

POSTERS

PS01-ISLET/CELL TRANSPLANT

P001

DONOR HEIGHT VALUE COMBINED WITH ISLET DONOR SCORE IMPROVES PANCREAS SELECTION IN CLINICAL ISLET TRANSPLANTATION

Lingjia Wang, Olivia Cochet, Michael J. Millis, Piotr Witkowski
University of Chicago

Background: In order to maximize the islet yield for successful islet transplantation, the key task is to select an ideal donor pancreas. By using Islet Donor Scoring (IDS) (O’Gorman et al. 2005) in the past years, we consistently obtained 50% transplant rate if the IDS reached above 80. In this study, we added donor height value as an independent variable in combination with the donor score to see if this addition can improve the pancreas selection.

Methods and Materials: Donor and islet isolation information ($n = 22$, 2011–2012) were collected and studied. Pearson Correlation Analysis was used in statistical analysis.

Results and Conclusions: Donor height value as an independent variable is significantly correlated to the pre-IEQ, post-IEQ, donor score and final pancreatic weight (all $r > 0.5$ and $p < 0.02$). When height (179 ± 3 cm) was used with IDS, islet transplant rate reached 80% in selected pancreases.

P002

CELL THERAPY WITH AUTOLOGOUS BONE MARROW STEM CELLS IN THE PREOPERATORY TREATMENT OF THE REMNANT LIVER IN PATIENTS SUBSIDIARY OF MAJOR HEPATECTOMIES. PRELIMINARY RESULTS

José-María Álamo¹, Carmen Bernal¹, Luis-Miguel Marín¹, Concepción Herrera², Magdalena Carmona³, Lydia Barrera³, Álvaro Iglesias², Juan Serrano¹, Gonzalo Suárez¹, Jordi Muntané⁴, Miguel-Angel Gómez-Bravo¹, Javier Padillo¹

¹Liver Transplant Unit. Virgen del Rocío Hospital; ²Reina Sofía Hospital; ³Virgen del Rocío Hospital; ⁴Instituto de Biomedicina de Sevilla, IBI3

Background: Pre-hepatectomy portal embolization is often ineffective. We present preliminary results from the application of stem cells from autologous bone marrow in the remaining liver of patients undergoing major hepatectomy after portal embolization to under clinical trial.

Material/Methods: Group treatment: preoperative portal embolization application of stem cells. Control group: without application of stem cells. Autologous bone marrow is extracted by puncture-aspiration of the iliac crest, and then the mother mononuclear cells separated, being administered in the remaining liver.

Results: We observed no morbidity or mortality associated with the procedure intrahepatic infusion of stem cells via portal. No portal vein thrombosis, no liver abscesses, no ischemia/hepatic necrosis, not sepsis. Was obtained remnant liver volume increased in all patients.

Conclusions: Cell therapy with autologous stem cells of the remnant liver of patients for major hepatectomy is safe.

P003

SELECTION OF TACTICS OF DAMAGED LIVER THERAPY BY USING CELL TRANSPLANTATION (EXPERIMENTAL STUDY)

Murat Shagidulin¹, Nina Onishchenko¹, Mikhail Krashenninnikov², Ludmila Bashkina², Alla Nicol'skaya², Igor Ilijinsky¹, Natalia Mogeiko², Pavel Avramov², Elena Volkova², Aleksey Lundup³, Nadezda Perova², Viktor Sevastjanov², Sergey V. Gautier¹

¹Federal V. Shumakov Research Center of Transplantology and Artificial Organs, I.M. Sechenov First Mosc.; ²Federal V. Shumakov Research Center of Transplantology and Artificial Organs; ³Sechenov First Moscow Medical State University

Background: It is known that severity of initial liver injury ought to be taken into consideration at the selection of effective therapeutic tactics.

Aim: To work out the algorithm of the therapy of chronic liver failure (CLF), by using cell transplantation (CTX) at the dependence of liver injury severity.

Methods: It was carried out five experimental groups with model of CLF. CLF was modeled on Wistar rats by using standard protocol of CCl₄ treatment. August rats were used as donors of cells. CT (MMSC or/and liver cells (LC)) was fulfilled after the ending of CCl₄ treatment. In the 1st gr. MMSC ($2 \times 2.5 \times 10^6$ cells) were iv. injected in 3 and 10 days. In the 2, 3, 4 gr. cells adhesioned on matrix <Sphero®GEL> were TX into liver in 7 days. There

were used: in 2nd gr.-MMSC (5×10^6 cells); in 3rd gr.-LC ($2.5-4.0 \times 10^6$ cells) and MMSC ($0.5-0.8 \times 10^6$ cells); in 4th gr.-LC and MMSC in the same doses as in the 3rd gr., but with immunosuppression by Prograf. 5th gr. was as a control. Biochemical (ALT, AST, ALP) and morphological indices of liver were examined during 90 days after CTx.

Results: In the 1, 2, 4 gr. ALT, AST, ALP decreased to normal in 30 days and in the 3rd gr.-in 18–20 days after CTx; in the 5th gr. these indices normalized in 90 days after CCl₄-treatment. Morphologically on the 14th day after CTx it was indicated the increasing of connective tissue area (CTA) in the 1st and 2nd gr. to comparison with the 5th gr. At the 30 days it was indicated decreasing of CTA in the 1st–4th gr. to comparison with the 5th gr. In 90 days in the 3th gr. it was revealed not only safety Tx cells, but also forming neo-hepatoid tissue - proliferating allogeneic viable hepatocytes with high level of glycogen, proliferating bile duct epithelium and neogenic vessels.

Conclusion: Because the increasing CTA took place after MMSC Tx MMSC ought to be used at the early reversible stage of CLF. At the stage of advanced and prolonged manifestation of CLF associates of LC and MMSC must be applied.

P004

ARCHITECTURE OF ISLETS AFTER THEIR TRANSPLANTATION

Domenico Bosco, Geraldine Parnaud, Philippe Morel, Raphael Meier, Laurianne Giovannoni, Vanessa J. Lavallard, Benoit Bédard, Thierry Berney
Geneva University Hospitals and University of Geneva

Background: Human pancreatic islets have a unique architecture that allows particular interactions between beta- and alpha-cells. The aim of this study was to assess whether this architecture was maintained in human islets after their isolation and transplantation.

Method/Materials: Human islets were isolated and kept in culture for 1–4 days. Then, they were transplanted under the kidney capsule of Scid mice. In addition, isolated islets were dispersed into single cells and either transplanted under the kidney capsule of Scid mice or kept in culture for 2 weeks allowing cell aggregation and pseudoislet formation. Histology of islets and islet cells was analyzed 2 weeks after transplantation and compared to that of islets and pseudoislets after culture. Immunofluorescence for insulin, glucagon and CD31 or CD34 was performed.

Results: By immunofluorescence we showed that in cultured islets alpha- and beta-cells lost their particular arrangement and were intermingled. In pseudoislets formed after 2 weeks of culture, alpha- and beta-cells had an inverted core-mantle position with alpha-cells at the center surrounded by beta-cells. Two weeks after transplantation, islet cells reorganized forming structures similar to native pancreatic islets with alpha-cells surrounding beta-cells and vessels lining alpha-cells. Similar results were obtained when islet cells were transplanted instead of islets.

Conclusion: These results indicate that islets and pseudoislets *in vitro* have a disorganized architecture and that alpha- and beta-cells have the ability to reorganize *in vivo* after transplantation forming structures similar to pancreatic islets.

P005

HUMAN BONE MARROW-DERIVED MESENCHYMAL STEM CELL: A SOURCE FOR CELL-BASED TRANSPLANTATION

Maryam Ayatollahi¹, Bitá Geramizadeh¹, Maryam Zakerinia²

¹Transplant Research Center, Shiraz University of Medical Sciences;

²Hematology-Oncology Research Center, Shiraz University of Medical Sciences

Background: The ability of mesenchymal stem cells (MSCs) to differentiate into many cell types, and modulate immune responses, makes these cells an attractive therapeutic tool for cell transplantation and tissue engineering.

Objective: This project was designed to isolation, culture, and characterization of human marrow-derived MSCs based on the immunophenotypic markers and the differentiation potential.

Material and Methods: Human bone marrow of healthy donors was aspirated from the iliac crest. Mononuclear cells were layered over the FicolI-Paque density-gradient and plated in tissue cultures dish. The adherent cells expanded rapidly and maintained with periodic passages until a relatively homogeneous population was established. The identification of adherent cells and the immune-surface markers was performed by flow cytometric analysis at the third passage. The *in vitro* differentiation of MSCs into osteoblast and adipocytes was also achieved.

Results: The MSCs were CD11b (CR3), CD45, CD34, CD31 (PCAM-1), CD40, CD80 (B7-1), and HLA-class II negative because antigen expression was <5%, while they showed a high expression of CD90, and CD73. The differentiation of osteoblasts, is determined by deposition of a mineralized

extracellular matrix in the culture plates that can be detected with Alizarin Red. Adipocytes are easily identified by their morphology and staining with Oil Red. **Conclusion:** All these data suggest that MSCs can be isolated and expanded from most healthy donors, providing for a source of cell based transplantation. **Keywords:** Cell transplantation, Mesenchymal stem cells, Human bone marrow.

P006

THE EXPRESSION OF NEUROGENIN3 IN ADULT HUMAN PANCREATA

Negar Azarpira¹, Anahita Shaer², Akbar Vahdati²

¹Shiraz University of Medical Science; ²Islamic Azad University, Oloom va Tahghighat Fars

Background: Neurogenin-3 is a protein that in humans is encoded by the NEUROG3 gene. Neurogenin-3 is expressed in endocrine progenitor cells and is required for endocrine cell development in the pancreas and intestine. It belongs to a family of basic helix-loop-helix (bHLH) transcription factors involved in the determination of neural precursor cells in the neuroectoderm during embryogenesis.

Method: Total RNA was extracted from fresh human pancreatic tissue using RNX-RNA extract kit. The pancreas belongs to a 12 years old boy died during car accident and after giving consent from his parents, the pancreas and liver was dedicated for transplantation. Because the organ was not good quality for whole organ transplant, it was used for research.

Result: The RT-PCR analysis showed Neurogenin-3 gene expression.

Conclusion: As the donor is young, it is suggested that the progenitor cells near the ducts or the residual stem cells in islets may be the source of Neurogenin-3 expression.

P007

HUMAN ISLET CELL ISOLATION PROGRAM IN SHIRAZ, SOUTH OF IRAN

Negar Azarpira, Mahdokht Aghdai, Saman Nikeghbalian, Masumeh Darai, Elahe Esfandiari

Shiraz University of Medical Science

Introduction: Pancreatic islet transplantation has become the minimally invasive procedure for the treatment of type 1 diabetes mellitus.

Method: Shiraz Organ Transplant Center is a leading center for organ transplantation especially pancreas transplant in Iran. For this reason, we intended to establish an islet transplantation program. Our experience in islet isolation on six pancreata from deceased donors is briefly presented. This required necessary equipment as well as well-trained professionals and a specially planned facility.

Results: The islet viability was good. We don't have a refrigerated COBE processor (COBE 2991; Cobe) for purification, therefore our yield was low. Our experience must be improved to achieve more islets in order to develop clinical grade cell therapy.

Conclusion: Overall, the isolation costs are high and accessing to a safer, more economic and persistent source of material and reagents will improve this technique.

P009

DIFFERENTIATION OF HUMAN INDUCED PLURIPOTENT STEM CELLS INTO INSULIN-PRODUCING CLUSTERS

Anahita Shaer, Negar Azarpira, Anahita Shaer

Transplant Research Center, Shiraz University of Medical Science

Background: It is hoped that in near future stem cells can be used in diabetes therapy through pancreatic beta cell replacement. IPS cells (Induced plurip-

otent stem cells) are a kind of pluripotent stem cell which are taken from non-pluripotent cell, an adult somatic cell, through 'stimulating' certain genes.

Objective: In diabetes type 1, it is beta cells that are mostly destroyed, but in diabetes type 2 the number of beta cells is reduced by a 40–60%. A way of producing immature islet-like clusters of insulin-producing cells taken from iPS cells will be introduced. **Methodology:** From the Iranian Royan Stem Cell Bank We got a human induced pluripotent stem cell line which had been derived from reprogramming a 42-year-old man's dermal fibroblast cells. Several steps were involved in this protocol. In the first place, embryoid bodies had to be formed and then plated in insulin-transferring-selenium medium. The medium was supplemented with N2, B27, and bFGF (basic fibroblast growth factor). In the next step, broke loose concentration in a medium was reduced, the bFGF was taken out, and nicotinic acid was added. Clusters were formed after the cells were isolated and cultured in suspension. An enhanced expression of pancreatic genes was observed through reverse transcription-polymerase chain reaction. The outgrowths were incubated in DTZ solution for 15 min.

Result: Gene expression of insulin-GlucagonPDX1- NGN3-PAX4-PAX6-NKX6.1- KIR6.2-GLUT2 was documented by Real-time qPCR analysis. DTZ-stained cellular clusters were observed after nearly 23 days but they were more observable after 31 days.

Conclusions: Since ips cells can be developed through reprogramming the patient's somatic cells, and due to the distinction between these cells and Beta cells they can produce sufficient insulin and there is no need to use suppressing drugs when applied to diabetic patients, they seem to be very promising. Thus in the present study we were able to produce clusters of cells, from IPS cells, which were quite capable of producing insulin. The present project may result in the formation of an unlimited source of cells appropriate for transplant.

P011

PANCREAS ISLET AUTOTRANSPLANTATION COMBINED WITH PANCREATECTOMY FOR TREATMENT OF GRADE C PANCREATIC FISTULA AFTER HEMIPANCREATODUODENECTOMY

Martin Oliverius, Matej Kocik, Milos Kucera, Peter Girman, Frantisek Saudek
Institute for Clinical and Experimental Medicine Prague

Background: Total pancreatectomy (TPE) is sometimes the only treatment option in severe pancreatic fistula (PF). Pancreas islet autotransplantation (PIT) performed at the time of completion pancreatectomy can rescue a part of endocrine tissue and prevent or minimize the bright diabetes. Data on long term outcomes are limited. We report our experience with patients who underwent TPE followed by PITx.

Methods/Materials: From 2007 to 2013 seven patients underwent TPE for grade C PF after hemipancreatoduodenectomy (five out of them for carcinoma and two for non-malignant tumours). Pancreatic islets were isolated from pancreatic tail using digestion with collagenase (Serva). Non-purified islet suspension was infused into the portal vein intraoperatively.

Results: A median number of islets transplanted was 210 000 ieq (range 70 000–365 000). One patient died postoperatively for reasons unrelated to PITx. One patient is 6 months after PITx with full islet function without insulin and without tumor recurrence (fasting C-peptide 0.45 nm). Other three patients have stable diabetes with partial graft function (fasting C-peptide levels 0.23, 0.61 and 0.22 nm). Two patients resected for ampuloma are alive. One patient with T3 pancreatic head carcinoma is alive 25 months after PITx with tumor recurrence. Another one with bile duct carcinoma died 47 months after PITx with tumor recurrence. Third patient with carcinoma of papilla of Vater with positive lymph nodes and angioinvasion died 12 months after PITx with local recurrence and solitary liver metastasis.

Conclusion: PITx after complete pancreatectomy for severe pancreatic fistula is able to prevent brittle diabetes and maintain some level of C peptide. The fear is about the possibilities of malignant tumour cells spreading. In our small series we did not observe any early development of multiple liver metastases, which could be caused by islet suspension contaminated with malignant cells.

PS02-COMPOSITE TISSUES

P012

ALLOTRANSPLANTATION OF STAPES

*Pavel Andreev**Donetsk National Medical University*

The aim of the work was to study the effectiveness of the stapes allotransplantation in the course of reconstructive operations on the middle ear on the basis of experimental and clinical research.

Material: According to the tasks set, the experimental part of the research of the stapes allotransplantation was conducted on cats. The operation was performed in the sterile conditions under the general anaesthesia. Electronic and microscopic examination of the stapes allotransplantation was conducted after one, three and six months after the operation, consequently. In the clinical research the effectiveness of using the stapes allotransplants was compared with the operations, during which the columella of the autobone was used as the prosthetic material. The results of the research. In six months after the operation, the periosteous formation of the bone starts due to the osteogenous cells, which accumulate themselves along the periphery of the transplant. However, the research of the transplant at the sub-microscopic level allowed to

find out that the first signs of bone-formation in it appeared considerably earlier. At three months already, on the surface of the transplant there accumulate multiple one-nuclear osteogenous cells, which contain granular endoplasmic reticulum; here also appear single osteoblasts, which have a developed endoplasmic reticulum with the homogenic secretion. It localizes itself mostly near the outer nucleus membrane. First of all, the reconstruction starts along the edges of the stapes's base. Obviously, it is caused by the fact that this is the very place where the physiologic stress during the sound transmission concentrates. Then, the intensive periosteous bone formation appears in the stapes's legs, and the bone formed here covers the inside cell-free structures of the transplant's legs as if a cuff. A year after the transplantation a nearly total reconstruction is observed in the outside layers of the stapes; the nearly-formed bone tissue begins to substitute the external side of the stapes's head. The cell elements of the bone tissue start to appear in the inside layers of the stapes, but they remain single units on the background of the cell-free fibrous structures so far. The layer of the osteoblasts on the stapes's surface modifies, becoming thinner, and the osteoblasts themselves look like thin flat formations, a little bit like the cambial layer of the periosteum. It is the stapes's head, where the process of bone-formation appears in the last turn. A characteristic feature is that here, together with the periosteous modification of the bone, there happen sections of intraosteal growth along the way of a vascular, growing into the head from the side of the stapes's leg, and it looks in it as a multi-layer tendon, which contains a great number of cell elements.

PS03-ALLOCATION

P013

FACTORS AFFECTING DELAY IN KIDNEY TRANSPLANTATION OF POTENTIAL RECIPIENTS REFERRED FOR REGISTRATION ON THE NATIONAL WAITING LIST

Antoine Barbari, Mahassen Jaafar, Farida Younan
Rafik Hariri University Hospital

Background: The number of deceased kidney transplant (DKT) performed in our center is relatively low in relation to the number of potential recipients seen in the pre-transplant clinic.

Methods: We analyzed retrospectively all 305 patients evaluated in our pre-transplant clinic by assessing: Demographic factors, referral pattern, financial coverage, withdrawal rate (WR) and causes from the preparation process and the cumulative time delay until wait-listing or Transplantation

Results: Mean age was 44 years with M/F and Muslim/Christian of 2/1. Fifty-five (18%) were obese (BMI > 30) and 74% were self-referred. Overall WR was 76.4% due to organ shortage (68%); poverty (56.4%); protocol refusal (15.1%); medical causes (10.5%). Only 20.7% were waitlisted within a mean time of 6.2 months (6.2–8.6). Of those, 13 patients (20.6%), six Muslims and seven Christians, representing 4.3% of all patients; received DKT within a mean time of 27 months (1–42).

Conclusion: Several factors seem to be responsible for the significant delay in patients wait-listing. Organ allocation appears to be equitable among communities and DKT occurs within an acceptable waiting time period.

P014

IMPACT OF AN ORGAN PROCUREMENT PROGRAM CREATION ON ORGAN AND TISSUE DONATION RATES

Mahassen Jaafar¹, Mustapha Itani¹, Wassim Nassredine¹, Farida Younan², Antoine Stephan², Antoine Barbari¹
¹Rafik Hariri University Hospital; ²National Organization Organ and Tissue Donation and Transplantation (NOOTDT-Lb)

Background: We evaluated the impact of the creation of Organ procurement program (OPP) in a 350 general and 13 adult intensive care unit (ICU) beds governmental hospital, on the rate of organ and tissue donations.

Methods: Following the creation of an OPP, all cardiac death (CD) and their related etiologies as well as the potential brain death (BD) cases were reported over 2 years period. BD was diagnosed clinically and confirmed by a flat electroencephalography and/or cerebral angiography. OP coordinator conducted family approach and obtained all family consents.

Results: Eight hundred and ninety-eight CD and 214 ICU deaths were reported. Only 104/128 (11.6%) families of potential donors were approached and 15 (14.4%) consented for the extraction of 24 corneas. Among 47 potential BD donors (BDD), 38 were diagnosed as BD and 18 were rejected for medical and/or legal reasons. The families of the remaining 20 were approached and only 1 (5%) consented to donation. The reasons for family refusal were religious and non-specific in 31.5% and 68.5% of cases, respectively.

Conclusion: Despite an acceptable conversion rate, the overall donation rate was remarkably low due to considerable high family refusal.

P015

THE CURRENT NUMBER OF PATIENTS ON THE NATIONAL WAITING LIST DOES NOT REFLECT THE EXPECTED NATIONAL NEED

Antoine Barbari¹, Antoine Stephan², Farida Younan², Mahassen Jaafar¹
¹Rafik Hariri University Hospital; ²National Organization Organ and Tissue Donation and Transplantation (NOOTDT-Lb)

Objective: The volume of any National Waiting List (NWL) for organ donation may be influenced by factors that impact both input and/or output. We assessed the size adequacy of our NWL in relation to the Lebanese dialysis population (LDP).

Methods: All database available since the creation of our national organ procurement program was reviewed in addition to data obtained from the Ministry of Health on the number of incident dialysis and new ESRD patients as well as the new yearly registered kidney transplants (KT).

Results: 173 renal/ 385 patients for all organs were actively waitlisted (WL) with an average annual rate of 58 patients /year for an estimated 3338 incident

ESRD patients, representing 5.1% of the LDP. Average donation and deceased KT rates were 2.6/million population and 13.2/100 WL patients, respectively. Positive PRA was present in 26% of patients and 12.3% were registered for pre-emptive KT. Yearly WL death rate and deceased to living donor KT ratio are 2% and 1/6, respectively.

Conclusion: Our data indicate that the current size of the Lebanese NWL under serves the true need of the country.

P016

LOW-DONOR AGE VERSUS LOW-MELD: DIFFERENT STRATEGIES, SIMILAR RESULTS? A LONG TERM US-ITALY STUDY ON DONOR TO RECIPIENT MATCH IN LIVER TRANSPLANTATION

Alfonso W. Avolio
Catholic University of Sacred Heart of Rome

A comparative analysis of D2Rm between US and Italy has not been performed. To investigate peculiarities & differences in D2Rm, UNOS and Italian D-MELD databases were merged (2002–2009). Pediatric cases, multi-organ Tx, SPLITs, living donor Tx, national share cases and DCDs were excluded.

There were 36.795 cases (US = 31.569, ITALY = 5226). Donor age (X, IQR) was lower in US than in Italy (43, 25–55 vs. 56, 40–68), MELD was higher in US than in Italy (20, 14–28 vs. 15, 11–21). D-MELD was similar. Low D-MELD class (<338) was prevalent in Italy. High D-MELD class (>1628) was prevalent in US. Un-adjusted patient survival (PS) between US and Italy were similar. Long term predictors of PS at 6-year Cox regression were: Recipient age (Rage) 50–64 (HR 1.1, p = 0.038) Rage >64 (HR 1.6, p < 0.001) Ethnicity: caucasian versus afro-american (HR 0.9, p < 0.001) Acute liver failure (HR 1.8, p = 0.001), HCV (HR 1.5, p < 0.001), HBV (HR 0.8, p = 0.003), Cholestasis (HR 1.5, p < 0.001), Low D-MELD versus Intermediate D-MELD (HR 0.7, p < 0.001), High D-MELD versus Intermediate D-MELD (HR 1.8, p < 0.001), Portal thrombosis (HR 1.3, p < 0.001), Italy versus US (HR 0.9, p = 0.007); $\chi^2 = 934$. US versus Italy difference in adjusted PS was significant.

D2Rm quantified by D-MELD remains a strong predictor of PS in US and Italy. The allocation of a graft from an elderly donor to an high-MELD patient, should be avoided especially if the recipient is HCV+. The Italian allocation system is more efficacious than the American one in the utilization of resources allowing better adjusted survival figures.

P017

EVALUATION OF ORIGIN OF PEDIATRIC LIVER TRANSPLANTATIONS IN SWITZERLAND

Danick F. Gut, Franziska Beyeler, Franz F. Immer
Swisstransplant

Introduction: We evaluated from where our pediatric organs for liver transplant originate from. We compared the rates of split liver donation and child to child donation with deceased donor organs from Switzerland and from foreign offers, and also from living donation. We compared the waiting time for children and adults on the waiting list.

Methods: We retrieved the data from the SOAS (Swiss Organ Allocation System). In the SOAS we have information concerning all donors and recipients. We evaluated the timeframe from the 1st of January 2008 to the 31st of December 2012. We considered all patients to be pediatric in the age range 0–16 years. From this data we compared the rates of split liver and child to child donations. We also compared where the organs came from. We compared the waiting time for children and adults on the waiting list.

Results: In the study period 6% (n = 44) of the recipients listed were pediatric. Sixty-two percent (n = 21) of the pediatric recipients received a split liver transplantation. Thirty-eight percent (n = 13) of all pediatric transplantation were child to child donations. Thirty-eight percent (n = 13) of all pediatric transplantations were from foreign offers. The mortality for pediatric recipients remained at 0% in these five years. We did not evaluate the patients that were taken off the waiting list and then deceased. In 2012 there were no splits performed in Switzerland; but there was an increase of 54% from 2008 (n = 6) until 2011 (n = 11) in pediatric transplantations. 2012 showed a drop in pediatric transplantations, this is compatible with the low donor numbers in Switzerland in 2012. The waiting time for adults was longer (mean 254d/median 191d) than the waiting time for pediatric recipients (mean 90d/median 52.5d).

Conclusions: In conclusion there is a very low mortality for children requiring a liver transplantation in Switzerland. This is in part due to an increase in split liver transplantation (n = 21/62% of all pediatric Tx) and Livers from foreign countries, mainly accepted in a critical medical situation (urgent, n = 7/53.8% of pediatric Tx from foreign offers) by the local liver transplantation program.

PS04-ETHICS/LAW/PSYCHOSOCIAL/PUBLIC POLICY

P018

RENAL TRANSPLANTATION IN THE ROMA (GYPSIE) MINORITY IN CROATIA

Nikolina Basic Jukic¹, Ivana Juric¹, Katarina Levarda-Hudolin¹, Petar Kes¹, Bojan Jelakovic¹, Dragan Novosec²

¹University Hospital Centre, Zagreb; ²University Hospital Centre, Osijek

Roma people are often socially deprived. We investigated characteristics of the Roma renal transplant recipients. Retrospective, and from the year 2002, prospective follow-up was performed. Out of 9463 registered Roma people in Croatia 25 patients require renal replacement therapy, giving the prevalence of 830 pmp; average age at the start of dialysis treatment was 29 vs. 67 years; waiting time to transplantation 48.9 vs. 53.5 months, mean age at the time of transplantation 33.18 vs. 48.01 years in the Roma and in the general Croatian population, respectively. One patient received kidney allograft from the spouse, and all other from the deceased donors. Patients were followed for 51.5 months (range, 6–240 months). The most frequent posttransplant complications were urinary tract infections. Three patients were non-compliant with immunosuppressive medications. Roma ethnicity has excellent access to renal transplantation in Croatia. They are younger than the average Croatian e.

P019

ATTITUDE OF WORKING STAFF TOWARD ORGAN DONATION IN AN ORGAN PROCUREMENT AND KIDNEY TRANSPLANT CENTER

Mahassen Jaafar, Najwa El Khazem, Mustapha Itani, Antoine Barbari, Rafik Hariri University Hospital

Background: We recently reported considerable low conversion rate of deceased donor (DD) to actual donors. We assessed the knowledge and attitude of the working staff toward DD.

Methods: A cohort of 100 working staff: 15 Physicians, 20 housestaff, 48 registered and 17 practical nurses answered a questionnaire covering the following: Demographic parameters, knowledge about all aspects of DD, brain death awareness and familiarity with the procedure of family approach and family consent.

Results: Majority (85%) had high education with a mean age of 33 years and slight female predominance (55%). Only 18% had ever discussed the subject, 98% did not carry a donation card. Whereas 65% acknowledge the need for BD confirmation prior to donation, only 30% knew it was associated with donor's death. Thirty percent still believed in donor's body disfigurement after donation, 87% acknowledged the approval of donation by law and 51% by religion. Sixty nine percent recognized the role of transplant coordinator in family approach and consent. Only 35/63 who supported organ donation would actually donate.

Conclusion: Our results clearly indicate a considerable unsupportive attitude among the working staff toward organ donation.

P020

QUALITY OF LIFE IN DIALYSIS PATIENTS: IMPACT OF A FUNCTIONING GRAFT

Sahier Khashab, Mohamed Nasr, Mohamed Ghallab, Mohamed Tag Eldin, Mohamed Monir, Hend Habiba, Ibrahim Samy, Amin Soliman, Cairo University

Background: Do modalities of renal replacement significantly affect quality of life (QoL) and lead to different levels of depression and anxiety?

Patients/methods: Fifty-nine patients (32 males, 27 females) were recruited. Thirty hemodialysis patients and 29 renal transplants (RTR) were compared regarding psychological condition and the QoL; which was assisted by Beck's depression inventory, Middlesex hospital questionnaire, life satisfaction scale and QoL scale.

Results: Depression stage, anxiety and somatization in RTR were significantly lower than hemodialysis. Higher "Life satisfaction" and "Physical quality" in RTR were found. Females showed higher degree of phobia. An inverse correlation between age and degree of Hysteria was shown.

Conclusions: QoL is better in RTR than on hemodialysis; yet financial QoL score of RTR is higher. Female RTR are usually more depressed, most likely due to associated social burden.

P021

COGNITIVE FUNCTION AFTER SUCCESSFUL KIDNEY TRANSPLANTATION COMPARED TO HEMODIALYSIS

Dalia Roshd, Amin Soliman, Ahmed Soliman, Cairo University

Objectives: To examine cognitive functioning in kidney transplant recipients (Tx) and a concurrently assessed group of hemodialysis patients (Hx) in relation to their estimated glomerular filtration rate (eGFR).

Methods: The study included 60 Tx divided into two groups according to eGFR compared to 30 Hx and were examined according to DSM IV TR criteria, Trail-Making Test, and Montreal Cognitive Assessment.

Results: Hx were significantly affected in trail making B, total attention, total visuospatial, delayed recall and total MoCA scores. Tx showed lower significant scores on trail making B test, total visuospatial, total attention, delayed memory recall and total MoCA scores. Level of eGFR did not show significant difference in cognitive functions in transplant patients.

Conclusion: The cognitive deficits are a prevalent and costly burden to chronic kidney disease patients impacting on a psychological and somatic level.

P022

LONG TERM QUALITY OF LIFE OF LIVER TRANSPLANT RECIPIENTS BEYOND SIXTY YEARS OF AGE

Georg Werggartner¹, Astrid Fahrleitner-Pammer², Regina Roller-Wirnsberger³, Daniela Kniepeiss⁴, Doris Wagner⁴

¹Department of Surgery, Division for General Surgery, Medical University of Graz; ²Department of Internal Medicine, Division for Endocrinology and

Metaboli, Medical University of Graz; ³Department for Geriatrics, Medical

University of Graz; ⁴Department of Surgery, Division for Transplantation,

Medical University of Graz

Introduction: Ameliorated surgical techniques and immunosuppression led to an extended survival after liver transplantation. This study aimed to investigate the health related quality of life after liver transplantation in aged recipients.

Methods: The quality of life of recipients above 60 years was screened using the SF36. Differences in the health related quality of life between the included aged recipients and age matched general population as well as among female and male recipients were assessed.

Results: Aged recipients showed lower scores in physical functioning (29 vs. 76 p = 0.001), role physical (42 vs. 73, p = 0.003), bodily pain (34 vs. 71, p = 0.003), general health (28 vs. 59, p = 0.001), vitality (25 vs. 61, p = 0.001), social functioning (36 vs. 87, p = 0.001), role emotional (46 vs. 89, p = 0.001) as well as the physical component score (28 vs. 76, p = 0.001).

Discussion: Quality of definitely is a restraint among aged recipients and should be assessed on a regular basis.

P023

COMPARATIVE ANALYSIS OF FIVE COLLABORATION MODELS FOR INTERNATIONAL ORGAN EXCHANGE – ESTONIA'S POINT OF VIEW

Virge Pall, Mart Einasto, Tartu University Hospital

Background: The Action Plan on Organ Donation and Transplantation supports various aspects of international cooperation. Our work has the objective to compare different collaboration models using generally accepted principles and Estonia's experience.

Methods: Comparative analysis includes five models: OEO-like fashion, twinning contract, agreement for exchange of surplus organs, membership in the OEO, EU-wide cross-border cooperation. We analyze the impact of a particular model to various aspects: availability of services, optimal usage of organs, demands for quality and safety.

Results: In our case the most important factors influencing all transplantation activities are the size of population and geographic location. The small population leads to limited donor pool, this results with minimal probability to find organs for urgent, paediatric or hyper sensitized patients. This is critical to develop national programs, as there is not enough capacity to ensure the qualification. As Estonian donation activity is quite good we can conclude that for us the key issue is not the lack of organs. Despite this we are not able to fulfil the standard criteria of OEO's about organ balance because of small numbers by specific age or blood groups. We have difficulties to find suitable organ in right time and maintain the effectiveness of the system. We need strong network on experts' level to obtain second opinion and put the patients on a waiting list abroad. Based on the geographic position the preferred choice is the collaboration with neighbours. This is important for ischemia time and allows optimal usage of organs. All this highlights the inevitable need for international network, but also raises a lot of ethic and economic questions, how to adopt our needs with the existing possibilities.

Conclusion: This analysis does not favor any model to another, but assesses their impact to one particular country.

P024

THE NEXT GENERATION TO LIVING KIDNEY DONATION: POTENTIAL POWER OF THE INTERNET

Aniko Smudla¹, Janos Fazakas¹, Henrik Backer², Laszlo Piros¹, Robert Langer¹

¹Department of Transplantation and Surgery, Semmelweis University;

²Semmelweis University

Background: Living related kidney transplantation can be influenced by the motivation of the next generation. The aim of this retrospective study was to estimate the way of motivation to living kidney donation in Hungary.

Methods: Seventy Hungarian living kidney donors were studied by self-completed questionnaire 2.4 years after donation. Besides socio-demographic data, we evaluated the correlation between motivation and psychosomatic health (shortened version of Beck Depression Inventory – BDI, 0–63 points; State-Trait Anxiety Inventory – STAI-T, 20–80 points). The data were analysed by SPSS 20.0.

Results: The average age of donors (23 men and 47 women) was higher than age of recipients (51.6 ± 10.25 years vs. 38.12 ± 13.48 years; $p < 0.01$). We found as main motivation the willingness to help ($p < 0.01$) based on the fact that the recipient was on dialysis and waiting list for a longer time. Younger donors got more information by internet ($p < 0.05$) but they were less confident in decision ($p < 0.05$). The educated participants searched information on internet, and they had more doubt that the kidney would work ($p < 0.05$). More women donated kidney to men than men to women ($p < 0.01$). The living donors' depression and anxiety were found less compared to the average value of the Hungarian society (BDI: 5.13 vs. 7.88; STAI-T: 36.66 vs. 43.56) (Hungarostudy 2002; Sipos, K. et al. Cross-Cultural Anxiety, Washington: Hemisphere, 1983; 27–39.)

Conclusion: To improve the number of donation, the next generation could be informed more accurately via internet by emphasizing the positive benefit of donation.

P026

MENTAL HEALTH STATUS DURING THE FIRST HOSPITAL EVALUATION FOR LUNG TRANSPLANTATION

Bouhon Sandrina, Romnee Amalo, Vastrade Christelle, Bulpa Pierre, Jacques Denis, Marchand Eric, Evraud Patrick
CHU-UCL Mont-Godinne - Dinant

Lung transplant candidates experience psychological distress. Our aim was to evaluate if this distress is already present during the first hospital evaluation (FHE) for being a candidate. During an 8 months period, 15 consecutive end stage pulmonary disease patients (pts) completed Hospital Anxiety and Depression scale (HAD). Anxiety or depression is defined as possible (P) with a score of at least 8/21 and certain (C) over 10/21. The majority of pts suffered from emphysema (60%). The mean age was 57 years (range 35 to 64) with 60% of men. The mean overall HAD scores were 11 (3–18) for anxiety and 7 (1–15) for depression. Anxiety occurred in 13 pts (87%) of which 8 quoted for C. All six women were anxious (5 as C). Depression disorders were only detected in six candidates (40%, 2 as C). Anxiety disorders are frequently encountered during the FHE for potential lung transplantation especially in women. In contrast, depression was less frequent. The patients considered that a booklet explaining this process.

P027

A STUDY OF RENAL OUTCOMES IN THE VICTIMS OF ORGAN TRAFFICKING

Igor Codreanu, Natalia Codreanu
Renal Foundation

Background: There is lack of data on chronic kidney disease (CKD) in the victims of organ trafficking. However, there are many reasons to believe that they may be at higher risk for long-term consequences.

Methods: We identified 32 victims which were invited to receive free health evaluation. Follow-up includes an interview on health status and lifestyle, anthropometric parameters and blood pressure. Spot urine (albumin, creatinine) and venous blood (creatinine, glucose, cholesterol) samples were collected. CKD was diagnosed based on urine albumin/creatinine ratio (ACR) >30 mg/g and/or GFR <60 ml/min/1.73 m² (as MDRD - 4 variables).

Results: Eighteen subjects (56.2%) accepted to participate in the follow-up. The mean age of the donors were 36.8 16.4 (SD) years, 13 (72.2%) were men. Time since donation 10.2 1.8 years. Two donors died, one of them required dialysis treatment. Two subjects (11.1%) had macroalbuminuria (ACR >300 mg/g), and five (27.7%) microalbuminuria (ACR >30 mg/g). GFR <60 ml/min/1.73 m² was documented in seven (38.8%) donors. CKD was found in 10 (55.5%) of screened donors.

Conclusion: The victims of organ trafficking experiences a substantial incidence of CKD. Future studies on larger number of victims are needed to determine the long-term consequences of kidney donation in this population.

P028

KNOWLEDGE ABOUT DIALYSIS, TRANSPLANTATION AND LIVING DONATION AMONG PATIENTS AND THEIR LIVING KIDNEY DONORS

Lotte Timmerman, Sohail Y. Ismail, Annemarie E. Luchtenburg, Willij C Zuidema, Jan N.M. Ijzermans, Jan J. Van Busschbach, Willem Weimar, Emma K. Massey
Erasmus Medical Centre

Background: In order to make a well-considered autonomous decision, potential living kidney donors and recipients should have sufficient under-

standing of renal replacement therapy options and risks. We explored knowledge about Dialysis & Transplantation (DT) and Living Donation (LD) among prospective donors and recipients.

Methods: Eighty-five donors and 81 recipients completed the Rotterdam Renal Replacement Knowledge-Test (R3K-T) in their native language (available in nine languages) one day before surgery.

Results: Recipients knew significantly more about DT than donors, donors more about LD than recipients. Both groups knew less about DT and LD if their native language was non-Dutch. Recipients undergoing pre-emptive transplantation knew less about DT and more about LD than patients on dialysis. Both groups knew less about LD if they had no paid employment.

Conclusions: We conclude that recipients and donors retain different information, while both lacked specific information about DT and LD. It appears that the decision to donate is not always based on consideration of risks and benefits. Extra attention should be paid to a person's understanding of information if his/her native language deviates from the professional's language. There is room for improvement in the knowledge about living donation among dialysis patients.

P029

DONOR AND RECIPIENT GENDER DISPARITY IN A LIVING-DONOR KIDNEY TRANSPLANT PROGRAM – A RETROSPECTIVE COHORT STUDY

Joseph Cairns¹, Sue Moore², Surinder Janduf², Adnan Sharif²
¹University of Birmingham; ²Queen Elizabeth Hospital Birmingham

Background: There is a paucity of information relating to gender disparity in live kidney donation between donors and recipients. We hypothesised that such inequality exists in a transplant centre based within a multicultural city and the aim of this study was to explore this in further detail.

Methods: This was a retrospective cohort study of all living-donor kidney transplant procedures performed at a single transplant centre. Data was obtained from the United Kingdom National Transplant Database, which maintains a mandatory record of all transplant activity, and cross-checked with locally held electronic databases. Donor/recipient demographics were collected including gender, age, ethnicity, religious belief (where stated) and relationship.

Results: About 623 living donor kidney transplant procedures have been performed (between 1987 and 2013) and formed the study cohort in this single-centre analysis. 53.4% of donors were female and 46.6% male. Mean age of donors versus recipients was 45 versus 40 respectively ($p = 0.003$). 18.9% of organ donors were from Black, Asian or Minority Ethnic backgrounds. No religious affiliation was documented in 72.1% of kidney donors, which limited our analysis of religion as a variable. Females donated more to males (69.3%) than females (30.7%), while male-to-female (48.8%) and male-to-male (51.2%) donations were similar ($p < 0.001$). Male donations were more common to paediatric recipients compared to females (10.8% versus 5.8% respectively, $p = 0.017$). South Asian partner-to-partner transplants ($n = 18$) were more likely to be female-to-male versus male to female (88.9% versus 11.1% respectively, $p = 0.007$). There was no difference in South Asian male versus female donations to paediatric recipients (16.0% versus 16.7% respectively, $p = 0.616$), but male donations were noted to be exclusively to boys (4/4) compared to an equal split for female donations (3/6 to boys).

Conclusion: We identify gender disparity in donor/recipient characteristics dependent upon the ethnic disposition and relationship of the donor/recipient pair. Our results can guide living donor kidney pathways and highlights areas for better public awareness and education.

P030

HOTT PROJECT: COMBATING TRAFFICKING IN PERSONS FOR THE PURPOSE OF ORGAN REMOVAL

Frederike Ambagtsheer¹, Susanne Lundin², Martin Gunnarson², Ingela Byström², Assya Pascalev³, Jordan Yankov³, Mihaela Frunza⁴, Jessicade Jong⁵, Ninoslav Ivanovskif⁶, Mike Bos⁷, Natalia Codreanu⁸, Willem Weimar¹
¹Erasmus MC, Internal Medicine, Kidney Transplantation, Rotterdam, The Netherlands; ²Department of Arts and Cultural Sciences, Lund University, Lund, Sweden; ³Bulgarian Center for Bioethics, Sofia, Bulgaria; ⁴The Academic Society for the Research of Religions and Ideologies, Cluj, Romania; ⁵National Police Services Agency, Utrecht University, Driebergen, The Netherlands; ⁶University Clinic of Nephrology, University St. Cyril and Methodius, Skopje, Macedonia; ⁷Eurotransplant International Foundation, Leiden, The Netherlands; ⁸Renal Foundation Moldova, Chisinau, Moldova

Background: The HOTT project addresses the crime of human trafficking for the purpose of organ removal. In particular, it addresses the lack of knowledge, the lack of awareness and the lack of non-legislative response to trafficking in persons for the purpose of organ removal by the following objectives: 1. to increase knowledge about the crime, 2. to raise awareness among target groups, 3. to organize an expert meeting where organ trafficking experts and competent authorities can express their views on project results, 4. to provide recommendations to improve the non-legislative response of this crime.

Methods: This project is executed by four partners, in close cooperation with a large group of associated partners. The project started in November 2012 for

the duration of three years. The main project activities are state-of-the-art research, identifying individual participants of target groups, organizing an expert meeting, developing indicators and recommendations and dissemination of results and recommendations.

Results: The planned deliverables are: (i) state-of-the-art report, (ii) report on transplant tourism, (iii) report on organ trafficking cases, (iv) a list of indicators to help data collection and identification of the crime, (v) recommendations to improve non-legislative response. Our reports will be published into a book.

Conclusion: This project aims to lead to increased knowledge and awareness of human trafficking for the purpose of organ removal, improved non-legislative response and partnerships to combat the crime more effectively.

P031

USE OF AN INTEGRATED CARE PATHWAY WITHIN THE RENAL TRANSPLANT SETTING

Richard Bowen

Nottingham University Hospitals

An Integrated Care Pathway (ICP) was introduced in our inpatient area because of the increasing complexity of the inpatient transplant pathway. The purpose of this was to improve documentation and audit processes and to make the transplant process simpler for staff and safer for patients. Method: MS Publisher was used to create a document which would cover the process from first receipt of a kidney offer to the patients' arrival in the operating theatre. The intention of the ICP is that it should be used by the multi-disciplinary team; the pathway includes a pro-forma for medical staff to document the initial assessment of the patient following their admission. The finalised document was then printed to form a 12 page "booklet" style document which can be included within the patients care records. Constituent parts of the ICP The first page describes donor characterisation and issues such as patient contact and arrival times. Pages two and three are dedicated to the crossmatch process; one for pre-transplant crossmatching, one for post-transplant (also described as "virtual") crossmatching. Subsequent pages are used for patient's medical assessment. And at the end there are two pages available for freehand notes for the use of the multi-disciplinary team. Trialling and Implementation a six week pilot program was performed before the final printing of the document. This allowed for a number of changes to be made. The completed version of the ICP has been in use since September 2011. The UK has adopted the European Union Organ Donation Directive (EUODD). The use of the pathway also allows clear unambiguous information to be recorded so that when this unit is subjected to the audit processes of the EUODD evidence of compliance should be clear. Conclusion: We plan to formally audit the use of the ICP within the next few months. This will allow any omissions to be rectified and also to determine the degree to which it has been used correctly by all grades of staff.

P032

ROLE OF TRANSPLANT COORDINATOR (TC) ON THE DONATION AND TRANSPLANTATION EFFICIENCY PROCESS

Maria Bodí¹, Elisabeth Colf², Alberto Sandiumenge¹, Jose Miguel Perez Villares³

¹University Hospital Joan XXIII, URV-IISPV, CIBER TARRAGONA; ²ONT;

³University Hospital Virgen De Las Nieves

Background: Quality evaluation of organ donation process (ODP) is based on its effectiveness assessment. To date no evidence exists on the role of TC on ODP efficiency assessment.

Method: A national questionnaire was distributed (November 2012) to TCs to determine their knowledge and decision-taking role on the ODP economic cost and hospital reimbursement. Their perception on the impact of the financial crisis on the ODP was also assessed.

Results: The survey was completed by 106 TCs (11.1 ± 7.8 experience years, 70% doctors, 90% actively involved in ODP quality assurance programs), 68% of whom worked on hospitals with at least one transplantation program. Only 45% of TC is aware of the impact of ODP on hospital budget (costs and reimbursement) and most of them (78%) do not participate on OPD efficiency assessment. Twenty-nine percent of the surveyed perceived logistics as the most aggrieved issue by the financial crisis.

Conclusion: Despite active role of TC on the ODP effectiveness evaluation, there is room for improvement on their participation in the ODP efficiency evaluation.

P033

MASTER'S DEGREE IN DONATION & TRANSPLANTATION OF ORGANS, TISSUES AND CELLS (D&T): 2ND EDITION MINUTES

Chloë Ballesté-Delpierre¹, Ricard Valero¹, David Paredes¹, Melania Istrate², Gloria Pérez², Martí Manyalich¹

¹University of Barcelona; ²TPM

Background: The second edition of Master D&T was offered by the University of Barcelona during 2011–2012, with 2 specialization paths:

Research and Professional. It was structured in three modules: donation, organ transplantation, tissues, cells & hematopoietic progenitors.

Methodology: To evaluate the efficiency of the Master we analysed the following aspects: students profile; participation and grades obtained (from 0 to 10); personal benefits from participation and lecturer's evaluation (from 1 to 5). Blended learning system (online + face to face) was used.

Results: Thirty participants from seven nationalities (15 Medical Doctors, 12 Nurses and three others). Student's grades: Donation (7.8 online / 8.6 simulations), Organ transplantation (7.9) and Tissues, cells & hematopoietic progenitors (8.0 online/9.3 simulation). Seventy-seven percent of participants developed Research projects and 23%, Professional Practices. All the Final Guided Projects were presented and approved by the ad-hoc tribunal. The lecturer's evaluation scores: Content of the materials (4.4 ± 0.3); presentation (4.4 ± 0.3); Questions/answers minutes (4.4 ± 0.3); Personal benefits (4.1 ± 0.3).

Conclusions: D&T offers the possibility to enlarge knowledge and skills of a large number of foreign professionals achieving their expectations and providing them with an official degree.

P034

KNOWLEDGE AND ATTITUDE OF HEALTH CARE PROFESSIONALS, STUDENTS AND PATIENTS TOWARDS THE AUSTRIAN ORGAN DONATION LAW

Vanessa Stadlbauer, Peter Steiner, Martin Schweiger, Michael Sereinigg,

Karlheinz Tscheliessnigg, Wolfgang Freidl, Philipp Stiegler

Medical University of Graz

Background: We conducted a survey on the knowledge and attitudes towards the Austrian organ donation legislation (an opt-out solution) of selected groups of the Austrian population taking into account factors such as age, gender, level of education, affiliation to healthcare professions and health related studies.

Methods: An online survey among three target groups (ICU nurses, health science students and non health science students) was performed and results were compared to the answers from transplantation patients to a paper questionnaire.

Results: Eighty-four percent of participants state that they know the Austrian organ donation legislation; this percentage varies within the target groups and is influenced by demographic variables of the participants. Seventy-four percent think that the law is good and 79% do not favour a change. Opinions and attitudes towards the legal situation are positively influenced by the affiliation to healthcare professions and health-related fields of study. Interviewed persons who were aware of the legislation before the survey had a more positive attitude towards the existing legislation.

Conclusions: The information level on Austrian organ donation legislation is high. ICU nurses and those who did not know the law before were most critical towards the existing legislation. Therefore education to increase knowledge in the general population and goal-oriented efforts to increase awareness in the target groups should be emphasized.

P035

DEVELOPMENT, CONTENT VALIDITY AND INTER-RATER RELIABILITY TESTING OF THE CIMI-BRIGHT: AN INSTRUMENT TO ASSESS THE LEVEL OF CHRONIC ILLNESS MANAGEMENT IN TRANSPLANT CLINICAL PRACTICE

Lut Berben¹, Cynthia Russell², Sandra Engberg³, Fabienne Dobbels⁴,

Sabina De Geest¹

¹Institute of Nursing Science, University of Basel; ²School of Nursing,

University of Missouri-Kansas City; ³School of Nursing, University of

Pittsburgh; ⁴KU Leuven, Center for Health Services and Nursing Research

Background: Guaranteeing organ transplant (Tx) recipients' successful long term outcome requires follow-up care that builds on principles of chronic illness management (CIM) (e.g. supporting self-management, guaranteeing continuity of care). We developed the CIMI-BRIGHT instrument to assess the level of CIM implemented in organ Tx centers.

Aim: The aim of this study was to describe the development of the CIMI-BRIGHT instrument and assess its initial content validity and inter-rater reliability.

Methods: The instrument was developed by the research team in consultation with a CIM expert and input from a focus group of Tx nurses. The development was based on the WHO's Innovative Care for Chronic Conditions' framework. The relevance of each item ($N = 51$) was rated on a 4-point Likert scale (1 = not relevant to 4 = highly relevant) by seven experts in CIM. The content validity index was calculated for each item and the total instrument. To evaluate inter-rater reliability, we conducted a pilot study in an abdominal and a renal Tx program. Percent agreement by center was calculated by averaging the percent agreement on individual items.

Results: Of the 51 items, 42 had a good content validity. Of the 9 items with low content validity two were deleted and seven were revised resulting in a 49 item instrument. The percentage agreement in the two Tx programs for the total instrument was 84.6% and 74.8%, indicating good inter-rater reliability.

Conclusion: The results of this initial validation of the CIMI-BRIGHT instrument are promising, suggesting its value as a tool to measure the extent

to which CIM is being implemented in Tx programs. We implemented the CIM-BRIGHT in a large multi-continental study in heart Tx centers, i.e. the BRIGHT study, which will also allow to further evaluate its psychometric properties.

P036

VOLUME-OUTCOME RELATIONSHIP IN ORGAN TRANSPLANTATION – A SYSTEMATIC REVIEW

*Annemarie Nijboer, Andreas A Schnitzbauer, Frank Ulrich, Wolf Bechstein
Klinikum der Johann Wolfgang Goethe-Universität*

Background: Volume-outcome relationships for transplant procedures has become one of the major topics in the discussions born from the organ transplantation scandal in Germany during the last six months. Proponents of the regulation argue, that highly specialized transplant centers may offer a higher quality but disregard the patients' wishes of a regionally available medical service. To investigate the relation between volume and outcome, in kidney, liver, and pancreas transplantation, a systematic review was performed.

Methods: 27 February 2013, the MEDLINE and PubMed databases were searched for the search terms: "kidney / liver / pancreas transplantation, and "volume-outcome relationship". The bibliographies of articles meeting the eligibility criteria were examined to identify additional studies. Only articles in English and German were included.

Results: Seventy-two articles were identified, of which seven articles were eligible. For renal transplantation different authors describe a significantly decreasing 3-month graft survival with decreasing center size. High-volume and medium (>100 transplants/year) transplant centers showed a significantly lower mortality rate, compared to low and very low volume (<60) centers. Furthermore, transplant surgeons' case mix was identified as a related factor; patients treated by "kidney only" transplant surgeons, were found to have an almost doubled operative mortality, compared to those treated by "multiorgan" transplant surgeons (1.7% vs. 0.9%). For liver transplantation various authors postulate a clear volume-outcome relation. Again, high-volume centers (>100) exceed low volume centers (<60–70), in the worst case with a 30% difference in mortality. Other authors report a cut-off of 20 transplants per year as the minimum acceptable standard. America's Medicare benchmark (minimum of 12 transplants/year, among other criteria), showed a significantly lower operative mortality. Pancreas transplant The largest study, analysing 6876 pancreas transplants failed to identify an outcome difference between low (<10), medium (10–20), high (21–50) and very high (>50) volume centers.

Conclusion: This systematic review demonstrated a volume-outcome relationship for kidney, liver, and less extensively, pancreas transplantation. For liver transplantation a minimum of 20 transplantations was proposed more than 14 years ago. However, especially for Germany, volume-outcome relationships have to be discussed critically; taking into account quality (acceptable survival and a low rate of re-transplantation) on one hand, and regional supply factors on the other hand. We propose an extensive prospective analysis, of volume-outcome and regional distribution of transplant centers, as basis for future regulative decisions in the German transplant environment.

P037

HOW TO TEACH EVIDENCE-BASED PRACTICE SKILLS IN 1.5 DAYS: THE EVIDENCE IN TRANSPLANTATION (EVIT) COURSE

Liset HM Pengel¹, Simon Knight¹, Akan Emir², John O'Callaghan¹, Jan H.P. Van der Meulen³, Vassilios Papalois⁴, Peter Morris¹

¹Centre for Evidence in Transplantation; ²Royal College of Surgeons of England; ³London School of Hygiene and Tropical Medicine; ⁴The West London Renal and Transplant Centre, Imperial College Healthcare NHS Trust & ESOT

Background: The Evidence In Transplantation (EVIT) course is aimed at transplantation professionals who want to increase their skills in evidence-based decision-making. The course was developed as part of the collaboration between the European Society of Organ Transplantation and the Centre for Evidence in Transplantation, together with the Clinical Effectiveness Unit, Royal College of Surgeons of England and the London School of Hygiene and Tropical Medicine.

Methods: During 1.5 quite intensive days participants were introduced to the principles of evidence-based practice through interactive lectures and small group discussions. They were taught how to critically appraise a paper on a therapeutic intervention, search common medical databases including the Transplant Library, and conduct a systematic review. Thereafter participants had to carry out a systematic review of Advagraf versus Prograf in small groups with some short cuts by going through the following steps: 1. Defining inclusion and exclusion criteria; 2. Designing search strategies for medical databases; 3. Selecting trials to include; 4. Critical appraisal and data extraction; 5. Constructing forest plots for outcomes; 6. Conclusions steps. The final step was a presentation of their findings.

Results: The course was highly rated by participants, with 80% of participants rating the course as very good and 20% as good. In particular, the practical sessions including the systematic review workshop were greatly valued.

Conclusions: Evidence-based practice skills essential to modern medical practice with high clinical standards can be taught in a comprehensive, 1.5 day course.

P038

IS IT FEASIBLE TO SCREEN FOR ALL RARE DISEASES PRIOR TO TRANSPLANTATION. CRITICAL INCIDENT REPORT OF A RARE LYMPHOMA DIAGNOSED AFTER POST MORTEM OF DONOR AFTER TRANSPLANT

*Hemant Sharma, Chang Wong, Adham El-Bakry, Daniel Ridgway, Sanjay Mehra, Ajay Sharma, Abdul Hammad
Royal Liverpool Hospital*

Background: Last year, kidneys from a DCD donor were transplanted to two recipients, the post mortem examination undertaken after death revealed the cause of death as a rare intra-vascular high grade B –cell Lymphoma. Pre mortem, donor presented with reduced consciousness and a CT report stated a cerebral lesion. The Organ donation offer was made after a reported benign brain biopsy. Retrieval team did not report any pathology. Both recipients decided to keep the kidneys and were successfully treated with chemotherapy. The worldwide press reported this as a critical incident. Huge public response was noted for a universal disease screening prior to all offers. An urgent investigation was performed to assess the root cause with-in the Organ Donation and Transplantation Directorate.

Results: Organs were offered after a documented Coroner's consent. A post mortem was done 2 days later, as a routine because of absence of a confirmed diagnosis as a cause of death. The Specialist Nurse in organ donation (SN-OD) referred the offer to Recipient Coordinator. Liverpool Centre based on the recorded contemporaneous notes accepted the kidneys. Electronic offering system (EOS) notes too made no reference to a possible lymphoma. Post mortem biopsy report 6 days post transplant showed high-grade intra-vascular B Cell lymphoma. Though liver was macroscopically normal but histology confirmed the lymphoma. On further review it was noted that the working diagnosis by the Intensivist was encephalitis and an abbreviation PCL (primary cerebral lymphoma) was used as one of the possible diagnoses. Consecutive teams possibly missed this abbreviation. It was also noted that SN-OD coordinating the donation was in training for SN-OD role. The possible errors were made at time of communication between the consecutive teams. Recommendations: Royal College of Pathologists has been contacted to expedite reporting and to immediately inform the NHSBT (NHS Blood and Transplant (NHSBT)). As this case was a very rare lymphoma, it is not possible to place a separate screening recommendation for it. All offers need to be electronic and in event of verbal offers all conversation are now recorded. Full review of SN-OD Training shall be under taken.

P040

LAPAROSCOPIC NEPHRECTOMY FOR LIVING DONORS: INITIAL EXPERIENCE AT MEXICO'S GENERAL HOSPITAL

*Luis Garcia, Dario Cantu, Alejandra Cicero, Alejandro Rossano, Hector Hinojosa, Diana Fernandez, Alejandro Luque, Roberto Bautista, Aldo Garcia, Hector Diliz
Mexico's General Hospital*

Laparoscopic nephrectomy (LN) is the gold standard for living donors, it is performed in most world-renowned transplant centers. However, its use is limited in some places due to lack of resources and training. OBJECTIVE. Present to the transplant community the experience with laparoscopic nephrectomy in a newly created transplant program in an underdeveloped country.

Materials and Methods: Retrospective review of living donor charts from March 1, 2009 to December 31, 2011 at Mexico's General Hospital Transplantation Unit. Demographics, bleeding, surgical time, days of hospital stay, renal function, donor and recipient creatinine, as well as surgical complications were reviewed.

Results: Hundred nephrectomies were performed, 75 on laparoscopic, hand assisted. Weck Hem-o-Lock clips were used for vascular control and ureter. Hundred percent had immediate graft function (IGF). 60% male, age: 34.87 years, BMI of 25.94. Mean surgical bleeding was 308.5 ml. Days of hospital stay: 3.89. Mean surgical time: 196.5 min. Patients required two analgesics. Three surgical complications, two required conversion to open surgery (1 aortic injury and 1 renal vein laceration); in one case the renal artery was injured. Preoperative creatinine: 0.84 mg/dl and 1.25 mg/dl at discharge. Recipient GFR was 72.73 ml/min/m² (MDRD) 1 month after transplant. Average cost was \$2300.

Conclusions: No recipient complications derived from the nephrectomy were seen. All had IGF. Laparoscopic hand assisted nephrectomy is a safe and effective procedure in living donors. Currently, we haven't had complications derived from the use of Weck Hem-o-Lock clips. It is possible to perform this procedure in centers with low budget.

P041

THE DEVELOPMENT OF TRANSPLANTATION PROGRAM IN MONTENEGRO

Marina Ratkovic¹, Marina Ratkovic¹, Nikolina Basic Jukic², Zeljko Kastelan², Josip Pasini², Jasna Stolic Brezak², Marija Topalovic Grkovic², Mirela Busic³, Branka Gledovic¹, Danilo Radunovic¹

¹Clinical Center of Montenegro; ²Clinical Center Zagreb, Croatia; ³Ministry of Health of Croatia

Background: In Montenegro there was no transplantation program until the September of 2012. On the other hand, there is 90 patients with transplanted kidney all transplantations were performed abroad. Twenty percent of these transplantations were performed in areas of black organ markets such as India and Pakistan. Beside the ethical problems, these transplantations carried high risk of medical complications. Preparing of all conditions for the beginning of transplantation program started in 2006 with activities including public, legal, medical and educational aspects.

Methods: These data refer activities brought on the development of organ transplantation in Montenegro.

Results: It was started with public campaigns focusing on the importance of organ donation and transplantation in our health system. The law about organ donation and transplantation was conducted in 2009. Since that it has been hardly worked on obtaining of all medical conditions for the beginning of the program. The best support was brought through collaboration with international groups and societies as RHDC (Regional Health Development Center) and SEEHN (South-Eastern Europe Health Network) and excellent collaboration with medical centers and colleagues from Croatia. The memorandum about collaboration between Montenegro and Croatia was signed in April of 2012. Medical staff from Clinical Center of Montenegro were on education in Clinical Center of Zagreb during the 2012. The first kidney transplantation from living donors in Clinical Center of Montenegro were performed on 25th and 26th September 2012 under the supervision of doctors and medical staff from Clinical Center Zagreb Croatia. Two others kidney transplantations from living donor were performed on 19th and 20th February of 2013 and we have prepared other pairs for living kidney transplantation for 2013.

Conclusion: We are working on the development of transplantation of the other organs and deceased donation program as our major aim in the next period.

P042

THE HIPPOCRATIC OATH AND THE ETHICS OF APPLICATION OF TELEMEDICINE SYSTEMS IN THE COORDINATION PROCESS AND IN THE VIRTUAL VOUCHING OF THE RENAL GRAFTS

Constantinos S. Mamas¹, Spyros Geropoulos², Adamantia S. Mamas³, Irene Grapsa², Vasileios Smyrmiotis¹, Georgia Kostopanagiotou¹, Chrysoula Lemonidou⁴, Andreas C. Lazaris⁴, Nikolaos Kavantzias⁴, Dionysios Venieratos⁴, Anastasia Konstantinidou⁴, Panagiotis Skandalakis⁴

¹Surgical laboratory Prof. C.TOUNTAS; ²Aretaieion University Hospital;

³Glasgow University; ⁴National and Kapodistrian University of Athens, Athens Medical School

Background: The study examines the medical ethics of the Hippocratic Oath (HO) in relation to the proposed integrated application of Telemedicine Systems (TS) in the coordination process (CP), and in renal graft (RG) procurement.

Material: The research is based on the rights of donors and recipients and on the current practice of CP and RG procurement with a reference: 1. to data about damaged RG in UK, and 2. to a simulation study in the University of Athens (Faculty of Nurse) applying simulating TS (CP) and 3. to results of another research, in the Medical School of Athens, about feasibility and reliability of the integrated remote evaluation of the RG applying TS based tele-radiology (TR) and tele-pathology (TP).

Results: The (HO) is an applicable ethical guidance in the ethical justification of the integrated application of TS in the (CP) and in (RG) procurement: 1. A 11% of grafted kidneys are considered damaged in UK, 2. The majority of participants (80%) considered TS as reliable in the management of donors, while specialists found them significantly more reliable, in notification and fulfillment of all medico-legal requirements in the (CP) ($p < .001$), and 3. The integrated remote evaluation of the renal graft is feasible and reliable (sensitivity = 96.7% and specificity = 100%).

Conclusion: TS coordination, TR and TP based remote evaluation of (RG), seem beneficial for the rights of patients, of donors, for surgeons and for the society.

P043

USING ONE PATIENT'S STORY TO CREATE A MULTIDISCIPLINARY EDUCATION SESSION TO INCREASE AWARENESS OF RENAL FAILURE AND TRANSPLANTATION AMONGST TOMORROW'S DOCTORS

Paul Herbert, Ros Herbert, Jeremy Crane
Imperial College Healthcare Trust

Background: Awareness of transplantation, as a treatment option, is an important part of medical training. We noted a knowledge gap amongst medical students and endeavoured to investigate and rectify this discrepancy.

Methods: A questionnaire was sent to all final year medical students at our institution to establish awareness and attitudes towards transplantation. We asked specifically about exposure to transplantation, awareness of it as a treatment option and interest in the speciality. To raise awareness we ran an educational interactive session for all first year medical students focussing on the clinical, psycho-social, ethical and practical issues surrounding transplantation. Participants were an expert renal patient, renal psychologist, general practitioner and transplant surgeon. In addition part of a recent documentary involving our patient's surgeon was screened. Feedback from the session was analysed and focus groups run, looking at longer term impact 9 months after the event.

Results: We received 161 complete responses to the initial questionnaire and found only 30% had exposure or would get exposure to transplantation by the end of their training. After the education session 330 feedback forms were completed. They showed greatly increased awareness of the difficulties of renal failure and the positive effect of transplantation (95%). The results from the focus groups were analysed using thematic analysis and showed good understanding of the holistic impact of renal failure and the benefits of transplantation. Interestingly a theme of the importance of team working also emerged.

Conclusion: An awareness of the impact of renal failure and the advantages of transplantation is important for medical practitioners. We used a novel method to instill the impact of renal disease into our first year students, and increased the knowledge, and we hope, acceptability of transplantation as an important means of managing renal failure in tomorrow's doctors.

P044

SETTING-UP AND RUNNING WEB-NET TOOL BASED AND NATIONWIDE SYSTEM FOR REFERRING AND MONITORING SERIOUS ADVERSE EVENTS AND REACTIONS IN THE AREA OF ORGAN TRANSPLANTATION

Jaroslav Czerwiński¹, Piotr Kaliciński², Anna Pszenny³, Roman Danielewicz¹

¹Department of Surg. and Transpl. Nurs. Med. Univ. of Warsaw, Polish Transplant Coord. Center Poltransplant; ²Department of Surgery and Transpl. Child Memorial Health Institute Warsaw; ³Polish Transplant Coordinating Center Poltransplant

Following Directive 2010/53/UE serious adverse events and reactions alerting system in the area of organ transplantation was implemented in Poland on technical basis of web-net platform connecting all transplant centers. Substantial issue of this system, distinctly problematic and widely discussed among professionals and decision makers was the catalog of events and reactions must be referred. Finally constructed catalog consists of: 1. Events related to organ recipients: transplantation from the donor with incomplete or incorrect characteristic, transplantation of organ after abnormal or too long preservation, absence of valid potential recipient's plasma for cross-match, organ transplantation from a donor with a viral infection (unrelated to the rules of allocation), severe and uncontrolled bacterial, fungal or protozoan infection, transplantation from a donor with cancer, unintentional transplantation from a donor with non-identical or incompatible blood group ABO. 2. Reactions related to organ recipients: resignation from transplantation due to organ damage at the time of donation, storage and implantation, transmission from a donor viral infection (unrelated to the rules of allocation), organ lost due to the absence of proper recipient, transmission of cancer, never function of the graft, recipient's death within 30 days after transplantation or during the initial hospitalization, graft loss within 30 days of transplantation or during the initial hospitalization, HIV transmission from the donor, severe bacterial, fungal, or protozoan infection. 3. Events related to living organ donor: organ procurement from the donor with incomplete or incorrect characteristic. 4. Reactions related to living organ donor: serious health consequences (illness, serious complications) in the donor associated with the donation.

P045

FOURTEEN YEARS CONSECUTIVE SEMINAR OF TRANSPLANTATION FOR PATIENTS AND CITIZENS FOR BETTER UNDERSTANDING

Masae Ikeda¹, Daisuke Ishii¹, Ryota Maeyama¹, Atsushi Sugita¹, Yoji Wakatabe¹, Haruki Wakai¹, Yasuo Takeuchi², Kenji Yamamoto³, Fumino Noguchi⁴, Noriko Arakawa⁵, Juntaro Ashikan⁴, Kazunari Yoshida¹, Masatsugu Iwamura¹

¹Department of Urology, Kitasato University School of Medicine; ²Department of Nephrology, Kitasato University School of Medicine; ³Department of Psychiatry, Kitasato University School of Medicine; ⁴Japan Organ Transplant Network; ⁵Department of Nursing, Kitasato University Hospital

Introduction: Only 0.8 per million populations donate organ for transplantation in Japan. This extreme shortage of donor organ insists the renal transplant waiting patients to expect longer than 15 years. Even after the change of transplantation act in 2010, total number of organ donor has not increased, although the percentages of brain dead donor increase. The number of end stage renal disease patients on the transplantation waiting list reached 12764 in Japan. Of these patients, 1741 (13.6%) have been waiting longer than 15 years. In our hospital, 18% of 256 waiting patients are as well. Most of these long-term waiting patients are high risk for renal transplant because of various complications due to long period of dialysis. It is mandatory to avoid the danger frequently encountered in transplant surgery and later. It is of course important to enlighten citizen to understand transplant medicine to increase the number of donation, but support these patients and their family to keep good condition.

Methods: We started and continued the annual seminar of renal transplant from 1999, 14 years ago. We have expanded the object of this seminar to citizen. This seminar aims to spread better understanding about transplant medicine and to share the information to maintain health condition better in long period of dialysis life and to reduce their anxiety. In this seminar, the information about donation and transplantation by Japanese organ procurement organization and transplant doctors have been shared, also talk by transplant patients, group work and discussion.

Results: The number of participant increased from 134 to 198 in 10 years. The total number exceeds 2000 in 14 years. Many questions about medication and post transplant life style were asked. The answer of questionnaire for the participant indicates that they desire detailed and accurate information. Discuss

P046

A PILOT RANDOMIZED CONTROLLED STUDY OF LIGHT THERAPY FOR SLEEP-WAKE DISTURBANCES IN RENAL TRANSPLANT RECIPIENTS

Burkhalter Hanna¹, Denhaerynck Kris¹, Wirz-Justice Anna², Cajochen Christian², Weaver Terry³, Steiger Jürg⁴, Fehr Thomas⁵, Venzin Reto Martin⁶, De Geest Geest Sabina¹

¹Institute of Nursing Science; ²Center for Chronobiology; ³Department of Biobehavioral and Health Sciences; ⁴Division of Nephrology, Basel; ⁵Division of Nephrology, Zürich; ⁶Division of Nephrology, Bern

Background: Morning light therapy has shown efficacy in synchronizing circadian misalignment. Sleep-wake disturbances are prevalent among renal transplant (RTx) recipients.

The aim of this study was to evaluate the efficacy of morning bright light therapy in RTx recipients who were diagnosed with sleep-wake disturbances on phase advancing bedtime (primary outcome), circadian and sleep parameters, cognitive performance and depressive symptomatology (secondary outcome).

Methods: This was a non-blinded, 1:1 randomized controlled wait-listed pilot trial. Thirty home dwelling RTx recipients aged 59.6 ± 12.6 year were randomly assigned to receive the intervention early (after 3 weeks) or usual care. The usual care group received the intervention after completion of the RCT periods (after 9 weeks). Morning light (10'000 lux) was scheduled according to chronotype daily for 30 min during 3 weeks. The rest-activity cycle was monitored throughout the whole period with a wrist actimeter. The RCT was analyzed using a random-intercept regression model to test group*time interaction. Effect sizes reflect the interaction estimate on standardized outcome variables. A second analysis combined intervention data of wait list design (pre-post analysis).

Results: RCT findings showed that morning bright light therapy induced a small phase advance for bed time (ES: -0.25; 95%CI -0.41; -0.09) and get up time (ES: -0.23; 95%CI -0.42; -0.03). The pre-post analysis showed a phase advance in get up time (ES: -0.21; 95%CI -0.32; -0.11). Post-hoc analysis revealed that controlling for beta-blockers and low-dose acetylsalicylic acid resulted in a significant increase in sleep efficiency (ES: -0.28; 95%CI -0.45; -0.10) and decrease in sleep latency (ES: 0.42; 95%CI 0.20; 0.65) for those not on these medications.

Conclusion: This pilot study indicated that light therapy in RTx recipients with sleep-wake disturbances can phase advance sleep time and improve sleep efficiency and sleep latency.

P047

INTERNATIONAL SURVEY OF NEPHROLOGISTS' PERCEPTIONS ABOUT NEW TRENDS IN TRANSPLANT: USE OF THE INTERNET AND MASS MEDIA FOR DONATION, ANONYMOUS AND PAIRED DONATION

Nasrollah Ghahramani

Pennsylvania State University College of Medicine

Background: The internet and mass media have become increasingly popular means of providing information about transplantation. Other new trends in transplantation include paired and anonymous donation. Nephrologists' perceptions and attitudes regarding these trends in transplantation have not been well-explored.

Methods/Materials: We used a web-based survey to investigate the perceptions of international nephrologists about five topics: (i) use of mass media for public education about kidney donation, (ii) use of media for promotion of kidney donation, (iii) use of the internet for solicitation of kidneys by patients, (iv) anonymous kidney donation, and (v) paired kidney donation. The relation between perceptions and demographic characteristics of 1280 nephrologists (age >50: 40%; female: 28%; rural practice: 11%; academic: 63%; transplant nephrologist: 51%) from 74 countries were examined by univariate and multivariable analyses.

Results: Used of mass media to educate the public about deceased donation and living donation were favored by 98% and 94% of the respondents, respectively. Use of mass media campaigns to promote deceased organ donation and living organ donation were favored by 74% and 58% of the respondents, respectively. Practice in an academic setting was more likely to be associated with favoring media advertisements to promote deceased organ donation (OR: 1.84; 95% CI: 1.32 to 2.56; p < 0.001). Nephrologists from North America (OR: 2.17; 95% CI: 1.61 to 2.94; p < 0.0001) and Western Europe (OR: 1.62; 95% CI: 1.08 to 2.46; p < 0.05) were more likely to favor media advertisement to promote living organ donation. Internet solicitation of organs by patients was favored by only 9% of the nephrologists. Nephrologist older than fifty (OR: 0.56; 95% CI: 0.35 to 0.88; p = 0.01), and those practicing in North America (OR: 0.30; 95% CI: 0.18 to 0.51; p < 0.001) or Western Europe (OR: 0.2).

P048

PRACTICE CHARACTERISTICS AND THE TYPE OF TRANSPLANT-RELATED PATIENT EDUCATION: A SURVEY OF NEPHROLOGISTS

Nasrollah Ghahramani

Pennsylvania State University College of Medicine

Background: There is wide variation in kidney transplantation (KT) referral rate. We hypothesize that the type of education patients receive from their nephrologists influences their choice of KT as an option, and that the nephrologists' demographic characteristics, training and practice environment impact the type of education they provide to patients about KT.

Methods/Materials: Invitations were sent to 3180 nephrologists in the eastern US. About 822 expressed interest, and 250 were randomly invited to complete a questionnaire about demographics, practice characteristics, and the types of educational material they provide to their patients. Two hundred and sixteen surveys with complete responses were analyzed by univariate analysis and stepwise logistic regression.

Results: Nephrologists noted availability of the following modes/materials of education: Printed material (85%), group sessions by representatives of a transplant center (TC) (78%); directions to access KT-related websites (63%); group sessions by members of their practice (55%); and educational CDs and DVDs (41%). Thirty-five percent provide four or more modalities. In multivariable analysis, practice in groups of >10 increased the likelihood of group sessions by a TC (OR: 4.91; 95% CI: 1.41–17.04; p = 0.01), or by members of the practice (OR: 2.96; 1.42–6.15; 0.004). Practice in locations where more than 2 TCs were within 50 miles was associated with higher likelihood of group sessions by a TC (OR: 3.34; 1.28–8.74; 0.01), availability of a tour of the TC (OR: 3.19; 1.58–6.44; 0.001), and availability of CDs and DVDs (OR: 2.26; 1.18–4.35; 0.01). Academic affiliation was associated with higher likelihood of offering four or more types of modality (OR: 2.46; 1.39–4.37; 0.002).

Conclusions: The majority of nephrologists provide some form of educational material/opportunity about transplantation as an option to their patients. The type and extent of material provided depend on the geographic location of the practice, its size and academic affiliation.

P049

HEALTH-RELATED QUALITY OF LIFE IN LIVER TRANSPLANT RECIPIENTS IN JAPAN

Estuko Soeda¹, Minoru Tanabe², Shigeyuki Kawachi³, Yuka Izawa⁴, Chie Takaoka⁴, Yuko Sano⁴, Tomohisa Hayakawa⁴, Masahiro Shinoda⁵, Satoshi Itano⁵, Hideaki Obara⁵, Minoru Kitago⁵, Taizo Hibi⁵, Yuta Abe⁵, Hiroshi Yagi⁵, Yuko Kitagawa⁵

¹School of Nursing, Keio University; ²Tokyo Medical and Dental University; ³Tokyo Medical University; ⁴Keio University Hospital; ⁵Keio University, School of Medicine

Background: This study aimed to identify retrospective evaluation of health-related quality of life (HRQOL) for liver transplant recipients in Japan.
Methods: Non-experimental descriptive study. Liver transplant recipients of one of transplant programs were invited to this study. The data of Short Form 35 (SF-36[®]) from liver transplant recipients were compared to the profile of the general Japanese population. This study was approved by the ethics committee of Keio University, School of Nursing and Medical Care.
Results: Baseline levels of SF-36[®] were as same as Japanese general scores; however, post-transplant complications and personal misfortunes (e.g., loss of spouse) contributed to some domains of SF-36[®], such as "Role functioning", "General Health", and "Social functioning" giving lower scores.
Conclusion: This study identified HRQOL of liver transplant recipients in Japan. Although the level of HRQOL is well as general population, transplant centers should give thorough check up of those recipients for long-term.

P050

ANKARA UNIVERSITY OF MEDICINE, LAW, THEOLOGY, FINE ARTS AND NURSING STUDENTS FACULTIES KNOWLEDGE AND ATTITUDE ON BRAIN DEATH AND ORGAN DONATION

Akyn Fyrat Kocaay¹, Nejat Emre Öksüz², Tefvik Eker¹, Cihangir Akyol¹, Yavuz Selim Apaydın², Taha Erkam Alptekin², Gökberk Özcar², Mustafa Özdemir², Acar Tüzüner¹

¹General Surgery, Ankara University of Medicine; ²Ankara University of Medicine

Background: Organ donation, among those brain death happened, plays an important role because many organs can be used in this situation. The aim of this project is to study the level of knowledge and attitudes of people in the Ankara University of Medicine, Law, Theology, Nursing and Communications who will be effective in future in this regard.
Materials and Methods: In order to determine perception of organ donation, 341 students from different faculties of the University of Ankara are participated in the survey. In the questionnaire a total of 30 questions that study the students' demographic data, and brain death, the level of knowledge and attitudes regarding organ donation and organ transplantation are found.
Results: While the most common answer for the donated organ is found to be the heart with a number of 291, the least one was the small intestine with 85 answers. Response to the question "Do you want to donate your organs?" revealed significant difference between faculties ($p = 0.006$). Answer yes were the highest in the Medical school students (60.2%) and the lowest in the students of the Faculty of Theology (32.3%)
Conclusion: In our study, it is seen that donatable organs are not well known. It shall be explained that many organs other than heart are transportable and with training, many patients' lives can be saved from transporting organs from brain death patients. Throughout the findings, it is clear that; the interest to organ donor card of those who want to donate organs is very low. For better functioning of the system, organ donation cards shall be promoted. The process of brain death and organ donation must work quickly. In this process, in order to avoid any problems adequate training should be given on the procedure to the related faculties.

P051

THE BELFAST-BIRMINGHAM MODEL - INCREASING RENAL TRANSPLANTATION NUMBERS IN THE SHORT AND LONG TERM

Tim Brown¹, John Connolly², Mohie Omar², Steve Mellor¹, Nicholas Inston¹, Aisling Courtney², Andrew Ready¹

¹University Hospitals, Birmingham; ²Belfast City Hospital

Background: Prior to 2009, the Northern Ireland (NI) transplantation service relied on cadaveric organs as the bedrock of activity. An inability to use organs retrieved after cardiac death combined with a reduction of numbers of organs from brain death donors impacted to create a rising waiting list. The NI population benefits from the preservation of a close extended family network and a strongly positive attitude to living donation.

Methods: The need to increase transplantation numbers was identified and given logistical and financial support from the Department of Health. A "one-stop" donor assessment clinic was instigated. This reduced the burden of multiple hospital attendances and made the donor pathway acceptable. The Birmingham transplant team were engaged on a peripatetic basis to provide a donor nephrectomy service on a regular basis "teaming up" with the Belfast team who provide the reimplantation service. To address succession planning for the NI unit, a surgical trainee was identified and received training in renal surgery by the Birmingham surgeons within their unit.

Results: The rate of living donor transplantation has increased exponentially (2008; $n = 9$; 2013; $n = 50$) since 2009. This has resulted in the NI transplant waiting list becoming shorter. The live donor transplant rate for NI is double the national average (33.5 ppm). The trainee has performed in excess of 100 transplants and 50 nephrectomies and is well placed to sustain this output into the future.

Conclusions: The Belfast-Birmingham relationship demonstrates how "twinning" of units can drive development. With appropriate logistical, political and financial support, this model may be transferable to similar units across Europe to increase transplant numbers and reduce waiting lists.

P052

BALNEOTHERAPY AS A PART OF A REHABILITATION PROCESS AFTER KIDNEY TRANSPLANTATION

Barbara Grandtnerova, Zuzana Beratsova, Miroslava Cervenova, Jan Cerven, Marian Markech, Hana Stefanikova
Golden Spa Turcianske Teplice

Background: Balneotherapy (BT) means bathing in thermal or mineral waters. It is known also as a spa therapy and is frequently used as a part of medical and rehabilitation process in many diseases of musculoskeletal system, neurologic disorders, diseases of circulatory system, for recuperation after treatment of oncologic diseases, etc. However, only scarcity of information exists about an effect of BT after kidney transplantation (KTx). In fact, as nephrologists we recommend to avoid bath tubs (bubble bath especially) as much as possible, not to contract urinary tract infection (UTI).

Aim: To evaluate the effect of BT after KTx, with a special emphasis on the risk of UTI.

Methods: Forty-three patients (29 women), median age 52 years (24-63), median time after KTx 9 months (9-12), 22% of transplants from living donors, wound healed, graft function stabilized, immunosuppression miscellaneous. All Ps were treated either in the bath tube (80%) or bubble bath (70%) for 15 min, 28 procedures in the average during 20-22 days of stay in the spa. The water was thermal (30-40°C), low mineralized (~1.5 g/l). Bathing was combined with other treatments, such as physical exercise, aquatic exercise in warm chlorinated mineral water, mud packs, massages and electro- or magnetotherapy for cervicocranial or low back pain syndromes.

Results: Only one female contracted uncomplicated UTI (cystitis) which quickly resolved after empiric antibiotic therapy. Infections of upper respiratory airways (10%) and acceleration of hypertension (10%) were much more common, refractory hypertension was a reason for an early discharge of 1 Ps. At the dismissal, remaining 42 Ps reported improved muscle strength in upper and lower extremities, raised well-being as well as better involvement in social life.

Conclusion: Balneotherapy together with physical rehabilitation, in an atmosphere free from stress, is a form of therapy that successfully complements medical treatment for allogenic KTx recipients.

PS05-CLINICAL IMMUNOSUPPRESSION & BIOLOGICALS

P053

IMPACT OF POST-RENAL TRANSPLANT LEUCOPENIA ON GRAFT AND PATIENT OUTCOME

Medhat Abdel Halim, Osama Gheith, Torki Al-Otaibi, Ahmed Musaad, Waleed Awadeen, Tarek Said, Prasad Nair, Narayanan M.R. Nampooray
Hamed Alessa OTC, Ibn Sina hospital

Background: Post-renal transplant leucopenia (PTL) is a common clinical problem with severe complications.

Methods: We studied renal transplant patients operated during 2010 in our center who received immunosuppression and chemoprophylaxis according to our protocol. Significant leucopenia was managed by reduction of valgancyclovir then MMF and giving granulocyte-colony stimulating factor.

Results: Seventy-nine patients divided into group 1 with leucopenia (34%) and group 2 without it. Valgancyclovir and septrin were stopped completely in 76.9% while MMF was reduced to $\geq 50\%$ in 85.7% in group 1, $p = 0.0001$. There were no significant differences in demographic data. Four cases of CMV infection were in group 1 while none were in group 2, $p = 0.01$. There was higher number of NODAT and mean rejection episode/patient in group 1 ($p = 0.03$) due to frequent drug manipulation.

Conclusion: PTL was complicated with higher CMV infection, NODAT, rejection rate and use of G-CSF without affecting graft or patient outcome at 1 year.

P054

ANALYSIS ON SWITCH BETWEEN CICLOSPORIN A AND TACROLIMUS IN THE TRIPLE IMMUNOSUPPRESSIVE

Yang Li, Wujun Xue, Xiaoming Ding, Ping Fan, Xiaohui Tian, Xinshun Feng, Xiaohong Wang, Xuzhen Wang, Chenguang Ding, Jin Zheng
The First Affiliated Hospital, Medical College, Xi'an Jiaotong University

Objective: To explore the clinical significance of switch between ciclosporin A (CsA) and tacrolimus (FK506) in the triple immunosuppressive agent including calcineurin inhibitors, mycophenolate mofetil, and prednisone after renal transplantation.

Methods: The data of 148 patients with CNIs switch were collected including 97 patients with FK506 switching to CsA and 122 patients with CsA switching to FK506. The clinical indexes were analyzed by paired T test.

Results: In patients with FK506 switching to CsA, the serum creatinine, urea and blood glucose significantly dropped and hemoglobin, bilirubin, cholesterol significantly increased compared to those before switch. In patients with CsA switching to FK506, the serum creatinine and urea began significantly dropping from 4 and 2 weeks respectively after switch. Platelet began significantly dropping from 20 weeks after switch. Albumin, globulin and bilirubin significantly increased from 20, 12 and 36 weeks respectively after switch. Blood glucose and cholesterol significantly decreased from 12 and 3 weeks respectively after switch.

Conclusions: The renal function of all patients were improved by CNIs switch between CsA and FK506 no matter what reason. So the switch of immunosuppressive agent has benefits to improve each clinical for patient.

P055

ERYTHROID RECOVERY AFFECTS TACROLIMUS CLEARANCE AFTER ENGRAFTMENT DURING STEM CELL TRANSPLANTATION

Noriyasu Fukuoka¹, Kumiko Tani¹, Osamu Imataki², Mari Kawano¹, Takaaki Fujimoto¹, Hiromi Ichinose¹, Kazunori Yamaguchi¹, Hiroaki Tanaka¹, Shinji Kosaka¹, Hitoshi Houchi¹

¹Department of Pharmacy, Kagawa University Hospital; ²Division of Hematology, Department of Internal Medicine, Faculty of Medicine, Kagawa University

The objective of this study was to identify which hematologic parameters affect tacrolimus clearance. Of the 13 patients, gradual dose reduction was required to combat elevated tacrolimus concentrations. The mean post-engraftment C/D ratio was higher than the pre-engraftment C/D ratio in each patient. The mean C/D ratio for all patients after engraftment was 1.56-fold higher ($p = 0.00004$, @range: 1.04–3.03) than that before engraftment. The variation ratio was calculated by dividing the C/D ratio by that on the engraftment day. Multivariate analysis revealed that the reticulocyte (RET) level (~ 103 count/ μ l) was the sole parameter influencing this ratio, and both parameters were expressed as: Variation ratio = $0.004 \sim \text{RET} + 1.0$. RET recovery of patients could influence the C/D ratio and tacrolimus clearance was affected by recipient original red blood cells, but not that of transfused red blood cells.

P056

THE MULTI-CENTRAL COMMON IMMUNOSUPPRESSIVE REGIMEN WITH EVEROLIMUS AND TAC FOR RENAL GRAFT

Kazunari Yoshida¹, Masae Ikeda¹, Daisuke Ishii¹, Ryota Maeyama¹, Yoji Watanabe¹, Atsushi Sugita¹, Fumino Noguchi², Noriko Arakawa², Kenji Yamamoto³, Juntaro Ashikari⁴, Yasuo Takeuchi⁵, Wakai Hariki⁶, Masatsugu Iwamura⁶

¹Kitasato University, Urology; ²Department of Nursing, Kitasato University Hospital; ³Department Psychiatry, Kitasato University School of Medicine; ⁴Japan Organ Transplant Network; ⁵Department of Nephrology, Kitasato University School of Medicine; ⁶Department of Urology, Kitasato University School of Medicine

Introduction: Only 0.8 per million populations donate organ for transplantation in Japan. This extreme shortage of donor organ insists the renal transplant waiting patients to expect longer than 15 years. Even after the change of transplantation act in 2010, total number of organ donor has not increased, although the percentages of brain dead donor increase. The number of end stage renal disease patients on the transplantation waiting list reached 12764 in Japan. Of these patients, 1741 (13.6%) have been waiting longer than 15 years. In our hospital, 18% of 256 waiting patients are as well. Most of these long-term waiting patients are high risk for renal transplant because of various complications due to long period of dialysis. It is mandatory to avoid the danger frequently encountered in transplant surgery and later. It is of course important to enlighten citizen to understand transplant medicine to increase the number of donation, but support these patients and their family to keep good condition.

Methods: We started and continued the annual seminar of renal transplant from 1999, 14 years ago. We have expanded the object of this seminar to citizen. This seminar aims to spread better understanding about transplant medicine and to share the information to maintain health condition better in long period of dialysis life and to reduce their anxiety. In this seminar, the information about donation and transplantation by Japanese organ procurement organization and transplant doctors have been shared, also talk by transplant patients, group work and discussion.

Results: The number of participant increased from 134 to 198 in 10 years. The total number exceeds 2000 in 14 years. Many questions about medication and post transplant life style were asked. The answer of questionnaire for the participant indicates that they desire detailed and accurate information.

Discussion: This seminar helped to support patients and could reduce their anxiety, but they need more information.

P057

THERAPY IN LIVER TRANSPLANT RECIPIENTS WITH ONCOLOGICAL DISEASE: A CASE-CONTROL STUDY

José-María Álamo¹, Luis-Miguel Marín¹, Carmen Bernal¹, Lydia Barrera¹, Gonzalo Suárez¹, Juan Serrano¹, Jordi Muntané², Javier Padillo¹, Miguel-Angel Gómez-Bravo¹

¹Liver Transplant Unit, Virgen del Rocío Hospital;

²Instituto de Biomedicina de Sevilla - IBI

Background: We have analyzed the efficacy of mammalian target of rapamycin inhibitor (mTORi) in patients with de novo malignancies or those transplanted because of a primary liver cancer.

Methods: A case-control study of patients with hepatocellular carcinoma (HCC; $n = 119$), cholangiocarcinoma ($n = 1$) or de novo malignancies ($n = 73$). Thirty-seven patients were treated with mTORi, and 167 with calcineurin inhibitors (CNI).

Results: No incidence of rejection, serious adverse events, or death was observed with an overall actuarial survival of 68.5% in the mTORi group versus 45.7% among the CNI group. Tumor recurrence were 15.2% and 36.8%, respectively ($p < 0.05$). In HCC, survival was 100% of mTORi with and 61.5% among CNI patients, with tumor recurrence rates of 6.2% and 19.1%, respectively ($p < 0.05$).

Conclusion: Differences in survival and tumor recurrence rates were observed. Switching from CNI to mTORi immunosuppressant therapy appeared to be safe. It's reasonable to employ this strategy in liver transplant.

P058

MINIMIZATION OF MPA-INHIBITORS COULD BE DANGEROUS FOR THE GRAFT

Dietmar Abendroth¹, Michael Marzinzig¹, Manfred Stangl²

¹University of Ulm, Center of Surgery; ²Ludwig-Maximilians-University Munich

Question was whether long term exposure for mycophenolate mofetil (MMF) or enteric coated mycophenolic acid (EC-MPS) is leading to an enzyme induction for IMPDH, thus decreasing MPA immunosuppressive properties.

Patients and Methods: By application of an IMPDH assay (HPLC based), enzyme activity was investigated in whole blood for the substrate xanthine monophosphate (XMP) and for xanthine (X) in isolated lymphocytes from stable renal transplant patients: Gr.I (MMF, $n = 23$); Gr.II ($n = 31$, EC-MPS).

Basic data from 60 healthy volunteers. Follow up measurements at week 1,2,3,4 and month 3–120.

Results: IMPDH activity increased with a high variability nearly 8 fold (318 vs. 2100 pmol/min/ml) in whole blood. In isolated lymphocytes the increase was up to 340% and higher in patients with rejection episodes; a decrease of IMPDH inhibition 3 to 43 months post tx.

Conclusion: Increase of IMPDH activity. Additional dose reductions might lead to underimmunosuppression. Drug "minimization" for MMF/EC-MPS might be hazardous for the graft.

P059

B-CELL DEPLETING THERAPIES DIFFERENTIALLY MODULATE DONOR SPECIFIC ANTIBODY DURING CHRONIC ABMR

Maxime Touzot¹, Gregoire Couvrat Desvergnés¹, Stéphanie Castagnet¹, Anne Cesbron², Karine Renaudin¹, Magali Giral-Classe³

¹ITUN; ²EFS; ³ITUN, INSERM 1064

Background: B cell-depleting therapy may be efficient in Chronic Antibody-mediated rejection (cAMBR).

Methods: Retrospective analysis of 17 patients with cAMBR, treated by Plasma Exchange (PE) and Rituximab (group I, $n = 10$) or by Bortezomib (group II, $n = 7$). Anti-HLA Donor Specific Antibody (DSA) were measured by Luminex

Results: Estimated Glomerular Filtration Rate (eGFR, MDRD) dropped from 27 to 19 ml/min and 42 to 33 ml/min in group I and II, respectively 12 months after treatment ($p < 0.05$). Graft loss was observed only in group I (3/5 patients). DSA were mainly class II (group I = 75%, group II=90%) with 2/3 of anti HLA-DQ. Class I and HLA-DR disappeared and remained negative after therapies for at least 6 months. Surprisingly, both therapies did not suppress HLA-DQ DSA during the follow-up.

Conclusion: Our results enlightened a differentially modulation of anti-HLA DSA during B-cell depleting therapy, raising questions about their pathophysiological significance.

P060

TUMOR INCIDENCE IN HEART TRANSPLANT RECIPIENTS RECEIVING CYCLOSPRIN A OR TACROLIMUS AS MAINTENANCE THERAPY

Fuchs Uwe

Heart Center North-Rhine-Westfalia

Background: Heart transplant (HTx) recipients are at an increased risk of developing tumors and administration of the calcineurin (CNI)-inhibitors cyclosporine (CSA) or tacrolimus (TAC) may contribute to this risk. We compared tumor incidence rates in HTx patients receiving either CSA or TAC as maintenance immunosuppressive therapy.

Methods: We included 145 patients into this retrospective data analysis. All patients were transplanted between 2003 and 2007 and were followed up until 2011. Group A ($n = 25$) received CSA and group B ($n = 120$) TAC as maintenance therapy. Those patients who died within the first postoperative year were excluded from data analysis.

Results: The two study groups were comparable with respect to sex, year of transplantation and primary and concomitant diagnoses. Group A was, however, significantly older compared to group B (58.8 ± 11.4 years vs. 49.1 ± 13.0 years; $p = 0.01$) and so was the donor age of group A (43.2 ± 11.2 years vs. 37.0 ± 11.7 years; $p = 0.02$). Mean follow-up was 60.7 ± 19.3 months in group A and 59.8 ± 18.1 months in group B ($p = 0.813$). In total, 16 tumors were diagnosed in 15 patients (five patients in group A and 10 patients in group B). In age-adjusted Cox regression analysis, freedom from malignancy according to study group did not differ in the CSA group compared to the TAC group (relative risk = 1.22 (95% CI: 0.39–3.78; $p = 0.730$). Moreover, age-adjusted overall survival was comparable between groups (relative risk for the CSA group = 1.89 (95% CI: 0.52–6.80; $p = 0.332$).

Conclusions: Our data indicate that tumor incidence does not significantly differ in patients receiving CSA or TAC as maintenance therapy.

P061

EFFICACY AND SAFETY OF EVEROLIMUS BASED IMMUNOSUPPRESSION ON DE NOVO KIDNEY TRANSPLANTATION WITH 4 YEARS FOLLOW-UP, ESPECIALLY IN PROTOCOL BIOPSY FINDINGS AND DONOR SPECIFIC ANTIBODY PRODUCTION

Yoshihiko Watarai¹, Takayuki Yamamoto¹, Makoto Tsujita¹, Takahisa Hiramitsu¹, Koji Nanmoku¹, Norihiko Goto¹, Shunji Narumi¹, Tsuneo Ueki², Akio Katayama², Asami Takeda¹, Kunio Morozumi¹, Kazuharu Uchida³, Takaaki Kobayashi⁴

¹Nagoya Daini Red Cross Hospital; ²Masuko Memorial Hospital; ³Aichi Medical University; ⁴Nagoya University Graduate School of Medicine

The impact of everolimus (EVR) based immunosuppression in De Novo Kidney Transplantation was evaluated with clinical outcomes, protocol biopsies findings and donor specific antibody (DSA) production.

Methods: During 2008 and 2009, twenty-six recipients were enrolled to compare the safety and efficacy between EVR based and mycophenolate mofetile (MMF) based immunosuppression. EVR group received reduced-exposure cyclosporine (CsA; target C0 25–50 ng/ml after 6 months) + steroid, and EVR-C0 were adjusted 3–12 ng/ml. MMF group received standard-exposure cyclosporine (CsA; target C0 100–250 ng/ml after 6 months) + steroid. Both group received basiliximab induction.

Results: With a mean observation period of 52 (49–59) months, current patient and graft survival is 100% in both groups (EVR; $n = 13$, MMF; $n = 13$). Renal function expressed as eGFR was similar 41.6;14.3 in EVR group and 37.2;7.0 in MMF group. Significant proteinuria, more than 300 mg/day, were observed more in EVR group (69%) than in MMF group (27%) respectively, however the proteinuria was successfully treated with angiotensin-II receptor blockade. Incidence of Cytomegalovirus (CMV) infection was significantly reduced to 15.1% in EVR group comparing to 46.2% in MMF group, especially none of seropositive recipients for CMV developed CMV infection under pre-emptive therapy principle. None of EVR and MMF group was treated for clinical T cell mediated rejection, similar incidence of Banff borderline change on 6 or 12 months protocol biopsies were observed in 7.7% of EVR group and 15.4% of MMF group, but none of both groups revealed peritubular capillaritis. Luminex solid phase assay revealed the similar incidence of class II DSA production in both groups, 7.7% of EVR group at 2 years after transplant and 15.4% of MMF group at 3 years

Conclusions: EVR based immunosuppression provides equivalent clinical outcomes as well as the incidence of De Novo DSA production with MMF based immunosuppression with 4 years follow-up.

P062

OPTIMIZATION OF IMMUNOSUPPRESSION IN DUAL KIDNEY TRANSPLANTATION (DKT) FROM ELDERLY DONORS (ED): WHICH CALCINEURIN INHIBITOR (CNI) GIVES A BETTER PERFORMANCE IN ASSOCIATION WITH EVEROLIMUS?

Lucrezia Furian¹, Cristina Silvestre¹, Lorenzo Vallese¹, Gaya Spolverato¹, Francesco Marchini², Luciana Bonfante³, Paolo Rigotti¹

¹Kidney and Pancreas Transplantation Unit, University of Padova; ²Nephrology Unit-Padova Hospital; ³Nephrology Unit-University of Padova

Background: Considering the reduced functional reserve of marginal kidneys, a CNI-sparing immunosuppressive approach in association with proliferation signal inhibitors (PSI) in DKT from ED could be beneficial for the minimization of acute and chronic nephrotoxicity; moreover it may reduce infectious, neoplastic and cardiovascular complications. Nevertheless, which CNI might be preferable in association with everolimus (EVE) in DKT offering a more effective prevention of acute rejection and a lower rate of adverse events is still unidentified. In the present study, the results of DKT from ED treated with extended-release tacrolimus (ER-TAC) + EVE compared with a historical group treated with cyclosporine (CSA) + EVE are reported.

Methods/Materials: From 09/2010 to 09/2012, 27 patients (median age 68 years, IQR62-69) underwent DKT from ED (median age 77 years, IQR73-84) and received ATG induction, low-dose ER-TAC (trough 3–5 ng/ml), EVE (trough 5–8 ng/ml) and steroids (G1). Renal function, incidence of acute rejection, delayed graft function (DGF), and side effects including surgical complications were compared with a historical group (G2) of 33 patients (median age 63 years, IQR60-69) who underwent DKT from ED (median age 72 years, IQR69-73) from 09/2008 to 08/2010, and received ATG induction, low-dose CSA (trough C2 400–700 ng/ml), EVE (trough 5–8 ng/ml) and steroids.

Results: No deaths or graft losses at 1-year occurred in either group. DGF occurred in three patients (11%) in G1 and in 11 patients (33%) in G2. Both groups of treatment resulted very effective in terms of prevention of acute rejection, with no episodes in G1 and 4 (12%) in G2. Renal function was similar between groups at 1-year with median S-creatinine of 120 $\mu\text{mol/L}$ (IQR 111–204) in G1 vs 124 $\mu\text{mol/L}$ (IQR103–149) in G2. Surgical complications included four lymphoceles (15%) in G1 and 3 (9%) in G2; 6 wound dehiscences (22%) in G1 and 13 (39%) in G2. CMV and BK-virus infection occurred in 7 (26%) and 4 (15%) patients in G1 vs 5 (15%) and 2 (6%) patients in G2.

Conclusion: Low-dose ER-TAC and CSA offered optimal renal function in DKT from ED in association with EVE; a lower rate of DGF and no cases of

acute rejections with ER-TAC suggest to explore the potential of this protocol with further minimization of TAC exposure.

P064

CLINICAL BENEFIT OF INDUCTION THERAPY WITH THYMOGLOBULIN IN MAJOR HISTOCOMPATIBILITY COMPLEX ANTIBODY POSITIVE HEART TRANSPLANT RECIPIENTS

Uwe Fuchs, Armin Zittermann, Stephan Ensminger, Jan Gummert, Uwe Schulz

Heart Center North-Rhine-Westfalia

Background: Major Histocompatibility Complex (MHC) antibody positive heart transplant (HTx) recipients have a high risk for clinical complications, including cellular and humoral rejections.

Methods: We assessed clinical outcomes in 39 MHC antibody positive heart transplant recipients who received thymoglobulin for induction therapy (T-group). Results were compared with 39 MHC antibody negative HTx patients as the control group who received standard immunosuppressive therapy (T group). Patients were followed for up to one year.

Results: Age and diagnosis were comparable between the two groups. In age- and -BMI adjusted Cox regression analysis, 1 - year survival did not differ significantly in the T group compared to the C-group (relative risk = 2.45 (95% CI: 0.20–29.8, $p > 0.1$). Freedom from biopsy-proven rejection was similar in group A and B (94.0% and 94.4%, respectively, $p = 0.925$). Freedom from CMV infection was 89.7% (T-group) and 97.4% C-(group; $p = 0.253$). During follow-up, 34 other infections occurred in the T- group and 35 in C-group ($p = 0.189$). In the surviving patients, white blood counts were comparable between groups, whereas C-reactive protein levels were significantly higher in T-group compared to the C-group ($p = 0.002$).

Conclusions: Our data suggest an elevated mortality risk in MHC positive HTx recipients despite thymoglobulin for induction therapy.

P065

ONCE DAILY TAC INITIATION IN KIDNEY AND LIVER TRANSPLANT: 3 MONTHS ANALYSIS OF AN OBSERVATIONAL STUDY

Olivier Cointault¹, Diego Cantarovich², Karine Moreau³, Elisabeth Cassuto⁴, Bruno Roche⁵, Alexandre Loupy⁶, Sebastien Dharancy⁷, Georges-Philippe Pageaux⁸, Michèle Kessler⁹

¹CHU Toulouse; ²CHU Nantes; ³CHU Bordeaux; ⁴CHU Nice; ⁵Paul Brousse hospital; ⁶Necker Hospital; ⁷CHU Lille; ⁸CHU Montpellier; ⁹CHU Nancy

Background: Once daily TAC (TAC-OD) is comparable to twice daily (TAC-BID) in Kidney (K) and Liver (L) transplantation (Tx). Impact of initiation strategies on patient outcomes and treatment compliance remains to be assessed.

Methods: Observational study with clinical data collection and patient self questionnaire at inclusion, 3 and 6 months after TAC-OD initiation in KTx and LTx. Data at 3 months are presented.

Results: About 1190 patients were included. Ninety-five percent were switched from TAC-BID, mg/mg associated with a mean decrease of CO ~10%. 10.5% of which needed a dose change during the first month. At 3 months after initiation, 98% of patients remained on TAC-OD with stable systemic exposure (mean CO 6.33 ng/ml). Four acute rejections were reported (3 KTx, 1 LTx), no graft loss. Twenty percent of patients assessed their compliance as improved.

Conclusion: Initiation of TAC-OD in a large cohort of KTx and LTx patients was associated with 20% improvement of treatment compliance without any safety concerns.

P066

DRUG-DRUG INTERACTION (DDI) ASSESSMENT TO GUIDE OPTIMAL USE OF HEPATITIS C (HCV) ANTIVIRALS WITH IMMUNOSUPPRESSANTS

Avantika Barve, Binfeng Xia, Heidi Einolf, Lucy Xu, Tao Zhang, Sven Kohler, Guido Junge, Patricia M. Lopez, Haiying Sun
Novartis

Background: Post-LTx recurrence of HCV infections is universal hence co-administration of Telaprevir (TPV) and Boceprevir (BPV) with cyclosporine (CsA), tacrolimus (TAC) or everolimus (EVR) is needed. A major concern is the risk of toxicity due to DDI between the two classes of drugs owing to interaction with CYP3A4. In this research work we present a modeling approach to aid in the identification of right dose for immunosuppressant and antiviral such that DDI is minimal without affecting efficacy or safety of individual therapies. Based on the degree of interaction and the predicted dose adjustment for the immunosuppressant, this approach has the potential to impact the choice of immunosuppressant that can be used with antiviral.

Methods: PBPK models for CsA and TPV were built using Simcyp (v12). The input parameters for CsA and TPV were obtained from in silico predictions, in-

house data or literature. The model for CsA and TPV as CYP3A4 substrate and inhibitor were qualified using clinical data. Simulations were run using different doses for CsA with TPV to achieve the steady-state C_{min} for CsA.

Results: The predicted PK parameters of CsA and TPV are in good agreement with the observed data (Table 1). The predicted C_{min} values for CsA when co-administered with TPV following different doses of CsA are shown in Table 2.

Conclusion: The model can be used to optimize dose selection of CsA with TPV. Similarly dose optimization of TAC and EVR with TPV will be evaluated.

P067

MARGINAL ADVANTAGE OF KNOWING PATIENT'S CYP3A5 GENOTYPE FOR TACROLIMUS DOSING

Anders Åsberg¹, Karsten Midtved², Mikevan Guilder³, Elisabet Størset¹, Sara Bremer², Stein Bergan², Roger Jelliffe³, Anders Hartmann², Michael Neely³

¹University of Oslo; ²Oslo University Hospital-Rikshospitalet; ³University of Southern California

Background: Tacrolimus (Tac) is an immunosuppressant with low bioavailability and initial dosing is based on bodyweight. Functional CYP3A5 affects Tac bioavailability and elimination. There is limited data on the clinical advantage of knowing CYP3A5 genotype at the time of transplantation (Tx).

Methods: To evaluate the advantage of knowing CYP3A5 genotype at time of Tx a non-parametric population model for dosing of Tac was developed and validated in 99 renal Tx recipients.

Results: The following covariates were included in the model; fat free mass, BMI, hematocrit, time post Tx and CYP3A5 genotype. Patients with functional CYP3A5 (CYP3A5^{1/*3}) had a 26% higher clearance and 37% lower bioavailability. Knowledge of CYP3A5 genotype provided a small advantage for prediction of the next Tac concentration until 3–4 trough concentrations were reported, after which a model without CYP3A5 genotype as covariate did just as well.

Conclusion: The population model for Tac described patient data well. When using the model for Tac dosing, knowledge of CYP3A5 genotype improved dose predictions the first few days.

P068

IMPROVEMENT OF LIPID AND LIPOPROTEIN PROFILE BY CONVERSION TO EXTENDED-RELEASE TACROLIMUS

Masayoshi Okumi¹, Yoichi Kakuta¹, Taigo Kato¹, Kazuaki Yamanaka¹, Koichi Tsutahara¹, Koji Yazawa¹, Naotsugu Ichimaru², Shiro Takahara², Norio Nonomura¹

¹Department of Urology, Osaka University Graduate School of Medicine;

²Department of Advanced Technology for Transplantation, Osaka University Graduate School of Medicine

Background: Extended-release tacrolimus (TAC-ER) is a once-daily extended-release formulation of tacrolimus (TAC). We have previously reported the effects of conversion from TAC to TAC-ER on treatment adherence in the maintenance phase after kidney transplantation. With lower C_{max}, TAC-ER may also be associated with a reduced risk of adverse effects, especially risk factors for cardiovascular disorder.

Objective: The effects of conversion to TAC-ER in improving lipid and lipoprotein profiles were evaluated in kidney transplant patients in the maintenance phase.

Patients and Methods: The study population consisted of 38 kidney transplant recipients with stable renal function who had been maintained on oral twice-daily TAC at a trough level of ≤ 10 ng/ml. They were converted from TAC to TAC-ER at the same daily dose within a range of plus or minus 20%. We analyzed the effects of the TAC-ER dose and trough level on graft function, triglycerides (TG), total cholesterol (T-Chol) and HDL cholesterol (HDL-C) at baseline and 1 year after conversion.

Results: The conversion to TAC-ER did not cause deterioration of renal function and none of the patients experienced any clinical adverse events such as rejection and infection. The mean dose at baseline and 1 year after the conversion was 2.8; 1.3 mg/day of TAC and 2.6; 1.0 mg/day of TAC-ER and the mean trough level of TAC decreased 6.6; 1.4 to 6.2; 1.2 ng/ml significantly. The mean T-Chol decreased 207.6; 29.0 to 197.7; 25.2 mg/dl and the mean TG decreased 105.2; 45.3 to 97.0; 40.5 mg/dl, significantly. However, no significant correlation between change in trough level and that in TG or T-Chol was seen.

Conclusion: These results suggest that the decrease of TG and T-Chol after conversion was not attributable to the trough level declining with conversion from twice-daily TAC to once-daily TAC-ER. It is possible to consider that C_{max} of TAC may affect the decrease of TG and T-Chol in kidney transplant recipients.

P069

PERIODONTAL INFLAMMATION IN LIVING KIDNEY DONORS AND RENAL TRANSPLANT RECIPIENTS RECEIVING EVEROLIMUS OR TACROLIMUS

Otilia Pereira-Lopes¹, Benedita Sampaio-Maia¹, Susana Sampaio², Ana C. Braga³, António Felino⁴, Manuel Pestana²

¹Faculty of Dentistry, University of Porto; ²Nephrology Research and Development Unity (FCT-725), Faculty of Medicine, São João Hospital Centre; ³Department of Production and Systems, University of Minho; ⁴Faculty of Dentistry, University of Porto

Background: The oral health of renal transplant recipients (RTR) can be affected by the oral manifestations of the chronic kidney disease as well as by oral complications related with transplantation. The aim of this study was to evaluate oral health status of RTR receiving tacrolimus (Tac) or everolimus (ERL) as immunosuppressants, and living kidney donors (LKD) as healthy comparison group.

Methods: Thirty-six RTR receiving Tac and 22 receiving ERL as well as 13 LKD were included in the study. Age, gender, literacy, body mass index, time since transplant and pharmacological data were recorded and oral health status was assessed through the evaluation of teeth, periodontal parameters, saliva, oral hygiene habits and oral symptoms.

Results: RTR receiving Tac (39 ± 9 year) were younger than ERL (50 ± 11 year) and LKD (44 ± 9 year) groups (p = 0.001). The prevalence of female gender was higher in LKD group (p = 0.001). No differences were found among the three groups concerning oral hygiene habits, oral symptoms and smoking habits. Although DMFT index did not differ among groups (11 ± 7 vs 11 ± 6 vs 16 ± 8), visible plaque index was higher in Tac group (92 ± 21) than both ERL (82 ± 23) and LKD (83 ± 14) groups (p = 0.035). Also, bleeding on probing in Tac group (15 ± 20.7) was higher than ERL (5.5 ± 9.6) or LKD (9.9 ± 10.5) groups (p = 0.047). No differences were found in clinical attachment level (2.8 ± 0.6 vs 2.9 ± 0.7 vs 2.6 ± 0.7), unstimulated (UNS) and stimulated (SS) saliva flow rate (UNS: 0.43 ± 0.33 vs 0.41 ± 0.27 vs 0.35 ± 0.29; SS: 1.59 ± 0.9 vs 1.51 ± 0.9 vs 1.42 ± 0.81) and pH (UNS: 7.11 ± 0.46 vs 7.2 ± 0.61 vs 6.89 ± 0.46; SS: 7.72 ± 0.4 vs 7.8 ± 0.27 vs 7.65 ± 0.36) among the studied groups.

Conclusions: Renal transplant recipients receiving ERL have lower periodontal inflammation than RTR receiving Tac and similar levels to LKD, suggesting that RTR receiving ERL may be better protected for the development of periodontal disease when compared to RTR receiving Tac.

P071

ORAL CANDIDA PREVALENCE IN RENAL TRANSPLANT RECIPIENTS RECEIVING CYCLOSPORINE, EVEROLIMUS OR TACROLIMUS AND LIVING KIDNEY DONORS

Otilia Pereira-Lopes¹, Susana Sampaio², Pedro Vieira-Marques³, Filipa Monteiro-da-Silva⁴, António Felino⁴, Manuel Pestana², Benedita Sampaio-Maia¹

¹Faculty of Dentistry, Nephrology Research and Development Unity (FCT-725), University of Porto; ²Nephrology Research and Development Unity (FCT-725), São João Hospital Centre and Faculty of Medicine; ³Center for Research in Health Technologies and Information Systems, Faculty of Medicine, University; ⁴Faculty of Dentistry, University of Porto

Aim: Given that Candida is a relevant opportunist microorganism, the aim of the present study was to evaluate oral Candida prevalence in renal transplant recipients (RTR) receiving cyclosporine (CsA), tacrolimus (Tac) or everolimus (ERL) as immunosuppressants and compare it with a control group, the living kidney donors (LKD).

Methods: Twenty-seven RTR receiving CsA (13 men and 14 women, age 55 ± 8 years), 29 receiving Tac (15 men and 14 women, mean age 39 ± 9 years) and 22 receiving ERL (16 men and six women, mean age 50 ± 11 years) as well as 13 LKD (1 men and 12 women, mean age 44 ± 9 years) participated voluntarily in the study. The number of decayed, missing and filled teeth (DMFT) index as well as saliva flow and pH were evaluated in all patients by a physician blind to the transplantation status and immunosuppressive treatment. Also, oral Candida prevalence was determined using stimulated saliva plated in CHROMagar[®] Candida.

Results: The DMFT index (p = 0.132), unstimulated saliva flow rate (p = 0.308) and pH (p = 0.200) as well as stimulated saliva flow rate (p = 0.551) and pH (p = 0.540) did not differ between RTR receiving CsA, Tac or ERL and LKD. Oral Candida prevalence did not differ between patients receiving CsA (37%), Tac (52%) or ERL (36%). Also, the mean value of oral Candida quantification was similar in patients receiving CsA (2.67 ± 0.22), Tac (2.77 ± 0.15) or ERL (2.48 ± 0.17). Additionally, oral Candida prevalence and quantification was similar between RTR (42%, 2.67 ± 0.10) and LKD (39%, 2.84 ± 0.38).

Conclusions: Although is established that immunosuppressed individuals are more susceptible to opportunistic Candida infection, the oral Candida prevalence as member of normal microbiota does not seem to differ between RTR and LKD or between different immunosuppressive regimens.

P070

ONCE VERSUS TWICE A DAY TACROLIMUS FORMULATIONS IN DE NOVO KIDNEY TRANSPLANTATION: EARLY AND LONG TERM OUTCOMES IN A SINGLE CENTER

Stefano Vittorio Impedovo¹, Michele Battaglia¹, Giuseppe Grandaliano², Carlo Bettocchi¹, Loreto Gesualdo³, Francesco Paolo Selvaggi¹, Antonio Schena³, Silvano Palazzo¹, Floriana Giangrande¹, Pasquale Ditunno¹

¹Department of Urology, Andrology and Kidney Transplantation Unit, University of Bari, Italy; ²Department of Nephrology, Dialysis and Transplantation Unit, University of Foggia, Italy; ³Department of Renal, Dialysis and Transplantation Unit, University of Bari, Italy

Introduction: Non-compliance after kidney transplantation, represents a major concern, leading to a worst graft survival. Tacrolimus is an immunosuppressive drug, commonly used for rejection prophylaxis after kidney transplantation. In order to improve patient's compliance, a once daily dosing formulation of tacrolimus was developed. Herein, we compare the efficacy and safety of twice versus once daily tacrolimus formulation in de novo kidney transplant patients.

Materials and Methods: we enrolled 174 patients who underwent kidney transplantations between January 2007 and December 2010. Patients were divided into two groups according to Tacrolimus formulation, once daily (QD, Group A, n = 85) and twice daily (BID, Group B, n = 89), both in combination with mycophenolate and corticosteroids and followed for 36 months.

Results: We did not observe significant difference between groups in tacrolimus trough levels, graft function and blood glucose levels during the hospital stay and throughout the observational period. Acute rejection rate (5.9% in group A vs. 11.2% in group B), delayed graft function (36.9% in group A vs. 29.2% in group B), onset of post-transplant diabetes (5.8% in group A vs. 6.7% in group B) were similar in the two groups. Three patients treated with Tacrolimus BID developed graft failure, one due to recurrence of the underlying disease and two from non-compliance to therapy. We counted two exits: one recipient of group A died because of severe acute respiratory syndrome by coronavirus, while another one of group B, died from urothelial cancer.

Conclusion: in our experience tacrolimus QD was well tolerated with similar short and long term safety and efficacy profiles of tacrolimus BID. Reduction in the number of pills is the best condition to improve treatment compliance, potentially reducing graft failure.

P072

TACROLIMUS FIRST DOSE DEPENDS ON RECIPIENT CYP3A5 AND ABCB1 (OR MDR1) GENOTYPES IN PEDIATRIC LIVER TRANSPLANTATION: EXPERIENCE IN LIVING DONOR RECIPIENTS

Vanessa Guy-Viterbo¹, Nadtha Panain¹, Magdalena Janssen², Laure Elens¹, Raymond Reding², Vincent Haufroid¹, Pierre Wallemacq¹

¹Louvain center for Toxicology & Applied Pharmacology (LTAP), Université Catholique de Louvain; ²Cliniques Universitaires St-Luc, Université Catholique de Louvain

Background: Finding adequate tacrolimus (TAC) dosing is difficult to handle in the early post pediatric liver transplantation period due to TAC interindividual pharmacokinetic (PK) variability. This variability is largely influenced by the activity of (donor and recipient) P-glycoprotein (P-gp) and (donor) hepatic and (recipient) intestinal CYP3A4 and CYP3A5 enzymes. Single nucleotide polymorphisms (SNPs) in genes coding for CYP3A5 (6986A>G, CYP3A5*3), CYP3A4 (CYP3A4*22) and P-gp (ABCB1, 3435C>T, 2677G>T/A) could influence TAC PK. Therefore, both donor and recipient genetic background could explain a part of the TAC PK variability. We wanted to study the impact of these donor and recipient genotypes on TAC PK in a pediatric liver transplanted cohort.

Methods: We retrospectively collected demographic and days 0–90 PK data from 83 children (0.5–14.3 years) who benefited from de novo living donor liver transplantation (2001–2011) and were immunosuppressed with a Basiliximab induction and TAC monotherapy. Fifty recipients and 44 donors were genotyped for CYP3A4, CYP3A5 and ABCB1 SNPs.

Results: As expected, donor CYP3A4*22 and CYP3A5*3 alleles were significantly associated with increased TAC trough level (C0) at days 3 and 10 (p = 0.008 and p = 0.024) and at day 10 (p = 0.021), respectively. At day 1 post transplantation, both C0 and dose-adjusted C0 displayed a significant reduction (p = 0.036 and p = 0.021, respectively) for recipients expressing CYP3A5*1 in their intestinal mucosa. Recipients with ABCB1 2677 TA and TT genotypes had higher C0 and dose-adjusted C0 at day 1 (p = 0.011 and p = 0.013). No effect of recipient or donor ABCB1 3435C>T SNP was observed.

Conclusion: As recipient CYP3A5 and ABCB1 2677 genotypes influence the TAC PK at day 1, they should be proposed as covariates for TAC first dose prescription.

P073

EFFICACY AND SAFETY OF SIROLIMUS AFTER LIVER TRANSPLANTATION

Silvia Schaffellner, Doris Wagner, Estrella Jakoby, Daniela Kniepeiss, Florian Iberger

Med. Uni. Graz Clinical Dep. of Transplantation

Background/Aims: The optimal immunosuppression after liver transplantation (LT) is still controversially discussed. Sirolimus (SIR) as m TOR inhibitor has been proposed to provide a calcineurin inhibitor (CNI) free immunosuppression but was associated with various side effects recently. The aim of the presented analysis was to follow up a cohort of LT recipients on SIR.

Methods: Patients after LT who received SIR off label over a time period of over 24 months as maintenance immunosuppression were included. Patients were worked up retrospectively. SIR was introduced originally in case of an existing renal impairment or hepatocellular carcinoma defined by the MDRD in combination to Mycophenolat Mofetil with target blood levels between 3–7 ng/ml. Potential side effects like dyslipidemia, renal impairment, cancer development or disease recurrence and the development of infections were recorded.

Results: Thirty-three patients were included into the analysis. Indications for LT were viral hepatitis (8), HCC (11) and alcoholic cirrhosis (14). The median time since LT was 8 a (2–15). Patients were on SIR based immunosuppression for 5.8 years at median (2–10). Sirolimus was administered due to HCC (10), viral hepatitis (13) and renal impairment. The median blood trough level of SIR was 4.5 ng/ml (2–7.1) with a median dose of 0.75 mg (0.5–1.5) SIR daily. None of the patients suffered an acute rejection or a recurrence of the viral disease or a HCC recurrence during the whole follow up. Five patients developed cancerous lesions (2 basaliomas, 1 prostate cancer, 1 tongue cancer, 1 leukaemia). In total seven patients suffered from bacterial, nine from viral and two from fungal infections. None of the patients needed dialysis.

Discussion: Sirolimus was safe and well tolerated as immunosuppression even in the longterm after LT. We did not observe severe side effects. This might be due to low trough levels of the administered therapy. Nevertheless the treatment was effective.

P074

INFLUENCE OF CYTOCHROME P450 3A5 POLYMORPHISM ON THE PROLONGED RELEASE FORMULATION OF TACROLIMUS METABOLISM ADMINISTERED DE NOVO AFTER RENAL TRANSPLANTATION

Martine De Meyer

Cliniques universitaires St Luc UCL

Advagraf (Adv), a prolonged release formulation of tacrolimus (tac) permits a once a day administration and improves medication adherence. Patients (pts) possessing at least one CYP3A5*1 allele (also called CYP3A5 expressors) have an increased tac metabolism. This prospective study evaluates the clinical interest of a new simplified starting dose protocol of Adv right after RT according to The CYP3A5 genotype status of the KTR.

Material and methods: CYP3A5 genotype (CYP3A5*1/*1, CYP3A5*1/*3, CYP3A5*3/*3) was determined at the time of HLA typing. All KTR received one Adv dose of 0.1 mg/kg prior to RT. On day 1, the Adv dose was adapted according to CYP3A5 genotype: 0.35 and 0.30 mg/kg/d in CYP3A5*1/*1 and CYP3A5*1/*3 respectively. CYP3A5 non expressors (CYP3A5*3/*3) were stratified to receive either 0.20 (control group) or 0.25 mg/kg/day. The daily dose (dd) remained unchanged during the first 3 days. The first tac trough level (TL) was determined at day 3 and the first dose adaptation performed on day 4. Associated therapy included MMF and CS. Pts needing plasma exchange because of prior sensitization were excluded.

P075

MULTI-CENTRAL DE NOVO REGIMEN OF EVR AND TAC-ER FOR RENAL TRANSPLANTATION IN JAPAN

Kazunari Yoshida¹, Daisuke Ishii¹, Michiro Nakamura², Junichi Teranishi³, Tatsuya Chikaraishi⁴, Hiroyasu Yamamoto⁵, Yuji Maru⁶, Yugo Shibagaki⁷, Hajime Suzuki², Yoji Wakatabe¹

¹Kitasato University, Urology; ²Tokai University, Transplantation Surgery;

³Yokohama City University, Urology; ⁴St Marianna @Medical University,

Urology; ⁵Atsugi Civic Hospital; ⁶Toranomon Hospital, Kidney Center Surgery;

⁷St Marianna Medical University, Nephrology

Introduction: We expect good renal graft function and little incidence of viral infection by the regimen with everolimus (EVR). Primary *de novo* regimen with EVR and tacrolimus-extended release (TER) is, however reported only little. We conduct multi-central *de novo* regimen with EVR and TER.

Method: Everolimus of 2 mg/day is initiated from 14 days after transplantation and control at the C0 of 5 ng/ml. PSL is started with 30 mg and gradually reduced to 2.5 mg by POD 30. TER is administrated with 0.15 mg/Kg and maintained with C0 level of 8 ng/ml until POD 14, then reduced to 5 ng/ml after EVR initiation. MMF is also reduced from 2000 to 1000 mg at same time. Other immunosuppressions are same as usual. We evaluated the results of the graft

and patient survival, graft function, incidence of acute rejection, and adverse events such as CMV infection, proteinuria and dyslipidemia.

Results: Entry cases were nine in 8 months. Mean age of the recipients were 47.2 years, M/F were 6/2, one was ABO incompatible, two were cadaver, HLA mismatch of AB/DR were 1.67/0.83. In all cases graft function result in good, the average eGFR were 34.3 ml/min. No BPAR, nor CMV infection were observed by mean follow-up of 6 months. Two cases had hyperlipidemia, and proteinuria of more than 1 g/day, stomatitis and wound trouble were occurred in one case each. The dose of EVR was unstable (1–3 mg/day) at beginning, but settled at 1–1.75 after two months. We had difficulty to control EVR and TAC dose, because C0 of EVR and TAC were certainly unstable (mean C0 of EVR: 4.78;1.76 (1.3*8.99) ng/ml), and C0/mg dose: 2.48;1.08. Special attention should be necessary for TER dose control when EVR is stopped because it flies high.

Conclusion: EVR and TER *de novo* regimen for renal transplantation resulted in good graft function, little incidence of rejection and viral infection, but in some risks of dyslipidemia and proteinuria. We need attention to control dose of EVR and TER with frequent drug monitoring.

P076

HIGH INPATIENT TACROLIMUS VARIABILITY PREDICTS WORSE SHORT AND LONG-TERM OUTCOMES AFTER KIDNEY TRANSPLANTATION

Henry Whalen¹, Julie Glen¹, Alan Jardine², Marc Clancy¹

¹NHS Greater Glasgow and Clyde; ²Glasgow University

Background: High inpatient tacrolimus variability (ITV) has been associated with worse clinical outcomes post-renal transplantation. High tacrolimus levels cause toxicity, whilst sub-therapeutic tacrolimus levels predispose to acute rejection (AR) and graft loss. We investigated the effects of ITV 6–12 months post renal transplant on episodes of AR, eGFR at 1 year and rates of allograft failure.

Methods: Data was collected for adult kidney transplants performed between 01/01/07 and 01/05/10. Patients 247 patients were included. Patients received Basiliximab at induction and triple therapy immunosuppression with prednisolone and mycophenolate. Target tacrolimus trough levels were 5–8 ng/dL. Median ITV 6–12 months post transplant was calculated according to the formula: $\{[(X_{\text{mean}} - X_1) + (X_{\text{mean}} - X_2) + \dots + (X_{\text{mean}} - X_n)] / n\} / X_{\text{mean}} * 100 =$ intra individual variability (%) (X mean is the mean tacrolimus level for all available samples, X1 is the first level available, X2 is the second, etc.) Patients were placed into High variability (HV) or Low Variability (LV) groups. HV was defined as variability > observed median and LV as.

P077

COMPARISON OF BASILIXIMAB TO ATG INDUCTION IN DCD KIDNEYS: A NON RANDOMISED OBSERVATIONAL TRIAL

Muhammad Jameel, Prodromos Laftsidis, Rafael Chavez, Argiris Asderakis Cardiff Transplant Unit

Background: DCD kidneys have a high incidence and suffer from a longer period of DGF compared to DBD kidneys. Avoiding early rejection in those patients might be even more important since it avoids additional injury and might also ameliorate the need for weekly biopsies during the duration of DGF. Aim of the study was to see if induction with ATG confers an advantage in terms of rejection in DCD kidneys compared to patients who received Basiliximab without increasing their morbidity.

Methods: This is a non-randomised observational study in patients transplanted in two different periods who received a DCD kidney and different inductions. Group A (n = 77) received ATG induction for 5 days (1.25 mg/kg/day). Group B (n = 36) received Basiliximab (20 mg on day 0 and day 4). Both groups received Tacrolimus to achieve levels of 4–8, Mycophenolate Sodium (up to 1 g BD) or Mycophenolate Acid (up to 720 mg BD), and 20 mg of steroids tapered down to 0, 3 months post transplant.

Results: The baseline characteristics were similar apart from total mismatches that were higher in the ATG group. One patient died in the Basiliximab and two in the ATG group. There were no patients with CMV disease in the ATG group and 1 in the Simulect group. There were two cases of BK viraemia in group B, and 1 in group A and 47.4% of the ATG group still received steroids at 12 months compared to 58% in the Simulect group. DGF, graft survival and acute rejections are summarized in table.

Conclusion: ATG induction in DCD kidneys is safe and results in significantly lower rejection rate, same graft survival and marginally better 1 year Creatinine Clearance.

P078

INDUCTION AND HIGH MPA, BUT NOT TAC, BLOOD LEVELS ARE ASSOCIATED WITH BK PREVALENCE IN KIDNEY TRANSPLANTATION

Alexander Yussim¹, Ruth Rahamimov¹, Tiki Mashraki¹, Pierre Marquet², Eytan Mor¹

¹Department Transplantation, Rabin Med Ctr, Tel Aviv University, Israel;

²Pharmacology, Toxicology and Pharmacovigilance Dep. at the Univ. Hospital of Limoges, France

Immunosuppression is accepted as a major risk for BK virus replication. The increased incidence of BK virus infection in kidney transplant recipients (KTR), coincidental with the introduction of tacrolimus /mycophenolic acid (Tac/MPA) immunosuppression, has emerged as an important cause of graft damage and loss. However, the specific contribution of individual medications to this risk has not been well established. To evaluate that, we have analyzed with serial (1–6, 9 and 12 mos.) quantitative PCR, the incidence of BK replication in urine and blood and its correlation with: (i) the usage of induction (anti IL2 receptor antibodies versus Thymoglobulin/Rituximab (Thy/Rit)) in 271 KTR on Tac/MMF/Pred protocol (groups A –213 KTR and B –58 KTR, respectively); and (ii) the blood levels of Tac or MPA in 53 additional KTR, receiving the same protocol as group A, in whom MPA levels were available (group C). The therapeutic and high levels of Tac and MPA were considered to be 6–12 ng/ml and >12 ng/ml and 30–40 ng/ml and > 60 ng/ml, respectively. PCR lowest, high and upper values of detection were 325, 10 000 and 3 250 000 copies/ml, respectively. The statistical significance was determined with Fisher's exact test. In urine and blood the BK prevalence <10 000 copies/ml was 14% and 24% in groups A and B (p 0.04) respectively, and 32% in group C (p 0.04 with group A and p 0.4 with group B), respectively. The prevalence of high viral load in blood was 21%, 35.7% and 0% in groups A, B and C (p 0.3 for group A vs. B (p 0.0002 for A and B vs. C), respectively. With regard to Tac and MPA levels, 10 and 12 instances of high levels were found respectively in 35 patients without BK, while 6 and 16 of such instances were detected in 18 patients with BK (p 0.7 for FK and p 0.0002 for MPA). We conclude, that Thy/Rit induction, or high MPA, but not Tac levels, were associated with a significant increase in BK viral prevalence.

P079

LOWER VARIABILITY IN TACROLIMUS 24 HOUR EXPOSURE AFTER CONVERSION FROM A TWICE-DAILY TO A ONCE-DAILY TACROLIMUS FORMULATION IN STABLE KIDNEY TRANSPLANT RECIPIENTS

Johannesvan Hooff¹, Frank Stiff², Leo Stolk³, Nasrullah Undre⁴, Maarten Christiaans¹

¹Department of Internal Medicine, University Hospital Maastricht; ²Department of Internal Medicine; ³Department of Clinical Pharmacy & Toxicology; ⁴Astellas Pharma

Background: Tacrolimus has originally been registered as a twice-daily formulation (Prograf, Tac BID). More recently, a once-daily formulation (Advagraf, Tac QD) is also available. It has been suggested to have a reduced intra-patient variability (expressed as coefficient of variation, CV) of Tac C_{min}, C_{min} is a surrogate marker for 24-h drug exposure (AUC₀₋₂₄). Improvement of CV can be caused by better adherence or by different intrinsic pharmacokinetic properties of the formulations. The change in CV of AUC₀₋₂₄ by conversion has never been studied prospectively yet. The main purpose of this study was to investigate the change in CV of Tac AUC₀₋₂₄ after conversion from Tac BID to Tac QD.

Methods/Materials: Forty stable renal transplant patients on Tac BID were converted on a 1:1 (mg:mg) basis to Tac QD in an investigator-driven comparative pharmacokinetic study. AUC₀₋₂₄ was determined five times, both before and after conversion, where each PK-profile consists of eight samples. Samples were collected in duplo by the patients themselves using the Dried Bloodspot method. Main outcome measure is change in intra-patient CV of AUC₀₋₂₄. Moreover, the influence of Cyp3a5 genotype polymorphism on change in CV was studied.

Results: All patients had 10 adequate PK-profiles; in total 400 AUC₀₋₂₄ were available for analyses. Conversion to Tac QD resulted in a significant improvement of intra-patient CV from 14.1% to 10.9% (p = 0.012). Patients with the Cyp3A5 *1/*3 genotype (n = 11) had a numerically larger improvement in CV (18.2% to 12.8%; p = 0.066) than patients with the CYP3A5 *3/*3 genotype (12.6% to 10.2%; p = ns).

Conclusion: The intra-patient CV of Tac AUC₀₋₂₄ is improved after conversion of Tac BID to Tac QD in stable renal transplant patients, especially in patient with the CYP3A5*1/3 genotype. Given the very strict protocol of this PK study, this improvement is most likely due to different intrinsic pharmacokinetic properties of Tac QD compared to Tac BID.

P080

OUTCOMES OF BARIATRIC SURGERY AFTER RENAL TRANSPLANT: SINGLE CENTER EXPERIENCE IN KUWAIT

Osama Gheith, Torki Al-Otaibi, Narayanan M.R. Nampoory, Medhat Halim, Tarek Said, Zakareya Zakareya, Prasad Nair, Waleed Hosni, Hani Adel OTC

Introduction: Obesity has been associated with poor graft and patient survival after kidney transplantation, requiring functional increase of anti-rejection drugs. Weight loss surgery may be a good alternative in this clinical scenario.

Aim of the study: To assess the outcomes of bariatric procedures performed in patients after renal transplantation compared to conventional group of patients.

Patients and Methods: In this retrospective study, collected database was conducted to analyze the outcomes of obese patients after kidney transplantation (BMI>38) who underwent bariatric procedures during the last 5 years (n = 11cases) in comparison to controlled obese group without this type of surgery (n = 41 cases). Roux-en-Y gastric bypass was the most common procedure. We aimed to evaluate this type of surgery among renal transplant patients in comparison to control group.

Results: The two groups of patients were matched regarding their demographic data, type of donor, cases with IHD, type of induction and maintenance of immunosuppression. Most of patients in bariatric group were females (60%) while males dominated the other group (84%, p = 0.03). The basal and last follow up BMI means were 38.3A ± 8.9 and 33.3A ± 7.3; while they were 44.2 ± 5.6 and 44.2 ± 6.7 in the control group. The mean percentage of excess weight loss at 6 months in bariatric group was 15.4A ± 5.1% vs. 0.4A ± 0.2% in the control group (p < 0.001). We found no significant difference in the two groups regarding number of cases with pre-transplant diabetes or NODAT, however the total number of diabetics in the control group was significantly higher (73.3% vs. 40%, p = 0.042). Moreover, we observed that rejection episodes, graft and patient outcomes were similar in both groups (p > 0.05). There were no postoperative complications except in two patients: one with strangulated hernia; and the second with postoperative deep venous thrombosis and pulmonary embolism.

Conclusion: Bariatric surgical techniques may be used safely and effectively with some precautions- to control obesity among renal transplant recipients. Further improvement in metabolic parameters and long term patient and graft outcome can be observed only with longer and larger studies.

P081

EPITHELIAL TO MESENCHYMAL TRANSITION MARKERS IN KIDNEY TRANSPLANT RECIPIENTS: THE CERTITEM TRIAL

Alexandre Hertig¹, Nassim Kamar², Dany Anglicheau³, Bruno Moulin⁴, Marc Hazzan⁵, Bruno Huraultde Ligny⁶, Fabienne Di Giambattista⁷, Eric Rondeau¹

¹Hôpital Tenon, Paris; ²Hôpital Rangueil, Toulouse; ³Hôpital Necker, Paris; ⁴Hôpital civil, Strasbourg; ⁵CHU Lille; ⁶CHU Caen; ⁷Novartis Pharma S.A.S.

Background: We conducted a randomized trial to determine whether epithelial to mesenchymal transition (EMT) markers would help to identify kidney transplant (tx) recipients at such a high risk of graft fibrogenesis that they would benefit from an early withdrawal of calcineurin inhibitor (CNI).

Methods/Materials: Initial treatment consisted in CsA, mycophenolate sodium (MPS), corticosteroids and basiliximab. We measured by immunohistochemistry the *de novo* expression of vimentin and the translocation of beta-catenin in tubular epithelial cells, on a first biopsy performed at 3 months post-tx. A biopsy in which iY10% of tubules expressed mesenchymal markers defined EMT+ patients (pts). We randomly assigned both EMT+ (n = 75) and EMT- (n = 119) pts to either continue CsA+full dose MPS (n = 98), or to withdraw CsA and to start on everolimus+low dose MPS (EVL/CNI-free) (n = 96).

Results: Study objective was to evaluate if the progression of interstitial fibrosis (IF) between the first and a second surveillance biopsy performed at 12 months post-Tx would be attenuated in EMT+ pts converted to a CNI-free regimen, when compared to those maintained on CsA. The primary endpoint (PE) was the progression of IF and tubular atrophy (TA) Banff score from M3 to M12 (Δ IF/TA \geq 1). In the modified intent-to-treat analysis (pts with adequate structural data at M3 & M12), the PE occurred in 16 of the 31 EMT+ pts maintained on CsA and in 12 of the 26 EMT+ pts converted to EVL/CNI-free (p = 0.68). Overall biopsy proven acute rejection (BPAP) occurred more frequently in the EVL/CNI-free group (25.0 vs. 5.1%, p < 0.001). Of these, subclinical BPAP was diagnosed on M12 biopsy in 10.4% of the EVL/CNI-free pts and 2.0% of the CsA pts (p = 0.015). Independent associated factor of BPAP was a dose of MPS inferior to the recommended one (720 mg/day in the EVL/CNI-free, 1440 mg in the CsA group) during >28 consecutive days. Pts with a trough level of EVL < 5.7 ng/ml were also particularly at risk of BPAP (8/22, 36.4%). Graft loss occurred in 5 pts in the EVL/CNI-free group (vs. 1 in the CsA group, p = 0.12).

Conclusion: An early CNI withdrawal with a switch from CsA to EVL does not prevent IF progression in patients at high fibrogenic risk and carries out a significant risk of rejection.

P082

**RECIPIENTS' MDR1 AND CYP3A5 GENOTYPES BOTH
IMPACT TACROLIMUS DOSE REQUIREMENTS AFTER
LIVER TRANSPLANTATION**

Miriam Maschmeier¹, Vito R. Cicinnati¹, Speranta Iacob², Arnold Radtke¹, Tina Schomacher¹, Iyad Kabar¹, Anna Hüsing¹, Christian Wilms¹, Hartmut Schmidt¹, Susanne Beckebaum¹

¹University Hospital Münster; ²Fundeni Clinical Institute Bucharest

Aims: This study sought to investigate the role of SNP CYP3A5(rs776746) and MDR1(rs1045642) on pharmacokinetics of prolonged-release tacrolimus (TAC-OD).

Methods: N = 69 stable liver transplanted patients were converted from TAC twice daily (TAC-BID) to TAC-OD. TAC doses and trough levels were determined at regular time intervals between baseline and month 6 postcon-

version. Sequencing of PCR-amplified genomic DNA was used to determine the recipients' genotype. Kruskal-Wallis test was performed to compare subgroups of patients with different genotypes. T-test or Mann-Whitney-U-test was used to compare continuous data.

Results: TAC-OD doses differed significantly according to CYP3A5 genotype at week 1 (p = 0.03), week 2 (p = 0.03), month 1 (p = 0.02) and month 3 (p = 0.04). Patients with G/G-SNP required significantly lower doses of TAC-OD than those with G/A- and A/A-genotypes (p < 0.05 at each time point). Moreover, there was a significant difference regarding the dose requirements of TAC-OD at month 6 for MDR1 genotypes (p = 0.02). Patients with C/C-genotype needed to be dosed significantly higher at month 6 (4.7 ± 1.96 mg vs. 3.3 ± 1.69 mg, p = 0.01) than those with other genotypes.

Conclusion: The recipients' CYP3A5 and MDR1 genotypes seem to affect the function of enzymes in TAC metabolism; this may explain differences in TAC pharmacokinetics among transplant patients.

PS06-TISSUE ENGINEERING

P084

**RAT KIDNEY BIOSCAFFOLD TRANSPLANTATION:
A QUICK AND PLAY PROTOCOL**

Andrea Peloso¹, Jacopo Ferrario di Tor Vajana¹, Carolina Bianco¹, Ilaria Benzoni¹, Benedetta Maiga¹, Annalisa Gaspari², Antonio Citro³, Lorenzo Piemonti³, Giuseppe Orlando⁴, Massimo Abelli¹, Marcello Maestri¹, Paolo Dionigi¹

¹IRCCS Policlinico San Matteo Pavia; ²University of Pavia; ³San Raffaele Scientific Institute; ⁴Wake Forest School of Medicine

Background: Kidney transplantation is the cure for end-stage renal diseases. The availability of organs is a scarce resource and is the real limit to a wider diffusion of organ replacement. Tissue engineering holds the promise to offer a potentially inexhaustible source of transplantable organs.

Material and Methods: Renal extra-cellular matrix (ECM) ($n = 10$) scaffolds were obtained in 4 h with decellularization of rat kidneys by sequential peristaltic perfusion of Triton X-100 and SDS-based solutions. In a second step the scaffold was implanted in a in a same-species recipient as it is, without any attempt to seed functional parenchymal cells.

Results: Preliminary results show the protocol feasibility. Kidneys were successfully and consistently decellularized while ECM framework remained well preserved. At the reperfusion ECM scaffolds reperfused well and sustained blood pressure. It was not observed any bleeding and the graft was normally perfused. Histological findings demonstrated the absence of cells and the maintenance of the entire 3D extra-cellular matrix.

Conclusions: Rat renal ECM scaffolds may represent an optimal platform for renal bioengineering and regeneration research.

P085

**CRITICAL EVALUATION OF KIDNEY EXTRACELLULAR
MATRIX AFTER PERFUSION DECELLULARIZATION AS A
STRUCTURAL BASIS FOR RENAL TISSUE
ENGINEERING**

Mireia Caralt¹, Stanca Iacob², Kyle Obergefell², Berke Akgun², Brent Bijonowski², Michael Abecassis², Zheng Zhang², Jason Wertheim²

¹Servei Cirurgia HBP i Trasplantaments, Hospital Universitari Vall Hebron, Barcelona, Spain; ²Department of Surgery, Comprehensive Transplant Center, Northwestern University, USA

Background: The kidney is the most frequently transplanted organ, yet few studies have focused on kidney tissue engineering. We compared three decellularization protocols in rat kidneys to create extracellular matrix (ECM) scaffolds for tissue engineering applications. We have further analyzed these scaffolds using rigorous methods for: (i) retention of critical matrix structures, (ii) efficient removal of cells and (iii) presence of structural and growth factor proteins.

Methods/Material: Three different protocols were used: Triton only (P1), Triton and SDS (P2) and Triton and Trypsin (P3). Hematoxylin & eosin (H&E) staining and scanning electron microscopy (SEM) was used to characterize the ECM. The presence of ECM structural proteins was analyzed by immunofluorescence and growth factors were determined by ELISA.

Results: After decellularization, kidneys were transparent and cells were not present in H&E staining (P2 and P3). The structure of glomeruli and tubules remained intact and was confirmed by SEM. Immunostaining showed the presence of collagen IV. FGF was detectable in P1 and P2.

Conclusions: P2 and P3 showed high efficiency of cell removal while maintaining preservation of the kidney architecture. However, P1 and P2 demonstrated retention of FGF. Taken together, the use of triton and SDS efficiently removes cells and retains FGF after decellularization in rat kidneys. This provides a basis for repopulating the parenchyma with renal progenitor and endothelial cells.

PS07-IMMUNOBIOLOGY / BASIC SCIENCE

P086

THE INTERLEUKIN-6 ROLE IN RENAL TRANSPLANT REJECTION

Alexey Zulkarnaev, Andrey Vatazin, Miroslav Krstic, Pavel Astakhov
M.F. Vladimirovsky Moscow Regional Research Clinical Institute

Background: IL-6 is one of the key inflammatory mediators. The role of IL-6 in the rejection reaction is not fully understood.

Methods/Materials: We have studied the role of IL-6 in the pathogenesis of rejection.

Results: Transplantation outcomes are largely determined by the activity of rejection. Great importance is the regulatory influence CD4-cells. Now known another type of T-helper cells: Th17. These cells can secrete IL-17 and come from the naive T-cells in response to IL-6 and transforming growth factor-stimulation. In the absence of TGF stimulation of naive T cells to differentiate into regulatory T cells – Tregs, expressing Foxp3, which is the opposite effect of Th17. IL-6 synergistically with TNF α prevent the development of tolerance to the transplant tissue.

Conclusion: Thus, IL-6 is an important mediator in the process of rejection. This may be a new target for specific therapy.

P087

IRF3 AND IRF7 PROTEIN EXPRESSION ARE SIGNIFICANTLY UP-REGULATED IN ACUTE REJECTION OF KIDNEY TRANSPLANTS

Paula Xavier¹, Susana Sampaio², Sérgio Gaião³, José G.G. Oliveira⁴
¹Instituto Portugues Sangue e Transplantação; ²Serviço Nefrologia, Hospital S.João; ³Serviço Cuidados Intensivos, Hospital S.João; ⁴Faculdade Medicina do Porto

IRF3 and IRF7 proteins regulate transcription of IFNs. Both can be induced by several factors in lymphoid cells and tissues. IFN α gene family is IRF7 dependent and we reported a higher production during acute rejections (AR) in human kidney transplants (KTX). KTX were divided into group I, rejection free and AR between day 6 and 4 years, group II. Aspiration biopsy (AB) was done on day 7 in I and on rejection day in II. Cytosolides were stained by a goat polyclonal IgG anti-human IRF3 and IRF7 by ABC. For IRF3, I and II included 39 and 15 cases and for IRF7, included 21 in I and 13 cases in II. IRF3 and IRF7 expression were higher in II whether +cells, $p = 0.0002$ and $p = 0.0009$, +kidney cells $p = 0.000$, $p = 0.002$, or +mononuclear cells, $p = 0.000$ and $p = 0.0002$ ratio, respectively. These results indirectly confirm our previous report on the importance of IFN- α in acute rejection of KTX and surmises the place unpecific, inflammatory, non cognate stimuli may find in the early fate of KTX.

P088

MITIGATION OF THE SMALL-FOR-SIZE-SYNDROME THROUGH HEPATIC HYPERPLASIA INDUCED BY CONSTITUTIVE ANDROSTANE RECEPTOR AGONISM

Christoph Tschuor, Ekaterina Kachaylo, Perparim Limani, Andrea Schlegel, Jae Hwi Jang, Dimitri A. Raptis, Emmanuel Melloul, Michael Linecker, Andrea Vuck, Yinghua Tian, Rolf Graf, Bostjan Humar, Pierre-Alain Clavien
Swiss Hepato-Pancreatico-Biliary (HPB) Center, Department of Visceral and Transplant Surgery, Univer

Background: Living donors left with marginal liver remnants or recipients of small/poor quality liver grafts are at risk of developing the Small-for-Size-Syndrome (SFSS). SFSS is characterized by an insufficient regeneration of liver mass. Constitutive androstane receptor (CAR) agonism induces liver hyperplasia. We investigated the potential of the CAR agonist TCPOBOP (TCP) to ameliorate experimental SFSS.

Methods: The effects of TCP were assessed in three murine models: 30% graft liver transplantation (0% survival), 86% Hx (75% survival) and 91% Hx (0% survival). Bilirubin, ALKP, and albumin served as measures of SFSS-like features. Proliferation-associated-molecules, including Foxm1b and miR375-dependent pathways, were analyzed.

Results: TCP markedly improved survival following 30% transplantation, 86% Hx and 91% Hx. Likewise, SFSS-associated features of bilirubinemia and reduced liver function were normalized by TCP. Furthermore, TCP reversed the abnormal induction of the Foxm1b/miR375 pathways, normalized upregulated p21 and restored the deficient regeneration.

Conclusions: TCP can prevent experimental SFSS. When given after extended resection or 30% graft liver transplantation, TCP rescues >40% of otherwise moribund mice. The underlying molecular changes suggest a contribution of pathways promoting cell cycle progression. TCP appears to override the regenerative deficits of marginal liver remnants.

P089

IL-33 A NEW (PREDICTIVE) BIOMARKER IN TRANSPLANTATION?

Dietmar Abendroth¹, Michael Marzinzig¹, Manfred Stangl²
¹University of Ulm, Center of Surgery; ²Ludwig-Maximilians-University, Munich

Innate inflammatory response either preexistent in the recipient or released by injured allografts may influence graft outcome. We retrospectively evaluated the influence of Kynurenine, HMGB-1, C5b-9 and IL-33 on delayed graft function (DGF), acute rejection (AR) and the long term outcome (GS).

Patients and Methods: A consecutive group of patients after renal transplantation (in total $n = 122$, mean age 42 ± 11 years). Probes were taken prior tx 0, wk1, wk2, wk3, wk4 and month3.

Results: HMGB-1 was predictive for DGF (donor) and correlated with duration of pop dialysis need. C5b-9, Kynurenin and HMGB-1 ($p < 0.001$) were significant elevated during DGF, but not IL-33. IL-33 was significant higher after 3 months in the DGF group. Predictive values for rejection were only given by Kynurenine. IL-33 was significant increased during AR. High IL-33 in the long-term (>3rd month) is correlated with a higher creatinine after 1–3 years ($r^2 = 0.685$). Prolonged GS was only predicted by Kynurenine and lower IL-33.

Conclusion: Kynurenine showed an excellent correlation to acute rejection as well as to long term graft function. HMGB-1 showed significant the injury of the graft and IL-33 showed a correlation to the graft function in the follow up <3 months.

P090

INCREASED SERUM LEVELS OF NEOPTERIN INDICATES ENHANCED LIVER DYSFUNCTION

Hani Oweira, Imad Lahdou
University Hospital of Heidelberg

Background: The Model for End-Stage Liver Disease (MELD) score is a well-established tool to assess the degree of hepatic insufficiency/ failure. Neopterin, a pteridine mainly synthesized by activated macrophages, is a marker of inflammation and immune system activation. Here we investigate whether the degree of systemic inflammation as measured by Neopterin and other parameters correlate with clinical liver dysfunction according to MELD scoring system.

Method: Serum samples from 180 patients with liver cirrhosis were categorized in two groups according to baseline MELD score (group I, MELD <20) and (group II, MELD ≥ 20). Serum levels of CRP, sCD30, and neopterin were assessed by ELISA.

Results: Serum levels of neopterin, and CRP, significantly correlated with MELD score whereas sCD30 showed no significant correlation.

P091

INHIBITION OF AUTONOMIC STORM DOES NOT IMPROVE MICROCIRCULATORY IMPAIRMENT AND INFLAMMATORY RESPONSE IN BRAIN DEAD RATS

Rafael Simas, Isaac Azevedo Silva, Laura Menegat, Sueli Gomes Ferreira, Cristiane Jesus Correia, Paulina Sannomiya, Luiz Felipe Moreira
Cardiovasc. Surg. and Circ. Pathophysiol. Lab., Heart Institute (Incor), University of Sao Paulo

Background: Brain death (BD) is usually followed by autonomic changes leading to hemodynamic instability, which seems to be associated with microcirculatory dysfunction and inflammatory activation. In this study, we evaluated the effects of autonomic storm inhibition by thoracic epidural anesthesia (TEA) on mesenteric microcirculatory changes and inflammatory response due to BD induction in rats.

Methods: Male Wistar rats (250–350 g) were anesthetized and mechanically ventilated. BD was induced by intracranial balloon inflation. An epidural catheter was placed to saline or bupivacaine infusion immediately before BD induction and these two groups were compared to sham operated animals. Mesenteric microcirculation was analyzed by intravital microscopy and the expression of adhesion molecules was evaluated 180 min after BD induction.

Results: Autonomic storm was blockade in bupivacaine group, with a significant difference in mean arterial pressure behavior in comparison with saline and sham groups ($p < 0.001$). However, proportion of perfused small vessels (<30 μm) in this group ($43 \pm 6\%$) was similar to BD with saline infusion ($39 \pm 7\%$) and lower than sham animals ($74 \pm 6\%$, $p = 0.002$). The expression of ICAM-1 did not differ among bupivacaine and saline groups (21 ± 5 and 23 ± 8 , respectively) and these values were significantly higher than sham obtained data (9 ± 2 , $p < 0.001$). Bupivacaine and saline groups also showed similar numbers of migrated leucocytes in perivascular tissue, which were significantly higher than those observed in sham operated animals.

Conclusions: TEA was effective to inhibit autonomic storm, but it did not affect mesenteric hypoperfusion and inflammatory changes after BD induction in rats.

P092

HUMAN MONOCYTES PRODUCE INTERFERON-GAMMA MRNA AND PROTEIN UPON STIMULATION WITH LPS

Marina D. Kraaij¹, Elly J.F. Vereyken¹, Pieter J.M. Leenen¹, Farhad Rezaee², Michiel Beijes¹, Carla Baan¹, Ajda T. Rowshani¹

¹Erasmus MC; ²UMC Groningen

Introduction: Representing a crucial T-helper 1 cytokine, IFN- γ acts as an important bridge between innate and adaptive immunity and is involved in many acute and chronic pathologic states, such as autoimmune diseases and solid organ transplant rejection. At present, debate still prevails about the ability of human monocytes to produce IFN- γ . We aimed to investigate whether human monocytes possess the capacity to produce IFN- γ at mRNA and protein level.

Materials and Methods: Using flow cytometric analysis and real time PCR, we investigated the capacity of freshly, isolated CD14⁺ monocytes of kidney transplant recipients to produce IFN- γ after stimulation with IFN- γ and LPS or LPS alone.

Results: We observed that stimulation of freshly isolated CD14⁺ human monocytes with LPS alone or combined stimulation with IFN- γ and LPS led to a significant increase in the percentage of TNF- α - and IFN- γ -producing monocytes ($p < 0.05$). In addition, IFN- γ mRNA levels in CD14⁺ monocytes increased after 2 h of stimulation as compared to the unstimulated controls. Moreover, these monocytes did not show a shift towards CD68 positivity.

Conclusion: We conclude that human monocytes possess the capacity to produce IFN- γ .

P093

CHARACTERIZATION OF ANTIGEN-SPECIFIC B CELLS USING NOMINAL ANTIGEN COATED FLOW-BEADS

Nicolas Degauque¹, Annie Elong Ngono¹, Ahmed Akl¹, Romain Crochette¹, Julie Lepourry¹, Magali Giral-Classe¹, Stéphanie Castagnet¹, Emilie Dugast¹, Anne Devys², David Laplaud¹, Arnaud Nicot¹, Sophie Brouard¹, Jean-Paul Souillou¹

¹INSERM UMR1064; ²EFS de Nantes

Background: Whereas antigen-specific antibodies have been extensively characterized, estimation of frequency, isolation and analysis of B cells with a defined antigen receptor remain a challenge. Here, we describe a new approach to quantify and characterize B cells engaging interaction with an antigen following the incubation with single or multiplex single antigen beads.

Methods: B cells were purified from human anti-MOG IGH transgenic mice, healthy volunteers ($n = 38$) and patients with known immunization against HLA molecules ($n = 34$). B cells reactivity was assessed using nominal antigen coated beads

Results: Using B cells purified from human anti-MOG IGH transgenic mice, we show that interaction between B cells and rMOG coated beads can be measured and inhibited by soluble MOG. Blood B cells purified from healthy volunteers were then tested for their ability to interact with various nominal antigens, including viral, vaccine or self and alloantigens. The frequency of B cells of male individuals interacting with the panel of HLA class I molecules was similar to the frequency of B cells interacting with Albumin (mean \pm SEM; 0.73 ± 0.17 vs. 0.61 ± 0.09 respectively). An increase frequency of B cell bound to self-antigen MOG ($1.53 \pm 0.16\%$), latent EBV antigen (EBNA1; $6.02 \pm 0.69\%$) and tetanus toxin ($6.44 \pm 0.88\%$) coated beads was measured. The B cell frequency in a context of over immunization against HLA antigens was finally tested. A significantly higher anti-HLA-A*0201 BBR frequency in HLA-A*0201 sensitized recipients compared to non-sensitized stable patients and healthy volunteers was detected. An important level of polyreactivity of the circulating B cells was observed when antigens with minor differences are tested. Finally, we show that both memory and resting B cells were able to bind to antigen-coated beads.

Conclusion: This method opens a new window for analyzing nominal antigen B cells precursors in various clinical settings.

P094

STABLE IMMUNOPHENOTYPE PREDICTS SQUAMOUS CELL CARCINOMA RISK POST-TRANSPLANTATION

Sam Sherston¹, Kathryn Wood¹, Paul Harden²

¹Transplant Research Immunology Group; ²Oxford Transplant Centre

Background: Malignancy remains a serious cause of morbidity and mortality in transplant recipients, with incidence rates 3 – 5 times higher than the general population. Of these, cutaneous squamous cell carcinoma (cSCC) is the most common cancer post-transplantation, with 30% of kidney transplant recipients (KTR's) developing at least one within 10 years of transplantation. In a previous study we have shown that high numbers of T-regulatory (Treg) and low numbers of Natural Killer (NK) cells in patients could predict cSCC development in KTR's (Carroll, R. P. et al. NEJM 2010). In this follow-up study we aimed to validate these results and ensure immune biomarker stability in patients on long-term immunosuppression.

Materials/Methods: We followed up previously gender, age, and duration of immunosuppression matched KTR's with ($n = 65$) and without ($n = 51$) cSCC.

During the follow up period (mean time = 1535 days) 36 KTR's from previous SCC group and 28 previously were re-assessed for known risk factors of cSCC and bled for assessment using multi-parameter flow cytometry of lymphocyte subsets.

Results: We found a higher proportion of Treg cells in patients with a history of SCC compared with those without ($p = 0.03$). No significant difference was identified between the proportion or number of NK cells between those with previous SCC and those without. Importantly we found no significant change in the proportions of T lymphocyte subsets in SCC or non-SCC group over the follow-up time. Interestingly, patients who are on Azathioprine have significantly reduced proportion and numbers of NK cells (Both $p > 0.01$). We found no difference in Treg numbers between immunosuppressive regimens.

Conclusion: Overall we have shown that monitoring of the immune system in these patients can provide insight into patients at an increased risk of developing a post-transplant malignancy. Furthermore, these immune markers remain stable over time despite chronic immunosuppression use.

P096

IMMUNOSENESCENCE DOES NOT ABROGATE ENGRAFTMENT OF ALLOGENEIC BONE MARROW

Karin Hock¹, Rupert Oberhuber², Ying-Lung Lee³, Thomas Wekerle¹, Stefan G. Tullius⁴

¹Medical University of Vienna; ²Innsbruck Medical University, Innsbruck;

³Harvard Medical School; ⁴Brigham and Women's Hospital, Harvard Medical School

Background: Tolerance induction through mixed chimerism holds promise for clinical translation but has only been investigated in young recipients so far. Therefore we investigated the consequences of recipient age on the outcome of mixed chimerism and tolerance induction.

Methods: Young (2mth; 20 g) and old (12mth; 30 g) recipients (B6) were treated with 5 different BMT protocols. In each protocols recipients were transplanted with Balb/c BM cells adjusted to body weight (1×103 /kg, i.e. young 20×106 ; old 30×106). 3 Gy TBI and an induction treatment of costimulation-blockade (CB: α -CD154mAb; CTLA4lg) or T cell depletion (TCD: α -CD4; α -CD8), 1 Gy and CB or rapamycin and without irradiation and rapamycin. Lymphocyte subsets and cytokine production were compared between young and old naive mice and multi-lineage chimerism was assessed by flow cytometry.

Results: Successful chimeras were achieved age-independently following non-myeloablative TBI (3 Gy) together with CB (7/8 old vs. 11/11 young). Of note, following T-cell-depletion chimerism levels were significantly higher in older recipients in all tested lineages (i.e. donor B-cell chimerism: 56.33% old vs. 18.17% young; $p < 0.0001$; by week 8 after BMT). Moreover, under a less vigorous conditioning regimen (1 Gy/CB), chimerism was achieved in most animals in an age-independent fashion (7/10 old vs. 6/6 young). In contrast, 1 Gy irradiation in combination with rapamycin led to chimerism in only 2/6 old recipients and none of the young recipients; neither old nor young recipients became chimeric when animals were only treated with rapamycin. Notably, frequencies of Tregs among splenocytes of old BMT recipients had significantly increased. Moreover, T cell proliferation and IFN- γ production after polyclonal but not allogeneic stimulation was increased in old mice.

Conclusion: BM engraftment and chimerism were successfully induced in older recipients through Treg maintenance and a reduced alloreactivity response.

P097

ACTIVATED PRIMARY HUMAN RENAL TUBULAR EPITHELIAL CELLS INHIBIT T-CELL PROLIFERATION VIA IDO

Martijn Demmers, Martin J. Hoogduijn, Thierryvan den Bosch, Marieke

Roemelingvan Rhijn, Jan N.M. Ijzermans, Michiel Beijes, Willem Weimar, Ajda T. Rowshani

Erasmus MC – University Medical Center Rotterdam

Introduction: Renal tubular epithelial cells (TECs) are one of the main targets of infiltrating T cells. Indoleamine 2,3-dioxygenase (IDO) has been shown to inhibit allogeneic T-cell proliferation. We hypothesise that renal TECs modulate alloactivated T-cell proliferation via IDO.

Methods/Materials: Primary human TECs were prestimulated with IFN- γ and TNF- α for 3 days to upregulate IDO. In the absence or presence of IDO inhibitor 1-methyl-L-tryptophan (1-MT), we tested the inhibitory effect of TECs on allogeneic and anti-CD3/CD28 induced proliferation of T cells.

Results: Activated TECs inhibited the allogeneic T-cell proliferation by 56%, while antiCD3/CD28 induced T-cell proliferation was inhibited by 95%. Preactivated TECs show IDO mRNA expression while unstimulated TECs did not. This expression was inhibited by 1-MT. Addition of the IDO inhibitor (1-MT) resulted in the recovery of allogeneic T-cell proliferation in a dose dependent manner, while only 50% recovery was found in the antiCD3/CD28 induced T-cell proliferation.

Conclusion: IFN- γ /TNF- α preactivated TECs inhibit allogeneic induced T-cell proliferation. Our results indicate a crucial role for IDO as the underlying

mechanism for this effect of TECs, and provide a potential immunosuppressive mechanism of TECs during renal allograft rejection.

P098

GENDER DIFFERENCES ON THE INFLAMMATORY PROCESS IN DIFFERENT ORGANS IN A RAT MODEL OF BRAIN DEATH

Ana Cristina Breithaupt-Faloppa¹, Sueli Gomes Ferreira¹, Micael Nunes da Silva¹, Cristianode Jesus Correia¹, Wothan Tavares-de-Lima², Paulina Sannomiya¹, Luiz Felipe Moreira¹

¹Cardiovasc. Surg. and Circ. Pathophysiol. Lab., Heart Institute (Incor), University of Sao Paulo; ²Department of Pharmacology, Institute of Biomedical Sciences, University of Sao Paulo

Rationale: Brain death (BD) triggers the immune system which is characterized by the expression of inflammatory mediators, edema and cell infiltration to the organs. There is evidence that the immune response differs between men and women, which could influence the donor state and the results of the transplant. Here we investigated the differences between the genders regarding the evolution of the inflammatory process in different organs and mesenteric microcirculatory changes in a model of BD in rats.

Methods: BD was induced by a sudden increase in intracranial pressure by rapid inflation of a balloon catheter in the extradural space. Groups of female in proestrus (time of maximal estradiol secretion) or estrus, and male rats were used throughout the experiments. Vascular permeability and myeloperoxidase (MPO) activity were assessed at 6 h as markers of organ inflammation. White blood cell counts and estradiol levels were analyzed. Mesenteric microcirculatory perfusion was observed after 3 h using intravital microscopy.

Results: Lung (L) and kidney (K) vascular permeability were increased in proestrus female ($L = 172i_{i}^{i} \pm 10$, $K = 274i_{i}^{i} \pm 17$) compared to male rats ($L = 105i_{i}^{i} \pm 8$, $K = 154i_{i}^{i} \pm 28$; $p < 0.05$). Regarding MPO activity, liver of female proestrus presented higher activity ($1.03i_{i}^{i} \pm 0.15$) when compared to male ($0.55i_{i}^{i} \pm 0.09$, $p < 0.05$). Male rats showed pronounced leukopenia ($7880i_{i}^{i} \pm 689$ cell/mm³), while proestrus female rats maintained the circulating cell number after 6 h ($11567i_{i}^{i} \pm 1628$ cell/mm³). Despite organ inflammation, proestrus female rats maintained the proportion of perfused small vessels ($78.6i_{i}^{i} \pm 3.5\%$) 3 h after BD, whereas estrus female ($50.4i_{i}^{i} \pm 8.9\%$, $p < 0.05$) and male rats ($39i_{i}^{i} \pm 7$, $p < 0.01$) presented hypoperfusion.

Conclusions: Our results evidenced important differences between genders after BD, suggesting that estradiol may exert a role on the inflammatory events triggered by BD and deserve, therefore, attention as a potential factor influencing the organ status. Supported by CNPq and FAPESP.

P099

BRAIN DEATH PARADOXICALLY INDUCES LEUCOPENIA AND REDUCTION IN THE NUMBER OF BONE MARROW CELLS

Laura Menegat¹, Primavera Borell², Rafael Simas¹, Julia Maria Caliman¹, Luiz Fernando Ferraz Silva³, Luiz Felipe Moreira¹, Paulina Sannomiya¹

¹Cardiovasc. Surg. and Circ. Pathophysiol. Lab., Heart Institute (Incor), University of Sao Paulo; ²Department Clinical Toxicological Analyses, Faculty of Pharmaceutical Sciences, University of São Paulo; ³Department of Pathology, University of Sao Paulo Medical School

Background: Brain death (BD) is associated with increased inflammatory response in the different organs. In this study, we evaluated the recruitment of bone marrow cells to peripheral blood in rats submitted to BD compared with BD-associated trauma.

Methods: Male Wistar rats (250–350 g) were anesthetized and mechanically ventilated. A balloon catheter was placed into intracranial cavity, through trepanation, and quickly inflated to induce BD. Sham operated rats (SH) were trepanned only. Bone marrow cells were obtained by flushing the femoral cavity with Iscoves medium 6 h thereafter. White blood cell (WBC) counts in the peripheral blood were determined at baseline, and after 3 and 6 h. Total bone marrow cells and WBC counts were determined using a hemocytometer. Differential counts were performed on smears stained with May-Grunwald Giemsa solution.

Results: BD rats exhibited a progressive leucopenia (Baseline: $13171i_{i}^{i} \pm 1377$; 3 h: $11086i_{i}^{i} \pm 1779$; 6 h: $8300i_{i}^{i} \pm 927$ cells/mm³), in contrast with SH group (Baseline: $12863i_{i}^{i} \pm 1283$; 3 h: $17013i_{i}^{i} \pm 6186$; 6 h: $17353i_{i}^{i} \pm 8286$ cells/mm³, $p = 0.012$). The leucopenia observed in BD animals was also associated with lower values for neutrophil/lymphocyte ratio in comparison with the values observed in SH rats at 6 h ($p = 0.004$). BD rats showed a significant reduction in the total number of bone marrow cells ($2.8i_{i}^{i} \pm 0.2 \times 10^7$ cells/ml) compared with SH animals ($4.9i_{i}^{i} \pm 0.9 \times 10^7$ cells/ml, $p = 0.03$), specially due to a significant reduction in the number of stabs ($p = 0.03$), and lymphocytes ($p = 0.06$).

Conclusions: Despite its pro-inflammatory effects, BD itself paradoxically induced progressive leucopenia and reduction in the number of bone marrow cells in this experimental model.

P100

VITAMIN K SUPPRESSES MIGRATION OF HEPATOCELLULAR CARCINOMA CELLS BY BLOCKING THE HGF/C-MET PATHWAY

Taejin Song, Samyool Yoon
Korean University

Background: Vitamin K (Vit K) is a fat-soluble vitamin involved in blood coagulation and bone metabolism. VK has been shown to suppress cancer growth and induce apoptosis and differentiation in various cancer cells including hepatocellular carcinoma (HCC) cells. In HCC patients, abnormal prothrombins (PIVKA-II) are detected at high frequencies in the blood as an important tumor marker.

Methods: In this study, we intended to reveal the migration suppression effect of Vitamin K through blocking the HGF/c-Met pathway. HepG2 cells (HCC cell line) were cultured and then treated with hepatocyte growth factor (HGF), in which E-cadherin expression were measured by using special immunohistochemical stains and Western Blot and cell migration was also measured by scratch tests.

Results: After treatment with different concentrations of HGF, E-cadherin expression was weakened reversely according to the concentration of HGF. In contrast, concurrent treatment with HGF and Vitamin K1/2 revealed no attenuation in E-cadherin expression. Migration of HCC cells were accelerated after HGF treatment, but this effect became much weakened after concurrent treatment with HGF and Vitamin K1/2. Attenuated expression of E-cadherin implicates that cell migration for HCC metastasis is facilitated by loss of adhesion molecules.

Conclusion: Treatment with Vitamin K1/2 in HCC cell lines resulted in down-regulation of N-cadherin and snail, and up-regulation of E-cadherin. The mechanism may take a part on the role of Vitamin K-associated anti-tumor effect during HCC progression. Further studies are necessary to integrate this pathway to the already-established action mechanisms of Vitamin K.

P101

GENETIC DISPARITY AT THE NATURAL KILLER GENE COMPLEX CAN AFFECT NK-CELLS' POTENTIAL TO NEGATIVELY REGULATE ALLOANTIGEN INDUCED T-CELL RESPONSES IN RAT

Daniel Pöhnert, Jürgen Klempnauer, Joachim Hundrieser
Medizinische Hochschule Hannover

NK-cells exhibit the capability to negatively regulate immune responses of adaptive immunity. For NK-T-cell interactions, involved NK-cell receptor proteins encoded by the Natural Killer Gene Complex (NKC) and ligand proteins expressed by T-cells in the course of activation have been identified. Herein we addressed whether genetic polymorphisms of NKC-encoded genes affect NK-cells' potential to negatively regulate T-cell responses. Purified NK-cells cultured in the presence of IL-2 of NKC-congenic rat strains LEW and LEW.TO-NKC differing exclusively in multiple genetic polymorphisms of NKC-genes were used to supplement MLC assays composed of lymph node cells of strains LEW or LEW.TO-NKC and irradiated MHC-disparate LEW.1U stimulators. NK-cells of LEW.TO-NKC inhibited autologous T-cell responses significantly stronger than LEW NK-cells respective T-cells even at low amounts. The inhibitory potential was rather mediated by NK-cells lacking expression of the inhibitory NKRP1B receptor than by NKRP1B positive NK-cells. This study strengthens that genetic polymorphisms of NKC-encoded surface proteins can influence immunoregulatory functions of NK-cells. Depending on the recipient's NKC-haplotype it is expected *in vivo* that survival of MHC-disparate tissues might differ.

P102

ALTERATIONS IN BOTH TH1 AND TH2 CYTOKINE PATTERNS AND INCREASED CD30 TRANSCRIPTS IN PATIENTS WITH END-STAGE RENAL DISEASE

Sonia Y. Velasquez¹, Caner Süsa², Gerhard Opelz², Mauricio Rojas¹, Cristiam M. Alvarez¹

¹Grupo de Inmunología Celular e Inmunogenética, Facultad de Medicina, Universidad de Antioquia; ²Department of Transplantation Immunology, Institute of Immunology, University of Heidelberg

Background: Measurement of sCD30 in serum has been considered a useful parameter to estimate the rejection risk in renal transplant recipients; however, little is known about the components of the immune system involved in the modulation of CD30 expression and sCD30 release during the alloimmune response in patients with end-stage renal disease (ESRD). Materials: We evaluated whether the genes related to expression and shedding (ADAM10, ADAM17) of CD30 and transcription factors associated with Th1 and Th2 (t-bet and GATA3) T-cell subsets are differentially expressed in circulating cells of ESRD patients and age- and gender-matched healthy controls (HC). By principal component analysis (PCA) we determined the interrelationship of the same gene transcripts, with the release of sCD30 and 32 different analytes into supernatants from allo- and polyclonally-stimulated CD3+ enriched T lymphocytes.

Results: ESRD patients exhibited circulating increased transcripts of both Th1 t-bet and Th2 GATA3 ($p \leq 0.005$). T cells of ESRD patients displayed higher expression levels of CD30 transcripts than HC in response to allogeneic and polyclonal stimulation (both $p < 0.001$), and higher basal *in vitro* expression levels of ADAM17 transcripts ($p < 0.001$). PCA enabled the establishment of differential interrelationships in allostimulated cell-cultures of ESRD patients, including (i) sCD30 with MIP-1 β , TNF- β , RANTES and GM-CSF, (ii) a high correlation of CD30 transcripts with t-bet transcripts and IP-10, IL-8, IL-1R α , MCP-1 and IL-13, and (iii) a higher correlation between sCD30 and CD30L, ADAM10 and ADAM17 transcripts.

Conclusion: Our findings suggest that activation of both Th1 and Th2 responses, active pathways leading to upregulation of CD30-expression and -shedding and their interrelationship with Th1 and pro-inflammatory responses, may explain the activated immune state in ESRD patients and the poor graft prognosis after transplantation in ESRD patients with higher serum levels of sCD30.

P103

RENAL TRANSPLANT STATUS CORRELATES WITH EXPRESSION OF BAFF AND REGULATORY B CELLS

Louise Onions¹, Arun Gupta², Cristina Navarrete³, Anthony Warrens¹

¹Queen Mary, University of London; ²Clinical Transplantation, The Royal London Hospital, London; ³NHSBT, Colindale, London

Background: Dysfunction in the B cell compartment may contribute to chronic allograft deterioration. B cell activating factor (BAFF), if in excess, has been associated with rejection and development of donor-specific antibody (DSA). Here we examined BAFF and regulatory B cells (Breg) to identify the relationships between differential expression and level of function of the allograft.

Methods: CD19+ cells from patients with deteriorating (gp 1), stably-impaired (gp 2) and well-functioning (gp 3) grafts were examined for CD19 & BAFF-R or cultured for Breg analysis and stained for CD19, CD24, CD38, IL-10. FACS-sorted-cells were stained with CD19, CD24 & CD38. Serum BAFF (sBAFF) levels were measured by ELISA. HLA antibodies were assessed using Luminex technology.

Results: Gp 1 had higher sBAFF and lower CD19 + BAFF-R+ cells. DSA with elevated sBAFF or low BAFF-R were only detected in gp 1. IL-10 producing-B cells, enriched in the CD24 high CD38 high compartment were lower in gp1 and cell-sorting showed the distinct CD19 + CD24 high CD38 high subset was minimal.

Conclusion: The expression of BAFF and Bregs correlates with deteriorating graft function, suggesting important roles in regulating B cell homeostasis. We are currently examining functional regulatory properties.

P104

T-CELL CFLIP KNOCK-DOWN IN PROLONGATION OF ALLOGRAFT SURVIVAL

Ryan Stott, James Kim, James Markmann, James McDavid

Harvard Medical School

ABSTRACT The success of transplantation is limited by allograft rejection, an unwelcome response of T-cells against the allograft. If alloreactive T-cell clones specifically could be removed from the host, allograft tolerance would result, without blanket pharmacologic therapies which suppress all immune responses. The goal of this project is to increase the longevity of transplanted organs by inhibiting T cell expression of c-FLIP, an important physiologic regulator of apoptosis, thereby promoting activation induced cell death (AICD) of alloreactive effector T-cells. As an important anti-apoptotic regulator of T-cells in normal immune responses, c-FLIP represents a novel target for manipulating the allograft immune response.

Materials and Methods: BALB/c and C57/BL6 mice were purchased from Jackson Lab. T cells were purified using a Miltenyi Biotec magnetic beads kit. siRNA and lentiviral vectors containing shRNA to cFLIP were purchased from Sigma. siRNA transfer into T cells used the Amaxa nucleofector, an electroporation technique. T cell apoptosis was measured using annexin V binding in flow cytometry. Skin grafting used colloidal glue and dressings for seven days. Cre-ER/lox-cFLIP mice were a kind gift of Dr You Wen He, Duke University

Results: Electroporation of BALB/c T-cells with siRNA to cFLIP resulted in knock-down of cFLIP protein expression as measured by Western Blot. This knockdown resulted in increased T cell apoptosis upon anti-CD3/CD28 stimulation, as measured by Annexin-V binding in flow cytometry.

Conclusions: cFLIP knock-down in T cells can be achieved using either siRNA nucleoporation or lentiviral vector bearing shRNA. Either method of gene transfer leads to increased T cell apoptosis and susceptibility to activation induced cell death. We plan experiments shortly with cFLIP conditional knockout mice in a ER-Cre/lox system which hopefully will show prolonged allograft survival.

P105

T CELLS ACTIVATION BY DENDRITIC CELLS GENERATED IN THE ENVIRONMENT OF IMMUNOSUPPRESSIVE AGENTS

Maja Machcińska¹, Grazyna Korczak-Kowalska¹

¹Faculty of Biology, University of Warsaw, Poland; ²Transplantation Institute, Medical University of Warsaw, Poland

Background: Dendritic cells (DCs) present antigen to T cells. The state of DCs maturation is crucial for induction of T cell response. It was noted that immature DCs play an important role in peripheral tolerance, whereas mature DCs induce a complete immune response. This is very important in transplantation, especially in allograft rejection. Immature DCs or DCs with tolerogenic properties may prolong allograft survival. It appears that this could be achieved using the immunosuppressive therapy with cyclosporine A and rapamycin.

We have studied the effect of dendritic cells generated in the environment of immunosuppressive agents: rapamycin and cyclosporine A on the expression of T cell activation markers and the proliferative T cells activity.

Methods: Human peripheral blood monocytes were induced by using cytokines: IL-4 and GM-CSF, in the direction of DCs in the presence of rapamycin (Rapa-DCs) and cyclosporine A (CsA-DCs) or without drugs. Immature DCs were then stimulated with LPS to create mature DCs. To evaluate effects of these DCs on T cells, mixed leukocyte reaction (MLR) was applied. At the end of MLR cultures the expression of T cells activation markers (CD25, CD69) was measured by flow cytometry. Additionally the proliferative T cells activity was determined by measuring the fluorescence intensity of CFSE dye using flow cytometry.

Results: We have observed a decrease in the percentage of CD69 + T cells when these cells were cultured with Rapa-DCs and CsA-DCs. The lowest percentage of T cells was noted in an environment of cyclosporine A. In contrast the percentage of CD25 + T cells was slightly increased in the presence of Rapa-DCs and CsA-DCs. We have also noted that the percentage of proliferating T cells do not change significantly after culture with Rapa-DCs and CsA-DCs.

Conclusions: Dendritic cells generated in the environment of immunosuppressive agents slightly change the expression of T cell activation markers.

P106

POSITIVE EFFECTS OF HYPERTONIC SALINE ON MICROCIRCULATION AND LEUCOCYTE-ENDOTHELIAL INTERACTION AFTER BRAIN DEATH INDUCTION IN RATS

Luiz Felipe Moreira, Cristianode Jesus Correia, Daniela Janolli, Sueli Gomes

Ferreira, Rafael Simas, Paulina Sannomiya

Cardiovasc. Surg. and Circ. Pathophysiol. Lab., Heart Institute (Incor), University of Sao Paulo

Background: Brain death (BD) induces hemodynamic instability with micro-circulatory hypoperfusion leading to increased organ inflammation and dysfunction. In this study, we investigated the effects of hypertonic saline on mesenteric microcirculatory changes and systemic inflammatory markers after BD induction in rats.

Methods: Male Wistar rats (250–350 g) were anesthetized and mechanically ventilated. BD was induced by intracranial balloon inflation. Hypertonic saline (7.5%) or normal saline solutions (4 ml/Kg) were infused immediately after BD induction. Mesenteric microcirculation and leucocyte-endothelial interactions were analyzed by intravital microscopy 180 min thereafter. The expression of serum concentrations of cytokines, chemokines and corticosterone were also obtained.

Results: There was no difference in mean arterial pressure behavior between Hypertonic and normal saline groups. On the other hand, proportion of perfused small vessels (<30 μ m) was significantly higher in Hypertonic group (69 \pm 7%) in relation to normal saline animals (40 \pm 6%, $p = 0.002$). Hypertonic rats also exhibited decreased numbers of rolling ($p = 0.036$), adhered ($p = 0.03$) and migrated leucocytes to the perivascular tissue in comparison with normal saline group (2.8 \pm 0.4 vs. 0.3 \pm 0.2, $p = 0.02$). Similar values in the cytokine, chemokine and corticosterone levels were observed in both groups.

Conclusion: Despite the absence of any influence on hemodynamic behavior and on systemic markers of inflammation, infusion of hypertonic saline improves mesenteric microcirculatory perfusion and decreases inflammatory cells migration after BD induction in rats.

P107

PARTIAL PORTAL VEIN LIGATION: A PORCINE MODEL FOR THE STUDY OF PRE-HEPATIC PORTAL HYPERTENSION

Duilio Pagano¹, Davide Cintorino¹, Sergio Li Petri¹, Elisabetta Oliva¹, Valeria Pagano¹, Marco Paci¹, Michela De Martino¹, Marina Romano¹, Calogero Ricotta¹, Pasquale Bonsignore¹, Rosa Liotta², Giovanna Occhipinti³, Bruno Gridelli¹, Marco Spada¹

¹Division of Abdominal and Transplantation Surgery, Istituto Mediterraneo per i Trapianti e Terapie a; ²Division of Pathology, Istituto Mediterraneo per i Trapianti e Terapie ad Alta Specializzazione (ISM); ³Division of Anesthesiology, Istituto Mediterraneo per i Trapianti e Terapie ad Alta Specializzazione

Background: This study aimed to devise a reproducible method of pre-hepatic portal hypertension (PH) in a large animal model. Materials and Methods

Eight pigs weighing a mean 23 ± 4 kg were treated with portal vein partial ligation (PVPL) using a cotton umbilical tape to determine a porto-systemic gradient of major of 12 mmHg (subtracting the central venous pressure from the portal venous pressure-PVP). Mean arterial pressure, heart rate and central vein pressure were monitored continuously. A venous line was surgically placed through a inferior mesenteric vein for PVP monitoring; while hepatic artery and portal vein flows were measured before and after PVPL using ultrasound transit time flow probes. Pigs were followed up for 7 days ($n = 4$) or 14 days ($n = 4$).

Results: Prior to PVPL, the average PVP was 15.2 ± 9.5 mmHg. After PVPL, porto-systemic gradient was 15.1 ± 1.8 mmHg, secondary to an increase of the mean PVP, which was 23.9 ± 8.1 mmHg. PVF dropped significantly after PVPL, from 463 ± 197 to 202 ± 119 ml/min, corresponding to a percentage decrease of 46%. Conversely, HAF had a 62% increase: from 24.3 ± 20.9 to 39.3 ± 24.16 ml/min, with a percentage increasing of 61.7%. After ligation, portal vein diameters passed from 47.7 ± 6.4 to 21.4 ± 4.0 mm. In all animals, at autopsy, we showed severe portal cavernomatosis with gastro-esophageal venous collaterals and splenic stiffness. Porto-systemic gradient was unchanged after 7 days and decreased of 6.3 ± 1.6 mmHg after 14 days ($p = 0.002$). Mean PVP was 26.3 ± 11.7 mmHg on day 7th and 9.5 ± 3.6 mmHg on day 14th ($p = 0.06$). PVF reduction was of 304 ± 159 and 460 ± 171 ml/min after 7 and 14 days, respectively ($p = 0.04$). No significant modifications occurred to the HAF and to the LFTs. Conclusion This technique has been shown to be easily reproducible of pre-hepatic PH and well tolerated by the animals and allow easy assessment of liver function and splanchnic blood flow redistribution in the postoperative period.

P109

INDUCTION OF HEME OXYGENASE -1 BY COBALT PROTOPORPHYRIN PROTECTS AGAINST MYCOPHENOLIC ACID INDUCED APOPTOSIS IN HUMAN T LYMPHOCYTE

Soo Jin Na Choi, Sang Young Chung

Department of Surgery, Chonnam National University Hospital

Background: This study demonstrated that pharmacologic induction of HO-1 along with catalytic activation significantly modulated apoptosis of Jurkat cells induced by mycophenolic acid (MPA).

Methods/Materials: We observed, cell viability, measurement of H₂O₂ generation, intracellular accumulations of Ca²⁺ and NO, and western blottings of apoptotic pathway proteins, such as caspase, HO-1, Bcl-2, and Bax proteins. Mitochondrial membrane potential transition (MPT) determination by JC-1 staining was performed. Results

Caspase-3 proteases expression on MPA treated-Jurkat cells in a time-dependent manner. Treatment of MPA resulted in reactive oxygen species (ROS) generation in Jurkat cells. 20 μM cobalt protoporphyrin (CoPPiX; HO-1 inducer) significantly increased HO-1 expression in MPA treated cells. Apoptosis rate is 3.53% in media only, 23% in MPA treated cells, 5.8% in MPA treated cells with CoPPiX. The cell viability was reduced 77% under MPA, but combination with CoPPiX, there was no increased MPA induced apoptosis. Induction of HO-1 decreased expression of Bax protein. Decreased HO-1 expression on MPA treated-Jurkat cells after 36 h. Change of mitochondrial MPT was also noted. Expression of Bax proteins was identified. CoPPiX, induced expression of HO-1 proteins in MPA treated Jurkat cells. CoPPiX inhibited generation of H₂O₂. CoPPiX also inhibited change of mitochondrial MPT. CoPPiX significantly inhibited the MPA induced apoptosis. Conclusion; CoPPiX, HO-1 inducer, significantly inhibited the MPA-induced apoptosis. CoPPiX attenuated ROS production and mitochondrial permeability transition in MPA-treated cells. In conclusion, the protective mechanism of HO-1 on MPA-induced apoptosis is associated with direct inhibitions of ROS generation and mitochondrial permeability transition.

P110

MICRO-RNA IN ACUTE LIVER GRAFT REJECTION IN DA-TO-LEWIS RAT ORTHOTOPIC LIVER TRANSPLANTATION

Eiichi Ishii, Akira Shimizu, Naomi Kuwahara, Takashi Arai, Arimi Ishikawa, Kyoko Wakamatsu, Yukinari Masuda, Yuh Fukuda
Nippon Medical School, Tokyo, Japan

Background: MicroRNAs (miRNAs) are short noncoding 21–24 nucleotide sequences that inhibits protein synthesis by targeting messenger RNAs in a sequence specific manner. It has been known that gene specific translational silencing by miRNAs regulates various inflammatory responses. The present study clarified the involvement of miRNAs in the acute liver graft rejection.

Methods/Materials: Orthotopic liver transplantation was performed from DA (RT1a) to Lewis (RT1 l) rats without immunosuppression. We studied liver grafts by day 11, focusing on the degree of acute liver graft rejection, and alteration of miRNA profile during the development of liver graft rejection. miRNAs in the liver grafts were examined by microRNA array, and analyzed by GeneSpring (Agilent Technologies).

Results: In DA-to-Lewis rat liver transplantation, the progressive acute T cell-mediated and antibody-mediated rejection occurred from day 5 and developed by day 11 with irreversible graft failure. During the development of liver graft rejection between day 5 and day 11, 193 microRNAs were up-regulated or down-regulated in rejecting grafts when compared with those in normal DA liver. These miRNAs were included miRNAs which are known as the pathways for various inflammatory responses, immune cells differentiation and signaling, development of immunity and molecular pathways for allograft rejection; up-regulated miRNAs (miR-146b, miR-223, miR-181, miR-34a, miR-326, miR-21) and down-regulated miRNAs (miR-150, miR-125b, miR-20a).

Conclusion: miRNAs may be involved in various immunological processes including development of innate and acquired immunity, inflammation, T-cell and B-cell mediated immune responses in transplant liver graft rejection. miRNAs in transplant immunobiology will provide an exciting framework for developing new biomarkers as well as new therapeutic interventions in transplantation.

P111

MODIFICATION OF IMMUNE SYSTEM BY CHRONIC HCV INFECTION AND UNIQUE PREDICTORS OF EARLY ACUTE REJECTION AFTER HCV LIVER TRANSPLANTATION VERSUS NON HCV LIVER TRANSPLANTATION

Takaaki Koshiba¹, Xiangdong Zhao², Ying Li², Alex Bishop³

¹Department of Disaster and comprehensive medicine, Fukushima Medical University; ²Department of Surgery, Graduate School of Medicine, Kyoto University; ³Transplantation Laboratory, Royal Prince Alfred Hospital, Sydney

Introduction: HCV disease is the leading cause of liver transplantation (Ltx). Since reinfection of HCV after Ltx can not be avoided, tailoring immunosuppression in the presence of biomarkers of early acute rejection (EAR) may improve outcomes after Ltx for HCV diseases. Immune system could be highly modified by chronic infection of HCV. If so, this modification must be taken into account to explore biomarkers of EAR after Ltx for HCV disease.

Method: 22 HCV (female/male = 6/16, 53.8 ± 4.5 years) and 26 non-HCV (female/male = 10/16, 41.5 ± 11.8 years) living-donor liver transplantation (LDLT) recipients were enrolled. Pre-Ltx peripheral blood mononuclear cells (PBMC) were systemically phenotyped by FACS analysis. The frequency of each phenotype within the lymphocytes was presented. The frequency of each phenotype was compared between recipients who experienced early acute rejection (EAR: < 3 months post-Ltx) and recipients who did not experience EAR both in HCV cohort and non-HCV cohort.

Result: The incidence of EAR was equivalent between HCV and non-HCV cohorts (8/22 in HCV vs. 11/26 in non-HCV, NS). HCV patients experienced EAR at 19 ± 14 days post-Ltx while non-HCV patients at 18 ± 14 days post-Ltx (NS). HCV patients with EAR exhibited low frequency of CD3 + CD8 +, $\gamma\delta$ T or NKT cells and high frequency of $\alpha\beta$ T cells, CD3 + CD4 + or CD4 + CD25 + cells compared to those without EAR. On the other hand, non-HCV patients with EAR exhibited high frequency of NKT cells and low frequency of CD19 + compared to those without EAR.

Conclusion: Our data suggest that chronic HCV infection modifies immune systems prior to liver transplantation (Ltx), which in turn results in differential correlation between PBMC phenotypes and EAR (early acute rejection) in HCV patients versus non-HCV patients. Thus, it is tempting to state that consideration of immunological modification by HCV infection may be needed when biomarkers of EAR after Ltx are explored.

P112

ANTI-MICA ANTIBODIES AND ACUTE REJECTION IN RENAL TRANSPLANTATION

Zuzana Zilinska¹, Silvia Chrenova², Michal Sapak³, Martin Chrastina¹, Jan Breza Jr¹, Daniel Kuba²

¹Department of Urology with Kidney Transplant Center, University Hospital Bratislava, Slovakia; ²Slovak Medical University, Bratislava, Slovakia;

³Department of Microbiology, Comenius University, Bratislava, Slovakia

Background: We studied anti-MICA antibodies (anti-MICA) and their connection with acute rejection (AR) after kidney transplantation. At the same time we observed presence of antibodies against HLA antigens class I and II (anti-HLA I and II). We correlated the findings with AR episodes.

Methods/Materials: The study group include 73 kidney transplant recipients. We used Luminex for detection of anti-MICA and anti-HLA I and II.

Results: We detected anti-MICA in 21 (28.8%) out of 73 patients (pts.), in 18 (85.7%) of them with biopsy proven AR (BPAR): in 17 (81%) cases AMR, only once TCMR. In 3 (14.3%) pts. AMR was associated with only anti-MICA. In 16 (76.2%) cases with anti-MICA we also detected anti-HLA I and in 17 (81.0%) pts. anti-HLA II using Luminex, both anti-HLA I and II we observed in 15 (71.4%) pts. In anti-MICA positive group graft loss occurred in 3 (14.3%) pts. due to AMR resistant to treatment. In group of 52 (71.2%) pts. no anti-MICA were detected. BPAR occurred in 34 (46.6%) pts.: AMR in 26 (50%) and TCMR in 8 (15.4%) out of them. AR was associated with antibodies in 29 (39.7%) pts., in 5 (6.8%) we didn't detect any antibody. In 10 (13.7%) pts. no anti-HLA I or II associated with signs of AR were found. In this group 5 (6.8%) grafts were lost: 1 due to active chronic AMR, 1 due to GNE because of health-threatening bleeding, 3 pts. died with functioning graft. AMR was significantly more frequent in group with anti-MICA ($p = 0.007$) in comparison with non-anti-MICA group.

Conclusion: In our study we detected anti-MICA in 21 pts., in 18 out of them associated with AR. In 3 cases AR was associated with isolated finding of anti-MICA. All lost grafts in this group were related to complications of AMR resistant to treatment. In the group without anti-MICA we found lower proportion of lost grafts (6.8 vs. 14.3%). Anti-MICA occurrence was associated with necessity of prolonged antirejection therapy.

P113

CHARACTERIZATION OF PRE-TRANSPLANT PARAMETERS ASSOCIATED WITH ACUTE REJECTION AFTER LIVING-DONOR KIDNEY TRANSPLANTATION

Florian Vondran, Kai Timrott, Sonja Kollrich, Ann-Kristin Steinhoff, Jürgen Klempnauer, Frank Lehner, Reinhard Schwizner

General, Visceral and Transplantation Surgery, Hanover Medical School

Background: Acute rejection remains a major cause for long-term kidney allograft failure. Reliable immunological parameters suitable to define the pre-Tx activation state and hence the individual risk for graft rejection are highly desired to appropriately adapt the immunosuppressive regimen in advance.

Methods: Donor- and 3rd-party alloreactivity were measured by mixed lymphocyte culture. Soluble forms of CD25, CD30 and CD44 were detected in patients' serum by ELISA. Various lymphocyte subsets were determined by flow-cytometry. All patients received immunosuppression with CNI/MMF/steroids and were grouped according to protocol and indicated biopsies within the first year post-Tx: non-rejector (NR, $n = 13$), borderline (BL, $n = 5$), acute rejector (AR, $n = 7$).

Results: Patients suffering from AR showed significantly higher pre-Tx alloreactivities than NR ($p < 0.02$). Highest levels of sCD25, sCD30 and sCD44 likewise were observed in the former ($p = 0.030$, 0.011 and 0.002 compared to NR). BL-patients were found between both other groups. Combination of these parameters enhanced differences seen between groups. Patients with graft rejection showed markedly increased frequencies of CD4 + CD28- and CD8 + CD28- T-cells pre-Tx.

Conclusions: Pre-transplant levels of alloreactivity, the overall activation state of recipient's immune system and the frequency of particular T-cell subsets seem to be associated with graft rejection after kidney-Tx and should be further evaluated for clinical applicability.

P114

EFFECT OF FK506 ON ENDOPLASMIC RETICULUM (ER) - MEDIATED APOPTOSIS OF JURKAT CELLS

Sang Young Chung, Soo Jin Na Choi

Department of Surgery, Chonnam National University Hospital

Background: The third apoptotic pathway is endoplasmic reticulum (ER) mediated apoptosis. We examined the effects of FK506 on ER mediated apoptosis of Jurkat cells.

Methods/Materials: We observed cell viability, measurement of H2O2 generation, intracellular accumulations of Ca²⁺ and NO, and western blottings of ER stress mediated apoptotic pathway proteins, such as phospho-PERK, PERK, CHOP, Grp78, Grp94, Bcl-2, and Bak proteins. Mitochondrial membrane potential determination by JC-1 staining was performed.

Results: Cells were cultured with the presence or absence of FK506. Flow cytometric analysis was performed after PI stain. Viability of Jurkat cells were decreased by the addition of FK506 in a dose-dependent manner. FK506 induced cytotoxicity was characterized by sub G0/G1 phase arrest. FK506 induced cell death was confirmed as apoptosis characterized by nuclear fragmentation and caspase-3 protease activation. Intracellular accumulations of Ca²⁺ and NO production were identified in FK506 treated Jurkat cells after 24 h. Expression of iNOS protein was also noted. Generation of H2O2 was identified. Deceased activation of procaspase-12 protease confirmed activation of caspase-12 after 48 hours. Activation of phospho-PERK protein peaked at 36 hours after FK506 treatment. Expressions of CHOP/GADD153, Grp78 and Grp94/BiP proteins were also identified after 36 hours. Expression of Bak protein was also noted. Change of mitochondrial membrane potential transition (MPT) was also noted.

Conclusion: FK506 treated Jurkat T cells increased the sub G0/G1 phase, nuclear fragmentation and activations of three and 12 caspases. FK506 also increased NO production through induction of iNOS and H2O2. Reactive oxygen species induced by FK506 resulted in the modulation of Bak protein expression and mitochondrial dysfunction through ER stress mediated pathway. FK506 induced ER mediated apoptosis in Jurkat T cells were identified.

P115

CLUES TO IMPROVE THE INTERPRETATION OF SAFB-DSA

Thomas BACHELET, Gwendaline Guidicelli, Jonathan Visentin, Lionel Couzi, Pierre Merville, Jean-Luc TAUPIN

CHU Bordeaux

Virtual crossmatch strategies and their definition of presumptive Donor Specific Antibodies (DSA) rely on single antigen flow beads (SAFB) assays. Technological limitations sometimes made its interpretation challenging (distorted HLA molecules, variable HLA density, prozone effect, inter and intra-test variation). Circumventing these limits is yet mandatory to extrapolate results to clinical practice. We here aimed to define which clues optimize the analysis by confronting acellular SAFB-DSA to cellular crossmatch (XM) DSA levels. To that end, 603 T-lymphocytes XMs combining flow cytometry (FCXM) and complement dependent cytotoxicity (CDC) assays (results expressed in Mean Channel Shift deviation (MCS) and using the CDC viability score) were performed by using 137 sera from sensitized patients, exhaustively characterized with SFAB on a Luminex platform and 90 organ donors' lymph nodes, with extensive HLA Class I typing. The correlation between SAFB-DSA and FCXM-DSA and CDC-DSA is better if (i) the sum of the Mean Fluorescence Intensity (MFI) of the different HLA DSA was taken in account rather than the MFI of the immunodominant DSA (for the whole tests: R^2 0.47 vs. R^2 0.46 and R^2 0.29 vs. R^2 0.21; for the tests with more than one mismatches-MM ($N = 187$): R^2 0.64 vs. R^2 0.57 and R^2 0.46 vs. R^2 0.33, respectively); (ii) MFI was doubled for homozygote sera (for the whole tests: R^2 0.47 vs. R^2 0.46 and R^2 0.29 vs. R^2 0.23; for the tests with homozygotic MM antigens ($N = 71$): R^2 0.65 vs. R^2 0.64 and R^2 0.49 vs. R^2 0.46, respectively). Noteworthy, information given by the different beads is not equivalent, likely in relation with the conformation of HLA Ag on the beads (each bead evaluated in more than 10 XM tests, being the unique DSA target): performant for HLA A11, B35, B38, B51, B57, B7 ($R > 0.6$, $p < 0.001$), correct for HLA A1, A2, A23, A24, A68, B44, B8 ($p < 0.05$) but results given by HLA A3, B18, B62 should be taken with caution ($p > 0.05$). Better apprehend the results from SAFB assay should enable the clinicians to better integrate this tool in their practice.

P116

HIGH NUMBER OF ACTIVATED NKT CELLS FOLLOWING LUNG TRANSPLANTATION DESPITE IMMUNOSUPPRESSION

Mary Gieschen-Krische¹, Sumiyya Mahmood², Josie Adams², Anna Rowan², Mohamed Al-Alouf², Nizar Yonan³, James Fildes³

¹The University of Manchester; ²UHSM; ³UHSM, The University of Manchester

Introduction: NKT cells have the potential to contribute to inflammatory and tolerogenic immune responsiveness, yet their role following lung transplantation is unclear. In this study we aimed to characterise and determine the differences in NKT cells and their function between lung transplant recipients and non-transplant controls.

Methods: Peripheral blood samples were collected from ($n = 87$) lung transplant recipients during routine clinical visits, and ($n = 10$) healthy controls). NKT cells were quantified by flow cytometry using fluorescent-labelled antibodies: CD3, CD16 and CD56. Phenotypes were characterised using activation markers (CD107a, CD161 and NKG2D) and tolerance markers (CD200 and CD200R). Differences between lung transplant recipients and controls were determined using Mann-Whitney U test, whereby p -values < 0.05 were considered statistically significant.

Results: Lung transplant recipients had significantly higher numbers of NKT cells expressing CD107a+ ($p < 0.01$), CD161+ ($p = 0.43$) and NKG2D+ ($p < 0.01$), compared to non-transplant controls. However, higher numbers of NKT cells expressing tolerogenic markers CD200+ ($p < 0.01$), CD200R+ ($p < 0.01$) and CD200+ CD200R+ ($p < 0.01$) were found in the control group. Differences in relative mean expression of markers of activation or tolerance were found to be non-significant between groups.

Conclusions: A higher frequency of activated NKT cells following lung transplantation suggests the existence of a signal inducing cellular maturation to an inflammatory phenotype. This is likely to be in response to alloantigen, and also indicates NKT cells are not sufficiently suppressed by immunosuppression. Clearly further work on this important cell is warranted in the transplant setting.

P117

AZATHIOPRINE ADMINISTRATION IS ASSOCIATED WITH AN INCREASE IN AIRWAY INHIBITORY NKT CELLS AND LOSS OF CIRCULATING ACTIVATED NKT CELLS FOLLOWING LUNG TRANSPLANTATION

Mary Gieschen-Krische¹, Louise Archer², Timothy Entwistle¹, Claire Cowan², Mohamed Al-Aloufi², Nizar Yonan³, James Fildes³

¹The University of Manchester; ²UHS; ³UHS, The University of Manchester

Introduction: Allograft rejection is a major complication following transplantation, requiring continuous immunosuppression. The mechanisms of action of immunosuppressive drugs have been well described. However, their effect on NKT cells following lung transplantation remains unclear. In this study, we assessed the association between NKT cells (peripheral blood and BAL) with immunosuppression doses in a lung transplant cohort.

Methods: Peripheral blood samples ($n = 87$), BALs ($n = 33$) and clinical data were collected during routine clinic visits. NKT cells were quantified by flow cytometry using fluorescent-labelled antibodies: CD3, CD16 and CD56. Cell function was characterised using CD200 and CD200R (markers of tolerance) and CD107a, CD161 and NKG2D (markers of activation). The relationship between administered doses of immunosuppression and NKT cells was performed by partial correlation co-efficient analysis, controlling for time.

Results: The percentage of NKG2D⁺ NKT cells negatively correlated with azathioprine dose ($p = 0.047$, $R = -0.338$). When assessing airway NKT cells, azathioprine dose again positively correlated with NKG2D⁺ NKT cell numbers ($p = 0.047$, $R = -0.338$), as well as the number of inhibitory CD200⁺ NKT cells ($p < 0.001$, $R = 0.952$).

Conclusion: Following gut absorption, azathioprine is converted to 6-mercaptopurine which inhibits purine synthesis, preventing DNA synthesis and therefore cell proliferation. Azathioprine associated NKT cell modulation and migration is therefore likely to be via another route. Further studies are required to delineate this pathway, and also to translate these phenotypic changes into clinical measures of outcome.

P118

CMV AND TUMOR STRESS SURVEILLANCE BY HUMAN Vd1 GD TCR BINDING TO EPHRIN RECEPTOR A2

Thomas Bachelet¹, Chrystelle Harly¹, Carrie Willcox², Vincent PITARD¹, Sonia Netzer¹, Romain Marlin¹, Jean-François MOREAU¹, Benjamin Willcox², Julie Déchanet-Merville¹

¹UMR CNRS 5164; ²Birmingham Cancer Research UK Cancer Centre, School of Cancer Sciences

Gamma-delta (gd) T cells are unconventional T lymphocytes combining innate-like and adaptive features. In immunocompromised patients, a subset of gd T cells markedly expands during cytomegalovirus (CMV) infection. These non-Vd2 gd T cells exhibit an *in vitro* dual reactivity toward tumor cells, which translate *in vivo* in solid organ transplant recipients: their expansion associates with resolution of CMV infection and with a reduced cancer-risk. Although their repertoire is restricted, they express diverse types of TCRs encoded by different V-genes suggesting the recognition of multiple stress-associated antigens common to CMV-infection and tumor transformation. In order to identify the antigens recognized by different non-Vd2 gd TCRs on infected and tumor cells, we immunized mice with these target cells and screened antibodies able to block their recognition by gd T cells. One such monoclonal antibody (6G8) specifically blocked the antitumor reactivity of Vg9Vd1 TCR transductants generated from a dually reactive Vg9Vd1 clone. Using immunoprecipitation and mass spectrometry, the 6G8 ligand was identified as EphA2 (Ephrin receptor A2), a member of the largest family of tyrosine kinase receptors. EphA2 is expressed on endothelial cells infected by CMV, and is heavily upregulated during tumorigenesis, with high EphA2 expression correlating with poor cancer prognosis. Immobilized recombinant EphA2 was able to activate Vg9Vd1 transductants and directly bound to the Vg9Vd1 TCR as assessed by AlphaScreen technology. Different Vd1-containing TCRs were shown to recognize EphA2, suggesting a shared reactivity toward EphA2 within the Vd1 T cell subset. We thus identified EphA2 as a new stress-regulated antigen targeting by non Vd2-gd T cells. These data suggest that in humans, a fortiori when immunosuppressed, gd T cells compose a lymphoid stress-surveillance compartment, capable of recognizing the dysregulated state of infected or transformed cells.

P119

A ROLE FOR TRIB1 IN REGULATORY T CELLS

Dugast Emilie¹, Kiss-Toth Endre², Docherty Louise², Danger Richard³, Chesneau Mélanie⁴, Pichard Virginie⁴, Judor Jean-Paul⁴, Pettré Ségolène⁴, Conchon Sophie⁴, Soullillou Jean-Paul⁴, Brouard Sophie⁴, Ashton-chess Joanna⁵

¹INSERM URM 1064; ²Department of Cardiovascular Science, University of Sheffield; ³UMR1064, INSERM; ⁴INSERM UMR1064; ⁵TcLand Expression

TRIB1, a serine-threonine kinase-like molecule, which was identified as a biomarker of chronic antibody-mediated rejection, is highly expressed in CD4 + CD25 + Foxp3 + Regulatory T-cells (Tregs). We isolated Tregs and non-Tregs counterparts and analyzed TRIB1 and Foxp3 mRNA expression by quantitative PCR. Physical interaction between the TRIB1 and Foxp3 proteins was analyzed by Protein Complementation Assay (PCA) using flow cytometry, microscopy and co-immunoprecipitation. Both TRIB1 and Foxp3 were expressed at higher levels ($p < 0.001$) and correlated tightly in Tregs (Spearman $r = 1.0$; $p < 0.001$) but not in CD4 + CD25 - T cells. The PCA revealed a direct physical interaction between TRIB1 and Foxp3, which is impaired upon deletion of the TRIB1 N-terminal but not the C-terminal domain, suggesting interaction in the nucleus. This interaction was confirmed in primary human Tregs by co-immunoprecipitation. By infecting CD4 + T cells with lentivirus expressing or not TRIB1, we showed that TRIB1 block CD4 + T cells proliferation after one cycle of cell division. Altogether, these data show a direct relationship between TRIB1 and Foxp3 in terms of expression and physical interaction and show that TRIB1 is an inhibitor of cell proliferation by blocking the cells before the G2 phase of the cell cycle.

P120

IN VITRO EFFECT OF STATINS ON INTRACELLULAR CYCLOSPORINE A CONCENTRATION IN HUMAN PERIPHERAL BLOOD MONONUCLEAR CELLS

Seok Ju Park¹, Ho Jung Shin², Min Hye Kim², Dong Hyun Kim², Yeong Hoon Kim¹, Young Chul Yoon³, Yang Wook Kim⁴, Jae-Gook Shin²

¹Department of Nephrology, College of Medicine, Inje University, Busan Paik Hospital; ²Pharmacology and Pharmacogenomics Research Center, Inje University, Busan Paik Hospital; ³Department of Cardiovascular surgery, College of Medicine, Inje University, Busan Paik Hospital; ⁴Department of Nephrology, College of Medicine, Inje University, Haeundae Paik Hospital

Background: It was known that declining intracellular T-lymphocyte concentration of cyclosporine A precedes acute rejection in kidney transplant recipients. The aim of this study was to elucidate the impact of various statins on intracellular cyclosporine A concentration in the PBMC (peripheral blood mononuclear cell).

Method: PBMCs were isolated from 30 ml of freshly collected blood which were obtained from healthy 4 volunteers with informed consent. PBMC were incubated in the media with 0.1 ml of ND96 buffer containing 200 nm of cyclosporine A in the presence and absence of rosuvastatin (10 μM, 100 μM), simvastatin (10 μM, 100 μM), atorvastatin (10 μM, 100 μM), fluvastatin (10 μM, 100 μM), pitavastatin (10 μM, 100 μM) for 30 min at 37 °C. The radioactivity was measured by a MicroBeta TriLux 96-well Scintillation/Luminescence detector (PerkinElmer). We also measured intracellular cyclosporine A concentration in the presence of the statins (100 μM) in the LLC-PK1 overexpressing P-glycoprotein cells.

Result: The intracellular concentration of cyclosporine A in the control and in the presence of verapamil was 30.5 ± 6.2 fmol/min/2*10⁵ and 55.8 ± 6.4 fmol/min/2*10⁵ ($p = 0.008$) respectively. The intracellular cyclosporine A concentration with simvastatin (10 μM, 100 μM) and with atorvastatin (10 μM, 100 μM) showed significant higher value, 67.1 ± 6.7 fmol/min/2*10⁵ ($p = 0.002$), 66.2 ± 4.5 fmol/min/2*10⁵ ($p = 0.001$), 45 ± 4.9 fmol/min/2*10⁵ ($p = 0.03$), 57.5 ± 2 fmol/min/2*10⁵ ($p = 0.002$), respectively. But the others were not ($p > 0.05$). It also revealed higher intracellular cyclosporine A concentrations in the presence of verapamil, atorvastatin and simvastatin, 398.7 ± 1.1 fmol/min/1*10⁴ ($p = 0.0002$), 108.3 ± 0.6 fmol/min/1*10⁴ ($p = 0.04$), 222 ± 0.8 fmol/min/1*10⁴ ($p = 0.01$), respectively, in the LLC-PK1 cells.

Conclusion: The intracellular cyclosporine A concentration could be affected variously with statins by p-glycoprotein mediated inhibition.

P121

LARGE ANIMAL SOLID ORGAN ALLOGRAFT TRANSPLANTATION MODEL USING PIGLETS

Ik Jin Yun, Kyung Sik Park, Jung Hwan Park, Jun Seok Kim, Hyun Geun Ji Konkuk University Hospital

Background: As for studying characteristics of solid organ transplantation, large animal model is very essential. However, large animal model is hard to handle and expensive for large group. Porcine and human beings have many aspects in common that make porcine a well-characterized animal model for solid organ allotransplant. So piglets which are small and relatively inexpensive

can be candidates for proper substitute for adult model. However, piglet allograft models have not been widely used in allotransplant model because of immunological and surgical problems. The aim of this study was to introduce our experience of kidney and heart transplantation using piglets.

Methods: We performed 12 kidney and 11 heart transplantations between wild type piglets. We use heart and kidney allograft using single donor in principle and monitored perioperative and immunological parameters before and after transplantation. Average weight of donor and recipient piglet is around 5 kg. Immunosuppressive protocols consisted of FK506, MMF and steroid.

Results: Average survival days of piglet recipients after transplant are 16.75 (4-89) in kidney and 17.10 (6-41) in heart without pathologic evidence of rejection. The major causes of death were not related to rejection, but other non-immunologic factors just like dehydration due to vomiting and diarrhea or stricture of ureter-bladder reconstruction. We performed second look up for evaluating and sampling the allograft of four cases among the porcines surviving the early postoperative period.

Conclusion: We successfully performed 12 cases of renal and 11 cases of heart allotransplant using piglet model with successful immunosuppression without acute rejection or early postoperative complication. However, we need to optimize protocols for immune modulation and post-operative care to attain long-term survival of piglet allotransplantation models.

P122

REDUCED HUMORAL RESPONSE TOWARDS HLA-C IS NOT ONLY DUE TO THEIR LOWER EXPRESSION BUT ALSO TO THEIR LOW IMMUNOGENICITY

Geert W. Haasnoot, Marian D. Witvliet, Frans Claas,

Ilias Doxiadis

Eurotransplant Reference Laboratory

The products of the 3rd classical MHC locus HLA-C were the last serologically discovered (Thorsby et al. 1970; Mayr et al. 1973). Hayek-Rosenmayer and Doxiadis (1984) displayed the products by 1-D-IEF and Bunce et al. (1996) achieved molecular typing reducing the incidence of C "blank" to 0. Recently, O'Huigin reported on the binding of miRNA-148a to the 3' untranslated region of HLA-C. Two groups were defined: C2,5,6,8,12,15,16 escaping down regulation and the C3,4,7,14,17, which are down regulated. In solid organ transplantation almost no information is available with respect to antibody formation towards HLA-C. Earlier, we showed that antibody production is closely related to the number of epitope incompatibilities (EI) expressed by the HLA antigens. We questioned whether the low immunogenicity of HLA-C is not only due to the differential expression of this locus but also to a lower degree of antigenicity, measured as EI. We selected HLA-A, B, and C molecularly typed phenotypes occurring at least twice in the normal population ($N = 126$). We simulated a situation in which these would occur as a single mismatch in transplantation ($N = 77$). Finally, we calculated the median EI per HLA locus. The mean EI for HLA-A was 5.2 vs. 4.0 for HLA-B and 2.4 for HLA-C ($p < 0.001$). When the HLA-B locus was divided into the Bw4/Bw6 epitopes and the HLA-C into NKC1 and NKC2 groups the results in terms of EI where Bw4 (EI = 5.3) > A (5.2) > C2 (3.6) > Bw6 (3.1) > C1 (2.0). HLA antigens, which were outliers with respect to their EI were: HLA-A2 (EI = 10), A1 (8), B44 (8), B60 (7), and HLA-C7 (8). HLA-C7 with a high number of EI belongs to the group of low expressed HLA-C, and leads to 18% specific antibodies in highly sensitized patients. Although the expression of the HLA-C in a transplanted graft certainly plays a role in antibody formation, the number and type of the EI is crucial as well. In general, the products of the HLA-C locus have a low immunogenicity on basis of their EI.

P123

ANTI-ANGIOTENSIN TYPE 1 RECEPTOR ANTIBODIES ASSOCIATED WITH ANTIBODY-MEDIATED REJECTION IN PATIENTS WITHOUT PREFORMED HLA-DONOR SPECIFIC ANTIBODY

J.W. In¹, H. Park¹, E.Y. Rho¹, S. Shin¹, K.U. Park², M.H. Park¹, Eun Young Song¹

¹Department of Laboratory Medicine, Seoul National University College of Medicine, Seoul, Korea; ²Department of Laboratory Medicine, Seoul National University Bundang Hospital, Seongnam, Korea

Introduction: Angiotensin II is a peptide hormone involved in renin-angiotensin-system (RAS). Anti-angiotensin receptor 1 (AT1R) antibodies are implicated in stimulating RAS and suspected to have some adverse impacts on renal transplantation outcome.

Methods: From Nov 2009 to Feb 2012, 42 remaining sera from renal transplantation recipients with biopsy-proven antibody mediated rejection (AMR) ($n = 6$), acute cellular rejection (ACR) ($n = 23$) and AMR+ACR ($n = 8$) without preformed HLA antibodies were tested with anti-AT1R antibody assay (Onelambda, USA). Forty two control patients without rejection were also analyzed.

Results: The frequencies of elevated anti-AT1R antibodies was higher in patients with AMR ($n = 14$) compared to controls (28.6% vs. 4.9%, $p = 0.03$, OR = 8.0). It was also higher in patients with AMR+ACR ($n = 8$) (37.5% vs. 4.9%, $p = 0.03$, OR = 12.0). There was no difference in frequencies of elevated anti-AT1R antibody in patients with ACR.

Conclusion: Anti-AT1R antibodies were suspected to have association with occurrence of AMR without preformed HLA antibodies in renal transplantation. Further studies in a larger number of patients are needed.

P124

INTRAGRAFT MRNA EXPRESSION OF GRANZYME A, GRANZYME B AND OX40 IN RENAL ALLOGRAFTS

Zuzana Zilinska¹, Daniel Kuba², Helena Bandzuchova², Branislav Trebaticky¹, Martin Chrastina¹, Jan Breza¹

¹Department of Urology with Kidney Transplant Center, University Hospital Bratislava, Slovakia; ²Medical University, Bratislava, Slovakia

Background: Acute antibody mediated rejection (AMR) and acute T-cell mediated rejection (TCMR) activates the immune system in different ways. Granzyme A (GZA) and Granzyme B (GZB) are cytolytic molecules expressed on effector cells of the immune system. Positive costimulatory molecule of T-lymphocytes is OX40. We studied the expression of biomarkers in renal allografts with AMR, TCMR, combined rejection (AMR + TCMR) and other diagnoses.

Methods/Materials: The study group included 55 kidney transplant recipients. We evaluated 79 biopsies from allografts: 28 samples (spl.) with AMR, 18 spl. with TCMR, 7 spl. with AMR + TCMR and 9 spl. with the recurrence of the disease in the graft (R). A group of 17 spl. without histologic signs of acute rejection had served as a control (K). Total RNA obtained from tissue was transcribed into cDNA, then amplified by real time PCR. Relative changes in gene expression of markers were calculated using the 2-DeltaCT. The results were evaluated by Mann Whitney U test.

Results: The results are given in the table. The values in the table are medians, P for U test in comparison with the control. Differences between AMR and TCMR are not statistically significant. Linear combination of results of GZA-GZB-OX40 has differentiated each group except R.

Conclusion: Acute rejection increases the expression of studied biomarkers. The highest levels of biomarker expression we found in TCMR group. In combined rejection the level of biomarkers (excluding GZA) is lower than the one in TCMR, which may indicate the different mechanism of activation of the immune system. The best differentiation among the groups was done by linear combination of GZA-GZB-OX40. Our results show that to obtain the better information value is advantageous to investigate more biomarkers together, which may be beneficial in the evaluation of ambiguous histologic or complicated clinical situations.

P125

FUNCTIONAL ANALYSIS OF VIRUS-SPECIFIC T CELLS WITH CROSS-REACTIVITY TO ALLO-ANTIGENS

Kirstin M. Heutink¹, Heleen van den Heuvel², Si-La Yong¹, Frans Claas², Ineke J. M. Ten Berge¹

¹Academic Medical Center; ²Leiden University Medical Centre

Background: Part of the antigen-specific memory T-cells generated against pathogens, such as cytomegalovirus (CMV) and Epstein-Barr virus (EBV) show also reactivity to allo-antigens, so called heterologous immunity. In kidney transplant recipients, the presence of virus specific T-cells with cross-reactivity to allo-antigens of donor origin might impair allograft function and survival. We here developed a method to analyze the characteristics of cross-reactive T cells *in vitro*.

Methods: Peripheral blood mononuclear cells (PBMCs) from five healthy individuals known to have circulating CMV- or EBV-specific T-cells, were labelled with CFSE. To expand allo- and virus-specific T-cells, PBMCs were cultured for 6 days either with allogeneic stimulator cells in a mixed lymphocyte reaction (MLR) or with viral peptide and IL-2. Cells were re-stimulated for 6 h with allogeneic cells or peptide loaded-autologous PBMCs and analyzed by flow cytometry. Cross-reactive CD8⁺ T-cells were identified as tetramer+ and CFSEdim in a MLR.

Results: Viral peptide dose-dependently induced expression of IFN γ , IL-2 and the degranulation marker CD107a in virus-specific T-cells expanded by either viral- or allo-antigen stimulation. Some cross-reactive T cells also produced cytokines in response to re-stimulation with allogeneic cells, which appeared to be dependent on the cross-reactive allo-antigen involved. For example, EBV B8 FLR-specific T cells, known to cross-react to HLA B44*02, produced large amounts of IFN γ and IL-2 (respectively 60% and 25% of the cells) in response to cells bearing this HLA molecule, whereas allo-stimulation evoked proliferation but no cytokine secretion in CMV B35 IPS-specific T cells.

Conclusion: Together these results show that frequency and function of cross-reactive T-cells can be analyzed *in vitro* and differ between cross-reactive epitopes.

P126

IN VITRO ANALYSIS OF ALLO-REACTIVE T CELL SUBSETS AND THEIR SENSITIVITY TO BELATACEPT-MEDIATED INHIBITION

Rakesh Sindhi¹, Bishu Ganguly², Robert Townsend¹
¹Plexision Inc; ²Bristol-Myers Squibb

Background: Belatacept (Nulojix™, Bristol-Myers Squibb) blocks CD28-mediated co-stimulation of T-cells. Variable dependency of T-cell subsets on CD28-mediated co-stimulation may affect the capacity of belatacept to inhibit their allo-responsiveness. The sensitivity of T-cell subsets to belatacept-mediated inhibition of allo-responses was evaluated *in vitro*.

Methods: Thirty-six CD3+ T-cell subsets were evaluated in PBMC from 20 NHV. Sensitivity of subsets to inhibition by belatacept (0–100 µg/ml) was tested in responder PBMC, stimulated with HLA-mismatched, T-cell-depleted stimulator PBMC (1:2 ratio). T-cell CD154 expression was used as a measure of T-cell activation as previously described. Allo-responses were stratified by T cell phenotypes (cytotoxic (Tc), helper (Th), memory (M) and naive (N)) and CD28 expression. Belatacept concentrations associated with half-maximal inhibition of allo-responses (EC50) were estimated for each T-cell subset.

Results: CD28-neg cells were more frequent among Tc (25.3 ± 2.8%) compared with Th (2.3 ± 0.76%, $p = 5.6 \times 10^{-9}$, $n = 31$) subsets. The least belatacept-sensitive T-cell subsets were ThMCD28-neg > TMCD28-neg > Tc > TcCD28-pos > TcCD28-neg (median EC50 = 35.8, 30.1, 26.5, 22.7, and 20.95 µg/ml, respectively, $n = 20$). The most belatacept-sensitive subsets included ThN, TcN, TcNCD28-neg, and TN and TM double-neg cells (median EC50 range = 9.4 to 3.15 µg/ml). Median EC50 values of the remaining 26 T cell-subsets ranged from 10.35 to 19.7 µg/ml. Conclusion CD28-neg TM and Tc populations are relatively insensitive to inhibition by belatacept *in vitro*, suggesting less dependence on CD28-mediated co-stimulation. Reduced inhibitory effect of belatacept on these donor-specific T-cell subsets may result in suboptimal immunosuppression and potentially increased risk of acute rejection. Understanding the effect of belatacept and co-therapies on these cell subsets may inform the selection of optimized belatacept-based treatment regimens.

P127

ROLE OF DENDRITIC CELLS AS BIOMARKERS FOR ACUTE CELLULAR REJECTION AFTER HEART TRANSPLANTATION

Markus J. Barten¹, Katja John¹, Jens Garbade¹, Stefan Dhein¹, Friedrich-Wilhelm Mohr¹, Hartmuth B. Bittner²
¹University Leipzig Heart Center; ²Florida Hospital Orlando

Objective: Over the last decade many studies evaluated the potential of certain biomarkers to predict acute cellular rejection (ACR) without finding their way in the clinical routine. Thus, in our study we monitored dendritic cells (DCs) in heart transplant recipients (HTxR) treated either with a tacrolimus (TAC) or cyclosporine A (CsA)-based immunosuppressive regimen in the context of ACR.

Methods: Both groups consisted of 14 maintenance HTxR. At different study time points (0, 3 and 6 months after study start) peripheral blood from all HTxR was drawn to analyse for (1) blood CsA or TAC concentration (trough value) and (2) to analyse myeloid and plasmacytoid (m and p) DCs with FACS. Histological rejection grading was performed of endomyocardial biopsies.

Results: TAC treated HTxR had significantly higher values of pDCs (CsA-group 53.9 ± 13.0%, TAC-group 67.5 ± 8.4%, $p < 0.05$) and significantly lower values of mDCs than CsA treated HTxR (CsA-group 57.9 ± 19.0%, TAC-group 45.2 ± 10.7%, $p < 0.05$). In general, HTxR with rejection grade of ≥2 ISHLT 1990 had significant ($p < 0.05$) lower values of pDCs (55.1 ± 16.2%) compared to HTxR without rejection (63.6 ± 10.5%). TAC treated HTxR had significantly less rejections compared to CsA treated HTxR (CsA-group 0.86 ± 0.95%, TAC-group 0.2 ± 0.4%, $p < 0.05$).

Conclusions: Our results showed that HTxR with high pDCs have a lower risk of rejection and that TAC treated HTxR had higher pDCs values compared to CsA treated HTxR. Future studies are needed to confirm if monitoring pDCs and mDCs have the potential value as biomarkers to identify HTxR at risk to develop ACR.

P128

CLINICAL IMPACT OF PREEXISTING AND DE NOVO ANTI-ENDOTHELIAL CELL ANTIBODIES DETECTED BY A NEW INDIRECT IMMUNOFLUORESCENCE ASSAY IN KIDNEY AND PANCREAS TRANSPLANTATION

Daniele Focosi¹, Chiara Biagini¹, Guido Ricchiuti¹, Fabio Vistoli¹, Fabrizio Scatena¹, Ugo Boggi¹
 Azienda Ospedaliero-Universitaria Pisana

Anti-endothelial cell (EC) antibodies (AECA) have been implicated in solid organ transplant dysfunction, but routine testing for donor-specific AECA has been limited to expensive flow-cytometry crossmatches (e.g. Xm-One™) employing circulating EC precursors. Since most EC antigens identified to date are not polymorphic, there is no need for donor EC. We have employed a new assay consisting of human umbilical vein endothelial cells (HUVEC) fixed onto slides and combined it with indirect immunofluorescence to detect AECA

(Titerplane™ technique, Euroimmun GmbH). Sun et al reported that *de novo* AECA detected by Titerplane™ were correlated to rejection after deceased-donor kidney transplantation in a Chinese cohort (Kidney Int. 2011 Mar; 79 (6):655–62). Among study criticisms was the lack of HLA typing for HUVEC lines used in the assays, since HUVEC also express HLA and thus the assay could have had false positives anti-HLA antibodies rather than AECA. We retrospectively replicated their study across a spectrum of 216 solid organ transplants (deceased donor and living donor kidney, pancreas transplant alone, pancreas-after-kidney, simultaneous pancreas and kidney) performed consecutively at the University of Pisa Transplant Centre in 2009–2012. Stored sera at posttransplant month +1, +3, +6, year +1 and +2 were available for 187 recipients. A single lot of Titerplane kits was used, and the HUVEC line was HLA typed (A/B/C/DRB1/DQB1), censoring all positive reactions occurring in the presence of donor-specific anti-HLA antibodies. Overall AECA prevalence was 7% in our cohort (vs. 25% in the Chinese study). We found a very low incidence of *de novo* AECA (0.1% vs. 10% in the Chinese study), likely due to the occurrence of 39% of living donor procedures (implicating shorter cold ischemia times) in our cohort. We report for the first time the occurrence of negativization of preexisting AECA (6 out of 13) after transplantation, likely due to maintenance therapy.

P129

STABLE IMMUNOPHENOTYPE PREDICTS CUTANEOUS SQUAMOUS CELL CARCINOMA (CSCC) RISK POST-TRANSPLANTATION

Sam Sherston¹, Robert Carroll², Paul Harden³, Kathryn Wood¹

¹Transplant Research Immunology Group; ²Clinical and Experimental Transplantation Group; ³Oxford Transplant Centre

Background: Malignancy post-transplantation has incidence rates 3–5 times higher than in the general population and is the second commonest cause of death. cSCC occurs in the UK in 30% of kidney transplant recipients (KTRs) within 10 years of transplantation. Previously we have shown that high numbers of T-regulatory (Treg) and low numbers of Natural Killer (NK) cells predicts cSCC development in KTRs. In this study we aimed to validate the presence and stability of high Treg /low NK phenotype in long-term KTRs.

Materials/Methods: We prospectively studied gender, age, and duration of immunosuppression matched long-term (mean = 17.1 years) KTRs with ($n = 60$) and without ($n = 50$) cSCC. Mortality during follow up (mean = 4.2 years) was 18.2% ($n = 20$); 9.1% ($n = 10$) failed grafts; 14.5% ($n = 16$) lost to follow up. Thirty-six KTRs from cSCC group and 28 cSCC-free KTRs were re-assessed. Flow cytometry to examine lymphocyte subsets was performed on fresh blood samples, and clinical phenotypic data collected using a questionnaire.

Results: We found increased Treg cells (CD3 + CD4 + CD25hiFOXP3 +) [$p = 0.03$], but no significant difference between the proportion or number of NK cells (CD3-CD19-CD16 + CD56 +) in patients with a cSCC compared with those without. Importantly we found no significant change in the proportions of T lymphocyte subsets in SCC or non-SCC group over the follow-up period. KTRs on azathioprine have significantly reduced proportion and numbers of NK cells ($p > 0.01$).

Conclusion: Monitoring immune phenotype in long-term KTRs can potentially identify patients at an increased risk of developing a cSCC. Immune phenotype remains stable over time in the setting of chronic immunosuppression. Immune markers could be incorporated into a useful clinical predictive index of cSCC risk in KTRs.

P130

METAGENOMICS OF URINE OF KIDNEY TRANSPLANT PATIENTS

David Perkins¹, Asha Rani¹, Halvor McGee¹, Patricia Finn¹, Daniel Brennar², David Perkins¹

¹University of Illinois; ²Washington University

Viral infections remain a major complication following transplantation and may be exacerbated by immunosuppressive treatments. For example, BK virus (BKV) develops in approximately 10% of kidney transplant patients resulting in the loss of the graft in 15–50% of affected grafts. The role of specific genotypes of BKV, other polyoma viruses including JC virus or other associated infections remains unknown. To investigate the role of urinary infections in kidney transplantation, we analyzed the metagenome of patients with a clinical diagnosis of BK infection (and control patients diagnosed BK negative) using deep sequencing by the Illumina HiSeq 2000 platform. We obtained 6–12 × 10⁶ reads per sample. After BLAST analysis to filter human sequences and assembly, we analyzed data with CLC and Megan software. Our results demonstrated: 1) detectable levels of BKV was identified in all transplant patients including the controls without a clinical diagnosis of BKV, 2) we identified 18 different genotypes of BKV, and 3) many patients had multiple different genotypes with a maximum of 9 different genotypes identified in a single patient. We also identified additional viruses including JC, torque teno and numerous less abundant viruses. We are currently correlating the BK genotypes with clinical outcomes following transplantation.

P132

MICRO-RNA-105 SUPPRESSES THE FRIZZLED-7/BETA-CATENIN PATHWAY IN HUMAN HEPATOCELLULAR CARCINOMA

Hong Sun, Vito R. Cicinnati, Miriam Maschmeier, Gang Wu, Iyad Kabar, Arnold Radtke, Hartmut Schmidt, Susanne Beckebaum
University Hospital Münster

Aims: Aberrant microRNA (miR) expressions have been observed in different types of cancer. Among the frizzled (Fzd) receptor family, Fzd7 is the Wnt receptor which is most commonly upregulated in a variety of cancers including hepatocellular carcinoma (HCC). FZH7 was predicted to be a potential target of miR-105 by the use of miR target prediction algorithms in HCC. Therefore, we sought to investigate the functional role of both miR-105 and FZH7 in hepatocarcinogenesis.

Methods: The expressions of FZH7 and miR-105 were analyzed in tumor and adjacent non-tumor tissues from 12 HCC patients by gene array and real-time quantitative RT-PCR (qRT-PCR). Transfection studies were performed in human hepatoma cell lines (HepG2, SUN-182) to elucidate the regulatory interrelationship between miR-105 and FZH7.

Results: A significant up-regulation of miR-105 was found in all (12/12) HCC tissues, whereas FZH7 expression was decreased in 25% (3/12) and similar in 33.3% (4/12) of tumor tissues as compared to non-tumor tissue. MiR-105 expression was negatively correlated with FZH7 expression. Transfection of miR-105 precursor dramatically inhibited whereas transfection of miR-105 inhibitor enhanced the expression of FZH7.

Conclusions: MiR-105 negatively regulates the FZH7 oncogene in HCC. These findings provide significant insights into molecular mechanisms of hepatocarcinogenesis.

PS08-HEART

P133

ANALYSIS OF FACTORS INFLUENCING OUTCOMES IN HEART TRANSPLANTATION: THE EXPERIENCE OF A TRANSPLANT CENTER IN THE MEDITERRANEAN BASIN

Gabriele Di Gesaro¹, Francesco Clemenza¹, Cesar Mario Hernandez Baravoglia¹, Calogero Falletta¹, Chiara Minà¹, Giuseppe Romano¹, Cettina Ruperto¹, Michele Piliato², Cesare Scardulla¹

¹Department of Cardiology, Mediterranean Institute for Transplantation and High Specialization Therap; ²Department of Cardio-Thoracic Surgery, Mediterranean Institute for Transplantation and High Special

Background: Advances in immunosuppressive therapy have led to better transplant outcomes, making heart transplantation (HT) a valid treatment for end stage heart disease. The purpose of this study was to identify which combination of variables potentially influences outcomes in our working area.

Methods: A retrospective analysis of 102 patients who underwent HT at our Institute from October 2004 to August 2012.

Results: Mean recipient age was 49.9 years. The majority was male (82.3%). Most frequent indications for HT were ischemic (46.1%) and idiopathic (29.4%) cardiomyopathy. Mean donor age was 34.4. There were 37 female donors (36.3%). Most frequent causes of death were cerebral bleeding in 37 patients (36.3%), head trauma in 54 (52.9%), and ischemic stroke in 4 (3.9%). Mean ischemic time was 173.8. Ischemic time was ≤ 120 min in 19 patients (18.6%), >120 and <180 in 27 (26.5%), ≥ 180 and 240 in 16 (15.7%). Actuarial survival was 84% at 12 months; 15 deaths occurred in the first 3 months, and 1 after 240 days. In this population, risk factors affecting outcomes were donor and recipient age ($p = 0.002$ and $p < 0.0001$), cause of death ($p = 0.036$), and ischemic time ($p = 0.023$). Donor age was correlated with cause of death ($p = 0.0001$). An ischemic time of >180 min was associated with higher mortality among the entire study population ($p = 0.014$), and we found a four-fold increase in mortality risk for the group of patients with an ischemic time of >180 min when compared with the group with an ischemic time of <180 min ($p = 0.017$).

Conclusions: This study identified an epidemiology different from northern Italian, and European, transplant centers in terms of donor age and cause of death, which appears to be closely linked to age. Recipient and donor age, ischemic time, and donor cause of death other than head trauma were associated with poor outcome. The fact that 42.2% of organs were procured outside the Sicilian region was not significantly associated with either higher donor age or lower incidence of head trauma as cause of death. Conversely, we found significant differences in ischemic time values when organs were procured outside of Sicily.

P134

LOW INCIDENCE OF REJECTION AFTER HEART TRANSPLANTATION WITH QUADRUPLE IMMUNOSUPPRESSION – IMPLICATIONS FOR THE SURVEILLANCE ENDOMYOCARDIAL BIOPSY

Iain Sim, Owais Dar, Georgios Rompolas, Andrew Mitchell, Alexandra Rice, Nicholas Banner

Royal Brompton and Harefield NHS Trust

Endomyocardial biopsy (EMB) is the gold standard for diagnosis of acute cardiac allograft rejection; however surveillance EMB protocols were developed with earlier immunosuppression regimens.

We retrospectively analysed the clinical and EMB findings during the 1st year following orthotopic heart transplantation in patients with a negative HLA crossmatch. Mean age at transplantation was 48 (range 18–65). Indications for transplantation included dilated cardiomyopathy (72%), ischaemic cardiomyopathy (21%) and 1 case of post partum cardiomyopathy, 1 restrictive cardiomyopathy and 1 hypertrophic cardiomyopathy. Immunosuppression was rabbit antithymocyte globulin induction followed by maintenance tacrolimus, mycophenolate and steroids

Four patients were treated for clinical rejection with a biopsy showing ISHLT 1R. Four patients were treated for ISHLT 2R biopsy proven rejection in the absence of symptoms, i.e. the true yield of surveillance biopsy without clinical indication was 0.88% and the incidence of treated asymptomatic rejection 9.3%. All episodes of rejection occurred within 83 days of transplantation

The scarcity of rejection episodes in patients transplanted with an HLA negative crossmatch and quadruple sequential immunosuppression has reduced the yield of routine surveillance EMBs and suggests that their frequency should be reduced or that other methods of monitoring be used. Furthermore, since all the ISHLT 2R rejections were asymptomatic, the issue of whether histologically diagnosed asymptomatic 2R rejection always requires increased immunosuppression in patients receiving quadruple therapy needs to be investigated further.

P135

PREVALENCE OF DONOR-TRANSMITTED ATHEROSCLEROSIS – A SINGLE CENTER ICUS STUDY

Helena Bedanova, Marek Orban, Petr Nemeč, Jiri Nicovsky
Center of cardiovascular and transplant surgery

Introduction: Coronary allograft vasculopathy (CAV) is one of the main factors limiting long-term survival following orthotopic heart transplantation (HTx). Whether or not and, if so, how donor-transmitted atherosclerosis (DCA) affects the post-transplant course is still unclear.

Patients and Methods: We performed a retrospective analysis of data of 119 patients (92 men) undergoing HTx from 8/2006 to 9/2012, who had survived their first post-transplant month and had coronary angiography and IVUS.

Results: DCA was present in 39 patients, and not documented in 80 patients. The main risk factors for DCA included donor age, cigarette smoking, and hypertension; the other parameters were not shown to be statistically significant. One-year mortality rates post-HTx were 15.4% in DCA positive, 15.0% in DCA negative group.

Conclusion: The prevalence of DCA in our patients was 32.8%, with major risk factors for DCA including donor age, cigarette smoking, and hypertension.

P136

PRESERVED MYOCARDIAL STRUCTURE AND FUNCTION IN LONG STANDING KIDNEY DONORS

Diego Bellavia¹, Cesar Hernandez-Baravoglia¹, Alessandro Cataliotti², Francesco Clemenza¹, Tullio Bertani¹, Angelo Luca¹, Bruno Gridelli¹, John Burnett², Cesare Scardulla¹

¹ISMETT Hospital; ²Mayo Clinic and Foundation

Background and Aims: Growing evidences have demonstrated a tight kidney-heart connection. However, while it is well established that compensatory and persistent hypertrophy occurs in the remaining kidney following unilateral nephrectomy (UNX), it remains unknown whether remodeling process also occurs in the heart following kidney donation. Thus, the aim of our study was to investigate long-term (≥ 5 years) myocardial structure and function in healthy kidney donors.

Methods and Results: A total of 12 kidney donors (≥ 13 years of age) and 13 sex matched healthy subjects were evaluated by standard and speckle tracking echocardiography (STE). In particular, longitudinal systolic strain (sS) and strain rate (sSR) for the inferoseptal and lateral walls were assessed. On average, patients donated one kidney 8.1 years before enrollment (range: 5.2–10.3). Left ventricular (LV) wall thickness (10 ± 0.8 vs. 9.2 ± 0.09 p 0.04) as well as stroke volume, cardiac output and cardiac index were lower in controls as compared to donors, although mitral inflow parameters, sS and sSR, were similar in the two groups (-22.6 ± 1 vs. -21.2 ± 2.2 p 0.11 and -1.5 ± 0.2 vs. -1.7 ± 0.3 p 0.21, for sS and sSR, respectively)

Conclusions: Kidney donors have no apparent structural or functional myocardial abnormalities by standard or speckle strain echocardiography 5 years post UNX. However, more sensitive evaluation (cardiac magnetic resonance, or cardiovascular biomarkers) are warranted for a definitive conclusion.

P137

CARDIAC SURGERY IN LIVER TRANSPLANT RECIPIENTS – SINGLE CENTER EXPERIENCE

Nils Reiss, Markus Fritz, Ursula Tochtermann, Mina Farag, Matthias Karck, Arjang Ruhparwar

Clinic for Cardiac Surgery, University of Heidelberg

Background: This was a single-center retrospective study to assess the surgical outcomes of liver transplant recipients undergoing cardiac surgery with the use of extracorporeal circulation.

Methods: Between 2002 and 2012, 21 patients with a functioning liver allograft underwent cardiac surgery (CABG $n = 6$; AVR $n = 10$; MVR $n = 1$; HTx $n = 1$; pulmonary embolectomy $n = 3$). The mean interval between liver transplantation and cardiac surgery was 4.5 ± 4.6 years. The patients were divided in to two groups according to their belonging to either Child-Pugh group A = 14 patients (66.6%) or B = 7 patients. (One patient classified as Child-Pugh C was excluded from our study). Pre and postoperative data were analyzed.

Results: The 30 days mortality was 9.5% (2 patients; 1 death after modified Trendelenburg's operation for pulmonary embolectomy, one after aortic root replacement and bypass surgery because of destructive endocarditis of the aortic valve and abscess formation). The survival rate was 76.1% at 1 year, 71.4% at 5 years and 66.7% at 10 years. Patients in the Child Pugh group A had a significantly better short time survival compared to group B: 92.9% compared to 42.9% at 1 year ($p = 0.02$). The long time survival did not differ between both groups. Cox regression analysis showed pulmonary embolectomy to be an independent risk factor predicting mortality (three patients; all passed within the first year).

Conclusions: Cardiac surgery in liver allograft recipients was associated with acceptable surgical results in. Grouping the patients according to their Child-Pugh status of their liver allografts may be a predictor of early mortality. A risk stratification according to the MELD score of the patients did not reach

statistical significance. The modified Trendelenburg's operation for pulmonary embolotomy was identified as an independent risk factor of early mortality.

P138

CLINICAL EXPERIENCES IN 11 PATIENTS WITH END STAGE HEART FAILURE CAUSED BY MUSCLE DYSTROPHY

Uwe Fuchs, Uwe Schulz, Bernd Schulze, Armin Zittermann, Stephan Ensminger, Kavous Hakim-Meibodi, Jan Gummert
Heart Center North-Rhine-Westfalia

Introduction: Muscle dystrophy (MD) has been considered a contraindication for heart transplantation. Nevertheless, the feasibility of heart transplantation in patients with inherited myopathies has been described in several recently published case reports. Here we present our clinical experience in heart transplanted recipients with MD.

Methods: We searched our patient records for heart transplant recipients with MD and evaluated their clinical outcome. Grad of mobilization was defined: Grad I bedridden, Grad II: confined to a wheel chair, Grad III: Walking aid (Rollator), Grad IV: confined to a cane, Grad V: self-sufficient and was evaluated prä-HTX, month 1 (t1), month 12 (t12), month 60 (t60).

Results: Between January 1989 and December 2009, 11 patients with MD were transplanted at our institution. Of these patients, five had an Emery-Dreifuss-MD, four had a Becker-Kiener-MD, one had a Neuromuscular-Typ-MD and one had a Multi-Core-MD. Mean age was 33.4 years (range: 18–58 years). Mean ischemic time was 205 min (range: 142–266 min). Maintenance immunosuppressive therapy was cyclosporine A plus cortisone ($n = 5$) and tacrolimus plus mycophenolate mofetil ($n = 6$). Median survival was 80.3 months (range: 0.6–236 months). One-year and 5-year survival rates were 91.7% and 81.5%, respectively. Of the three patients who died, causes of death were rejection ($n = 1$); graftvasculopathy ($n = 1$); and technical complications ($n = 1$). Currently, all eight patients who are still alive are in good clinical condition. There is no evidence for an increased risk of adverse events such as neurological complications or myalgia. Referring the mobilization grading a significant improvement was seen ($p < 0.05$): prä HTX: Grad I 54%, Grad 46%, t1: Grad II 10%, Grad III 40% and Grad IV 50%. T12: Grad II 10% and Grad V 90%. t60: six of six patients Grad V.

Conclusion: To our opinion, in patients with end-stage heart failure due to MD, heart transplantation is a reliable treatment option with acceptable long term results.

P140

HEART RATE REDUCTION WITH IVABRADINE HAS NO EFFECT ON PERIPHERAL CHEMOKINE PROFILE FOLLOWING HEART TRANSPLANTATION

Baskar Sekar¹, William Critchley², Louise Archer², Timothy Entwistle², Lorna Beresford³, Nizar Yonan¹, Simon Williams¹, Steven Shaw¹, James Fildes²

¹The Transplant Centre, Wythenshawe hospital, University hospital of South Manchester NHS foundation; ²Manchester Collaborative Centre for Inflammation Research, University of Manchester, Manchester, Un; ³Faculty of life sciences, University of Manchester, Manchester, United Kingdom

Background: Sinus tachycardia is common after heart transplantation due to graft denervation. Given heart rate reduction is linked to improved clinical outcomes in patients with native cardiovascular disease, the merits of lowering post transplant sinus tachycardia (PTST) warrants further investigation. Tachycardia can predispose to localised inflammation and immune activation within the transplanted heart (by increasing myocardial metabolism), yet to date the effects of heart rate on inflammatory status remain unknown.

Methods: We prospectively studied immune profile in 11 heart transplant recipients with PTST (HR >90 bpm). Patients were administered Ivabradine (5 mg twice daily) and dose adjusted based on tolerance. Peripheral blood samples were taken prior to drug initiation, then at 6 and 10 weeks. A total of 8 chemokines were quantified via a multiplexed bead based luminex assay.

Results: Ivabradine induced significant heart rate reduction (mean bpm [95% CI] 100.6 [97.4–103.7] vs. 77.3 [73.0–81.6] vs. 73.8 [70.7–76.8] for baseline, 6 and 10 weeks respectively, $p < 0.001$). However, heart rate reduction does not alter the circulating chemokine environment in this cohort. No significant difference was observed in the concentration of: RANTES ($p = 0.146$), eotaxin ($p = 0.363$), MIP-1 α ($p = 0.159$), IL-8 ($p = 0.369$), MIP-1 β ($p = 0.705$), MCP-1 ($p = 0.100$), IP-10 ($p = 0.431$) or MIG ($p = 0.746$) and heart rate at any time point

Conclusions: Ivabradine had no effect on the peripheral chemokine profile in this cohort, despite significant heart rate reduction. This suggests that while being effective in lowering heart rate, Ivabradine has no systemic effect on cellular trafficking following heart transplantation.

P141

COMPARISON OF TPE CHANGES ON ECG PRE & POST-DIALYSIS AND AFTER TRANSPLANTATION

Ali Monfared, Mohammadreza Feizkhal, Ehsan Kazemnezhad, Mohammad Asadian, Masoud Khosravi, Mohammadkazem Leبادi
Urology Research Center, School of Medicine, Guilan University of Medical Sciences

Introduction: According to Tpe index and T wave analysis in predicting dangerous arrhythmias, in this study the effects of dialysis and renal transplantation on Tpe, Tpec, Qtc, Qtd, Tpe/Qtd parameters & also the association between electrolyte change, arterial blood gas and these parameters would be assessed.

Materials and Methods: In a retrospective study, 42 transplant patients in the case of not having the existing criteria were selected, under the supervision of a cardioelectrophysiologist information as well as electrolyte information, arterial blood gas (ABG) before & after dialysis, and after transplantation were analyzed.

Results: The mean Pre-dialysis and post-dialysis Tpe were respectively 0.063 ± 0.002 & 0.058 ± 0.002 ($p = 0.087$). Two weeks after transplantation, it was 0.052 ± 0.002 which was significant before ($p < 0.001$) & after dialysis ($p = 0.019$). The mean pre-dialysis and post dialysis TpeC were 0.0672 ± 0.003 & 0.0614 ± 0.002 which was statistically significant ($p = 0.030$). After transplantation, it was 0.059 ± 0.002 , that just comparing to pre-dialysis was significant ($p = 0.005$). The mean pre-dialysis and post-dialysis QTD were respectively 0.073 ± 0.005 & 0.070 ± 0.004 ($p = 1.000$). After transplantation, it was 0.066 ± 0.004 which wasn't significant before and after dialysis. The mean pre-dialysis and post-dialysis Tpe/Qt was respectively 0.162 ± 0.006 & 0.146 ± 0.005 which was a significant change ($p = 0.014$). After transplantation, it decreased to 0.143 ± 0.005 , comparing to pre-dialysis it was significant ($p = 0.018$). The mean pre-dialysis and post-dialysis QTC were respectively 0.396 ± 0.005 & 0.403 ± 0.005 ($p = 0.319$). After transplantation, it decreased to 0.386 ± 0.004 , comparing to post-dialysis it was significant ($p = 0.0003$).

Conclusion: According to the role of Tpe in arrhythmia & amending it by a successful transplantation, it can be considered as an arrhythmogenicity index in end stage renal disease (ESRD), and a rationalization for improving the survival in transplant patients.

P142

FEAR OF WEANING? TRANSESOPHAGEAL ECHOCARDIOGRAPHY (TEE) MANAGEMENT IN PATIENT WITH PRIMARY GRAFT FAILURE (PGF) AFTER HEART TRANSPLANTATION (HTX) AND EXTRA-CORPOREAL SUPPORT

Gianluca Santise, Giuseppe Raffa, Gabriele Di Gesaro, Sergio Sciacca, Maria Scarlata, Simona Servetti, Marco Turrisi, Vincenzo Stringi, Alessandro Armario, Michele Pilato
ISMETT

Background: Echocardiography is fundamental in managing patients with PGF after Htx supported by extra-corporeal membrane oxygenation (ECMO) from cannula placement to weaning decision. Several echocardiography parameters as well ejection fraction (EF) >35% to 40%, an left ventricular (LV) outflow tract velocity-time integral >10 cm, absence of LV dilatation, aortic valve opening (AVO) rate and eventually, mitral regurgitation (MR) degree may predict a successful weaning. The aim of our study is to analyze the role of TEE in complications detection, cardiac recovery and readiness for ECMO weaning in patients with PGF.

Methods: Over 104 orthotopic HTx performed between 2006 and 2013, 10 patients developed PGF requiring ECMO and IABP support. TEE was performed daily to: 1) exclude ECMO dysfunction 2) evaluate: EF, left ventricular end diastolic diameter (LVEDD), AVO, degree of MR; 3) establish the optimal weaning time.

Results: The mean age was 46 years and eight were male. Four patients had severe MR. Central/peripheral ECMO ratio was 6/4. Mean support time was 139 h. During ECMO support TEE evaluation evidenced: 1) pericardial effusion compressing heart chambers despite a properly ECMO flows (patients); 2) no adequate AVO requiring decreasing ECMO speed in one; 3) EF improvement (mean 18% to 66%), decreasing of MR, conserved LVEDD (mean 53.5 mm) and increased AVO rate (Fig 1). Eight patients were successfully weaned from ECMO (average length of support 6.1 ± 2.3 days) and 7 (70%) survived to hospital discharge and are still alive. Causes of death were multi organ failure.

Conclusion: TEE is a powerful tool to monitor the heart during ECMO support. Despite early complications detection as well strict cardiac recovery monitoring by daily TEE can favorable affect weaning successful rate, the decision to wean and its timing are still a complex issue.

P143

VAP-1 AND RENALASE IN HEART AND KIDNEY TRANSPLANTATION

Jacek Malyszko¹, Piotr Przybylowski², Ewa Koc-Zorawska¹, Michal Mysliwiec¹, Jolanta Malyszko¹

¹Department of Nephrology and Transplantation; ²Department of Cardiac Surgery and Transplantation

VAP-1 (vascular adhesion protein-1) is a copper-containing SSAO (semi-carbazide sensitive amine oxidase) secreted by vascular smooth muscle cells, adipocytes, and endothelial cells. Elevation of SSAO activity is observed in atherosclerosis, diabetes mellitus and obesity. Renalase, a novel protein believed to participate in the regulation of blood pressure, is also monoamine oxidase, present in endothelial cells. Considering all these data, the aim of the study was to assess VAP-1 and renalase in 128 prevalent patients after orthotopic heart transplantation [OHT] (96 males) and 130 renal allograft recipients (90 males).

Methods: Complete blood count, urea, serum lipids, fasting glucose, creatinine, were studied by standard laboratory method. We assessed VAP-1 and hsCRP with commercially available assays.

Results: The mean serum VAP-1 in OHT and Tx was significantly higher comparing to the control group (231.00 ± 88.62 vs. 158.34 ± 56.89 ng/ml, $p < 0.01$ and 239.83 ± 115.12 vs. 158.34 ± 56.89 ng/ml, $p < 0.01$, respectively). The same applied for renalase. In heart transplant recipients VAP-1 correlated with age, presence of diabetes, insulin therapy, ejection fraction, eGFR by MDRD, eGFR by CKD-EPI, use of tacrolimus, LVIDD left ventricular internal end-diastolic dimension, NYHA class, NT-proBNP. Diabetic patients ($n = 13$) had higher serum VAP-1 than non-diabetic (280.68 ± 81.16 ng/ml vs. 225.83 ± 88.79 ng/ml, $p < 0.05$). Patients with eGFR below 60 ml/min had higher VAP-1 when compared to those with eGFR ≥ 60 ml/min (261.84 ± 112.16 ng/ml vs. 222.81 ± 82.07 ng/ml, $p < 0.05$). The same applied for renalase. In multiple regression analysis VAP-1 was predicted in 25% by LVIDD (beta value 0.23, $p = 0.049$), and use of tacrolimus (beta value -0.27, $p = 0.048$), $F = 2.94$, $p < 0.00685$, $SE = 81.94$. In multiple regression analysis VAP-1 was predicted in 25% by LVIDD, and use of tacrolimus in OHT. Diabetic kidney transplant patients ($n = 17$) had higher serum VAP-1 than non-diabetic (265.74 ± 49.31 ng/ml vs. 205.05 ± 97.79 ng/ml, $p < 0.05$). Patients with eGFR below 60 ml/min had higher VAP-1 when compared to those with eGFR ≥ 60 ml/min (254.54 ± 134.87 ng/ml vs. 184.43 ± 68.87 ng/ml, $p < 0.05$) similar findings were observed for renalase. In kidney transplant recipients VAP-1 correlated only with time after transplantation, and serum glucose. There were no predictors of VAP-1 in multiple regression analysis.

Conclusion: VAP-1, elevated in heart transplant recipients, is predominantly dependent on left ventricular diameter and use of tacrolimus, however, precise associations between VAP-1 and immunosuppressive regimen warranted further studies. VAP-1, elevated in kidney transplant recipients might be related to glucose control. Renalase appeared to related mainly to kidney function.

P144

PUS BONUM ET LAUDABILE ? – WOUND HEALING COMPLICATIONS AFTER HEART TRANSPLANTATION IN THE 21ST CENTURY

Martina Gröemmer, Arezu Aliabadi, Olivia Salameh, Günther Laufer, Andreas Zuckermann

Cardiac Surgery, Med. University Vienna

Background: Today transplant recipients are older, sicker and have more comorbidities than in earlier eras. The aim of this analysis was to evaluate incidence, risk factors and outcome after sternal-wound complications in a current heart transplant cohort

Methods: A retrospective analysis was performed in 534 heart patients, transplanted between 1998 and 2011. Complications were defined according to tissue involvement and presence of infection. Therapy was defined as conservative or surgical. Risk factor analysis was performed to evaluate previously published variables. Survival was compared between patients with versus without wound complications by Kaplan Meier analysis.

Results: Twenty-six (4.9%) patients developed sternal wound complications. 15.4% of cases were non-infectious complications, whereas 61.5% were bacterial and 23.1% were fungal infections. Tissues involved were skin/subcutaneous (61.5%), deep soft tissue (15.4%) or sternum/retrasternal space (23.1%). Median time to bacterial and non-infectious complication infection was shorter than in fungal infections (24 vs. 110 days). Conservative therapy was used in three cases (11.5%) whereas surgical therapy was used in 23 (88.5%). In 17 patients (77%) vacuum assisted closure therapy was used; six underwent (23%) surgical debridement. We identified six significant risk factors ($p < 0.05$): transfusion requirement post transplantation (12.9% vs. 2.8%), preoperative status (stable 3.3%, hospitalised 2.15%, inotropic support 8.9% versus assist device 10.8%), primary graft dysfunction (9.3% vs. 3.9%), body mass index ≥ 30 (14.3% vs. 4.2%), and preoperative intubation (28.6% vs. 4.6%). 6 and 12 month survival of patients with infection was significantly lower in patients (6-months: 74.1% vs. 86%; 12-months: 66.4% vs. 84.5%; $p < 0.01$).

Conclusion: Sternal wound complications have not increased over time. Pre-transplant and peri-operative risk factors are associated with increased incidence. Wound infections are associated with decreased survival after TX.

P145

MINIMALLY INVASIVE TREATMENT OF TRICUSPID REGURGITATION AFTER HEART TRANSPLANTATION

Sandro Sponga, Giorgio Guzzi, Cristian Daffarra, Enrico Spagna, Vincenzo Tursi, Ugo Livi
University Hospital

Background: Tricuspid valve insufficiency is common after heart transplantation (HTx) but need for replacement or repair is rare. Patients with signs of advanced right-sided heart failure are considered at higher risk for surgery. Aim of this study is to evaluate if a minimally invasive approach for tricuspid valve surgery can guarantee better results.

Methods: We reviewed our overall experience between 1985 and 2012 (497 HTx). Five patients (1%) developed symptomatic severe tricuspid regurgitation (TR) with right ventricular failure requiring surgical treatment after a mean interval of 81 (8–138) months after transplantation. TR mechanism was: leaflet prolapse due to chordal rupture after biopsy injury in three patients, leaflets theating in 2, both combined with annular dilatation. Surgical approach was right minithoracotomy, peripheral vessels cannulation for extra corporeal circulation, and beating heart procedure.

Results: Treatment was bioprosthetic valve replacement in three patients, ring implantation in 2. Two patients died due to refractory right ventricular failure despite temporary mechanical circulatory support. One patient developed renal failure and cerebral ischemia, one needed prolonged ventilatory support. During follow-up (27 ± 13 months), survivors improved their functional NYHA class (<2 in all), had no recurrence of right failure with minimal dose of diuretics (furosemide 25–75 mg/die), and no prosthetic or repair failures occurred.

Conclusions: Treatment of patient with right failure due to tricuspid regurgitation after HTx is associated with high morbidity and mortality even if minimally invasive technique is employed. Early surgery could get better results.

P146

CD34/CD45 POSITIVE CELLS CONCENTRATION IN PERIPHERAL BLOOD OF HEART RECIPIENTS BEFORE AND AFTER HEART TRANSPLANTATION

Olga P. Shevchenko¹, Rivada Kurabekova¹, Vitaliy Poptsov¹, Nadezhda Kuncovich¹, Timur Khalilulin¹, Svetlana Lugovskaya², Elena Naumova², Ekaterina Spirina¹, Vladimir Dolgov², Sergey V. Gautier¹

¹Federal V. Shumakov Research Center of Transplantation and Artificial Organs; ²Russian Medical Academy of Postgraduate Education

Background: It is proposed that circulating hematopoietic stem cells (HSC) may have some impact on pathogenesis of cardiac allograft vasculopathy (CAV). It was shown that in heart recipients high plasma levels of placenta growth factor (PIGF), soluble CD40 ligand (sCD40L) and pregnancy associated protein A (PAPP-A) are negative predictors of CAV development. The aim of the study was to determine relationship of HSC number in peripheral blood before and after HTx with plasma level of the biomarkers.

Methods: We studied 42 pts. (33 men; 43 ± 15 years) with heart failure caused by ischemic (25 cases, 21 men; 51 ± 10 years) and dilated cardiomyopathy (17 cases, 12 men; 33 ± 12 years), 28 of them received HTx (22 men; 39 ± 14 years). HSC (as CD34/CD45 positive cells) were measured in peripheral blood by flow cytometry and expressed in mean number of the cells per 10⁶ events ± SD, plasma level of the biomarkers - by ELISA.

Results: The number of CD34/CD45+ cells in pts. with heart failure (196 ± 169) was similar to those in healthy individuals (208 ± 124) but there was significant difference ($p = 0.03$) in the cell number between pts. with ischemic (168 ± 159) and dilated cardiomyopathy (245 ± 195). The cell number did not correlate with age, sex, body weight, blood cells counts and preoperative levels of PIGF (25.9 ± 15.0 ng/l), sCD40L (5.0 ± 3.0 ng/ml) and PAPP-A (42.0 ± 20.7 mIU/L). In 2–5 days after HTx the cell number decreased to 96 ± 86, $p = 0.01$ and did not differ in pts. with previous ischemic (100 ± 86) or dilated (98 ± 97) cardiomyopathy. After HTx the cell number correlated with WBC ($r = -0.45$) and did not correlate with age, sex, body weight, ischemia and hypothermia duration, blood loss volume and preoperative level of the biomarkers.

Conclusion: Circulating HSC number is lower in pts. with ischemic cardiomyopathy than in those with dilated cardiomyopathy and decreases after HTx. The cell number before and after transplantation does not correlate with plasma levels of the negative predictors.

P147

CARDIAC TRANSPLANTATION IN A DEVELOPING COUNTRY: A TWENTY TWO YEARS SURVIVING PATIENT INTO A COSTA RICAN SOCIAL SECURITY SYSTEM

Eduardo Induni

Hospital México Caja Costarricense de Seguro Social

Background: To present the case of a patient who had a cardiac transplantation 22 years ago for severe ischemic heart disease in functional class IV who has a class I since then.

Methods/Materials: This was a 38 years female patient at the transplantation time, with a medical history of hyperlipidemia and smoking which had severe Coronary Artery Disease, with multiple myocardial infarctions, refractory angina and severe LV dysfunction. In 1991 an orthotopic cardiac transplant was performed with an ischemic graft period of 120 min. She required peritoneal dialysis during 10 days before being discharged at 21 postoperative days.

Results: The first endomyocardial biopsies revealed a light rejection grade 1a, becoming negative after six months. Her immunosuppressive therapy was based on Cyclosporine, Prednisone and Azathioprine scheme, drugs that she has tolerated very well and has been the immunosuppressive treatment with slight changes to present day. The follow up angiograms have been normal. Lately, she has had an appendectomy, salpingectomy and hysterectomy. The medical condition is overall good, receiving medication for hypertension, diabetes mellitus and hyperuricemia with a mild secondary renal failure. The last echocardiogram shows a slight aortic regurgitation with a 45% ejection fraction and type 2 diastolic dysfunction. She is in a NYHA 2 functional class with some knee movement limitation due to degenerative arthropathy. At the present time, she is 61 years old, currently living in a rural community, married and fully integrated to the society.

Conclusion: This case represents a landmark in the Social Security system of Costa Rica. The follow up after more than two decades reveals a prolonged survival time in a limited resources environment with an unique health system in Latin America. She is part of a group of patients (the first in Central America) admitted into a heart transplant program that started in 1990 with a one year survival of 80%.

P148

SINGLE CENTER EXPERIENCE WITH THE USE OF EVEROLIMUS AS PRIMARY DE NOVO IMMUNOSUPPRESSOR: 5 YEARS EXPERIENCE ON 47 PATIENTS

Cristiano Amarelli¹, Federica Agrusta², Daniela Pinto², Gianpaolo Romano¹, Claudio Marra¹, Emanuele Durante², Riccardo Utili², Ciro Maiello³

¹Monaldi Hospital, Azienda dei Colli; ²Second University of Naples; ³Monaldi Hospital, Azienda Ospedaliera dei Colli

Background: Long-term survival after heart transplant (HTx) is impaired due to rejection, opportunistic infections and malignancies, and metabolic disorders. Everolimus (RAD) has been introduced more recently and could affect in a different manner the most significant clinical end points. The aim of this study was to assess results of de novo immunosuppression with RAD + CyA in terms of death, graft failure, rejection, kidney disease and infections.

Methods/Materials: In a retrospective analysis of our single center experience, we studied 47 consecutive patients undergone heart transplant from 2006 through 2011. The clinical outcomes evaluated were death, graft dysfunction, infections, cancer, kidney disease and lipid abnormalities. Cytomegalovirus (CMV) replication was also assessed.

Results: Three patients died. Causes of death were cardiac allograft vasculopathy for one patient and a malignancy for two patients. Acute cellular rejection (ACR) occurred in 11 (23%) while cardiac functional impairment was observed in 12.7% in the RAD group. Opportunistic infections were observed in only two patients, but CMV infection or disease was observed in 8/47. After HTx, median eGFR declined up to 3 years post-transplant with a better profile in patients with GFR less than 60 (10 patients whose Renal function at 3 years was higher than the preoperative).

Conclusions: RAD use is associated on the short term with a low rate of CMV infections/disease. Renal function showed a decline on the long run clearly more evident in patients with a better preoperative renal function. This results could be related with the higher CNi exposure achieved in patients with good renal function. An aggressive reduction of CNi is desirable when using RAD as denovo primary immunosuppressor.

P149

ROLE OF EVEROLIMUS ON PROGNOSIS OF SOLID ORGAN MALIGNANCIES AFTER HEART TRANSPLANTATION: A FEEBLE LIGHT IN THE DARKNESS

Marco Masetti¹, Luciano Potena¹, Valeria Pece¹, Gaia Magnani¹, Maria Abbondanza Pantaleo², Margherita Nannini², Valentina Manfredini¹, Giorgio Isidoro Bianchi¹, Francesco Fallani¹, Francesco Grigioni¹, Angelo Branzi¹

¹Heart Failure and Heart Transplant Unit, University Hospital S.Orsola-Malpighi, Bologna; ²Department of Oncologica, University Hospital S.Orsola-Malpighi, Bologna

Background: Malignancies are a major cause of death after heart transplant (HT). While several risk factors have been suggested to promote carcinogenesis after HT, data about markers and strategies influencing outcome after cancer onset are lacking. The use of mTOR inhibitors reduces the occurrence of malignancies after transplant, and everolimus (EVE) has been registered for the treatment of several solid organ cancers in the general population, but its effect as immunosuppressant in HT recipients with a concurrent malignancy is unknown.

Methods/Materials: From clinical charts of all patients followed in our Center between October 1988 and July 2012, we collected data about cancer incidence, staging (presence (M1) or not (M0) of metastasis), treatment, immunosuppression, and 5-years survival after cancer diagnosis.

Results: Out of 500 patients, 71 (14.2%) developed a solid organ cancer (16.8 ± 2.2% at 10 years after HT), with a poor 5-years survival (43.4 ± 6.8%). Although cancer incidence did not differ between study eras (before-after 2002), after a standardized protocol for malignancy surveillance was established, cancer-related death (p = 0.02) and incidence of M1 status (47.9% vs. 19.0%, p = 0.02), significantly reduced. As expected, M1 predicted negative outcome (p < 0.01) while availability of surgical treatment was protective (p = 0.03). Treatment with EVE after cancer diagnosis (20 patients) was associated with a 64% reduction of relative risk for death (p = 0.01, Figure). Benefit of EVE therapy was more evident in patients who were M0 at diagnosis.

Conclusions: Despite several limitations, this study supports the concept that early diagnosis of solid organ malignancies after HTx may provide a more favorable prognosis, suggests the feasibility of an aggressive surgical treatment, and provide a strong rationale for the introduction of EVE as an effective rescue strategy in patients with malignancies, in particular in the subgroup diagnosed at early cancer stage.

P150

EXCELLENT LONG-TERM OUTCOME FOLLOWING ORTHOTOPIC HEART TRANSPLANTATION PERFORMED FOR ANTHRACYCLINE INDUCED CARDIOMYOPATHY

Ramesh Kutty¹, R.V. Venkateswaran², Clive Lewis¹, Pedro Catarino¹, Catherine Sudarshan¹, John Dunning¹, David Jenkins¹, Steven Tsui¹, Jayan Parameshwar¹

¹Papworth Hospital; ²Wythenshawe Hospital

Objectives: Advances in the oncological management of many cancers have led to improved cancer specific survival of patients. However, this leads to increased numbers of patients presenting with end stage heart failure caused by anthracycline induced dilated cardiomyopathy (AIDCM). Successful cases of heart transplantation for AIDCM have been reported, but their long-term outcome is unknown. This study evaluated the long-term outcome following heart transplantation for AIDCM.

Methods: All heart transplants performed in a single unit between January 2000 and November 2010 were retrospectively analysed. Patients with pre-transplantation diagnosis other than idiopathic DCM were excluded. The case notes of all idiopathic DCM recipients were reviewed to identify pre-transplant diagnosis of AIDCM. The pre-transplant parameters, incidence of acute rejection and infection were collected. The long-term outcome was analysed using Kaplan-Meier survival analysis.

Results: A total of 347 heart transplants were performed of which 164 (47.2%) were for DCM. Nine (5.5%) were performed for AIDCM; with 6 in the last 4 years. Five were male and mean age was 38 ± 19 years. Primary cancer sites included breast (3), acute leukaemia (3), lymphoma (1), hepatoblastoma (1) and sarcoma (1). Following treatment, the mean time to diagnosis of heart failure was 102 ± 41 months and 3 patients (33%) required urgent transplantation. Routine surveillance identified acute rejection in seven patients (77%). The 1 and 5 year survival was 100% and 71% respectively. Kaplan-Meier survival analysis showed no difference in the long-term outcome between AIDCM and DCM recipients (p = 0.64).

Conclusion: Heart transplantation for AIDCM is rare, with an apparent increase in incidence in the last 4 years at our centre. Development of symptomatic heart failure often appears late after initial cancer treatment. The immediate and long-term results are comparable to other DCM recipients.

P151

PSYCHOLOGICAL VULNERABILITY PREDICTS QUALITY OF LIFE HEART TRANSPLANT RECIPIENTS

Irena Milaniak¹, Ewa Wilczek Ruzyczka², Karol Wierzbicki³, Piotr Przybyłowski³, Jerzy Sadowski³

¹John Paul II Hospital; ²Andrzej Frycz Modrzewski Krakow University;

³Jagiellonian University, Collegium Medicum

Background: Heart transplantation (HT) can significantly improve the quality of life, but the patient will have to adapt to multiple limitations and other health problems. HT requires substantial personal, financial, and psychosocial resources. Purpose. This study investigates psychosocial vulnerability as a predictor of quality of life HT recipients.

Methods: One-hundred and nineteen patients after heart transplantation were assessed. Psychological vulnerability markers were cognitive beliefs (sense of coherence, optimism and self efficacy), affect (depression and stress). All participants completed a self-report quality of life instrument. Data was statistically analyzed.

Results: All psychological variables were associated with measures of quality of life heart transplant recipients. Cognitive variables explain 50% and affect 49% of the variance quality of life.

Conclusion: The multidimensional vulnerability model is suitable for predicting posttransplant quality of life. Patients with high vulnerability should receive ongoing psychosocial counseling.

P152

HYPOTHERMIC CONTINUOUS MACHINE PERFUSION IMPROVES METABOLIC PRESERVATION AND FUNCTIONAL RECOVERY IN HEART GRAFTS

Olivier Van Caenegem¹, Christophe Beauloye¹, Alain J. Poncelet², Peter Demuylder³, Pierre Gianello², Luc Marie Jacquet¹, Jean-Louis Vanoverschelde¹

¹UCL, Institut de Recherche Expérimentale et Clinique - pole of cardiovascular research; ²UCL, Institut de Recherche Expérimentale et Clinique - pole of surgical research; ³Organ Recovery Systems

Background: The number of heart transplants performed by year is declining since the 2000s because of organ shortage. Increasing the donor pool could be achieved by improving graft preservation. This would allow to prolong cold ischemic time or to use extended criteria donors. Hypothermic machine perfusion (MP) has been shown to better preserve kidney, liver or lung grafts. We investigated in a large animal model whether this would be the case in heart grafts.

Methods: Sixteen pig hearts were retrieved after cardioplegia and randomized to 4 h preservation on static cold storage (CS) or MP (Modified Lifeport® System, Organ Recovery Systems®, Itasca, IL). The preservation solution was KPS-1 in both groups. After preservation, the grafts were reperfused on a Langendorff during 60 min. Myocardial biopsies were performed at baseline, post-preservation and post-reperfusion to quantify oxidative metabolism by measuring lactate, nucleotides, phosphocreatine (Pcr) and creatine (Cr). Contractility index (CI) was assessed *in vivo* before cardioplegia with a Millar catheter and during reperfusion with an intraventricular balloon.

Results: Compared to MP, hearts preserved on CS showed significant higher lactate levels, higher AMP/ATP ratio and lower Pcr/Cr ratio after preservation and during reperfusion (Figure 1). Coronary flow was similar in both groups during reperfusion (CS = 107 ± 9 vs. MP = 125 ± 9 ml/min/100 g heart; p = ns). Compared to baseline, CI decreased by 25 ± 10% in the CS group while it remained stable in the MP group.

Conclusion: Compared to MP, hearts preserved on CS suffer more severe ischemia during preservation, as shown by a higher lactate and lower energy states. These differences remain after reperfusion despite equal coronary flow in both groups, probably due to oxidative defects in CS group. Functional recovery is better in the MP group.

P153

CORONARY HEART DISEASE RISK ESTIMATION AND ITS IMPROVEMENT WITH A GENETIC RISK SCORE IN PATIENTS WITH KIDNEY DISEASE

Emilio Rodrigo¹, Isaac Subirana², Sara Pich³, Carles Ferrer³, Gema Fernández-Fresnedo⁴, Ramón Brugada⁵, Roberto Elosúa², Manuel Arias⁴, Eduardo Salas³

¹Servicio de Nefrología, Hospital Universitario Marqués de Valdecilla, Santander; ²IMIM, Barcelona; ³Gendiag.exe, Esplugues de Llobregat; ⁴Servicio de Nefrología, Hospital Universitario Marqués de Valdecilla, Santander; ⁵Gencardio, Girona

Background: The spectrum of kidney disease (KD) is broad ranging from mild chronic kidney disease to end-stage renal disease, which requires dialysis and kidney transplantation. Coronary heart disease (CHD) is prevalent in KD patients, and contributes substantially to the morbidity and mortality of these patients. However, the classical CHD risk equations have shown limited clinical utility in KD patients.

Aims: The aims were: a) to develop and assess the predictive capacity of a CHD risk function based on clinical variables; and b) to evaluate whether the inclusion of genetic variants improve CHD risk estimation.

Methods: Our cohort study included 632 KD patients with a median follow-up of 9.13 years. Mean age was 53.4 (±10.6) years and 32.4% of the patients were male. Seventy three coronary events (fatal- or non-fatal acute myocardial infarct or acute angina) were identified in the follow-up. The clinical CHD risk score included KD status, age, sex, HDL, diabetic condition, hypertension condition, dyslipemic condition, hemoglobin A1c. In a second model, we also included a weighted genetic risk score (GRS) [Cardio inCode Score] with variants previously identified to be associated with CHD and not related with classical cardiovascular risk factors (rs10455872, rs12526453, rs1333049, rs17465637, rs501120, rs6725887, rs9818870, rs9982601, rs10507391, rs17222842, and rs9315051).

Results: The discrimination of the CHD risk function improved with the GRS (c-statistic = 72.0 vs. 68, p-value = 0.015). The calibration assessed by the Howmer Lemeshow test was 9.6, p = 0088 (i.e., calibration was good with no statistical differences between the events predicted and the observed). The reclassification of the patients also improved with the GRS (Net reclassification improvement = 22.0; 95%CI: 5.5; 38.6).

Conclusion: The inclusion of a GRS improves risk prediction of CHD in patients with KD. Genetic screening could help to prevent CHD events in this group of patients.

P154

STEROIDS WITHDRAWAL AND USE OF MYCOPHENOLATE ACID FOR MAINTENANCE IMMUNOSUPPRESSION IMPROVES SURVIVAL IN HEART TRANSPLANTATION: A SINGLE CENTER EXPERIENCE

Alain J. Poncelet¹, Thierry Timmermans², Olivier Gurne³, Anne-Catherine Pouleur², Dominique Latinne⁴, Olivier Van Caenegem³

¹Pole of surgical research, UCL, Institut de Recherche Expérimentale et Clinique; ²Cliniques Universitaires Saint-Luc; ³Pole of cardiovascular research, UCL, Institut de Recherche Expérimentale et Clinique; ⁴UCL, Institut de Recherche Expérimentale et Clinique

Background: Early severe rejection in heart transplantation has become unusual and drug-related morbidity accounts partially for the gradual attrition of the heart transplant population. Therefore, maintenance immunosuppression (IS) is now being investigated as improvement in late outcomes is still being contemplated.

Methods: A retrospective transversal study of 348 primary heart transplantation patients operated on between 1985 and 2006. Of the 302 first-month survivors, complete pharmacologic and angiographic follow-up was available in 296 patients (98%). Induction IS was used in all instances (ATG Fresenius). Maintenance IS was based on triple-drug therapy. Since 1996, an attempt to systematically withdraw steroids before 12 months was initiated. Study primary endpoints were patient/graft survival, severe cellular rejection and coronary allograft vasculopathy (CAV).

Results: Cyclosporin A (CsA) and tacrolimus were given in 230 and 62 patients, respectively. The antiproliferative drug was azathioprine (AZA) in 127 patients and mycophenolate acid (MPA) in 115 patients, while 53 patients received neither. Weaning from steroids was accomplished in 143 patients (48.3%). Conditional to one-month survival, patients had a 5- and 10-year survival of 81% and 64%, respectively. In univariate analysis, the type of calcineurin (CNI) used had no influence on survival. Maintenance IS with AZA (HR 2.4 [95%CI: 1.5-4]) or with steroids (HR 3.0 [95%CI: 2-4.5]) were both significant risk factors for death/graft failure. Neither incidence of severe rejection nor incidence of CAV was influenced by the type of CNIs or by the antiproliferative agent administered. However, patient still on steroids were at greater risk for developing CAV (HR 1.65 [95%CI: 1.03-2.63]).

Conclusion: This study confirms the beneficial effect of mycophenolate acid as the antiproliferative agent of choice and also supports our current practice of early steroids weaning, without additional risk.

PS09-DONATION / RETRIEVAL

P155

DONOR SAFETY IN LIVING DONOR LIVER TRANSPLANTATION IN A LOW VOLUME TRANSPLANT CENTER*Seong-Hwan Chang**Konkuk University School of Medicine*

Background: The safety of the donor after donation is still one of the main issues in living donor liver transplantation. We are going to evaluate the overall safety of living donors in our low volume center.

Methods: Among the 49 liver transplants, which is total number in our institution and starting from June 2006, 29 living donors of adult living donor liver transplantations, performed from June 2006 to December 2012, were analyzed.

Results: There was no operative mortality and no re-operation. The mean age of donors was 27.76. Mean remnant volume was 38.985%. The mean operation time was 5 h and 38.31 min. The mean hospital stay was 12.86 days. There was no intraoperative blood transfusion. There was one major complication which was biliary stricture and it was improved with endoscopic retrograde biliary drainage (ERBD). There were three minor complications which were one mild depression with poor diet, one wound infection, and one postoperative blood transfusion.

Conclusion: A well prepared transplant team could guarantee a favorable safety of donors even in a low volume transplant center.

P156

FEASIBILITY RESEARCH ON REASONABLE REIMBURSEMENT TO DONATIONS BY CARDIAC DEATH IN CHINA*Fei Teng¹, Youmin Wu², Zhengxin Wang¹**¹Shanghai Changzheng Hospital; ²New York Medical College*

The global shortage of organ donors has become the key factor halting the progress of organ transplantation. Research and trials have been made to expand donor banks in various countries, but problems of organ transplant tourism, organ trafficking and ethical debates follow at heel, which have aroused extensive attention and further reflection. In this article, we analyze possible strategies to narrow the donor-recipient imbalance, and explore the ethical preferences and ways of compensation to donations by cardiac death (DCD). In our opinion, the fixed compensation mode may be the most reasonable mode, given the actual situation in China at present. The total amount of compensation should be measured comprehensively according to the economic situation in different regions, the cost of transplantation there, and the interests obtained by both the donor and the recipient.

P157

LOCALISED WOUND TREATMENT IN HAND ASSISTED RETROPERITONEOSCOPIC DONOR NEPHRECTOMY*Sarah Heap¹, Yahya Khan¹, Mohammad A. Hossain¹, Nicos Kessar²**¹St George's Healthcare NHS Trust; ²Guys Transplant Unit*

Introduction: Hand Assisted Retroperitoneoscopic Donor Nephrectomy (HARDN) is an established technique for live renal graft donation that confers advantages over laparoscopic methods, potentially reducing complications. The incidence of seroma formation following kidney donation before and after the institution of localised wound treatment was observed.

Methods: Retrospective review of all live donor cases (June 2011 to June 2012). A comparison of two distinct groups was made. Group 1 – HARDN cases without a drain and Group 2 nephrectomy patients with routine insertion of 10fr Redivac drain. Seromas diagnosed clinically and/or with Ultrasound in outpatient clinics.

Results: In group one there were a total of six seromas ($n = 24$, mean BMI 26.9). Three were aspirated in clinic (mean volume 40 ml) and three underwent drainage (mean vol. 123 ml). In group two, only one seroma was diagnosed. ($n = 24$, mean BMI 26.6) which spontaneously discharged.

Conclusion: The reduced incidence of seroma formation in Group 2 favour localised wound treatment in patients undergoing HARDN. It is now routine practice at our unit to insert a superficial operative drain in all live kidney donors.

P158

PROFILE OF DECEASED ORGAN DONATION IN A GOVERNMENT HOSPITAL*Rose Marie Liquete¹, M.A. Zsarin Tuazon²**¹InfORT, Inc., QMMC-AUFMC; ²QMMC*

Introduction: Despite the Organ Donation Act of 1991 organ donation in the Philippines barely advanced. The Quirino Memorial Medical Center is a typical

government facility lacking in logistics and manpower, but networking with a private foundation can push forward the frontiers of transplantation.

Objective: To analyze organ donation activity at the QMMC and identify factors that influence family decisions and make recommendations.

Method: Referred cases for donation and interview data of donor families were analyzed.

Results: From 2010 to 2012, 60/209 (29%) of head trauma admissions at QMMC became brain dead but only 37 (62%) were referred for organ donation. Together with 13 other non-trauma patients, 50 potential donors were evaluated. Only 21/50 (42%) were found suitable for donation. Donor creatinine ranged from 37.9 to 187.38 mmol/l (mean – 97.52). It took 10–93 h (mean – 34 h) for them to deteriorate to brain death from time of injury, and 6–17 h more (mean – 15 h) from brain death to retrieval. Retrieved were 41 kidneys, one liver and six corneas. There was doubling in the annual referral (11–23 cases) implying increased awareness, being a transplant center, with a surgical residency program and a neuroscience institute. However, actual retrieval declined annually from 46.6% to 19.4%. This is attributed to more fatal injuries, late referrals and comorbidities. Some families still have misconceptions. In decision-making, opinions of distant relations, common law partners and friends had always played a pivotal role. Cost of donor maintenance were shouldered by the private foundation.

Conclusion: Government hospitals can partner with private entities for logistics to intensify advocacy, improve neurointensive care and address misconceptions and fallacies.

P159

MINI-INVASIVE LIVING DONOR NEPHRECTOMY USING THE HAND-ASSISTED LAPAROSCOPIC TECHNIQUE: OUR FIRST EXPERIENCE*Jacopo Romagnoli¹, Maria Paola Salerno¹, Nizam Mamode², Francis Calder³, Josè Alberto Pedrosa¹, Evaldo Favi¹, Gionata Spagnoletti¹, Valentina Bianchi¹, Franco Citterio¹**¹U.O. Trapiantologia Renale, Università Cattolica del Sacro Cuore, Roma;**²Renal and Transplant Unit, Guy's & St Thomas' NHS Trust, London UK;**³Renal and Transplant Unit, Guy's Hospital, Guy's & St Thomas' NHS Trust, London UK*

Background: Hand assisted laparoscopic nephrectomy (HALN) is gaining popularity because of its increased safety, especially in the donor operation setting, and its positive impact on the donor pool. HALN has been recently introduced in our program, we report our initial experience with this mini-invasive technique.

Methods: From January 2011 to september 2012, 43 patients underwent HALN via a transperitoneal approach, using a manual assistance device. Indications were living donation in 38 patients, native kidney tumors of small size (<3 cm) in five patients. Surgical blood loss, operative time, warm ischemia time, intra and postoperative complications and length of stay were also recorded.

Results: Mean operative time was 219 min (range 180–295), mean blood loss 105 ml (range 50–280), mean warm ischemia time 1.9 min (range 1.0–3.5). All transplanted kidneys displayed immediate function. There were no deaths, no conversions to open surgery, no intraoperative complications, no major postoperative complications except for one pulmonary microembolism in a female donor successfully reversed with i.v. heparin. Minor postoperative complications were one wound infection requiring readmission and open drainage, one wound seroma, treated conservatively, two cases of prolonged postoperative ileus requiring NG tube positioning and iv fluids for 48–72 h, 1 UTI treated with oral antibiotics. All patients were restarted on oral intake on postoperative day 1, mean post-operative in-hospital stay was 3.7 days (range 3–10).

Conclusions: Our initial experience confirms that HALN offers several advantages in terms of safety, minimal blood loss and short postoperative stay. It is a relatively easy technique compared to the pure laparoscopic approach, allowing for a shorter learning curve, especially considering the transition from an open technique. HALN is now the preferred method in our unit and our first results are encouraging.

P160

TELEPHONE SURVEY AFTER DONATION*Nicola Campe, Detlef Bosebeck, Thomas Breidenbach,**Angelika Eder**Deutsche Stiftung Organtransplantation*

Background: Trustful cooperation between the organ procurement organisation (DSO), and the donor hospitals is essential. The "Region Bayern" of the DSO established a telephone survey after organ donation. Hospitals get the possibility to discuss problems and comment the donation process.

Methods: The telephone surveys were conducted under the following conditions: -skilled and informed coordinator ("caller"), not involved in donation process himself -caller contacts physician who was responsible for organ donation in the hospital Due to results from our first evaluation in 2011 we

focused from 2012 on following categories. -feedback on conflicts and problems during donation process -unsolved questions -problems in the hospitals themselves

Results: Nine hundred and fifty-four surveys were analysed between 2006 and 2012. In 2012 reported problems or need for action increased significant. (2006-2012: 25%; 2012 41%) Details will be presented.

Conclusion: In time of staff shortage the telephone survey can be a simple tool to improve continuously the relationship to donor hospitals and the organ donation process.

P161

EVALUATION OF THE STAKEHOLDERS IN THE DONATION PROCESS: THE COORDINATOR'S VIEW

Nicola Campe, Uta Tessner, Thomas Breidenbach, Angelika Eder
Deutsche Stiftung Organtransplantation

Background: Organ donation in Germany is a complex process with many different stakeholders. The process is coordinated by staff (coordinators) from the German organ procurement organisation, which are not employees of the donor hospital. In 2011 the "Region Bayern" started a questionnaire to detect problems in the donation process caused by collaboration with different stakeholders.

Methods: The questionnaire is filled out by the coordinators following the organ donation and evaluates the following stakeholders: hospital staff, explant surgeons, eurotransplant, and other service providers. Two hundred and forty-eight questionnaires are evaluated.

Results: In 32% one or more problems were documented: The main problems (73%) were reported in collaboration with hospital staff (e.g. lack of medical knowledge, family approach, access to the operating theatre, etc.). In 14% coordinators reported about problems with surgeons and in 13% with other service providers.

Conclusion: In the German transplant law organ donation is a common task of all hospitals in cooperation with the organ procurement organization. However, the separation of responsibilities and additional work load is often a problem leading to little appreciation of the organ donation. Reasons and solutions will be presented.

P162

EXPANDING THE DONOR POOL IN THE EMILIA-ROMAGNA REGION

Angelo Ghirardini, CarloDe Cillia, Lorenza Ridolfi
Emilia - Romagna Transplant Reference Center

Introduction: Aim of this study is to explain the model applied in Emilia-Romagna region to expand the donor pool.

Methods: We shared the process in seven steps (Identification, Consent, Evaluation, Maintenance, Allocation, Retrieve and Transplantation) and analyzed the measures adopted over the years in order to expand the donor pool.

Results Identification: The Donor Action program was implemented in 1998 allowing about 200 potential donors/year; analysis of potential donors outside the ICUs was implemented in 2005. Consent: information regional campaign started in 1996 as well as education programmes for nurses and doctors.

Maintenance: National Guidelines were continuously implemented at regional level. Evaluation: regional Microbiology and Pathology laboratories are available 24/24 h; Adohners programme to improve heart donors started in 2005. Allocation: infective (506 organs transplanted) and neoplastic (141 organs transplanted) risk donor programmes started in 2003; allocation patient oriented was implemented.

Retrieve: Perfusion Machines for kidney are in use. Transplantation: living kidney and liver transplantations were performed.

Conclusion: This study shows that multidisciplinary organization is paramount to expand the donor pool.

P163

RESULTS OF THE DONOR ACTION PROGRAM IN THE EMILIA-ROMAGNA REGION

CarloDe Cillia, Maria Bonanno, Angelo Ghirardini, Lorenza Ridolfi
Emilia - Romagna Transplant Reference Center

In order to reach high quality levels in organ donation, Donor Action program (DA) started in 1998, to check whether all brain deaths are diagnosed, referred and assessed in Emilia-Romagna ICUs.

Methods: The program involved 29 regional ICUs, seven belonging to hospitals with neurosurgical department, identifying deceased patient charts through the regional computer network by 22 Hospital Transplant Coordinators collaboration, to avoid missing any potential donor.

Results: Total deaths in ICUs rose from 1998 to 2012, in spite of a decrease in the percentage of deaths with severe brain damages on total deaths (43.9% vs. 20.15%) and a significant increasing brain death assessments (86 vs. 198). In the last years is reported a decrease of family refusals too. Over the years, organ donation improved and transplant centres achieved high level activity standards.

Conclusions: Despite severe brain damage death reduction, a remarkable brain death assessment gain was observed in Emilia-Romagna ICUs. These results confirm that: a) DA is an efficient quality control program in ICUs; b) it is correct to extend identification of brain injured patients in departments other than ICUs.

P164

SOME SHADES OF GREY IN ORGAN PROCUREMENT: A REVIEW OF LAZIO SITUATION SINCE 2000

Gianfranco Teti, Roberta Durante, Paola Piovano, Aurela Meçule, Teresa Altobelli, Nicola Tortone, Maurizio Valeri, Domenico Adorno
Centro Regionale Trapianti Lazio

Some shades of grey in organ procurement: a review of Lazio situation since 2000 Background In the first 13 years organ procurement in Lazio was changed, both from a qualitative and a quantitative point of view: since 2004 Regional Transplant Coordination Center of Lazio (CRTL) manages on line all the donation and transplant activities of organs and tissues in Lazio.

Material/Methods/Results: If we compare the year 2000 to the 2012, we can observe different data.

Conclusions: But we have not to read these data like two well defined situations, or two colours: black or white. Many factors have changed the evolution of organ procurement towards the present situation in Lazio. Maybe we should analyze all this information like different shades of grey, to find a path from 2000 to this day.

P165

DEVELOPMENT OF THE DECEASED ORGAN DONATION SYSTEM IN A CARIBBEAN COUNTRY: SEUSA MODEL

Maria Paula Gómez¹, Marti Manyalich¹, Anton Fernandez², Jose Garcia-Buitron², Lesley Ann Roberts³, Bridgit Elcock⁴, Prisca Bradshaw⁵
¹DTI Foundation; ²Juan canalejo Hospital; ³NOTU; ⁴Port of Spain hospital; ⁵San Fernando Hospital

Background: The WHO approved on 2010 the "Madrid Resolution" to achieve self-sufficiency in organ donation for transplant. SEUSA is a model to improve the organ donation and transplant based on the best practices of the Spanish, European and USA systems. The objective of the present study is to collect evidence of the effectiveness of the SEUSA model and to analyze what are the adjustments needed depending on the country. SEUSA was implementing in South of Italy (La Puglia) and Lebanon increasing the deceased organ donation.

Methodology: The SEUSA included following phases: (i) To Diagnosed the organ donation and transplantation activity through the "Organ Donation Diagnosis Survey" (ODDS); (ii) Establishment of the Transplant Procurement Management Team; (iii) Implementation of the "Deceased Alert System" (DAS); (iv) Application of the "Essential in Organ Donation" (EOD) and 5) Hospital Audit. Monthly monitoring meetings to make needed adjustments based on the specific characteristics of the country were done.

Results: During the 4 years before of the SEUSA model implementation, two deceased organs donors were procured in Trinidad. The SEUSA Started in July of 2010, it has been implemented the phases 1-3. In 2012, 167 alerts of possible Donor Circulatory Death and 35 alerts of possible Donor Brain Death happened, 13 cases were diagnosed as Brain Death and seven family approaches were done. Seven forensic cases reported and one authorized. Finally two actual donors were obtained in one year. The main reason that explains the difficulties of the organ procurement was the lack of guidelines when a coroner case occurs.

Conclusion: The application of the SEUSA model helps the countries to identify their main obstacles in deceased organ donation as well as help to improve the technical knowledge and the Transplant Procurement Management capacity of the healthcare professionals involved.

P166

BRAIN DEAD DONORS DUE TO PRIMARY BRAIN TUMORS: GOOD SOURCE OF HEART AND LUNG FOR TRANSPLANTATION

Fariba Ghorbani, Omid Ghobadi, Keyhan Hadisadegh, Shadi Shafaghi, Katayoun Najafzadeh

Lung Transplantation Research Center, Masih Daneshvari Hospital, Shahid Beheshti University of Medic

Background: From non-head trauma brain dead donors, organs and recipients of donors with primary brain tumors (PBT) and donors of Cerebrovascular Accident (CVA) or Hypoxemia were compared together.

Methods: Between 2003 and 2011, 83 and 492 organ transplantations were performed from 24 brain dead donors with PBT and 164 donors with CVA or hypoxemia respectively. In cases of cranial manipulation determined histology of tumor was evaluated, otherwise neurologist's opinion was assessed for decision making about the risk of donating the organs. Ratio of procured Organ quantity per donor, tumor transmission and rate of suitable lung and heart were compared in brain tumor donors (group A) with CVA or Hypoxemia ones (group B).

Results: Twenty-four donors were in group A (6.09%) and 164 were in group B (48%). There was significant difference in organ per donor ratio (4 organ per donor in group A vs. 2.3 in Group B) ($p < 0.05$) and more suitable heart and lungs in group A. Mean follow up was 39 months and there was no report of transmission in group A.

Conclusion: In non-head trauma donors, if the donors with brain tumor are selected carefully, with higher rate of the usable organs they are a good source of organs specially heart and lung for transplantation. Keywords: Brain death, brain tumor.

P167

WHAT CAN EFFECT ON THE RATE OF SPINAL REFLEXES IN BRAIN DEAD

Mahsa Hosseini, Omid Ghobadi, Mahdieh Hazrati, Fariba Ghorbani, Katayoun Najafzadeh

Lung Transplantation Research Center, Masih Daneshvari Hospital, Shahid Beheshti University of Medic

Background: Diagnosis of brain death is determined when loss of all brain stem reflexes and apnea is permanently observed. Reflex motor activities known as spinal reflexes occur frequently in brain-dead and they do not disprove the diagnosis of brain death. This study aimed to evaluate the association between different factors and rate of medullary reflexes in brain-dead.

Methods: Brain-dead bodies transferred to the organ procurement unit of Masih Daneshvari Hospital during a one year period starting from June 2011 were evaluated for the spinal reflexes. Demographic characteristics, vital signs; serum electrolytes and arterial blood gases were compared among those with or without reflexes.

Results: Forty cases (33%) of the heart beating cadavers in this study showed one or more spinal reflexes. Mean systolic blood pressure was 126 ± 19 vs. 116 ± 17 in patients with and without reflex and this was the only significant difference between these two groups ($p = 0.007$).

Conclusion: This study showed that spinal reflexes are more probable to occur when heart beating cadavers become hemodynamically stable. Enhancing awareness about these reflexes among medical team is essential to reduce uncertainty about the death and afterward organ donation. Keywords: Brain death, spinal reflex.

P168

HOW THE RATE OF FAMILY CONSENT FOR ORGAN DONATION INCREASED FROM 32 TO 90% IN SBMU- OPU IN IRAN

Katayoun Najafzadeh, Omid Ghobadi, Fariba Ghorbani, Keyhan Hadisadegh, Hamid Reza Khoddami Vishteh

Lung Transplantation Research Center, Masih Daneshvari Hospital, Shahid Beheshti University of Medic

Background: Family consent is mandatory for organ donation in some countries like Iran and in countries like Spain that first person consent law has been approved, for preventing the bad effect on the society, organ donation is cancelled if the family refuses to donate. We in Shahid Beheshti University Organ Procurement unit, by changing our family interview system increased the rate of consent for organ donation significantly.

Methods: Only the coordinators with history of more than 60% success in taking consent were chosen for family interview. We also hired six knowledgeable & interested psychologists. Regular teaching classes were holding every other week for the interviewer group.

Results: With using experienced interviewers, without any other intervention, the rate of family consent for organ donation went up from 32% to 77.8% (25 out of 32 detected potential brain dead donors) in one month and stayed between 70-94% since then.

Conclusion: Brain dead family interview for organ donation is a science and needs to be done by experienced people. Keywords: Family consent, Organ donation.

P169

HOW COULD WE GET TO PMP OF 25 FOR ORGAN DONATION IN SHAHID BEHESHTI UNIVERSITY OPU OF IRAN

Katayoun Najafzadeh¹, Omid Ghobadi¹, Fariba Ghorbani¹, Hamid Reza Khoddami Vishteh¹, Badiozaman Radpay¹, Ali Khalili¹, Azizollah Abbasidezfouli¹, Zahra Ansari¹, Zargham Hossein Ahmadi¹, Mohammad-Reza Masjedf², Ali-Akbar Velayati²

¹Lung Transplantation Research Center, Masih Daneshvari Hospital, Shahid Beheshti University of Medic; ²Masih Daneshvari Hospital, Shahid Beheshti University of Medical Sciences

Background: The most important problem in our country such as the rest of the world is the shortage of organs for transplantation. We could recognize four

changeable aspects: 1- Donor detection 2- Family approach 3- Donor maintenance 4- Social awareness

Methods: We handled these problems with designing some new projects: 1- Creating a team consisted of some expert nurses for inspection of ICUs "Inspector project" 2- Training the coordinators and some psychologists for family approach 3- Active donor management right after detection 4- Performing many social awareness activities such as: 5- Online registry for Donor card 6- Taking cooperation of the other organizations such as mass media 7- Annual Organ donation celebration 8- Volunteers' project (using the volunteers help in social awareness activities)

Results: 1- Jumping the family consent rate from 32% to 90% 2- Increasing the PMP from 5.7 to 25 3- Improving the quantity and quality of retrieved organs

Conclusion: The mentioned projects have been the most effective way for increasing the pool of potential donors in Iran.

P170

INCREASING THE BRAIN DEAD POTENTIAL DONOR DETECTION RATE, INSPECTOR PROJECT

Omid Ghobadi, Katayoun Najafzadeh, Fariba Ghorbani, Keyhan Hadisadegh, Hamid Reza Khoddami Vishteh

Lung Transplantation Research Center, Masih Daneshvari Hospital, Shahid Beheshti University of Medic

Background: The most important step in organ donation process is potential donor identification. There are different methods for brain dead detection in ICU like regular call to ICU, having a person responsible for informing the OPU of brain dead, unexpected visits of ICU and in hospital coordinator. Shahid Beheshti University of medical sciences (SBMU) OPU as the most active Organ procurement Unit of Iran beside all of the above methods started a new project for detection of potential organ donors since July 2011.

Methods: Six experienced nurses were employed and were taught how to detect a brain dead. They started to visit all of the hospitals (108 hospitals) by a regular schedule. The rate of visits was defined according to the number of ICU beds and existence of neurosurgery ward.

Results: Mean rate of brain dead detection rose from 60 to 150 per month. **Conclusion:** Active ICU visit by trained inspectors is the most effective way for detecting all potential organ donors especially in developing countries which having in-hospital coordinators is not possible easily in all of the hospitals. Keywords: Brain death, potential donor, detection rate.

P171

BRAIN DEAD DONOR'S LUNGS ASSESSMENT OF MASIH DANESHVARI-OPU OF IRAN

Shadi Shafaghi, Sareh Parto, Shahabedin Mohammad Makki, Abolghasem Daneshvar, Frahnaz Sadeghbeygi, Jamileh Faeghi, Hamid Reza Khoddami Vishteh, Omid Ghobadi, Fariba Ghorbani, Katayoun Najafzadeh

Lung Transplantation Research Center, Masih Daneshvari Hospital, Shahid Beheshti University of Medic

Background: The shortage of suitable lung is a major cause of waiting list mortality of lung transplant candidates. Selecting inappropriate lung can lead to post operation complications. So, assessment of lungs in brain dead cases has an essential role. The aim of this study was to assess the lungs of donors step by step.

Methods: This study was performed on 127 donors of Masih Daneshvari OPU from August 2008 to August 2012. Evaluation was carried out in five steps including history taking and physical examination, chest-x-ray (CXR), O2 challenge test, recruitment maneuver and bronchoscopy. Finally, patients with normal CXR and bronchoscopy and PaO₂/FIO₂ > 300 mmHg were considered as a suitable candidates.

Result: Mean age of donors was 33 ± 14 year and 80 (63%) were male. Sixteen percent of cases had chest trauma and 58 (45.7%) had turbid tracheal secretion. CXR was abnormal in 49 (38.6%) cases. Recruitment was carried out in 31 donors who could increase the mean of PaO₂/FIO₂ significantly and finally 26 donors (20.5%) considered suitable lung donors.

Conclusion: Findings of this study showed that only one fifth of donors had acceptable lungs for transplantation that needs active interventions including recruitment maneuver. Keywords: Brain death, lung Assessment, lung transplantation.

P172

IMPACT OF MULTISLICE SPIRAL COMPUTED TOMOGRAPHY ON DONOR SELECTION AND SURGICAL PLANNING IN LIVING-RELATED LIVER TRANSPLANT

Ibrahim Abdelkader Salama¹, Basma Dessouky², Enas Korayem¹, Sayed Abdel Aal¹

¹National Liver Institute, Menophya University; ²Faculty of medicine, Menophya University

Objectives: Living-donor liver transplant is used with increasing frequency to help compensate for the increasing shortage of deceased-donor liver grafts.

However, donor safety is a primary concern, and selection of the preoperative imaging modality is important in preserving donor's health by excluding unsuitable candidates, and tailoring the surgical procedure according to anatomic variations. In this study, we evaluate the impact of multislice spiral computed tomography on potential donor selection and surgical planning before living-related liver transplant.

Materials and Methods: One-hundred seventy-five potential living-liver donors (62 women and 113 men; age range, 23–34 years; mean, 32 years) were included in our study. All subjects underwent multiphasic multislice spiral computed tomography. Postcontrast acquisitions were obtained for the arterial and venous phases. There were 139 potential donors for the right lobe and 36 potential donors for the left lateral segment. All data were analyzed to detect vascular variants, exclude focal liver lesions, and determine hepatic volume, and preoperative findings were correlated with intraoperative findings in 65 patients. **Results:** Of the 175 potential liver donors evaluated with multislice spiral computed tomography, 56 (32%) were excluded for the following reasons: portal vein anomalies in 11 (19.6%), hepatic venous anomalies in 9 (16.1%), fatty liver in 17 (30.3%), small liver volume in 12 (21.4%), and a focal lesion in the liver in 7 (12.5%). Of the 65 candidates, surgical planning and technique were modified in 24 donors and recipients, in 23 candidates, and the donor only in one candidate. **Conclusions:** Multislice spiral computed tomography provides parenchymal, vascular, and volumetric preoperative evaluation of potential donors for living-related liver transplant and has an effect on surgical planning: It allows the surgeon to reduce postoperative complications by modifying the surgical technique.

P173

INTERNATIONAL REGISTRY IN ORGAN DONATION AND TRANSPLANTATION (IRODAT)

Maria Paula Gómez¹, Martí Manyalich², Blanca Pérez¹
¹DTI Foundation; ²Hospital Clínic de Barcelona

Background: IRODaT is the first registry in this field, which contains statistics of deceased/living donors and transplants. Out of the 105 countries with organ donation or transplantation activity, 86 national reporters submit data to IRODaT.

Methods: IRODaT is a friendly, easy to use database. Reporters introduce the figures of their countries directly to the webpage. Experts validate and update the data. IRODaT staff process the information and produce different materials to meet users' needs and requirements.

Results: The registry enables the analysis of donation activity at national level. For example we are able to identify a decrease in donation activity in Austria from 24.3 dpm in 2006 to 23.5 dpm in 2011. A further analysis reveals an increase of donation activity between 2008 and 2009 when the rate reached 25 dpm. Currently Austria has higher donation rates than the European average rate of deceased organ donation. The new IRODaT work line aims at offering activity data at REGIONAL level. It will analyze regions with homogenous number of inhabitants helping to identify peer developments.

Conclusions: IRODaT is able to provide basic statistics within a short timeframe, based on a worldwide network of experts involved in organ donation and transplantation. The data have proved to be of an extreme value to scientific programs, social and governmental bodies.

P174

LESSONS LEARNED FROM REGIONAL VARIATIONS IN ORGAN DONATION IN SAUDI ARABIA

Hussien Elsiey¹, Faisal Abaalkhail¹, Almoataz Hashim¹, Mohammed Al Sebayel¹, Waleed Al Hamoud²
¹KFSHRC; ²King Saud University

Background and Aim: There is marked regional variation in organ donation among different region of Saudi Arabia. Mobile donor team was active in Central region since 2006. Our aim is to study the reasons for this variation in order to improve organ donation in areas of low donation rate.

Methods: Saudi Center for organ transplantation (SCOT) data for cadaveric organ donation from 2006–2011 detailing the number of cases reported, documented, consented and harvested, as well as the distribution by region (central 29.4% of the total population Saudi Arabia, western 32%, eastern 15%, northern 8%, southern 15.6%). The number of contributing ICU stratified by size of ICU and the region was also reviewed. The overall donation rate as well as the percentage of harvested cases per region as well as the conversion rate (harvested/Documented) was reviewed.

Results: Between 2006–2011, 448 cases procured from Saudi Arabia, of which 343 were procured from central region representing 76.5% coming from 30 out of 97 contributing ICU's (31%), the eastern region came second with 49 cases (11%) followed by the western region with 35 cases (7.8%) while northern and southern region had 12 and 9 cases (2.7&2%) respectively. The conversion rate followed a similar trend. This is related to the presence of active mobile donor team in Riyadh (the capital) as well as active transplant centers.

Conclusion: There is marked variation with regards of contribution to organ donation in different regions in Saudi Arabia from 2% in the southern area to 76.5% in central area. This is related to the presence of active mobile donor team in the central region. A similar trend towards increasing number of cases and conversion rate was observed in the eastern region after having a new

mobile donor team. We suggest that having active well trained mobile donor team in each region will increase the number of cadaveric donor at least 3 folds in the next 3–5 years.

P175

EXPANDING THE DONOR POOL FOR LIVER TRANSPLANTATION

Irinel Popescu, Mihnea Ionescu, Vladislav Brasoveanu, Doina Hrehoret, Emil Matei, Bogdan Dorobantu, Sorin Alexandrescu, Razvan Grigorie, Radu Zamfir
 Fundeni Clinical Institute

Aim: The organ shortage associated with the increased waiting list time have led to the acceptance of marginal donors. On the other hand, a "perfect liver" can expand the graft pool by using the split liver technique. The purpose of this study is to evaluate our liver transplantation experience using graft from deceased donors and alternative liver transplantation technique.

Patients and methods: From January 2010 to December 2012 we performed 191 liver transplantations, 146 by using grafts from deceased donors. There were transplanted 140 patients using whole graft technique and six patients using split liver technique. Donor and recipient data were analyzed by both uni- and multivariate Cox proportional hazard model analyses. The grafts from marginal donors were used in patients with hepatocellular carcinoma and liver cirrhosis (30 patients).

Results: Primary graft non-function was recorded in two cases (one in case of a marginal donor). Four patients were retransplanted (2 primary graft non-functions, one hepatic artery thrombosis and one ischaemic type bile lesion). The postoperative survival was 90% (27/30) in the series using the marginal donors and 92.7% (102/110) in all the other patients. There was no death recorded in the split liver group.

Conclusions: This discrepancy between the graft pool and the number of the patients on the waiting list can be partially solved by accepting marginal donors or by using the split liver technique.

P176

COULD A DECEASED POSSIBLE DONOR AFFECTED BY A RARE DISORDER BE ELIGIBLE FOR ORGAN DONATION?

Olivier Huot, Geraldine Malaquin, Jean Paul Jacob, Candide Font-Sala, Hervé Creusvaux, Christian Lamotte, Conte Ludovic
 Agence de la biomédecine, 93212 LA PLAINE SAINT DENIS Cedex France

Over the past 15 years organ donation criteria were extended to older or vascular BD donors in an attempt to overcome organ shortage. Among non-optimal donors, we performed a 5-years retrospective study to analyse the results of organ transplantations from donors affected by a rare disease. From January 2007 to December 2012 we found 388 donors with rare diseases in the French Agency of biomedicine registry out of 9250 donors (0.4%). Three hundred and thirty were retrieved. We classified diseases as neurodegenerative and non-neurological. Those procurement rates increased between 2007 and 2012, mainly (40%) in neurodegenerative diseases (ALS, multiple sclerosis, chorea etc., fig 1). The average number of organ retrieved was three per donor. The cohorts were rather young excepted for the neurodegenerative group whose average age was higher than the national one. Reasons for organ refusal was the rare disease status, either by following recommendations that the disease was a procurement contraindication (von Hippel, lymphoma) or by precautionary principle. The pathway of organs retrieved and accepted and the success of transplantation were studied 1 year, 3 years, and 5 years. Some of these diseases appear to have a significant transplant failure rate. For most of them (cohort 2007/2009) the 3-years survival looks identical to standard donors. This study showed that potential donors carrying rare disorders can be eligible and utilized donors and that organs pathway can be extrapolated in accordance to the type of pathology. Collaboration between Agency of biomedicine and "Orphanet" will develop eligibility sheets for these potential donors based on the literature and experience drawn from this study.

P177

OXIDATIVE STRESS AND APOPTOSIS IN A PIG MODEL OF BRAIN DEATH (BD) AND LIVING DONATION (LD)

Philipp Stiegler¹, Michael Sereinigg¹, Thomas Seifert-Held², Iris Wiederstein-Grasser³, Bettina Leber⁴, Florian Iberer¹, Elke Stadelmeyer⁵, Nadja Dandach⁵, Vanessa Stadlbauer-Köllner⁴

¹Department for Surgery, Division for Transplant Surgery, Medical University Graz; ²Department of Neurology, Medical University Graz; ³Division of Biomedical Research and Section for Surgical Research; ⁴Department for Gastroenterology and Hepatology, Medical University Graz; ⁵Department of Internal Medicine, Division of Oncology, Medical University Graz

Introduction: As organ shortage is increasing, the acceptance of marginal donors increases, which might result in poor organ function and patient

survival. Mostly, organ damage is caused during brain death (BD), cold ischemic time (CIT) or after reperfusion due to oxidative stress or the induction of apoptosis. The aim of this study was to study a panel of genes involved in oxidative stress and apoptosis and compare these findings with immunohistochemistry from a BD and living donation (LD) pig model and after cold ischemia time (CIT).

Methods: BD ($n = 6$) was induced in pigs; after 12 h organ retrieval was performed; heart, liver and kidney tissue specimens were collected in the BD and in a LD model. PCR analysis for NFKB1, GSS, SOD2, PPAR-alpha, OSXR1, BAX, BCL2L1, and HSP70.2 was performed and immunohistochemistry was used to show apoptosis and nitrosative stress induced cell damage.

Results: In heart tissue NFKB, GSS, SOD2, PPAR-alpha and HSP70.2 gene expression was higher in BD after 4 h of CIT; in liver tissue, BCL-2L1, GSS, OSXR1, NFKB1, SOD2 and BAX gene expression was significantly higher in BD after 6 h of CIT. No differences could be observed in kidney tissue. In all organs, activated caspase-3 and nitrotyrosine positivity was significantly higher in BD after CIT.

Conclusion: Our results showed an up-regulation in most of the genes encoding for enzymes protecting the organs from oxidative stress in BD; however after CIT apoptosis was more likely to occur in BD organs as compared to LD.

P178

RENAL AXIAL MALROTATION IN THE LIVING DONOR: SHOULD WE PROCEED?

Fiona Kelly, Mohammad Hossain, Sarah Heap

Department of Renal Transplantation, St Georges Hospital NHS Trust

Background: Outcome data of live donors with axially malrotated (AM) kidneys in the context of normal function is unknown. Unilateral AM is not an absolute contraindication for live donor nephrectomy. The decision to proceed is made on an individual basis at the multidisciplinary level, with anecdotal evidence. The estimated incidence of AM in a donor population is <1%, although may be larger in the general population. As such, a dilemma is faced as to whether it is appropriate to leave a healthy donor with a known anatomical abnormality in which long term outcome is unknown. This unknown can lead to the rejection of a suitable donor. In this report the outcomes of donors with a contralateral AM kidney are presented from the experience of a single UK centre.

Methods: Four potential donors presented over a 6 month period during 2012. CT angiogram of these patients demonstrated a unilateral right malrotated kidney. Split function was performed on all patients alongside routine screening protocols. In all cases, the left kidney was favored for donation due to vessel anatomy or function. Follow up after donation was undertaken and is currently on going.

Results: Three patients (all female, mean age 58 years) were selected for left donor nephrectomy, with the 4th declined due to a potential tumour on CT imaging. To date two patients have successfully donated the anatomically correct left kidney, with a 3rd awaiting paired exchange. Follow up serum creatinine at 1 week and 6 months for the first patient was 92 $\mu\text{mol/l}$ with no associated hypertension. The 2nd patients' renal function at 2 weeks was stable at 102 $\mu\text{mol/l}$. Her procedure was uneventful, and she was discharged without compromise to her renal function or blood pressure.

Conclusions: This report supports the safety of donor nephrectomy in the case of a contralateral AM kidney. The series provides evidence of good overall renal function at early follow up.

P179

POTENTIAL BRAIN DEATH ORGAN DONORS, CHALLENGES AND PROSPECTS. A SINGLE CENTRE REVIEW

Yousef Al Maslamani, Omar Ali, Riadh Fadhil, Ausama Abdul Muhsin, Abdel-Hadi Abu-Jeish

Hamad Medical Corporation

Objective: Brain death (BD) organ donation is an option for patients with end stage organ disease ESOD. The objective of this study is to evaluate the demographic criteria and challenges of organ donation among potential brain dead (BD) organ donor patients and plan a strategy to improve organ donation in Qatar.

Materials and methods: This retrospective review was carried out from January 2011 to April 2012. Various criteria of BD patients in the intensive care units (ICUs) of HMC, and possible reflection on organ retrieval were studied. The time intervals analyzed to determine the possible causes of organ retrieval delay were: time of diagnosing fixed dilated pupils in the ICU, to performing the first BD test, then second BD test, to family approach, to organ retrieval and/or circulatory death (CD) without organ retrieval.

Results: File records of 116 potential BD organ donor patients were reviewed of whom 96 (82.75%) were male and 20 (17.25%) were female patients. Brain hemorrhage and head injury contributed to 37 (31.9%), and 32 (27.6%) of BD cases respectively. Time interval between the diagnosis of (fixed dilated pupil) and performing first test of BD was delayed >24 h in (79%) of cases. Similarly time interval between first and second BD tests was delayed >6 h in (70.8%) of cases. This delay is not compatible with HMC policy for BD patients' management.

Conclusion: In addition to living donors, BD organ donation is a potential source for organs to save patients with ESOD. This source of donation

however, has pitfalls and every effort should be done to increase medical personnel awareness of proper management and maximum cooperation with transplantation team to optimize donation efficacy. Key words: Brain death (BD), organ donation, kidney.

P180

SOCIOECONOMIC FACTORS, RATHER THAN RACE, IMPACT ON CONSENT RATES FOR ORGAN DONATION

Delawir Kahn¹, Fiona McCurdie¹, Alexia Michaeledes²

¹University of Cape Town; ²Christiaan Barnard Hospital

Background: The critical shortage of donor organs remains a major limiting factor in organ transplantation. Strategies to increase the number of donor organs include improving public awareness about transplantation. However it remains unresolved whether these public awareness campaigns have made any difference. Thus the aims of the study were to measure consent rates for organ donation over the last 20 years and critically evaluate factors which influenced the consent rates.

Methods: All potential donors referred to two Transplant Units, one at the Academic Hospital (GSH) and one in the private sector (CBH), between 1991 and 2011 were included in the study. The families were asked about organ donation using standard counselling techniques. We analysed the consent rates at 5-yearly intervals.

Results: A total of 241 families were asked about organ donation and 134 (55%) agreed. The overall consent rates changed from 55% in 1991, to 55% in 2001 and 44% in 2011. In GSH the consent rates declined from 55% in 1991 to 50% in 2001 and to 32% in 2011. In CBH the consent rates have remained relatively stable at 73% in 2001, 94% in 2006 and 78% in 2011. The overall consent rates in white families were good at both hospitals (80% and 93%) and poor in black patients (33% and 33%). However the consent rates in families of mixed race was significantly higher in the private hospital (CBH) - 70% vs 40%.

Conclusion: The consent rate for organ donation is influenced by race but there are over-riding socioeconomic factors.

P181

ORGAN DONATION AND CONFIRMATORY TESTS FOR BRAIN DEATH DIAGNOSIS

Flavia Marini Paro¹, Pablo Cardozo Rocon¹, Larissa Pechincha Ribeiro¹,

Rayssa Florentina Scardua¹, Adauto Vieira de Almeida²

¹Universidade Federal do Espírito Santo; ²Associação Pró-Vidas Transplantes

Background: The realization of confirmatory test (CT) for brain death (BD) diagnosis is mandatory in Brazil and CT should demonstrate: absence of brain electrical activity or absence of cerebral metabolic activity or absence of cerebral blood perfusion. The objective of this study was to investigate whether difficulties in performing the CT contribute to reduce the number of BD notifications in three public hospitals in the state of Espírito Santo, Brazil.

Methods/Materials: This study was approved by the Ethics Committee for Human Experimentation of HINSG. Data collection was performed during 6 months, in 2010, from forms filled out daily by the Commission for Organ and Tissue Donation of the hospitals. The inclusion criteria were all patients who had opened the protocol for BD diagnosis, during the period of study, totaling 28 patients.

Results: For all 28 patients the cerebral angiography was used for BD confirmation, although these public hospitals didn't have infrastructure to perform this test and the patients had to be transported to other services where the CT was performed and driven back to the hospital. The BD was confirmed in 20 patients (71.43%). In eight patients (28.57%) CT could not be performed due to difficulties to schedule the test and patient transportation. One patient had cardiac arrest after CT. Only nine patients (32.14%) have become effective donors.

Conclusion: The data showed that difficulties in performing the CT contributed to reduce the number of BD notifications in the studied hospitals. In Brazil and other Countries, several hospitals use electroencephalogram or Transcranial Doppler to BD diagnosis confirmation in specific cases. These results demonstrate the importance of assessing which is the CT that best suits the needs of each service. In order to this, it is essential to consider scientific evidence, logistical and structural factors, hemodynamic status of the patients, needs of the examination at the bedside, costs, among other aspects.

P183

DECEASED ORGAN DONATION AND TRANSPLANTATION ACTIVITY IN THE KINGDOM OF SAUDI ARABIA: A DECADE OF PERSPECTIVE IN THE 21ST CENTURY

Faissal Shaheen¹, Beshar Al Attar¹, Mohammed Souqiyeh¹, Mohammed Kamal¹, Abdullah Al Sayyar²

¹Saudi Center for Organ Transplantation; ²King Abdul Aziz Medical City and National Guard Hospital - Riyadh

Objective: Organ transplantation is the best existing method for the treatment of end-stage organ failure. However, the need for viable organ supply limits its

progress; thus, we studied the algorithm of process for deceased heart beating donors with the rate of adapting the critical pathways of organ donation from possible to potential to eligible to consent and to actual deceased donors (DD) in the kingdom.

Methods: A retrospective study comparing the nationwide figures and composition of the Critical Pathway of DD cases in a decade from 2001–2005 vs. 2006–2010 to Saudi Center for Organ Transplantation (SCOT).

Results: The Study showed a remarkable increase in the total number of Possible Deceased Donor cases from 1827 of 2001–2005 to 2651 (+45%) of 2006–2010. The mean possible case per year in relation to the number of population for the first half of the decade is 16 PMP as compared to 22 PMP in the last 5 years of the decade. The rate of conversion from possible to potential is 63% (1151 and 1674 respectively). Moreover, Eligible Donors ascends its number from 956 to 1336 (+39%) of which 270 (28% with 2.2 PMP) and 511 (38% with 4.1 PMP) respectively were consented for organ donation. The Actual DD for the year 2001–2005 was 248 and 453 for the year 2006–2010. As a result, the number of Utilized DD organs increased from 244 to 441 (+81%) cases.

Conclusion: There is a notable increase in the number of Possible DD reported and consented in the second half of the decade. There is also a significant increase in the Actual DD. In relation to this, the various strategies being implemented to promote organ donation in every region of the kingdom are relatively effective in applying the critical pathways of deceased organ donation.

P184

DO WE USE TWO CONCEPTS OF DEATH: ONE FOR ORGAN RECOVERY AND ANOTHER FOR DEATH CERTIFICATION?

Maciej Kosieradzki¹, Roman Danielewicz², Tomasz Kubik³, Anna Jakubowska-Winecka⁴, Wojciech Rowinski⁵

¹Department of General and Transplantation Surgery, Medical University of Warsaw, Poland; ²Poltransplant, Warsaw, Poland; ³2nd Department of Anesthesiology and Intensive Care, Medical University of Warsaw, Poland;

⁴Department of Health Psychology, Children's Memorial Health Institute, Warsaw, Poland; ⁵Polish Union for Transplantation Medicine, Warsaw and Department of Surgery, University of Warmia and

The mean DD organ recovery in our country reached 16 pmp last year, and is similar to that observed in Germany, the Netherlands and a number of other European countries. However the number of people dying in ICUs and neurological and neurosurgical utilities is much higher. Donation rate in various regions of our country differs greatly (from 5 to 28 pmp). In our previous studies we showed that there is a great difference in attitude of physicians toward the recognition (and acceptance) of brain death and organ recovery. Seven hundred and forty-four anesthesiologists, neurologists and neurosurgeons (i.e. physicians involved in brain death diagnosis) were interviewed. Physicians from regions with low donation rates (LDR) were twice more reluctant than their colleagues from high donation rate regions (HDR) to start the diagnostic procedure when clinical signs suggesting brain death were present (14% vs. 7% would not diagnose death, respectively). In 2012 we monitored the death rate among patients treated in the ICUs, and neurological and neurosurgical utilities of three regions of the country and calculated theoretical potential of deceased organ donors according to DOPKI donation index. Results are shown below: In conclusion, low donation activity seems to be mostly due to the medical staff attitude. Moreover, the tendency to diagnose brain death exclusively for purpose of organ recovery was observed. Does this mean that two concepts of death are in use?

P185

SINGLE CENTER EXPERIENCE IN HAND ASSISTED LAPAROSCOPIC DONOR NEPHRECTOMY

Tomasz Jakimowicz, Sławomir Nazarewski, Tomasz Ciacka, Lukasz Romanowski, Amro Alsharabi, Jacek Szmidt

Medical University of Warsaw, Department of General, Vascular and Transplant Surgery

Objective: The advantages of minimally invasive nephrectomy are: faster recovery, shorter hospital stay and better quality of life for the donors. It helps potential donors to make the decision to donate and therefore expands the donor pool. The aim of the study was to present the biggest Polish single center experience in hand assisted laparoscopic donor nephrectomy (HALDN).

Material and Methods: First HALDN in Poland has been done in our department on 18.06.2003 and was performed retroperitoneally as well as next two cases. Those three were left kidneys. From 06.06.2011 we changed the method to transperitoneal approach and started to harvest also right kidneys with hand assisted laparoscopic method. From this time we used it in all consecutive donors except one who refused laparoscopy and three with multiple renal arteries which we considered contraindication for laparoscopy on the beginning. Our total experience is 32 operations – 18 left (3 retro- and 15 transperitoneal) and 14 right kidneys (transperitoneal). All but one had single renal artery. In all cases we used hand-port (Gelport in last 29 cases) and renal vessels were closed with endo-staplers. WIT was 80–420 s (mean 217, 8 s).

Results: All surgeries were uncomplicated and all donors were discharged home after 2–7 days with the creatinine level in normal range. The follow-up was uneventful in all cases. None of the kidneys had nephrectomy dependent complications however there were two cases of transient DGF and one kidney was lost in third postoperative week due to the urethra necrosis and infection.

Conclusion: Our limited experience shows, that minimally invasive donor nephrectomy is safe and should be used as the preferred method.

P186

SHOULD WE BE AFRAID OF RIGHT-SIDE LAPAROSCOPIC DONOR KIDNEY NEPHRECTOMY?

Tomasz Jakimowicz, Sławomir Nazarewski, Tomasz Ciacka, Lukasz Romanowski, Amro Alsharabi, Jacek Szmidt

Medical University of Warsaw, Department of General, Vascular and Transplant Surgery

Introduction: Right-side minimally invasive donor nephrectomy is considered more challenging. The aim of this study was comparison of left and right hand assisted laparoscopic donor nephrectomy (HALDN).

Materials and Methods: We always aim to take worse kidney from the donor, and refuse to take right when the vein is shorter than 1.5 cm. From 06.06.2011 we started "active" HALDN program taking into account all patients for laparoscopic approach first. Since then we performed 14 right and 15 left HALDN. We compared time of operation, WIT, graft function and complications in both groups.

Results: There were no donor-related complications in both groups. Mean WIT was 260 and 178.4 s in right and left nephrectomies. Time of operation was 152.7 and 136.4 min respectively. There were no significant difference in none of the parameters. One left and one right kidney recipient developed DGF. One right kidney was lost due to urethra necrosis and infection in 3rd postoperative week that we found impossible to reconstruct.

Conclusion: Our limited experience shows, that results of right and left HALDN are similar. We should not be afraid to take right kidney utilizing hand-assisted laparoscopic method.

P187

FEAR OF KIDNEY FAILURE: DIFFERENCES BETWEEN GENETICALLY-RELATED AND UNRELATED LIVING KIDNEY DONORS

James Rodrigue¹, Aaron Fleishman¹, Tanya Vishnevsky¹, James Whiting², John Vella², Krista Garrison², Deonna Moore³, Liise Kayler⁴, Prabhakar Baliga⁵, Kenneth Chavin⁵, Didier Mandelbrot¹

¹Beth Israel Deaconess Medical Center; ²Maine Medical Center; ³Vanderbilt University; ⁴Montefiore Medical Center; ⁵Medical University of South Carolina

Introduction: While psychological outcomes for living donors (LD) are favorable, anxiety about possible renal failure is unknown. Some LDs may feel a heightened sense of anxiety about future kidney failure due to their biological relationship to someone who required kidney transplantation. Therefore, we hypothesized that genetically-related LDs would be more likely than unrelated donors to report fear of kidney failure.

Methods: Former LDs from 5 US centers were invited by mail or phone to anonymously complete questionnaires assessing fear of kidney failure, QOL, and psychological symptoms.

Results: Study participants were 304 LDs (172 related, 132 unrelated). Mean age was 51 (±11) years, 68% were female, 91% were White, and median time since donation was 73 months. Overall, 62% endorsed some fear of kidney failure. Compared to unrelated LDs, a higher proportion of genetically-related LDs reported fear of kidney failure (59% vs. 70%, $p = 0.04$). Related and unrelated LDs did not differ significantly on demographic characteristics, physical QOL (53.6 vs. 53.4, $p = 0.67$), or somatization symptoms (2.2 vs. 1.9, $p = 0.61$).

Conclusion: Related LDs may harbor more anxiety about renal failure or injury than unrelated LDs due to their biological relationship to the recipient, perhaps believing that this predisposes them to higher risk. Strategies to attenuate fear of kidney failure in all LDs, especially those who are genetically-related to the recipient, should be implemented prior to donation and reinforce during follow-up care. This study also shows that the Fear of Kidney Failure questionnaire may be a useful clinical tool that can easily be integrated into the follow-up assessment of LDs.

P188

LEVEL OF INFORMATION OF STUDENTS AT THE UNIVERSITY OF REGENSBERG CONCERNING ORGAN DONATION AND TRANSPLANTATION – INFORMED OR NOT INFORMED CONSENT IN ORGAN DONATION?

Bernhard Banas¹, Bernhard Bleyer², Hans Gruber², Jochen Pfirrstinger¹, Oliver Schaller², Barbara Dietl¹

¹University Hospital Regensburg; ²University of Regensburg

Background: As a result of the actual amendment of the German transplantation law, every citizen will be regularly asked by health insurance companies

about his attitude towards postmortem organ donation – without the obligation to decide. The aim is to increase the willingness of donations as well as the availability of organs. Therefore, we investigated the level of information of students at the University of Regensburg and their agreement to organ transplantation regarding an informed consent.

Methods: Using an interdisciplinary developed questionnaire (Medicine, Theology, Educational Science) the level of information concerning process and possibilities of organ donation, the possession of an organ donor card, as well as the active or passive consent to donate organs was investigated.

Results: Out of 1225 respondents 31.5% had an organ donor card, 49.1% wanted to donate organs, 32.1% were unsure. Ninety-eight percent generally favoured organ donation. However, serious information deficits about brain death were identified: 37.4% did not know that brain death is a prerequisite for a post-mortem organ donation, 18% thought brain death is reversible, 52.7% were not aware of the necessity of intensive medical care. Furthermore, providing information about other potential donor organs including lungs, pancreas, small intestine, and tissue is required.

Conclusion: Health insurance companies and responsible authorities need to close the identified gaps in knowledge in order to achieve “informed” consent with organ donation, which might increase the availability and number of donor organs.

P189

ORGAN RETRIEVAL ANAESTHESIA: LONDON TRAINEE PERSPECTIVE AND TRAINING NEEDS

Anneliese Rigby¹, Rebecca Campbell², Thomas Bishop³, Mae Johnson², Daniel Abell⁴

¹King's College Hospital; ²St George's Hospital, London; ³Whipp's Cross University Hospital, London; ⁴King's College Hospital, London

Background: Organs are retrieved from approximately 900 deceased organ donors in the UK each year, yielding about 3000 organs for transplantation (NHS Blood and Transplant. National standards for organ retrieval from deceased donors. 2010 v1.2). Optimisation of donor management can increase the number and quality of organs retrieved from each donor. We surveyed anaesthetic trainees in London, United Kingdom, regarding their knowledge and experience of organ retrieval.

Methods: A link to a “Survey Monkey” Questionnaire was sent to trainees from the South East School of Anaesthesia (SESA), St George's School of Anaesthesia and Bart's and the London School of Anaesthesia. Results were collated and analysed using Microsoft Excel.

Results: Results are shown in the table below.

Conclusion: Although organ retrieval anaesthesia is part of the curriculum for CCT in anaesthesia in the UK, few trainees have received formal training. Most organ retrieval cases occur out of hours, often with distant supervision. It is therefore important to provide trainees with the supervision & skills to deal with these cases. We have demonstrated a trainee requirement for additional training. As a result we have developed an e-learning module on organ retrieval anaesthesia and plan to pilot simulator sessions for trainees.

P190

POSITIVE BK VIRUS-KIDNEY DONORS CAN BE ACCEPTED SAFELY FOR NEGATIVE RECIPIENTS IN THE PRESENCE OF THE PROTECTIVE LOCUS HLA-CW7

Osama Gheith, Zakareya Zakareya, Torki Al-Otaibi, Medhat Halim, Narayanan M.R. Nampoory
OTC

Introduction and Aims: BK nephropathy is increasing problem in renal transplant recipients which has been correlated with newer Immunosuppressive agents and the decline in acute rejection rates. We aimed to evaluate the impact of BK positive kidney donors on the outcome of kidney transplant recipients after mean follow up period of 21 months.

Methods: Out of 18 kidney donors with positive BK virus in blood and urine, five were found fit for donation. Here in we present five kidney transplant recipients who received kidney allografts from such donors with mean age of 35 ± 3 years.

Results: All patients-except one –were males with mean age 49.4 ± 4.2 years; mean body weight 68.2 ± 4 kg and mean follow up duration 33.6 ± 4 months. All patients –except one - received thymo induction and steroid, tacrolimus, MMF as maintenance therapy; and ureteric stenting was a routine procedure in each case . HLA-CW7 locus was detected in four out of five recipients and the 5th was detected in the donor. Moreover, at last follow up all patients are enjoying functioning grafts without recurrence of BK infection.

Conclusions: BK positive persons can be accepted safely for kidney donation especially if the locus HLA-CW7 is present either the patient or the donor.

P191

HAND-ASSISTED RETROPERITONEOSCOPIC LIVE-DONOR NEPHRECTOMY, SINGLE CENTRE EXPERIENCE: 100 CONSECUTIVE CASES

Jiri Fronek, Libor Janousek, Tomas Marada, Jiri Mendl, Pavel Trunecka
Institute for Clinical and Experimental Medicine

Background: This is a report of 100 consecutive hand assisted retroperitoneoscopic live donor nephrectomies (HARS). The main benefit of this approach is increased safety for the donor. Risk of bleeding and intraabdominal injury is low thanks to hand assistance and extraperitoneal approach. This method has been introduced at our unit in January 2003, since June 2011 is being used for all the donors including right sided and complex anatomy cases.

Methods: This study reviews last 100 consecutive cases of living-donor nephrectomies performed since the HARS has been introduced for all the cases with no exclusions. Data were collected prospectively. The operation is performed in the manner described by Wadström et al 2002, with minor modifications.

Results: There was no conversion to open nephrectomy, one donor was re-operated on the first postoperative day for bleeding from paraaortic lymphatics, this donor was also given two units of blood. The median blood loss was zero otherwise, meaning no use of suction or no blood in container. The median post-operative hospital stay was 2 days. Minor complications include one wound infection and three wound haematomas. Major complications included bleeding from paraaortic lymphatics mentioned above required retroperitoneoscopic exploration and one incisional hernia. All donors have life-long follow up. All transplanted kidneys had immediate function, we did not observe any delayed graft function.

Conclusions: HARS is a safe way of performing living-donor nephrectomy with minimal morbidity and fast recovery. It is safe and quick alternative to the intraperitoneal approach, or other nephrectomy techniques. It can be used safely for all the anatomical variations as well as right sided cases.

PS10-INFECTIONS

P193

TREATMENT RENAL GRAFT SEPTIC NEPHROPATHY WITH ENDOTOXIN ADSORPTION

Pavel Astakhov, Alexey Zulkarnaev, Mirolub Krstic
M.F. Vladimirovsky Moscow Regional Research Clinical Institute

Background: It is known that in some cases the progression of infection complicated by renal dysfunction.

Methods/Materials: We studied the effect of endotoxin adsorption on renal graft function in gram-negative or mixed infections.

Results: As we have stated, the development of systemic inflammatory response initiated by bacterial infection has negative impact on graft function. This is reflected in a decrease of the diuresis, glomerular filtration rate, increased creatinine concentration in plasma, disturbance of microcirculation. At the same time early application of adsorption of endotoxin can significantly improve the function of the graft. Also, adsorption of endotoxin increases the survival of patients in the main group, mainly, we believe, by preventing the progression of systemic inflammatory response with subsequent formation of multiple organ failure.

Conclusion: Thus the use of endotoxin adsorption can significantly improve the function of the kidney transplant.

P194

COUPLED PLASMA FILTRATION AND ADSORPTION IN TREATMENT OF SEPTIC COMPLICATIONS AFTER RENAL TRANSPLANT

Alexey Zulkarnaev, Andrey Vatazin, Mirolub Krstic
M.F. Vladimirovsky Moscow Regional Research Clinical Institute

Background: Systemic inflammatory response in sepsis leads to poor graft function, as well as other organ and systems and can lead to multiple organ failure and death. Extracorporeal therapy can effectively intervene in the pathogenesis of sepsis.

Methods/Materials: In the study were included 30 patients, 15 of which were randomized in main group (in this patients we did coupled plasma filtration adsorption (CPFA))

Results: In the main group, we observed a significant reduction in the concentrations of cytokines during the procedure. This is associated with improvement of central hemodynamics in all main group patients. In comparing group cytokine concentrations remained stable. There was a slight decrease in cytokine concentrations only in patients with positive dynamics of clinical status.

Conclusion: We believe that the removal of cytokines is an effective procedure for patients with sepsis. In renal transplant recipients with complex immunosuppression, CPFA has great potential.

P195

ACUTE GRAFT PYELONEPHRITIS DURING FIRST YEAR AFTER RENAL TRANSPLANTATION

Justyna Gołębiewska, Alicja Dębska-Ślizień, Bolesław Rutkowski
Department of Nephrology, Transplantology and Internal Medicine, Medical University of Gdańsk

Introduction: Urinary tract infections (UTIs) are the most common infections in renal transplant recipients. Acute graft pyelonephritis (AGPN) is considered a potential risk factor for poorer graft outcomes, however its clinical impact still remains controversial.

Methods: We performed a retrospective cohort study reviewing medical records of patients who received a renal transplant at Gdańsk Transplantation Centre between January 2007 and December 2009. We analyzed urine cultures performed within first 12 months after RTx with reference to clinical data. Renal function assessed by creatinine concentration and eGFR was recorded 24 months after RTx.

Results: We studied urine cultures and clinical data from 209 renal transplant recipients, including 59.3% of male gender, with mean age of 46 ± 14 years. We observed 70 AGPN episodes defined as the presence of significant bacteriuria, fever $>38^\circ\text{C}$ and/or graft pain and/or acute graft function impairment, including 13 cases of bacteraemia in 46 patients. This accounted for 22% of all diagnosed UTIs. Over 80% of all AGPN episodes were diagnosed beginning from the second month post-transplant and the most frequently isolated uropathogen was *Escherichia coli* (65.7%, $n = 46$). Female gender, vesico-ureteral reflux or strictures at the uretero-vesical junction and history of CMV infection emerged as independent predictors of AGPN. The evolution of renal graft function over the period of 24 months measured by serum creatinine concentration and MDRD eGFR did not differ significantly between patients with and without AGPN.

Conclusions: AGPN may be a marker of underlying impairment of urine flow e.g. due to vesico-ureteral reflux or strictures at the uretero-vesical junction, while it does not affect graft function in renal transplant recipients.

P196

A LARGE PRIMARY INTRAMUSCULAR HYDATID CYST OF THE THIGH: CASE REPORT

Ahmed Hussein, Ahmed Nabil
faculty of medicine cairo university

Intramuscular hydatid cyst is a rare disease representing 0.2–2.2% of all cases of Echinococcosis. It should be suspected in patients from endemic areas. ELISA is a good positive but not a good negative test. MRI is the corner stone of diagnosis. We present a case report of a 50 year old male, from Yemen, presenting with a painless cystic swelling in his left thigh. It was diagnosed by proper history taking, ultrasound and MRI. Needle biopsy was avoided. Cyst excision was done together with intraoperative injection of hypertonic saline. Albendazole was administered perioperatively. Histopathological examination confirms the diagnosis.

P197

A PILOT STUDY IN KIDNEY TRANSPLANT RECIPIENTS TO MONITOR EBV-SPECIFIC CELLULAR IMMUNITY WITH ACTIVATED BZLF1

Ludwig Deml¹, Sascha Barabas¹, Florian Zeman², Hanna Bendfeldt¹, Astrid Starke¹, Andreas Pfister³, Bernd Krüger⁴, Wolfgang Jilg³, Hans Wolf², Michael Koller², Bernhard K. Krämer⁴, Bernhard Banas⁵

¹Lophius Biosciences GmbH; ²Center for Clinical Studies, University Medical Center Regensburg; ³Institute for Medical Microbiology and Hygiene, University Medical Center Regensburg; ⁴Medical Faculty Mannheim of the University of Heidelberg; ⁵Department of Internal Medicine II, University Medical Center Regensburg

Epstein-Barr virus (EBV) infections are effectively controlled by cell-mediated immunity (CMI). Inadequate impairment of CMI by immunosuppressive treatment after transplantation (tx) occasionally causes EBV-reactivation potentially associated with serious complications (PTLD). The prospective pilot study aimed to investigate the suitability of activated BZLF1 to monitor functional EBV-reactive CMI in kidney transplant recipients in the course of immunosuppressive treatment. We performed a 2-years prospective observational study in 83 patients, of whom 92.8% had a positive EBV serostatus. Blood was collected pre and post tx to measure functional activated BZLF1-reactive effector cells with an IFN- γ ELISpot. EBV load was determined from serum by quantitative PRC. Prior to tx, a significant activated BZLF1-reactive CMI was detected in 63.8% of EBV-seropositive patients followed by a substantial decrease within the first 3 weeks post tx. In some patients, EBV-specific CMI started to recover in month 6 to 18. Transient and weak, clinically inapparent EBV-reactivations occurred in 53% of the patients. Individual patient courses revealed that reactivations appeared preferentially at time points with low numbers of activated BZLF1-reactive leukocytes. Monitoring of functional activated BZLF1-reactive CMI may be an interesting novel strategy to assess the risk for EBV-reactivation in immunocompromised transplant recipients.

P198

OUTPATIENT PARENTAL ANTIBIOTIC THERAPY IN RENAL TRANSPLANT RECIPIENTS: A SINGLE CENTRE EXPERIENCE

Jade Harrison, Mohammad A Hossain, Mohamed A Morsy, Abbas Ghazanfar
St George's NHS Healthcare Trust

Background: Outpatient antimicrobial therapy (OPAT) has been established as a clinically and cost-effective way of treating infections in medical and orthopaedic specialties. There are no specific guidelines regarding OPAT use within renal transplant recipients. We describe our experience of OPAT within a single centre renal transplant unit.

Methods: A retrospective case record study was performed over a 12 year period. Nine patients, with functioning grafts, received 635 OPAT delivered antimicrobial episodes during 12 discrete OPAT courses. Renal function, mapped by eGFR and clinical response to infection, mapped by CRP and leukocyte count, was collected. Adverse incidences and a crude cost analysis of OPAT were also reported.

Results: Indications for OPAT were osteomyelitis ($n = 4$, 33.3%), mycotic aneurysm ($n = 2$, 16.7%), abscess ($n = 3$, 25%), pyelonephritic sepsis ($n = 2$, 16.7%), and cytomegalovirus infection ($n = 1$, 8.3%). No significant change in graft function occurred during any of the OPAT courses compared to baseline (Kruskal Wallis ANOVA $p = 0.06$). Eleven out of 12 courses were deemed successful and cleared infection to a level requiring no further i.v antimicrobials. The one remaining OPAT course required a digital amputation for chronic osteomyelitis. One patient developed immunosuppressive related neutropenia. This was successfully managed by switching OPAT to oral agents, reducing mycophenolate mofetil dose, and commencing granulocyte colony stimulating factor. No major lines complications were reported. Crude cost analysis showed a saving of over £4000 per course.

Conclusions: OPAT is safe and clinically effective in renal transplant recipients. The incidence of adverse events, specifically related to line complications, was lower in our population than those reported in the general OPAT population. Future work should focus on the development of guidelines

for the use of OPAT within renal transplant patients and aim to outline the degree of monitoring required.

P199

CLINICAL CONSIDERATIONS FOR CO-ADMINISTRATION OF THE NOVEL ANTIFUNGAL ISAVUCONAZOLE WITH IMMUNOSUPPRESSIVE AGENTS

Robert Townsend¹, Amit Desai², Corrie Howieson², Donna Kowalski², Helene Pearlman², Takao Yamazaki², Salim Mujais²

¹Astellas; ²Astellas Pharma Global Development, Inc.

Background: Isavuconazole (ISA) is a novel, broad-spectrum, triazole undergoing Phase III clinical development for the treatment of invasive fungal infections (IFIs). Patients undergoing organ transplantation are at increased risk of IFIs, raising the likelihood of co-administration of ISA with immunosuppressive drugs. Therefore, the pharmacokinetics and safety of ISA and the transplant drugs cyclosporine, mycophenolate mofetil, prednisone, sirolimus, and tacrolimus were investigated.

Methods: Five Phase I, open-label, drug-interaction studies were conducted in healthy subjects. Pharmacokinetics and safety of single doses of cyclosporine, mycophenolate mofetil, prednisone, sirolimus, and tacrolimus were assessed in the presence and absence of multiple doses of oral ISA.

Results: Co-administration with ISA increased the area under the whole blood/plasma concentration-time curves of tacrolimus (+125%), sirolimus (+100%), mycophenolic acid (+35%), cyclosporine (+29%), and prednisolone (+8%). Pharmacokinetics of ISA were mostly unaffected; however, maximum plasma concentration of ISA was higher during co-administration with cyclosporine (+30%) and tacrolimus (+26%). No major safety concerns were reported in any of the studies.

Conclusions: Attention to systemic drug levels and possible dose adjustments are required following administration or discontinuation of ISA in subjects receiving immunosuppressive drugs, in particular cyclosporine, sirolimus, and tacrolimus.

P200

CALCINEURIN INHIBITORS PROMOTE BUT MYCOPHENOLIC ACID INHIBITS HEPATITIS E VIRUS INFECTION IN CELL CULTURE

Yijin Wang, Luc J Wvan der Laan, Robertde Man, Petrade Ruiter, Jaap kwekkeboom, Maikel Peppelenbosch, Herold J. Metselaar, Qiuwei Pan
Erasmus Medical Center Rotterdam

Background: Hepatitis E virus (HEV) infection often results in rapid development of chronic hepatitis in organ-transplant recipients, which may be associated with immunosuppression. The aim of this study is to investigate the effects of different immunosuppressants on HEV infection in state-of-the-art cell culture models.

Methods/Materials: A subgenomic model containing a luciferase reporter gene and the full-length HEV infectious model were used.

Results: Steroids did not significantly affect HEV replication. However, calcineurin inhibitor (CNI) FK506 significantly enhanced HEV infection in both subgenomic and infectious models. Another CNI, cyclosporin A (CsA), which potently inhibit hepatitis C virus (HCV) infection, also resulted in enhancement of HEV infection. Forty-eight hour treatment of 5 µg/ml of CsA increased luciferase activity up to 2.5-fold ($p < 0.01$) in the subgenomic model and increased HEV genomic RNA by 9.6-fold ($p < 0.01$) in the infectious model. Using an RNAi gene silencing approach, the CsA-induced enhancement of HEV infection was found to be mediated by its cellular targets cyclophilin A and B. In contrast to CNIs, mycophenolic acid (MPA), an inhibitor of the IMPDH enzyme, inhibited HEV replication. Treatment with 10 µg/ml of MPA for 24 h resulted in 52;A3% ($p < 0.01$) inhibition of HEV luciferase activity. Ribavirin is another IMPDH inhibitor without immunosuppressive property that is often considered as an off-label drug for treating chronic HEV. Similarly, 100 µmol/l of ribavirin resulted in 51;A8% ($p < 0.01$) inhibition of HEV luciferase activity. Supplementation with exogenous guanosine partially restored their antiviral activity, suggesting depletion of cellular nucleotide pool contributing to the antiviral action.

Conclusion: Both CsA and FK506 enhance HEV infection. Similar to HCV, MPA was found to suppress HEV replication. These findings may help to choose the right immunosuppressive medication for post-transplant patients who are infected with HEV.

P201

CLINICAL IMPACT OF BACTERIAL CONTAMINATION OF PERFUSION FLUID IN KIDNEY TRANSPLANTATION

Andrea Ranghino¹, Francesca Simonato¹, Alessandro D. Quercia¹, Davide Diena¹, Maria Messina¹, Giuliana Tognarelli¹, Manuel Burdese¹, Valentina Piraina², Giuseppe Paolo Segoloni¹, Luigi Biancone¹

¹Nephrology, Dialysis and Transplantation Center, Molinette Hospital and Department Medical Sciences, University; ²Nephrology Unit, Magna Graecia University, Catanzaro, Italy

Background: Contamination of perfusion fluid (PF) could lead to serious infections. Nevertheless, it remains unclear if modifications of the antibiotic prophylaxis (AP) might help to avoid infections in presence of bacterial contamination. Aims of the study were to determine the incidence of PF contamination and the impact of AP modifications in presence of bacterial contamination on clinical outcome.

Material and Methods: We analyzed 290 PF samples and the clinical data of the recipients from 01/2010 to 12/2012. From 01/2012, recipients with positive PF and no signs of infection did not change AP, except in the case of fungal contamination.

Results: The incidence of positive PF was 34.8%, mainly staphylococci, 9.9% C. albicans. Urine culture was positive for the same bacteria of PF in four recipients. In 30/101 positive PF, the bacteria isolated were sensitive to AP. The infection rate between recipients changing AP according to PF (51/101) and recipients maintaining AP regardless PF (21/101) was not different.

Conclusion: Although PF contamination is frequent, the incidence of PF-related infections is low and changing of AP does not cause a reduction of recipient bacterial infections. Nevertheless, culture of PF should be routinely performed to identify fungal contamination.

P202

NATURAL HISTORY OF LIVER DISEASE POST KIDNEY TRANSPLANTATION IN PATIENTS WITH HEPATITIS C VIRUS, BIOPSY BASED, PROSPECTIVE COHORT STUDY

Hassan Aleid¹, Khalid Hamawi², Mai Altalhi¹, Ammar Abdulkaki¹, Hadeel Al-manea¹, Tariq Ali¹, Abeer Pall¹, Khalid Almeshari¹

¹King Faisal Specialist Hospital; ²King Fahad Specialist Hospital-Dammam

Kidney transplantation outcome is affected by liver disease in patients with HCV infection. Factors associated with progression of liver disease were not studied before with sequential liver biopsy. The aim of this research is to study the natural history of liver disease post kidney transplantation in patients infected with HCV supported by sequential liver biopsy.

Methods: This is a prospective longitudinal study of all kidney transplantation patients infected with HCV in a tertiary care centre in Saudi Arabia, study started January 2007 and is still ongoing. Patients were planned for liver biopsy at year 1, 5 10 and 15 post kidney transplantation. All patients had liver biopsy before kidney transplantation.

Results: About 1951 kidney recipients were screened, 285 had HCV, 136 patients underwent liver biopsy. Mean age was 43 + 15 years. Males were 55%. Tacrolimus was used in 70% of patients. Majority (> 90%) of patients were also on prednisone and MPA. Viral genotype 1, 4 and 2 were found in 82 (60%), 44 (32%) and 10 (7%) patients. Twenty percent of patients had persistent elevation of liver enzymes and 50% had transient elevation. Metavir scoring system was used to grade inflammation and stage fibrosis. Patients who crossed one grade of inflammation or one stage of fibrosis in comparison to baseline biopsy were classified as progressors. Safety data showed two patients had in adequate tissue, 13 had mild pain responding to oral pain killer. No patients had bleeding, required admission or blood transfusion. Table 1
Necro-inflammation and fibrosis based on metavir scoring system 0 1 2 3 4
Total progression Grade 25 66 41 2 0 134 49 Stage 15 73 28 14 4 134 46

Conclusion: Around one third of patients had progression in liver biopsy inflammation and or fibrosis post kidney transplantation. 20% had persistent and 50% had transient transaminitis. Biopsy was well tolerated with no major complication.

P204

CMV INFECTION IS RELATED WITH TUBULAR INJURY IN RENAL TRANSPLANTS

Lucio Requião-Moura¹, Ana Matos¹, Eduardo Tonato¹, Rogério Chinen¹, Erika Arruda¹, Thiago Filliponi¹, Marcelino Durão Jr¹, Niels Camara², Alvaro Pacheco-Silva¹

¹Hospital Israelita Albert Einstein; ²Universidade São Paulo

Background: The indirect effects of CMV infection can be related with IF/TA in renal transplants. The aims of this work are to evaluate the impact of CMV infection in a marker of early proximal tubular injury and in the renal graft function.

Methodology: One hundred and fifty nine patients undergoing renal transplantation were followed prospectively with serial measurements of urinary RBP and analyzed according CMV infection.

Results: The prevalence of CMV infection was 72.9%. The urinary RBP at the time of diagnosis of CMV infection was elevated in 81.8% of patients with infection in 30.5% of patients without infection ($p = 0.013$). In the serial assessment of uRBP levels found to increase markedly among infected patients on the time of diagnosis (16.9 ± 41.1 vs. 1.90 ± 1.50 mg/l, $p = 0.025$) and three months posttransplant (4.7 ± 8.6 vs. 1.70 ± 2.1 mg/l, $p = 0.041$). In multivariable analysis CMV infection was related with high RBP levels (OR=4.33, CI95% 1.66–11.27, $p = 0.003$). 3-years graft function was lower in patients who had infection: 54.4 ± 23.0 vs. 63.8 ± 28.9 ml/min, $p = 0.03$ (CKD-Epi).

Conclusions: The CMV infection is associated with a profile of the proximal tubule injury assessed by measurements of uRBP, as well as lower renal graft function until 3 years of follow up.

P205

EMERGENT LIGATION OF EXTERNAL ILIAC ARTERY IN ORDER TO CONTROL BLEEDING DURING POST-TRANSPLANTATION ALLOGRAFT KIDNEY NEPHRECTOMY, A DISASTROUS DREAM FOR ANY SURGEON PRACTICING KIDNEY TRANSPLANTATION

Afshar Zomorrodi¹, Sahar Zomorrodi¹

¹Tabriz medical science university

Kidney transplantation is the best modality treatment for any chronic renal failure patient, but sometimes it associates with horrible complications that one of them is allograft nephrectomy and post allograft nephrectomy bleeding. The vascular complications of post transplant allograft kidney is rare but they sometimes result in very bad outcomes (1). In our kidney transplant department with more than 20 years of experience, there were two cases of post allograft transplantation nephrectomy bleeding due to weakness of carell patch caused by it's infection after nephrectomy. For controlling the bleeding, the external iliac artery was ligated without any consequent ischemic finding at corresponding foot with subsequent reperfusion of it with collateral artery especially superficial femoral artery.

P206

CLINICAL CHARACTERISTICS OF OUTBREAK OF PNEUMOCYSTIS JIROVECI PNEUMONIA

Ieva Ziedina¹, Arta Gertner², Sabine Svikle³, Janis Jushinskis³, Rafail Rozental¹, Pauls Aldins⁴

¹Transplantation center of Latvia; ²Liepaja Regional Hospital; ³Riga Stradins University; ⁴Stradins Clinical University Hospital

Background: *Pneumocystis jiroveci pneumonia* (PJP) was not detected in our kidney transplantation center from 1973 till the end of 2008, so prophylaxis was not prescribed routinely.

Materials: A PJP outbreak of 15 cases occurred from November 2008 till June 2012 with a maximum of 5 cases in 2011. The PJP developed 1–5 months after surgery in 12 cases and 67–81 months posttransplant in three cases.

Results: The most common symptoms were dry cough (80%), fever (73%), dyspnea (60%), hypoxemia (SpO₂ less than 85%; 47%) and weight loss (40%). Chest x-ray was interpreted as normal in all cases, but 'ground-glass' infiltrate was found on chest CT in 67%. Graft function was not deteriorated during PJP, except of 3 cases when chronic hemodialysis was restarted. Treatment with trimethoprim-sulfamethoxazole (TMP-SMX) was successful in 80%, but none of patients was able to tolerate the recommended dose of the American Society of Transplantation guidelines (Am J Transplant 2004; 4 (suppl. 10): 135–141) due to side effects. The mean tolerated dose was 960 mg bid. The mortality rate was 20% and was associated with graft loss ($p = 0.01$) and development of pneumothorax ($p = 0.03$). The growing incidence of PJP led to necessity of implementation of universal TMP-SMX prophylaxis in middle of 2011, what resulted in relative decrease of the number of PJP (Figure) and absence of PJP from June 2012.

Conclusions: The symptoms of PJP were typical and pronounced. The death related to PJP was associated with development of pneumothorax and graft loss in renal transplant recipients.

P207

INTERNATIONAL MULTI-CENTRE DATA GATHERING FOR THE ESTABLISHMENT OF A DATABASE AND A RADIOLOGIC SOFTWARE THAT CAN BE USED FOR THE DIFFERENTIAL DIAGNOSIS OF BRAIN LESIONS OF AN INFECTIOUS ORIGIN

Natalia Maximova¹, Floriana Zennaro², Daniele Grosso³, Davide Zanon², Tiziano Minuzzo⁴

¹Institute for Institute for Maternal and Child Health, IRCCS Burlo Garofolo, Trieste, Italy; ²Institute for Maternal and Child Health, IRCCS Burlo Garofolo, Trieste, Italy; ³University of Genoa, Genoa, Italy; ⁴Consiglio Nazionale delle Ricerche-ISMAR, Venice, Italy

Brain infections in patients undergoing haemopoietic stem cell transplants or solid organ transplants, thus seriously immunosuppressed, are very complex to

deal with and lead to higher mortality rates. It would very important for diagnostic images to be interpreted in a more accurate and consistent way so that treatments could be applied more rapidly. The Brain Supporters Project aims at creating an international database capable of gathering an extensive collection of radiologic images of brain lesions together with the relevant clinical, laboratory and microbiological data. Starting from this database the possibility is envisaged to develop an "intelligent" software that through the use of multi-dimensional analysis techniques, variational methods and classification procedures taking advantage also of neural networks and Bayesian forecasting models, can detect, highlight and differentiate the minimal and yet peculiar differences in the "radiologic footprint" connected with the local alterations of brain tissue produced by each individual pathogen, thus becoming an objective diagnostic aid not influenced by the individual interpretation given by the operator. An internet site will be created, www.brainsupporters.eu, freely accessible to transplant centres world-wide. The radiologic images with confirmed diagnosis collected in the database will then be subject to a blind evaluation (without knowing the microbiologic diagnosis) by a team of specialists belonging to at least two of the Centres taking part in the project, so as to obtain an independent confirmation of the diagnosis. The images will then be classified by aetiological agent and subsequently by age group and by clinical characteristics of the patients. It will thus be possible to evaluate if and how the "radiologic footprint" of lesions due to the same pathogen is modified depending on the different characteristics of the host.

P208

PROSPECTIVE LONG-TERM STUDY ON PRIMARY CMV INFECTIONS IN ADULT LIVER TRANSPLANT RISK PATIENTS (D+R-) RECEIVING VALGANCICLOVIR PROPHYLAXIS

Heikki Mäkisalo, Krister Höckerstedt, Raisa Loginov,

Irmeli Lautenschlager

Helsinki University Hospital

Background: To prevent cytomegalovirus (CMV) disease, most transplant centers use antiviral prophylaxis to the CMV (D+R-) risk patients. However, late primary infections after cessation of prophylaxis may occur. In this study, we investigated the long-term efficiency of valganciclovir prophylaxis in preventing primary CMV infections in adult liver transplant patients.

Methods: Of 154 consecutive adult liver transplant recipients transplanted 2006–2009, 20 (13%) CMV D+R- recipients received valganciclovir prophylaxis up to 3 months after transplantation. The patients were frequently monitored for CMV by quantitative real-time PCR for one year after transplantation. After excluding the recipients with incomplete prophylaxis or monitoring, 13 (D+R-) patients with follow-up of >4 years were included in the study.

Results: During valganciclovir prophylaxis no break-through CMV infections occurred. After cessation of prophylaxis 12/13 (90%) patients developed CMV infection mean 165 days (range 95–320 days) post transplantation. Two low-level CMV infections were asymptomatic and were not treated with antivirals, 6 infections were successfully treated with valganciclovir, and four severe cases of CMV disease with intravenous ganciclovir and secondary valganciclovir prophylaxis. No intra-graft infection was seen, but one patient developed gastrointestinal CMV. Recurrent asymptomatic low-level CMV replication was recorded in three patients, 6 months, 3 years and 3.5 years after transplantation. One patient died of bacterial sepsis, but no patient or graft was lost due to CMV.

Conclusions: During valganciclovir prophylaxis no break-through CMV infections were recorded. Primary CMV infections after cessation of prophylaxis were common, but were successfully treated with valganciclovir (or ganciclovir).

P209

DELAYED SEROCONVERSION AND RAPID ONSET OF LYMPHOPROLIFERATIVE DISEASE AFTER TRANSMISSION OF HTLV-1 FROM A MULTI ORGAN DONOR

Ilona Glowacka¹, Klaus Korn², Sebastian A. Potthoff², Ulrich Lehmann⁴, Hans H. Kreipe⁴, Katrin Ivens³, Hannelore Barg-Hock⁵, Thomas F. Schulz¹, Albert Heim¹

¹Institute of Virology, Hannover Medical School, Hannover, Germany; ²Institute of Clinical and Molecular Virology, University of Erlangen, Erlangen, Germany;

³Department of Nephrology, Medical Faculty, University of Düsseldorf;

⁴Institute of Pathology, Hannover Medical School, Hannover, Germany;

⁵Department of Visceral and Transplantation Surgery, Hannover Medical School, Hannover, Germany

Background: Human T-cell lymphotropic virus type 1 (HTLV-1) screening of blood and organ donors is not mandatory in Germany because of its low prevalence (about 7/100 000). An HTLV-1 transmission event caused by a multiple organ donor was investigated. Validity of diagnostic procedures and HTLV-1 disease association in immunosuppressed organ recipients were analyzed.

Methods: Two CE marked screening immunoassays and an immunoblot (confirmatory assay) were used for detection of HTLV-1 antibodies. Proviral DNA was quantified in blood and biopsies of organ recipients by HTLV-1 real-time polymerase chain reaction (RT-PCR).

Results: Proviral HTLV-1-DNA was detected in all blood samples of organ recipients (1×10^4 – 1×10^6 copies/ml) but seroconversion was delayed for up to 2 years in screening assays and more than 6 years in the confirmatory assay. In two of three organ recipients a cutaneous T-cell lymphoma was diagnosed 2 and 3 years after infection, respectively. Proviral HTLV-1 DNA concentration was almost 1 copy/cell in cutaneous lymphoma biopsies whereas in biopsies of other tissues ≤ 0.03 copies/cell were found. The organ recipient did not suffer from lymphoma but detailed clinical data on this patient were not available to us.

Conclusions: Biopsy results support an etiological role for HTLV-1 in these cases of primary cutaneous T cell lymphoma after solid organ transplantation. Diagnosis of potentially HTLV-1 associated disease in organ recipients may require PCR because of delayed seroconversion and rapid onset of disease.

P210

THE NEGATIVE LONG TERM IMPACT OF HEPATITIS C VIRUS INFECTION ON PATIENT SURVIVAL AND GRAFT FUNCTION IN RENAL TRANSPLANT RECIPIENTS- SINGLE CENTER EXPERIENCE

Pavlina Dzekova-Vidimliski, Elka Masin-Spasovska, Irena Rambabova-Busljetic, Igor Nikolov, Aleksandar Sikole, Ninoslav Ivanovski
University Clinic of Nephrology

Background: Hepatitis C virus (HCV) infection is an independent risk factor for renal transplant recipients. The aim of the study was to present the long term clinical outcome of HCV positive renal transplant recipients.

Methods: A retrospective study was performed in order to analyze the long term clinical outcome of 54 HCV positive living donor kidney transplant recipients, transplanted in the period from 1992 to 2008. The 1, 5 and 10 years patients and graft survival rate, GFR-MDRD, the renal and extra renal morbidity and mortality were analyzed. Anti-HCV status was determined before transplantation. The results were compared with outcome of 69 HCV negative patients who were recruited during the same period. The usual triple drug immunosuppression was used in both groups of recipients. There was no difference regarding donor and recipient's age, HLA mismatch, delayed graft function and rejection episodes between the groups.

Results: The 1, 5, and 10 years HCV positive patients survival rate was 96%, 94.4 and 79.4% compared with 98%, 96.9% and 84.3% in HCV negative recipients, which is statistically significant ($p < 0.05$). The cardiovascular morbidity and mortality was predominant in HCV positive patients compared with infection and sepsis in HCV negative recipients. Calculated GFR-MDRD was significantly lower in HCV positive than in HCV negative patients (43.4 ± 9.5 vs. 55.9 ± 13.2 ml/min/1.73 m², $p < 0.000$). There was no significant difference in graft survival rate among the groups (98.1%, 92.6% and 83% vs. 98.6%, 94.2% and 90.7%, respectively, $p < 0.87$). None of the recipients developed cirrhosis and diabetes mellitus during the follow up.

Conclusion: Our study confirmed the harmful impact of HCV infection on patient's survival, renal and extra renal morbidity and mortality and graft function. The authors recommended the whole eradication of HCV infection before transplantation or avoidance to transplant HCV positive patients.

P211

EARLY INVASIVE FUNGAL INFECTIONS (IFI) AND UNIVERSAL ANTIFUNGAL PROPHYLAXIS (UAP) AFTER LIVER TRANSPLANTATION (LTX): CHANGING THE APPROACH ACCORDING TO THE RISK

Andrea de Gasperi, Laura Petrò, Ernestina Mazza, Manlio Prosperi, Jessica Bastreghi
Ospedale Niguarda Ca Granda, Milan, Italy

Background: IFIs occur in 4% to 15% of LTx patients. Candida and Aspergillus account for nearly all IFIs with high attributable mortality (30–70%). While targeted antifungal prophylaxis (TAP) seems justified in high risk (HR) pts, more controversial, in spite being used, is AP in low risk (LR) pts.

Material and Methods: Retrospective review of 192 consecutive LTx recipients who received universal AP (UAP) to determine 1) the incidence of early IFIs and the associated risk factors (RF); 2) the proportion of pts at high (HR) and low risk (LR) for IFI; 3) how appropriate was UAP in this series. Immunosuppression included antithymocyte serum, steroids and IL2 inhibitors. UAP included oral nystatin, and Fluconazole. Amphotericin B lipid formulations (ABL) were used as TAP (3–5 mg/kg/day, 7–10 days) in case of fulminant hepatic failure (FHF), post-transplant abdominal reexploration, retransplantation, renal failure, CRRT, acute rejection, documented mould colonization and/or positive galactomannan assay.

Results: Median age was 54 years, MELD score 15 ± 7 . LTx indications were viral cirrhosis (70%), ETOH cirrhosis (25%), miscellaneous (5%) Mortality rate at 3 months was 5%. Infections episodes were present in 40 pts (21%). 45 pts were at HR for IFI (24%), 147 (76%) at LR. 4 IFIs were recorded in 4 pts (2%, CI 95% 0.02–3.98%), more represented in HR pts (6.6%, vs. 0.7%, $p = 0.04$): 2 had C. Glabrata candidemia and recovered; two had invasive Aspergillus (1 proven, 1 probable) and recovered. Independent RFs for IFI were HR, CRRT, FHF, fungal colonization, peritonitis, blood stream infection.

Conclusions: TAP approach with broad spectrum antifungals (ABL) in the HR group might have played a role in achieving these good results. Our study confirms the utility of UAP with FLU in LR pts. Due to the different risk factors for Candida and Aspergillus, broad spectrum antifungals (ABL vs. echinocandins) are to be considered for TAP.

P212

FATAL LATE ONSET PNEUMOCYSTIS PNEUMONIA FOLLOWING RITUXIMAB ADMINISTRATION FOR POST-TRANSPLANT RECURRENCE OF FSGS – CASE REPORT

Dominika Deborska-Materkowska¹, Olga Kozinska-Przybyl¹, Malgorzata Mikaszewska-Sokolewicz², Magdalena Durlik³

¹Department of Transplantation Medicine and Nephrology; ²1st Department of Anaesthesiology and Intensive Therapy, Medical University of Warsaw;

³Department of Transplantation Medicine and Nephrology, Medical University of Warsaw

Background: Recurrence of focal segmental glomerulosclerosis (FSGS) is an important cause of graft loss following kidney transplantation. The management of patients with recurrent FSGS is not well established because there are no prospective randomized studies with a view to the impact of FSGS on graft survival. Recent studies suggest that rituximab – an anti-B-CD20 monoclonal antibody may be therapeutic alternative in selected cases resistant to conventional therapy. Opportunistic infections with rituximab have not been studied extensively, but recent studies suggest an increased risk for Pneumocystis jirovecii pneumonia (PJP) following rituximab therapy.

Methods: We report the case of a kidney transplant recipient with the recurrence of FSGS in the graft, who developed fatal Pneumocystis jirovecii pneumonia subsequent to treatment with rituximab. Our patient was treated with plasmapheresis and a complex immunosuppressive drug scheme for the recurrence of FSGS in transplanted kidney. However this treatment had no effect on the amount of proteinuria which increased to maximal 15 g per day after 18 session of plasmapheresis. Thereafter 500 mg i.v. of rituximab was administered at a four week interval.

Results: The number of CD19 positive B lymphocytes decreased from 9% to 0.57%. 2 months after the second dose of rituximab proteinuria decreased to 2.1 g per day. 10 months after transplantation and five months after first dose of rituximab was administered the patient developed severe PJP pneumonia and died despite all efforts with antibiotic therapy.

Conclusions: It seems to be essential that all renal transplant recipients treated with rituximab should currently be considered at an increased risk for PJP. This case suggest that prolonged or restarted prophylaxis for PJP should be recommended following not only conventional treatment for acute rejection episodes but after use of rituximab in combination with other immunosuppressive therapy as well.

P213

BACTERIAL INFECTIONS IN THE EARLY PERIOD AFTER LIVER, KIDNEY, SIMULTANEOUS PANCREAS AN KIDNEY TRANSPLANTATION – ETIOLOGICAL AGENTS AND SUSCEPTIBILITY TO ANTIMICROBIAL DRUGS

Dariusz Kawecki¹, Andrzej Chmura², Grazyna Mlynarczyk³

¹Department of Medical Microbiology, Medical University; ²Department of General Surgery and Transplantation, Medical University of Warsaw;

³Department of Medical Microbiology, Medical University of Warsaw

Bacterial infections remain serious complications in solid organ transplant recipients, despite professional medical care, the introduction of new immunosuppressive drugs and management which decreases the risk of infections. Therefore it was justified to analyse the frequency at which microbe strains occur, their biochemical profile and susceptibility to antimicrobial agents in patients after solid organ transplantation in the early posttransplant period in Poland. The study sample was composed of 511 consecutive solid organ transplant recipients (295 – kidney transplant, 190 – liver transplant, 26 – simultaneous pancreas-kidney transplant) who underwent transplantation at the Department of General Surgery and Transplantation at the Medical University of Warsaw between September 2001 and December 2007. This six-year-period of observation of transplant patients had been subdivided into two subperiods: from 2001 to 2004 and from 2005 to 2007. Clinical samples were taken from these recipients before transplantation, intraoperatively and during the first month after the operation. Cultured bacterial and fungal strains were identified and characterised at the Chair and Department of Medical Microbiology at the Medical University of Warsaw using standard microbiological methods. The differences between isolated strains in these four periods have been evaluated by statistical analysis using SAS 9.1 program: chi-square test, Fisher test. Differences between the incidence rate in two periods (2001–2004 vs. 2005–2007) was performed using bootstrap method. The significance level was considered to be $\alpha = 0.05$. In the analysed clinical materials a high prevalence of multidrug resistant strains was demonstrated: *Staphylococcus aureus* (MRSA) – 59.7%, methicillin-resistant coagulase-negative staphylococci (MRCNS) – 82.2%, *Enterococcus* spp. (HLAR) – 84.4%, *Enterococcus* spp. (VRE) – 12.4% and ESB(+) Gram-negative rods of the Enterobacteriaceae family – 31.1%.

P214

A SIMPLE POST-TRANSPLANT IMMUNE MONITORING STRATEGY IS USEFUL IN PREDICTING THE OCCURRENCE OF INFECTION AFTER KIDNEY TRANSPLANTATION: THE SIMPLICITY SCORE

Mario Fernández-Ruiz, Francisco López-Medrano, Luis M. Allende, Pilar Varela, Rafael San Juan, Carlos Lumberras, Amado Andrés, Esther González, José María Morales, Estela Paz, José María Aguado
Hospital Universitario "12 de Octubre", Madrid, Spain

Background: To develop a practical score –based on readily available immunological parameters– to predict the risk of infection in kidney transplant (KT) recipients.

Methods: We included 245 patients who undergo a KT between November 2008 and July 2011. Total lymphocyte count and peripheral blood lymphocyte subpopulations (PBLs), serum immunoglobulin levels (IgG, IgA and IgM), and serum complement levels (C3 and C4) were investigated at months 1 and 6. Predictors for overall and opportunistic infection in different post-transplant periods (intermediate [months 1–6] and late [>6 months]) were assessed by Cox regression models. One point was assigned to each of the following: IgG hypogammaglobulinemia (<700 mg/dL), C3 hypocomplementemia (<83 mg/dL), and low counts in some PBLs ($CD8 + T-cell <0.200 \times 10^3/\mu\text{l}$ at month 1 and $CD3 + T-cell <0.500 \times 10^3/\mu\text{l}$ at month 6). The index was collapsed into three groups: low- (score of 0), intermediate- (score of 1–2), and high-risk (score of 3). **Results:** According to the score value at month 1, cumulative incidences of overall infection at the end of the intermediate period were 19.3%, 41.8% and 77.8% in low-, intermediate- and high risk-groups, respectively ($p < 0.001$). Cumulative incidences of opportunistic infection were 8.8%, 25.9% and 55.6%, respectively ($P = 0.001$). In the multivariate analysis, compared to the low-risk group, the hazard ratios for overall infection in the intermediate- and high-risk groups were 1.96 (95% confidence interval [CI]: 1.01–3.79) and 4.14 (95% CI: 1.82–9.41), respectively. The area under receiver operating characteristics (auROC) curve of the model at month 1 for predicting infection in the intermediate period was 0.68 (95% CI: 0.61–0.75). In the late period, cumulative incidences of overall infection were 8.6%, 23.2% and 50.0% in low-, intermediate- and high risk-groups, respectively ($p = 0.011$). The auROC of the model at month 6 for predicting late infection was 0.65 (95% CI: 0.55–0.75).

Conclusions: A simple score, on the basis of scheduled monitoring of PBLs and serum IgG and C3 levels, is useful for evaluating the risk of infection after KT.

P215

RECOMMENDATIONS FOR HYGIENE MANAGEMENT OF METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS (MRSA) IN ORGAN DONATION AND PROCUREMENT

Gunnar Urban, Christina Schleicher, Carl-Ludwig Fischer-Fröhlich
Deutsche Stiftung Organtransplantation

Since 2001 hygiene management in Germany is regulated by law according to the Infection Protection Act (IPA; Infektionsschutzgesetz, IfSG). After revision in 2011, the act highlights the legal character of guidelines published by the Robert Koch Institute (Division of Applied General and Hospital Hygiene and Commission for Hospital (healthcare associated). Mentioned amendment had become necessary inter alia after reality stroke expectations regarding presupposed control of MRSA in Germany: In 1997 MRSA-prevalence (KISS-data from 200 ICU) rose from an average of 8% to 30% until year 2003. Moreover at least 400 000–600 000 nosocomial infections are presupposed in Germany annually, whereof 14 000 MRSA-infections. As this situation has impacts on organ transplantation programs, too, consequently case reports regarding the spread of MRSA via organ donation have been published. Moreover, there is evidence suggesting that the outcome of *S. aureus* donor-to-recipient-transmitted infection might be poor in cases of solid organ transplantation. Today, regarding hygiene management, organ donation programs in Germany usually refer to respective hospital hygiene guidelines which are not specially adapted to the needs of multi-organ donations involving multiple teams arriving from different places bringing along their own equipment for organ recovery, preservation and transportation. Regarding the above, it is of major importance to apply and adapt standardized guidelines for hygiene management of MRSA in organ donation and transplantation programs, too. The present recommendations on hygiene management of MRSA in organ donation and procurement refer to mentioned regulations and guidelines but as well take into account other actual published literature. As it is generally agreed upon that the course of nosocomial infection is mostly due to transmission via contaminated hands, hygienic hand disinfection remains the most important measure in organ transplantation setting, too.

P216

ORGAN TRANSPORT FLUID CULTURES: AN ANALYSIS OF OUTCOMES

Harkiran Sran¹, Sarah Heap¹, Hersharon Sran², Atul Bagul¹
¹St. George's Hospital, London; ²Brighton & Sussex University Hospital, Brighton

Background: Following the potential contamination of organ preservation fluid (2012), recommendations were that transport fluid be routinely cultured.

This study aims to evaluate the impact of positive transport fluid cultures following deceased-donor kidney transplantation.

Materials and Methods: A retrospective analysis over an 8-month period assessed 41 consecutive transport fluid cultures. Recipient demographics: median age 56.9 ± 12.9 , inpatient-stay 5.7 ± 2.1 days, 31 DBD, 11 DCD. All patients received prophylactic antibiotics as per institution protocol. Patients were followed-up for 90 days.

Results: Ten recipients had culture-positive perfusion fluid (CP) and 31 were negative (CN). There was no difference in white cell count, serum creatinine and eGFR at Day 7, 30 and 90. Patients in the CP group had a numerically higher rate of culture-proven infective episodes (urinary, wound, bacteraemia) compared to the CN group (8/10 vs. 14/31, $P 0.0578$). Of these eight episodes, 50% had similar organisms cultured to that of the transport fluid. One patient in this group required graft nephrectomy for ongoing sepsis.

Conclusions: This study suggests that positive transport fluid cultures are associated with increased incidence of infections. This should prompt clinicians to be pro-active in ascertaining culture results and establishing appropriate treatment early in the post-transplant period.

P217

MICAFUNGIN AS ANTIFUNGAL PROPHYLAXIS IN HIGH-RISK LIVER TRANSPLANTATION: RANDOMISED, MULTICENTRE TRIAL

Faouzi Saliba¹, Lutz Fischer², Marcus Bahra³, Olivier Cointault⁴, Pierre-Francois Laterre⁵, JanDe Waele⁶, Umberto Cillo⁷, Carlos Cervera⁸, Lorraine Tweddle⁹, Andreas Karas⁹

¹Hôpital Paul Brousse Villejuif; ²Univ-Krankenhaus Eppendorf; ³Charité Universitätsmedizin; ⁴Hôpital de Rangueil Toulouse; ⁵UCL Saint-Luc; ⁶Ghent University Hospital; ⁷Az. Osp. Di Padova; ⁸Hospital Clinic i Provincial; ⁹Astellas Europe

Background: Amphotericin B (AmB) and fluconazole are recommended for antifungal prophylaxis after liver transplant (LTx). In this open-label, randomised, multicentre trial, the efficacy and safety of micafungin was compared with site-approved standard care prophylaxis (SC) in LTx pts at high risk of invasive fungal disease (IFD).

Methods: After LTx, pts were randomised 1:1 to iv micafungin 100 mg once daily (od) or iv SC (fluconazole 200–400 mg od; liposomal AmB 1–3 mg/kg/day; or caspofungin 70 mg loading, 50 mg maintenance od). The primary endpoint was clinical success (absence of a proven/probable IFD and no additional antifungals) at end of prophylaxis (EOP). Non-inferiority (10% margin) of micafungin versus SC was assessed in the per protocol set (PPS) and confirmed in the full analysis set (FAS). Safety assessments were adverse events (AE) and liver and kidney function.

Results: The FAS comprised 172 micafungin and 172 SC pts. Mean age was 51.2 years, 48.0% had a MELD score ≥ 20 . Most common risk factors for IFD were post-operative renal impairment (31.4%), abdominal re-operation within 5 days of LTx (21.5%) and pre-operative renal impairment (20.3%). 60 (17.4%) pts had intra-operative transfusion of ≥ 20 units of cellular blood product. 13.4% of pts had a previous liver transplant. 22.7% of donors were >65 years old. At EOP (mean drug duration 17 days), clinical success was 98.6% for micafungin ($n = 140$) and 99.3% for SC ($n = 137$; $\Delta[95\% \text{ CI}]: 0.7 [-2.7, 4.4]$) in the PPS and 96.5% and 93.6% ($-2.9 [-8.0, 1.9]$) in the FAS. There were four Aspergillus and eight Candida infections at EOP. 70% of pts completed prophylaxis. Incidences of drug-related AEs for micafungin and SC were 11.6% and 16.3%, leading to discontinuation in 6.4% and 11.6% of cases, respectively. Liver and kidney function were similar between groups.

Conclusions: Micafungin was shown to be safe and non-inferior to SC as antifungal prophylaxis in high-risk LTx patients.

P218

SAFETY AND EFFICACY OF PROPHYLAXIS WITH AEROSOLIZED AMPHOTERICIN B LIPID COMPLEX (ABLC) IN LUNG TRANSPLANT RECIPIENTS

Marta Fiscon¹, Monica Loy², Federico Rea², Anna Ferrari¹, Veronica Zanichelli¹, Serena Marinello¹, Dino Sgarabotto¹

¹Infectious Diseases Transplant Unit, Transplantation Deptment, Azienda Ospedaliera di Padova; ²Thoracic Surgery Unit, Transplantation Deptment, Azienda Ospedaliera di Padova, Italy

Rationale, Goals and Aims: Invasive fungal infections severely affect lung transplant morbidity and mortality. However, a safe and effective antifungal prophylaxis has not been established yet. The aim of this study is to determine safety and efficacy of antifungal prophylaxis with short-course intravenous ABLC followed by Aerosolized ABLC.

Patients and Methods: In this longitudinal retrospective study from Jan 2008 to Jan 2012, we evaluated lung transplant patients of Padova General Hospital, Italy. We analyzed, in two follow-up periods (within 2 and 6 months), the following variables: presence/absence of invasive aspergillosis, concomitant other antifungal prophylaxis, culture-oriented or empiric antifungal therapies, severe bacterial infections, and other risk factors for invasive fungal infections

such as adjunctive immunosuppressive drugs, high-dose steroids for rejection, diabetes, dialysis and ECMO.

Results: Eighty-four patients were enrolled in the study. Eleven patients could not receive aerosolized ABLC because of clinical incompatibility or intolerance (1/11) and received only intravenous ABLC. The other 73 patients were treated with intravenous ABLC (median 5 days) followed by a median of 4 weeks aerosolized ABLC (50 mg/weekly). Forty-five patients received antifungal therapy within 8 weeks after transplant: in five cases invasive aspergillosis was diagnosed, in 14 patients invasive candida infection was present, and finally in 26 cases antifungal therapy was administered empirically. Between 2 and 6 months we observed two other cases of invasive aspergillosis.

Conclusions: Unlike safety, efficacy of ABLC prescribed as prophylaxis in lung transplant patients has not been completely proved. Our study suggests that this strategy could be appropriate. More effort is needed to establish the correct dosage and the adequate length of therapy.

P219

IDENTIFICATION OF NEW FACTORS THAT IMPACT SUBCUTANEOUS HBIG REQUIREMENT AFTER LIVER TRANSPLANTATION

Susanne Beckebaum¹, Speranta Iacob², Arnold Radtke¹, Iyad Kabar¹, Miriam Maschmeier¹, Vito R. Cicinnati¹

¹University Hospital Münster; ²Fundeni Clinical Institute Bucharest

Aims: High interindividual variability of anti-HBs consumption may be of multifactorial etiology. We therefore aimed to identify predictive parameters for sc HBIG consumption in a prospective study.

Methods: Transplanted HBV patients were switched from iv HBIG to weekly sc HBIG. According to SPC, sc doses of 500 IU/week and 1000 IU/week were initiated in 24 (55.8%) and 19 patients (44.2%) respectively. At baseline, relevant parameters were determined and repeated at day 8, 15, monthly between month 1–6, at month 9 and 12, and comprehensive body composition was assessed using a bioelectrical-impedance-analyzer.

Results: Mean body weight, BMI and waist circumference (74.9 ± 14 kg, 26.2 ± 4.9 kg/m² and 96.9 ± 13.2 cm) measured at baseline did not significantly change during follow-up. The same was true for renal function and total protein. Pearson correlation analysis showed that anti-HBs titers were negatively associated with MDRD ($p = 0.04$), total protein ($p = 0.04$), total body water ($p = 0.007$), fat-free mass ($p = 0.005$) and muscle mass ($p = 0.01$) and positively associated with creatinine ($p = 0.03$), body weight ($p = 0.02$), BMI ($p = 0.003$), body waist ($p = 0.03$) and fat mass ($p = 0.005$).

Conclusion: This is the first study showing that body composition and renal function impact HBIG levels. Given these findings, future studies are warranted to investigate individualized HBIG schedules.

P220

CYTOMEGALOVIRUS (CMV) INFECTION PROPHYLAXIS AFTER ORTHOTOPIC LIVER TRANSPLANTATION (OLTx)

Efstathios Antoniou¹, Gregoris Hatzis², George Daikos³, Gerasimos Tsouroufflis⁴, Panorea Paraskeva⁴, Anastasios Smyrnis⁴, Paul Vernicos⁵, John Floros⁵, Gregoris Kouraklis⁴

¹2nd Department Of Propedeutic Surgery, University Of Athens, Laikon Hospital, Athens, Greece; ²Department of Pathophysiology, University Of Athens, Laikon Hoospital, Athens, Greece; ³1st Propaedeutic Department, University Of Athens, Laikon Hoospital, Athens, Greece; ⁴2nd Department Of Propedeutic Surgery, University Of Athens, Laikon Hospital, Athens, Greece; ⁵Itu Laikon Hospital, Athens, Greece.

Background: CMV infections have been among the most fatal post-OLTx complications. However, post-OLTx CMV prophylaxis has been a controversial issue during the last two decades. Our aim is to present the results of our unit, of long-term post-OLTx CMV prophylaxis.

Materials and Methods: Thirty-two adults (7 female) underwent OLTx, within 3 years. Twenty-four recipients were CMV (IgG) positive (R+) and 8 CMV negative (R-). Donors CMV status: 21 were CMV (IgM) positive (D+) and 11 negative (D-). Liver-grafts distribution: 18 R+ received 18 D+ grafts and 6 R+ received 6 D(-). Eight R (-) received 8 D(-) grafts. IV Ganciclovir 5 mg/kg/day, was administered for as long as recipients stayed in ITU. Valganciclovir 900 mg bd given then orally for three months, followed by dose once daily for further three months. Their dose reduced further to one tabl, every other day for six more months.

Results: No particular side effects were noted during CMV prophylaxis treatment. Three recipients presented severe infection during their staying in ITU, suspicious for CMV infection. Specific CMV examinations (CMV-IgM, CMV-PCR) did not reveal CMV infection. Two more recipients, while in the ward, presented intra-abdominal infection and one severe acute rejection, mimicking CMV infection. Again, the CMV investigations on these patients were negative.

Conclusion: These preliminary results show, although the number of recipients is small, that long term CMV prophylaxis could prevent OLTx recipients from a possible fatal CMV infection.

PS11-KIDNEY

P221

INTIMAL CALCIFICATION IN ILIAC ARTERY IS PREDICTIVE FOR POOR LONG-TERM RENAL ALLOGRAFT SURVIVAL

Hyeon Seok Hwang¹, Sun Woo Lim², Byung Ha Chung¹, Bum Soon Choi¹, Suk Young Kim¹, Chul Woo Yang¹

¹Division of Nephrology, Department of Internal Medicine, the Catholic University of Korea, Seoul, Korea; ²Transplant Research Center, Seoul St. Mary's Hospital

Background: The impact of pre-existing intimal calcification on clinical outcome after kidney transplantation has not been investigated.

Methods: The iliac artery segments were obtained at the time of transplantation in ninety renal transplant recipients. We examined the presence of intimal microcalcification using von Kossa stain.

Results: The intimal microcalcifications were found in 56 (62.2%) patients. The ten-year renal allograft survival rate (patient death censored) was significantly lower in patients with intimal calcification than in patients without intimal calcification (51.4% vs. 89.1%, $p = 0.022$). The chronic allograft nephropathy as a cause of renal allograft loss was observed more frequently in patients with intimal microcalcification than in patients without intimal calcification (60.7% vs. 14.3%, $p = 0.041$).

Conclusion: The pre-existing intimal microcalcification is closely associated with renal allograft loss caused by chronic allograft nephropathy.

P222

DOUBLE FILTRATION PLASMAPHERESIS IN TREATMENT OF RENAL GRAFT ACUTE HUMORAL REJECTION

Alexey Zulkarnaev, Andrey Vatazin, Mirolub Krstic, Rusudana Kantaria
M.F Vladimirsky Moscow Regional Research Clinical Institute

Background: It is known that the rejection significantly worsens the prognosis of renal graft survival at all stages of the postoperative period.

Materials and Methods: The study included 18 patients after kidney transplantation. All patients were classified as high-immunologic risk group. In all patients we performed the double filtration plasmapheresis (DFPF). All patients got three to five DFPF treatments. To prevent ricochet syndrome after treatment, all patients received intravenous immunoglobulin.

Results: In all patients, we noted 40–64% reduction in the concentration of IgG and IgM after procedures. All grafts and recipients survived at 1.5 years after therapy. Graft function was good and stable. We noted no signs of recurrence of rejection by biopsy after 1 year.

Conclusion: DFPF can safely and effectively reduce the high titers of antibodies that are responsible for humoral rejection of renal allograft.

P223

EVEROLIMUS VERSUS MICOPHENOLATE AFTER 5 YEARS OF TRANSPLANTATION

Paolo Carta, Maria Zanazzi, Giulia Antognoli, Lorenzo Di Maria, Leonardo Caroti, Enrico Minetti
Careggi University Hospital

Background: We compared retrospectively 56 kidney transplanted patients receiving everolimus (8–12 ng/ml), Cyclosporin (C2: 250–300 ng/ml) + steroids, Vs 50 patients treated with Enteric coated Mycophenolate (1440 mg/day) + Cyclosporin (C2 500–700 ng/ml) + steroids.

Methods: Efficacy was evaluated at 5 years. Statistical analysis included χ^2 test and Fisher exact test, Mann-Whitney test, Log rank test for the difference of the Kaplan–Meier curves.

Results: In the everolimus group we found a non statistical trend towards a better graft survival (86% Vs 72%) and towards a better graft function: 77.34 ± 36.38 vs. 60.36 ± 25.34 ml/min ($p = 0.052$). The Everolimus group had higher level of proteinuria 306 (range 47–2196) vs. 174.5 (12–1012) mg/24 h, and a comparable levels of cholesterol but a greater use statin. (55% vs. 17%)

Conclusion: Everolimus was associated to a trend towards a better renal function and graft survival than Mycophenolate.

P224

DOES LOW DOSE TRIMETHOPRIM-SULFAMETHOXAZOLE AFFECT SERUM CREATININE AFTER RENAL TRANSPLANTATION?

Shigeyoshi Yamanaga, Mariko Toyoda, Yuji Hidaka, Umi Fukuda, Kouta Hori, Takashi Senba, Youei Miyabe, Kenichirou Tokunaga, Hiroshi Yokomizo, Seishi I, Sohichi Uekihara

Kumamoto red cross hospital kidney center

Background: By inhibiting creatinine secretion, it has been well known that high dose trimethoprim (TMP) increases serum creatinine (S-Cr) level without changes in real glomerular filtration rate. But there has been no report regarding the effect of low dose TMP on S-Cr level after renal transplantation (RTx).

Materials and Methods: Retrospectively, we investigated fifty-one out-patients who required re-administration of TMP-sulfamethoxazole (TMP-SMX) to prevent the possible outbreak of pneumocystis pneumonia (PCP). Thirteen patients who were not available during the same period were set as a control. Dosage was 80/400 mg (single strength) three tablets per week and administrated about 30.6 ± 13.5 days until the diagnosis of the patient to be PCP was denied.

Results: S-Cr was raised significantly in the case group (from 1.40 ± 0.64 mg/dl to 1.48 ± 0.70 mg/dl, $p < 0.01$) while not in the control group (from 1.39 ± 0.50 mg/dl to 1.38 ± 0.45 mg/dl, not significant). Δ S-Cr (before and after the administration) was significantly higher in the case group ($p < 0.05$). S-Cr returned to baseline level after cessation. No adverse events were observed and all patients completed re-administration without failure. Other laboratory data such as serum total bilirubin, serum blood urea nitrogen, serum potassium and urine protein (UP) were not changed significantly. The higher the initial S-Cr levels, the greater the increase of Δ S-Cr ($R = 0.59$, $p < 0.001$). Gender, baseline UP levels, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker use, donor type and time after renal transplantation did not affect Δ S-Cr. S-Cr returned to baseline levels after cessation.

Conclusion: Low dose TMP-SMX significantly raised S-Cr by 6% after RTx. Effect of TMP-SMX is supposed to be dose dependent and large prospective studies are warranted.

P225

THE ASSOCIATION BETWEEN INFLAMMATION MARKERS, MALNUTRITION AND QUALITY OF LIFE WITH VOLUME STATUS IN THE PRE-POST TRANSPLANT PERIOD

Hülya Colak¹, Ismail Sert², Yusuf Kurtulmus¹, Cezmi Karaca¹, Hüseyin Töz³, Seyhun Kursat⁴

¹Tepecik Training and Research Hospital; ²Van Regional Training and Research Hospital; ³Ege University; ⁴Celal Bayar University

Background: The aim of the study was to evaluate the relationship between inflammation markers [(interleukin-6 (IL-6), high-sensitivity C-reactive protein (hsCRP)], malnutrition and health-related quality of life (HRQoL) with volume parameters [echocardiography (ECO), blood pressure measurements] taken before and 6 months after renal transplantation.

Material and Methods: Forty-one patients received deceased donor kidney transplantation were included in this trial. The short form (SF-36) HRQoL scale adapted to Turkish society was used for the HRQoL assessments. Systolic and diastolic blood pressure (BP), echocardiography measurements were used for the evaluation of the volumetric status of patients. Routine biochemistry parameters and demographic data were recorded. Malnutrition scores (Subjective Global Assessment, SGA) and anthropometric measurements were obtained, and inflammation markers (IL-6, hsCRP) were measured.

Results: All of the subscales of HRQoL except vitality (energy) were improved after transplantation. Malnutrition and HRQoL were assessed in the preoperative period; SGA, arm circumference, MAMC (mid-arm muscle circumference) and in the post-operative period; albumin, SGA were statistically significant. When we evaluated the inflammation markers and HRQoL, we found relationships between hsCRP and the pain subscale and between IL-6 and the vitality (energy) subscale. For the postoperative period, we found a relationship between hsCRP and the physical function subscale and between IL-6 and the general and mental health subscales.

Conclusion: Hypervolaemia and uraemia may cause inflammation, decreased HRQoL and malnutrition. Therefore, the establishment of a normovolaemic status and the decrease in uraemia that occur after renal transplantation can contribute to the decline of uremic inflammation, the improvement of the HRQoL and recovery from malnutrition.

P226

IS THE GRAFT FUNCTION OF LIVING DONOR RENAL TRANSPLANTS ASSOCIATED WITH RENAL MASS MATCHING BY CT ANGIOGRAPHIC VOLUMETRY?

Ji Yoon Choi

Department of Surgery, College of Medicine, Hanyang University

Background: Low functional renal mass and mismatch of donor kidney-recipient body size can lead to progressive renal injury and poor graft function.

So, we evaluated the association between living donor renal volumes and graft function after Tx.

Methods: We analyzed 51 consecutive living donor renal Tx carried out between January 2005 and December 2011. The patients were divided into two groups by donor-recipient BSA ratio: group I ($n = 31$, $iA1$) and group II ($n = 20$, >1).

Results: Serum creatinine after renal Tx was correlated with transplanted renal volume at 1 and 12 months ($r = -0.319$, $p = 0.048$; $r = -0.472$, $p = 0.002$). Serum eGFR was also correlated with transplanted renal volume at 3 and 12 months ($r = 0.318$, $p = 0.049$; $r = 0.388$, $p = 0.015$). Serum creatinine levels at 6 and 12 months was higher in group I ($p = 0.022$, $p = 0.007$) and serum eGFR at 6 and 12 months after renal Tx was significantly lower in group I ($p = 0.042$, $p = 0.049$).

Conclusions: Donor's renal volume may reflect allograft function and have a significant impact on graft outcomes.

P227

POST-TRANSPLANT DIABETES MELLITUS: IS IT ASSOCIATED WITH POOR ALLOGRAFT OUTCOMES IN RENAL TRANSPLANTS?

Ji Yoon Choi, Jin Young Kwak

Department of Surgery, College of medicine, Hanyang University

Background: PTDM is associated with poor graft outcomes and increased infections and cardiovascular disease following renal Tx. We assessed the incidence and association between PTDM and graft function.

Methods: We investigated 565 renal Tx and divided into two groups: group 1 ($n = 228$, January 1990 to December 1995) and group 2 ($n = 377$, January 1996 to December 2011). All patients in group 1 received CsA and patients in group 2 received CsA or tacrolimus. We analyzed the clinical characteristics of recipients and long-term graft outcomes.

Results: The incidence of PTDM was 11.7% ($n = 66$). There was a higher incidence of PTDM in the recipients who received tacrolimus than in those who received CsA (25.0% vs. 9.5%, $p = 0.000$) and the delay before the appearance of PTDM was shorter (38.5% vs. 75.8%, $p = 0.017$). Serum creatinine levels at 10 years after renal Tx ($p = 0.756$ in group 1 and $p = 0.559$ in group 2) and long-term graft survival in those groups were not significantly different ($p = 0.067$ in group 1 and $p = 0.125$ in group 2).

Conclusion: Allograft function and outcomes are more impaired in patients with PTDM than in either non-DM or pre-DM. However, if early diagnosis and appropriate treatment of PTDM are carried out, the risk of complications can be minimized and the long-term outcomes improved.

P228

ANALYSIS OF RENAL GRAFT THROMBOSIS AFTER DECEASED DONOR RENAL TRANSPLANT: OUR 5 YEAR EXPERIENCE

Rahul J. Sinha, Chang S. Wong, Hemant Sharma, Adham El-bakry, Daniel Ridgway, Sanjay Mehra, Ajay Sharma, Abdul Hammad

Royal Liverpool University Hospital

Background: This retrospective study was undertaken to analyze the possible etiological factors that caused renal graft thromboses after deceased donor renal transplant.

Material and Methods: Ten patients who had graft thrombosis following deceased donor renal transplant between 1st April, 2006 and 1st April, 2012 were included.

Result: 2.75% of the recipients had renal graft thromboses within the given time period. Mean deceased donor age was 44 years (range 10-68 years). Mean warm ischemia time was 47 min (range 30-54 min). Mean cold ischemia time was 19 h (range 11-28 h). Renal Doppler ultrasound was performed to assess the status of the graft in post transplant period. Mean time interval between transplant and graft thromboses was 3 days (range 2-10 days).

Conclusion: Renal vein thromboses appeared to be the most frequent cause of early graft failure. More effort is required to look for possible etiological factors which could help reduce this problem.

P229

DUPLICATED URETERS AND RENAL TRANSPLANTATION: A CASE-CONTROL STUDY AND REVIEW OF THE LITERATURE

Victor Alberts, Robert Minnee, Frederike J. Bemelman, Pilar Laguna, Mirza Idu

Academic Medical Center

Background: Ureteral duplication in a renal graft might result in an increased complication rate after transplantation. We analyzed our data of double ureter renal transplantations using a case-control study design and we performed a review of the literature.

Methods: From January 1995 to April 2012, twelve patients received a donor kidney with a double ureter (0.8%). We created a control group of 24 patients that matched in age, sex, donor type and ureteral stenting. Patient charts were reviewed retrospectively.

Results: In seven patients both ureters were separately anastomosed to the bladder. In four patients a common ostium was created. In one patient one of the two ureters was ligated. No postoperative urological complications occurred. In the single ureter group, the urological complication rate was 17% ($p = 0.71$). Mean creatinine levels after transplantation were comparable between the groups.

Conclusion: We conclude that transplantation of a kidney with a duplicated ureter is safe.

P230

TRANSPLANT NEPHRECTOMY: WHAT ARE THE SURGICAL RISKS?

Victor Alberts, Robert Minnee, Frederike J. Bemelman, Mirza Idu
Academic Medical Center

Background: Whether or not to remove a failed renal graft has been subject of much debate. We analyzed the morbidity, mortality and risk factors of renal transplant nephrectomy at our center.

Methods: We included 157 cases of transplant nephrectomy in 143 patients, performed between January 2000 and May 2012 at our study center. Patient data were collected retrospectively.

Results: A total of 32 surgical complications occurred after transplant nephrectomy (20%) and 16 patients needed surgical re-intervention (10%). Haemorrhage and infection are the most frequent causes of surgical complications (14%). The mortality rate was 3.2%. There were no significant differences in characteristics and timing of transplant nephrectomy between the group with surgical complications and the group without. A total of 59 re-transplantations were performed in 57 patients (38%).

Conclusion: We found no significant risk factors for surgical complications following transplant nephrectomy.

P231

SUDDEN DEAFNESS WITH THE USE OF ANTI-THYMOCYTE GLOBULIN: CAUSE OR CO-INCIDENCE?

Sheneen Meghji, Clare Pattenden, Michael L. Nicholson
The Renal Transplant Department, Leicester General Hospital, Leicester.

Anti-thymocyte Globulin (ATG) is used to treat acute cellular transplant rejection unresponsive to intravenous steroids. ATG contains antibodies against human T-cells but has numerous adverse drug reactions. There is one case report of hearing loss linked to ATG whereby transient sudden unilateral deafness occurred post-treatment. We describe a patient who experienced sudden deafness 90 min post-infusion. An audiogram demonstrated 93 dB loss in the right and 17 dB loss in the left compared with a baseline audiogram. MRI brain revealed a 3.7 mm right-sided vestibular schwannoma. The post-insult audiogram shows bilateral hearing loss. The schwannoma could not account for this. Timing of onset correlates closely with ATG use, favouring a link. Hearing loss can have a profoundly debilitating impact upon a patient's life. It might be prudent to advise patients of the risk when consenting and patients with predisposing ear pathology may be recommended to get an audiogram pre-treatment.

P232

THE IMPACT OF LONG-FUNCTIONING ARTERIOVENOUS FISTULA ON LEFT VENTRICULAR HYPERTROPHY

Aureuliusz Kolonko, Agata Kujawa-Szewieczek, Magdalena Szotowska, Piotr Kuczera, Jerzy Chudek, Andrzej Więcek
Medical University of Silesia

Background: The aim of this study was to evaluate the impact of long-functioning arteriovenous fistula (AVF) on left ventricular hypertrophy (LVH) in kidney transplant (KTx) recipients.

Methods: This study enrolled 162 patients at 8.7 ± 1.8 years after KTx. LVH was defined based on left ventricular mass (LVM) indexed for body surface area (BSA) or for height^{2.7}.

Results: Patients with patent fistula were characterized by significantly larger LVM and greater percentage of LVH, based on both LVM indexes (66.7 vs. 48.4%, $p = 0.02$ for LVM/BSA and 86.6 vs. 74.7%, $p = 0.06$ for LVM/height^{2.7}, respectively). The OR for LVH in patients with patent fistula was 2.39 (1.19-4.76), $p = 0.01$, and 2.52 (0.99-6.47), $p = 0.05$, respectively. Regression analyses confirmed an independent contribution of patent fistula to the presence of LVH and higher LVM.

Conclusion: Long-lasting patent AVF after KTx plays the important role in the increased prevalence of LVH in kidney transplant recipients.

P233

DETERMINANTS OF RESISTANCE INDEX (RI) IN STABLE KIDNEY TRANSPLANT RECIPIENTS (KTR) DURING LONG-TERM OBSERVATION

Aureliusz Kolonko, Magdalena Szotowska, Piotr Kuczera, Jerzy Chudek, Andrzej Wiecek
 Medical University of Silesia

Background: Increased RI has been associated with poor allograft and patient survival. We evaluate nonrenal determinants of kidney graft RI in stable KTR.

Methods: The study enrolled 174 patients at 8.2±1.8 years after transplant. Echocardiography, kidney graft Doppler, and the assessment of pulse wave velocity (PWV) were performed. Patients were divided into quartile subgroups based on RI value (Q I: RI ≤0.68, Q II: RI 0.69–0.72, Q III: RI 0.73–0.76, Q IV: RI ≥0.77).

Results: The values of age, serum phosphate, PWV, and left ventricular mass index (LVMI) were higher in subsequent RI quartile subgroups. In backward stepwise multivariate regression analysis, the RI variability was strongly explained by age, LVMI, and serum phosphate. PWV has shown an independent contribution to RI variability after the exclusion of age from explanatory variables.

Conclusion: Arterial stiffness and left ventricular hypertrophy may significantly influence intrarenal RI measured in stable KTR.

P234

SERUM FABP4 LEVELS POSITIVELY CORRELATE WITH ARTERIAL STIFFNESS IN KIDNEY TRANSPLANTATION PATIENTS

Ming-Che Lee, Bang-Gee Hsu
 Tzu Chi General Hospital and Tzu Chi University, Hualien, Taiwan

Background: Relationship between fasting serum fatty acid-binding protein 4 (FABP4) levels and arterial stiffness among kidney transplant (KT) patients was evaluated.

Methods and Materials: Fasting blood were obtained from 74 KT patients. Brachial-ankle pulse wave velocity and plasma FABP4 was measured using an automatic pulse wave analyzer and commercial ELISA kit.

Results: Age, KT duration, triglyceride, systolic blood pressure, and FABP4 were positively correlated with arterial stiffness, while serum HDL-cholesterol level was negatively correlated with arterial stiffness. Multivariate forward stepwise linear regression analysis showed that systolic blood pressure (β): 0.259; R² = 0.186, p < 0.001, KT duration (β): 0.353; R² = 0.083, p = 0.006, FABP4 (β): 0.299; R² = 0.069, p = 0.009, and HDL-cholesterol (β): -0.265; R² = 0.061, p = 0.010) were the independent predictors of arterial stiffness.

Conclusion: Serum fasting FABP4 level was positively associated with arterial stiffness among KT patients.

P235

FASTING SERUM ADIPONECTIN REDUCED IN RENAL TRANSPLANT RECIPIENTS WITH PERIPHERAL ARTERIAL DISEASE

Ming-Che Lee, Bang-Gee Hsu
 Tzu Chi General Hospital and Tzu Chi University, Hualien, Taiwan

Background: To evaluate the relationship between peripheral arterial disease and fasting serum adiponectin concentration in renal transplant recipients.

Material and Methods: Fasting blood were obtained from 74 renal transplant recipients. The ankle-brachial index (ABI) values were measured using an ABI-form device by an oscillometric method. Left or right ABI values <0.9 were included in the peripheral arterial disease group.

Results: Ten patients were enrolled in peripheral arterial disease group. Increased triglyceride levels and decreased serum adiponectin levels were noted in the peripheral arterial disease group. Multivariate forward stepwise linear regression analysis of the significant variables revealed that serum adiponectin (β): -0.282; F² = 0.080, p = 0.015) level was independent predictor of the peripheral arterial disease in renal transplant recipients.

Conclusions: Serum adiponectin concentration reduced in renal transplant recipients with peripheral arterial disease.

P236

DOES PREGNANCY AFTER RENAL TRANSPLANTATION AFFECT THEIR ALLOGRAFT AND PREGNANCY OUTCOMES?

Ji Yoon Choi, Jin Young Kwak
 Department of Surgery, College of Medicine, Hanyang University

Background: The number of pregnancies in renal transplant recipients has been increased. Many studies show that it increased the risk of graft, fetal, and maternal complication and doesn't affect on long-term graft outcomes, however, there are limited. Therefore, we assessed the incidence of pregnancy after renal transplantation and examined their graft, fetal, and maternal outcomes.

Materials and Methods: We included 145 women recipients who were in child-bearing age (15–45) in our center from January 1990 to December 2011. All recipients were divided into two groups: pregnancy (n = 17) and control (n = 128). Twenty-six pregnancies in 17 recipients were also classified into live births (n = 10) and no-live births (n = 16) and analyzed to evaluate pregnancy outcomes, graft function and long-term graft survivals.

Results: Pregnancy outcomes included 10 live births, eight therapeutic abortion, seven spontaneous abortion, and 1 stillbirth. The mean serum creatinine levels of pregnant recipients diminished during first trimester (1.14±0.37 mg/dl) and slightly restored to baseline (1.23±0.37 mg/dl) during third trimester (1.18±0.37 mg/dl). It maintained stable ranges. The mean interval from transplantation to pregnancy was 20.73±3.57 months. Live births were associated with the time from transplantation to pregnancy (71.78±37.75 in live births vs. 19.38±12.71 in no-live births, p = 0.000). There were no significant differences in graft function, graft failure rates and survivals.

Conclusion: Pregnancy does not appear to have adverse effect on the graft function and long-term outcomes. If recipients who want to become pregnant maintain their renal function stable, they can have successful pregnancies.

P238

WHAT IS THE TRUE CAUSE OF THE POST-TRANSPLANT LYMPHOCELE IN PATIENTS WITH POLYCYSTIC KIDNEY DISEASE?

Jaroslav Pacovsky¹, Pavel Navrátil¹, Radomir Hyspler², Lukas Holub¹, Milos Brodak¹

¹Department of Urology, Regional Transplant Center, Charles University Medical School Hradec Kralove; ²Clinic of Gerontology and Metabolism, Charles University Medical School Hradec Kralove

Objective: Adult polycystic kidney disease (APKD) is as a risk factor for the lymphocele (LY) formation. The objective of this work was to describe APKD metabolic role.

Method: We have analyzed data of 40 patients who were treated for LY. The Lymphocele Formation Risk Index (LFRI) was calculated. LFRI = albumin/(α1 globulin + γ globulin) the total protein and albumin pre-transplant levels were analyzed. The data of APKD and non-APKD patients were compared.

Results: Eight APKD patients (25%) were found in cohort. The protein levels in APKD resp. in non-APKD were 57.1, resp. 58.2 g/l (ns), albumin levels were 31.4, resp. 36.2 g/l (p 0.06). Median LFRI in APKD, resp. non-APKD patients were 2.29, resp. 3.44 (p 0.02).

Conclusion: The APKD is metabolic factor of high incidence LY in APKD. Not absolute protein and albumin levels, but protein subgroups spectrum are fundamental circumstances. Supported by the project for conceptual development of research organization 00179906.

P239

EVALUATION OF THE PARATHYROID GLANDS REVEALS THE THYROID GLAND INCIDENTALOMAS

Ana Danic Hadzibegovic¹, Ljubica Bubić Filipić², Tomislav Jukic³, Nikolina Basic Jukic², Davor Danic¹, Petar Kes², Lea Katalinic²

¹General hospital Slavonki Brod; ²University hospital centre Zagreb; ³Clinical hospital centre Sisters of mercy

Papillary thyroid carcinoma (PTC) is the most common endocrine malignancy with the increasing incidence in general population. From 1973 to December 2012, 1458 patients received kidney allograft at our institution. We retrospectively reviewed medical files to identify cases of PTC. In five female and three male patients aged 46–59 years, PTC were discovered incidentally based on ultrasonographic screening for evaluation of parathyroid glands pathology 1–19 years after transplantation. Patients underwent total thyroidectomy. The mean size of the largest tumor nodule was 0.72 cm. Postsurgical radioiodine administration was applied. Immunosuppressive protocol was modified, with sirolimus introduced instead of the calcineurin inhibitor in all patients. During the mean follow-up period of 24 months all patients remained disease-free with the stable graft function. Increased rate of PTC may be a consequence of increased diagnostic work-up for evaluation of the parathyroid pathology.

P240

HIGH-URGENCY RENAL TRANSPLANTATION: INDICATIONS AND LONG-TERM OUTCOMES

Lampros Kousoulas, Nikos Emmanouilidis, Wilfried Gwinner, Jürgen Klempnauer, Frank Lehner
 Hanover Medical School

The concept of high-urgency (HU) renal transplantation was introduced in order to offer to patients, who are not able to undergo long-term dialysis treatment, a suitable renal graft in a short period of time. The goal of this study was to evaluate the patient and graft survival after HU renal transplantation and compare them to the outcomes of the non HU renal transplant recipients. The course of 33 HU renal transplant recipients operated on at our center between 1995 and 2010 was retrospectively analyzed. The patient survival of the study

population was 67%, 56% and 56% whereas the graft survival was 47%, 35% and 35% at 5-, 10- and 15-years respectively. In the comparison between our study population and the non HU transplant recipients, our study population presented statistically significant lower patient survival rates. The HU transplant recipients also presented lower graft survival rates, but statistical significance was reached only in the 5-year graft survival rate.

P241

PRE-TRANSPLANT ADYNAMIC BONE DISEASE INCREASES POST-TRANSPLANT OSTEOPOROSIS AND ARTERIAL STIFFNESS

Siren Sezer¹, Emre Tuta¹, Mehtap Erkmn Uyar¹, Zeynep Bal¹, Bahar Gurlek Demirci¹, Orhan gulyev¹, Turan Colak¹, Mehmet Haberal¹
Baskent University Medical School

Background: Previous literature showed strong associations between vascular calcifications and adynamic bone disease. The aim of this study is to evaluate the relationship between pre-transplant bone activity and post-transplant osteoporosis and arterial stiffness in kidney transplant recipients.

Methods: Eighty-three patients' clinical and biochemical parameters, pre-transplant PTH levels, post-transplant lumbar t-scores and pulse wave velocity (PWV) levels were cross sectionally analyzed.

Results: In patients with adynamic bone disease (PTH<100 pg/ml, $n = 24$) post-transplant serum PTH levels were significantly lower than in patients with those pretrans PTH levels>100 (118.5 ± 14.5 vs. 178.9 ± 17.6 pg/ml, $p = 0.029$). In linear regression analysis of factors influencing lumbar t-score; pre-transplant and post-transplant PTH levels were associated with post-transplant osteoporosis ($p = 0.0049$, $p = 0.004$). Pre-transplant PTH levels were negatively correlated with lumbar t-scores ($r = -0.345$, $p = 0.005$). PWV levels were significantly higher in adynamic bone disease group than in normal or hyperdynamic bone disease (7.6 ± 2.5 vs. 6.4 ± 2.0 respectively, $p = 0.08$). In regression analysis for factors influencing PWV pretransplant PTH levels ($p = 0.07$) and age ($p = 0.046$) were the major determinants of PWV.

Conclusions: Pre-transplant serum PTH level is an important determinant of post-transplant osteoporosis and increased arterial stiffness.

P242

10-YEARS FOLLOW-UP OF 753 RENAL TRANSPLANT RECIPIENTS

Krzysztof Mucha¹, Bartosz Foroniewicz¹, Artur Kwiatkowski¹, Tomasz Cieciera¹, Monika Krajewska¹, Slawomir Nazarewski², Maria Nowaczyk¹, Teresa Baczkowska¹, Magdalena Durlik¹, Jacek Szmidt², Andrzej Chmura¹, Leszek Paczek¹

¹Transplantation Institute, Medical University of Warsaw; ²Medical University of Warsaw

Background: The aim of the study was to assess if the choice of immunosuppression (IS) may result in different patient and graft survival and incidence of adverse events (AES).

Methods: Seven hundred and fifty three Renal Transplant Recipients (RTR) Were Divided Into four Groups Depending On the Is: Tacrolimus (TAC), cyclosporine, mycophenolate mofetil, azathioprine (AZA). Graft Function At Month 3 and Every Year, Incidence Of New Onset Diabetes Mellitus (NODAT), Malignancies and Hospitalization Length (Patient/year) were assessed for 10 years.

Results: Ten years patient and graft survival was 88.3% and 78.2%, respectively. Malignancy was diagnosed in 5.4%.no differences were found between is regimens with respect to the studied endpoints, excluding nodat. combination of TAC and AZA resulted in higher nodat incidence than other is combinations ($p < 0.05$).

Conclusion: Is did not influence patient and graft survival. this suggests a need for economic evaluation of is. The patients at risk for diabetes mellitus probably do not benefit from TAC and AZA.

P244

PAINFUL CRURAL ULCERATIONS AND PROTEINURIA AS COMPLICATIONS AFTER SEVERAL YEARS OF THERAPY WITH MTOR INHIBITORS IN THE RENAL ALLOGRAFT RECIPIENT

Lucyna Józwiak, Andrzej Ksiązek
Nephrology Department

The use of mTOR inhibitors is limited because of high incidence of adverse reactions (Sanchez-Fructuoso, A.I. et al. Transplantation Proc 2010; 42: 3050-3052). We report a patient with proteinuria and painful crural ulcerations which appeared after a few years of mTOR inhibitors' therapy and necessitated their withdrawal. A cadaveric kidney recipient, was converted to sirolimus after being diagnosed with carcinoma of his own removed cystic kidney. After 5.5 years of fairly good tolerance of the treatment, the proteinuria and painful crural ulcerations appeared. Because of the progressive character of the adverse reactions and no results of the applied treatment, the mTOR therapy was

discontinued, which reduced proteinuria, relieved pain and favoured healing of the ulcerations. Presented case indicates that adverse reactions may develop as a result of mTOR inhibitor use even after many years of good tolerance of the drug and they may necessitate its withdrawal.

P245

DONOR CISH POLYMORPHISM IS ASSOCIATED WITH ALLOGRAFT OUTCOMES IN KIDNEY TRANSPLANTATION

Tai Yeon Koo¹, Jong Cheol Jeong¹, Hyuk Yong Kwon¹, Yoon Jung Kim², Seon Ha Baek², Hayne Cho Park², Myung-Gyu Kim³, Han Ro⁴, Young-Hwan Hwang⁵, Woo-Kyung Chung⁴, Curie Ahn², Jaeseok Yang¹

¹Transplantation Center, Seoul National University Hospital; ²Department of Internal Medicine, Seoul National University College of Medicine; ³Department of Internal Medicine, Korea University Anam Hospital; ⁴Department of Internal Medicine, Gachon University of Medicine and Science, Incheon; ⁵Department of Internal Medicine, Eulji General Hospital

Background: We evaluated the association of two single nucleotide polymorphisms (SNPs) located in cytokine-inducible SH-2 containing protein (CISH), a negative regulator of IL-2 signaling, with kidney allograft outcomes. Methods

SNPs in CISH (rs414171 and rs2239751) were genotyped in 339 donor-recipient pairs of living-donor kidney transplantation (KT).

Results: There was no association with acute rejection (AR). eGFR tended to be lower in the group with donor rs2239751 AA genotypes for more than 10 years, after correcting for AR, year after transplantation, donor age, gender of donor and recipient, and immunosuppressant regimen (beta = -3.3, $p = 0.057$). Graft survival rate was significantly lower in subjects with donor rs414171 TT than TA+AA genotypes (HR 2.7, 95% CI 1.1-6.9, $p = 0.033$), and it was higher in subjects with donor rs2239751 AC+CC than AA genotype (HR 0.33, 95% CI 0.13-0.84, $p = 0.02$).

Conclusion: Donor CISH polymorphism was associated with long-term graft survival in living donor KT.

P246

HLA MISMATCHES ROLE IN KIDNEY ALLOGRAFT REJECTION IN PATIENTS INDUCED WITH IL-2R ANTIBODIES

Jorge Malheiro, Hugo Silva, Isabel Fonseca, La Saete Martins, Manuela Almeida, Sofia Pedrosa, Leonidio Dias, António Castro-Henriques, António Cabrita

Nephrology and Kidney Transplant Unit, Centro Hospitalar do Porto

Retrospective analysis of acute rejection (AR) during the first 6-months posttransplant, and its influence on graft function and survival in 255 adult renal graft recipients treated with a quadruple IS regimen (TAC, MMF, Pred, IL2Rantibody), between 2004 and 2010 in our centre. Thirty (11.8%) patients were treated for AR in the first 6 months posttransplant. Population characteristics and group comparison are shown below. In a multivariate (recipient gender, panel reactive antibody >15%, second graft, number of HLA mismatches by each locus) logistic regression analysis, only increasing number of HLA-DR mismatches was an independent predictor of AR (OR 1.98 per each HLA-DR mismatch, $p = 0.014$); no association was found between HLA-A ($p = 0.52$) or -B ($p = 0.16$) mismatches and AR. Death-censored graft survival according with AR status is shown below. Only HLA-DR matching was a significant predictor of AR and, therefore, remains an important tool in improving kidney graft outcomes.

P247

HLA IDENTICAL LIVING DONOR KIDNEY TRANSPLANTATION: LONG TERM OUTCOMES

Mediha Boran¹, Ertay Boran², Mertay Boran³

¹Department of NDT, Turkish Higher Education Hospital, Ankara, Turkey; ²Izmir Katip Celebi University, Ataturk Training and Research Hospital, Izmir, Turkey; ³Cankiri State Hospital, Cankiri, Turkey

Background: We aimed to assess the clinical outcomes of kidney transplant recipients (KTR) with human leukocyte antigen (HLA) identical living donor (HLAID) receiving different immunosuppressive treatments (IT).

Methods: Data of 25 HLAID KTR between 1994 and 2010 years were collected. Patients were divided into 3 groups based on IT: Cyclosporine A (CsA); Tacrolimus (TAC) and Sirolimus (SRL). All groups received also mycophenolate mofetil (MMF) 1000 mg/day. If there was no acute rejection (AR) until 90th posttransplant day (PTD) and until 180th PTD, CsA and TAC doses were reduced 50% and 75%, respectively, with prednisone 2.5 mg/day maintenance.

Results: Table 1. At median follow-up of 84 (range 32–232) months, patients survival and graft survival was 100% without any CMV disease or BK nephropathy.

Conclusion: The maintenance IT with low doses of mTOR (mammalian target of rapamycin) inhibitors and MMF provides very effective and safe regimen with perfect patient survival, graft survival and renal function for HLAID kidney transplantation.

References: Alloway RR et al. *Am J Transplant.* 2011;11:408.

P248

FIVE TIMED ORAL GLUCOSE TOLERANCE TEST AS A PREDICTOR OF NEW-ONSET DIABETES AFTER KIDNEY TRANSPLANTATION

*Kazuaki Tokodai, Noritoshi Amada, Hiroyuki Kikuchi, Izumi Haga, Tetsuro Takayama, Atsushi Nakamura
Sendai Shikaihoken Hospital*

Background: New-onset diabetes after transplantation (NODAT) is a serious complication after kidney transplantation. It is of great importance to identify the high-risk group to develop NODAT for its prevention. The efficacy of 2-h plasma glucose (2 h-PG) in pretransplant oral glucose tolerance test (OGTT) has already been reported. However, the predictive power of five timed OGTT remains unknown. In this study, we sought to evaluate the predictive power of postload plasma glucose of each time point. To elucidate the utility of pretransplant OGTT, we also assessed the predictive models based on 1-h plasma glucose (1 h-PG) and 2 h-PG.

Materials and Methods: We performed a retrospective study of 146 nondiabetic patients who received living donor kidney transplantation in Sendai Shikaihoken Hospital from March 2000 to June 2011. We compared five timed OGTT values and demographic variables of patients who developed NODAT with those who did not.

Results: Seventeen patients (11.6%) developed NODAT within 1 year after transplantation. All of the postload plasma glucose concentrations were higher in patients who developed NODAT, while fasting plasma glucose showed no significant difference. Univariate and multivariate analyses indicated each of the postload plasma glucose as an independent risk factor for NODAT. Furthermore, patients with normal glucose tolerance (NGT) and with impaired glucose tolerance (IGT), who were classified using the American Diabetes Association criteria, could be stratified with a 1 h-PG cut point of 152 mg/dl; the rates of the incidence of NODAT were 23.5%, 16.7%, 9.1%, and 0% for patients with (IGT + 1 h-PG \geq 152 mg/dl), (IGT + 1 h-PG < 152 mg/dl), (NGT + 1 h-PG \geq 152 mg/dl), and (NGT + 1 h-PG < 152 mg/dl), respectively.

Conclusion: The postload plasma glucose at each time point during pretransplant OGTT is a strong predictor of NODAT. A 1 h-PG cut point of 152 mg/dl plus NGT/IGT can be used to identify intermediate- and high-risk groups to develop NODAT.

P250

SUCCESSFUL SALVAGE OF RUPTURED LIVING RELATED KIDNEY TRANSPLANT

*Mohammad Hamshow, Basem Hegab, Abdulrahman Altamimi, Noura Aloudah, Khaled Alsaad, Mohamad Nouredin Almarastani
National Guard Health Affairs, King Abdulaziz Medical City*

Forty-two years old female with end stage renal disease on hemodialysis underwent living related kidney transplant from her son. On post day four patient had right lower quadrant pain with hypotension and tachycardia. Bed side ultrasound showed large perinephric hematoma extending retroperitoneal for 20 cm above the upper pole of the kidney. Patient was taken to the operation room for exploration which showed a large crack on the lateral side of the graft extending from the upper pole to the lower pole around 10–12 cm length. Bleeding was controlled using argon and tacho seal was put in the crack and Biogluce injected over it and pressure applied by wet gauze for 10–15 min. The bleeding stopped and biopsy was taken from upper pole using 18 gauge needle gun biopsy. Biopsy showed antibody mediated rejection. Kidney function improved and patient discharged in a good condition with serum creatinin 54 μ mol/l. Graft nephrectomy is not a must in acute rupture of kidney transplant.

P251

BONE LOSS IN KIDNEY TRANSPLANT RECIPIENTS

*Ruzica Smalcelj, Ivan Barisic
University Hospital Center Zagreb*

Bone mineral density (BMD) changes were estimated in kidney recipients. In 62 patients creatinine clearance was > 50 ml/min over the study period, BMD was estimated in the lumbar spine, femoral neck and the distal third of the radius using dual energy absorptiometry 0.1–4, 12–19 and 23–36 months after transplantation. BMD changes (delta BMD, \pm %) between measurements were calculated per 12 months (median); (i) first: second measurement; lumbar spine -2.87 , femoral neck -1.925 , distal radius -1.505 , (ii) second: third

measurement; lumbar spine 1.59 , femoral neck 1.955 , distal radius -0.88 . Dialysis duration prior transplantation correlated significantly negatively with radius BMD at all measurements. During the first posttransplant year, the majority of patients lost cortical and trabecular bone. For cortical bone, this trend continued after this period. The time spent on dialysis was a risk factor for cortical bone loss.

P252

CLINICAL ANALYSIS OF POST-TRANSPLANT LYMPHOPROLIFERATIVE DISORDERS

*Hyun Hee Lee, Yeon Ho Park, Woo Kyung Chung, Ji Yong Jung, Jae Hyun Chang, Han Ro
Gachon university*

Post-transplant lymphoproliferative disorders (PTLDs) are rare major complications of organ transplantation with poor patient prognosis. We collected data from different published studies in the transplant centers of Korea. Overall 88 patients were identified from 14 792 solid organ and 10 310 bone marrow transplant recipients. There were 64 adults (age ≥ 18 year) and 24 children (age < 18 year). The number of male patients were 61 (69.3%) and female were 27 (30.7%). The mean interval between transplantation and PTLD was 58.5 months (range, 2–240). The rate of Early onset (<1 year) and late onset (1A 1 year) PTLDs were 39.6% and 60.4%, respectively. At the time of PTLDs, 53.8% of patients showed EBV infection or activation. EBV infection status and disease onset time were not related to outcomes of patients. Multiple organ involvement was 45.2% and showed poor prognosis. Monomorphic PTLD histology was most common and slightly associated with poor patients survival. All the patients were treated with discontinuation or reduction of immunosuppressive agents and/or additional modalities. Overall patients survival was 59.5%. We need to early diagnosis and treatment of late onset PTLD in transplant recipients. Because the incidence of late onset PTLD is high, poor response to treatments, and long post-transplant latency period.

P253

THE RELATION BETWEEN EPICARDIAL ADIPOSE TISSUE WITH VOLUME MARKERS AND INFLAMMATION MARKERS, WITHIN DIALYSIS AND TRANSPLANT PATIENTS

*Hülya Colak¹, Bary Kılıççalan¹, İsmail Sert¹, Mehmet Tanrısev¹, Cenk Ekmekci¹, Cezmi Karaca¹, Seyhun Kursat², Hüseyin Töz³
¹Tepecik Training and Research Hospital; ²Celal Bayar University; ³Ege University*

The aim of the study was to evaluate the relation between epicardial adipose tissue with volume markers and inflammation markers within chronic hemodialysis, peritoneal dialysis, renal transplant patients and control group. Total number of 160 patients, 40 people in each group, chronic hemodialysis (CHD), peritoneal dialysis (PD), renal transplant (RT) patients and the control group were evaluated. To evaluate volume status of patients, left atrium (LA), LA index (LAI), left ventricular mass (LVM), LVM index (LVMI), collapse of the inferior vena cava index (IVCCI), ejection fraction (EF), and the EAT were evaluated by echocardiography (ECHO) and additionally, systolic-diastolic blood pressures (BP) of the patients were recorded. Inflammation markers (IL-6, hsCRP) were measured. Biochemistry markers were tested. IL-6, hsCRP, systolic-diastolic BP, LA, LAI, LVM, LVMI for CHD patients were significantly higher than the other three groups. On the other hand, IVCCI and EF values were lower than the others. EAT values for CHD patients were higher than the other groups. Correlation analyses were done for CHD patients to evaluate the relation between anthropometric markers, laboratory data and ECHO parameters with EAT. Significant data for these analyses were BMI, hsCRP, IL-6, LAI, LVMI, IVCCI. BMI, LAI and IVCCI were found independent predictors for high EAT values. Significant relation was found between volume markers and EAT in CHD patients with the highest volume overload in present study. It is considered that EFT follow-up could give some information regarding volume condition and EAT might be accepted as a new marker for volume evaluation.

P254

TLR9 GENE POLYMORPHISM: ASSOCIATION WITH ACUTE REJECTION IN RENAL TRANSPLANT RECIPIENTS

*Yeong Hoon Kim, Seok Ju Park, TaeHee Kim, Sun Woo Kang
University of Inje*

The Toll-like receptors (TLRs) are related to innate immunity. We investigated the association between TLR9 polymorphisms and kidney allograft outcomes. To investigate whether TLR9 polymorphisms are associated with acute rejection after renal transplantation, two SNPs of TLR9 gene (rs187084, -1486; rs352140, G2848A) were selected and genotyped by direct sequencing in 342 renal transplant recipients. Both SNPs, TLR9 rs187084 - 1486 and rs352140 G2848A, of recipients were associated with the risk of acute rejection in renal transplantation. C allele of rs187084 - 1486 and A allele of rs352140

G2848A were protective genotype for acute rejection (OR 0.6, 95% CI 0.40–0.92; $p = 0.018$, OR 0.64, 95% CI 0.42–0.98; $p = 0.04$, respectively). rs187084 CT and rs352140 GA genotype were associated with a lower eGFR after a year of renal transplantation. TLR9 polymorphisms of recipients were associated with the risk of acute rejection and a lower eGFR after a year of renal transplantation.

P255

IMPACT OF THE COMBINATION OF CYTOMEGALOVIRUS INFECTION AND ACUTE REJECTION ON CLINICAL OUTCOMES IN KIDNEY TRANSPLANTATION: A SINGLE CENTER EXPERIENCE

Takuzo Fujiwara¹, Shinichiro Tanaka¹, Kouichiro Okada¹, Kei Namba¹, Haruchika Yamamoto¹, Hiroaki Matsuda²

¹Okayama Medical Center/National Hospital Organization; ²Saiwaicho Memorial Hospital

Background: Cytomegalovirus (CMV) Infection and acute rejection (AR) are major complications of organ transplantation.

Patients and Methods: We analyzed outcomes in 145 kidney transplant recipients at our center. Patients were categorized according to the occurrence of AR and/or CMV infection within the first 12 months after transplantation. Group 1 ($n = 79$) without AR or CMV; Group 2 ($n = 21$) with AR; Group 3 ($n = 22$) with CMV infection; and Group 4 ($n = 23$) with both AR and CMV.

Results: Death-uncensored graft survival rates in the four groups were 94.9%, 90.5%, 83.8%, and 65.2% ($p = 0.007$), whereas mean eGFR 1 year after transplantation in these 4 groups was 54.1, 14.4, 42.9, 11.2, 44.8, 10.6, and 37.4, 13.9 ml/min/1.73 m², respectively ($p < 0.001$). When patients in Group four were subdivided into those with AR and CMV occurring with intervals of <40 days ($n = 9$) and >40 days ($n = 13$), graft survival rate was worse in the former (35.3% vs. 85.7%, $p = 0.019$).

Conclusion: The combination of CMV and AR after kidney transplantation was associated with poor outcomes, especially when the interval between complication was shorter.

P256

DRUG AND PILL BURDEN IN KIDNEY GRAFT RECIPIENTS

Jadranka Buturović-Ponikvar, Ales Christian Mihelac, Jakob Gubensek, Miha Arnot, Aljoša Kandus, Rafael Ponikvar

Department of Nephrology, University Medical Center Ljubljana

Objective: To assess drug and pill burden in kidney graft recipients.

Methods: All Slovenian adult patients with functioning kidney graft at the end of 2012 were included in the retrospective cross sectional study. Number of drugs and pills reported in medical chart from the last outpatient visit in 2012 were counted. Estimated glomerular filtration rate (eGFR/1.73 m², MDRD), duration of renal replacement therapy (RRT) and time after transplantation were evaluated in multivariate model.

Results: About 634 kidney graft recipients, 55% males, aged 54 A ± 14 years (median 55) participated in the study. Average time after transplantation was 100 A ± 75 months (median 94 months, range 1–438), duration of RRT was 179 A ± 125 months. Mean eGFR was 58 A ± 21 ml/min/1.73 m² (median 58). The mean number of drugs prescribed per day was 10.5 A ± 3.5 (median 10, range 2–26). The mean number of pills prescribed per day was 19.9A±9.1 (median 19, range 3–46). In multiple linear regression analysis age ($B = 0.05$, $p < 0.001$), male gender ($B = 0.81$, $p = 0.001$), diabetes ($B = 1.19$, $p < 0.01$), eGFR ($B = -0.05$, $p < 0.001$) and time after transplantation ($B = -0.01$, $p < 0.001$) were identified as independent predictors of number of drugs, while time on RRT was not. Independent predictors of number of pills per day were male gender ($B = 2.15$, $p < 0.001$), eGFR ($B = -0.05$, $p < 0.001$) and time after transplantation ($B = -0.04$, $p < 0.001$).

Conclusions: Drug and pill burden in kidney graft recipients is high. Male gender, lower eGFR and shorter time after transplantation were independent predictors of number of drugs and pills prescribed. Strategies to reduce drug and pill burden should be explored in future, to avoid drug interactions and improve patients' adherence.

P257

IMPACT OF COMBINED ACUTE REJECTION ON BK VIRUS-ASSOCIATED NEPHROPATHY IN KIDNEY TRANSPLANTATION

Tai Yeon Koo¹, Woo Kyung Cheong², Hyuk Yong Kwon¹, Jong Cheol Jeong¹, Curie Curie Ahn¹, Jaeseok Yang¹

¹Transplantation Center, Seoul National University Hospital; ²Department of Internal Medicine, Gil Hospital

Background: BK virus-associated nephropathy (BKVAN) can occur concurrently with acute rejection (AR).

Method: We retrospectively analyzed biopsy-proven BKVAN in kidney transplant patients from 2000 to 2011.

Results: Among 14 patients of BKVAN, nine patients had BKVAN alone. There were two graft losses and one patient death. Five patients were found to have both BKVAN and AR. BKVAN in BKVAN/AR group was detected earlier than in the BKVAN alone group (6.39 vs. 21.77 months, $p = 0.03$). Histological grade was more advanced ($p = 0.034$). Steroid pulse and ATG were administered to four and one patient, respectively. After anti-rejection therapy, all patients reduced immunosuppression, and two patients received IVIG. Graft loss occurred in one patient. BKV load, dose of immunosuppressants, and tacrolimus level showed a lower tendency in the BKVAN/AR group. Renal functional deterioration over 1 year after BKVAN diagnosis was similar.

Conclusion: The prognosis of BKVAN/AR might be similar as that of BKVAN alone.

P258

SUCCESSFUL WITHDRAWAL OF ANTIVIRAL TREATMENT IN KTR WITH CHRONIC HEPATITIS B VIRUS INFECTION

Chan-Duck Kim, Jeong-Hoon Lim, Hee-Yeon Jung, Seung-Chan Park, Kyung-Hoon Kim, Owen Kwon, Ji-Young Choi, Jang-Hee Cho, Sun-Hee Park, Yong-Lim Kim

Department of Internal Medicine, Kyungpook National University Hospital

Background: We proposed criteria for withdrawal of antiviral agents and reported long-term outcomes after withdrawal in kidney transplant recipients (KTR) with chronic hepatitis B virus (HBV) infection.

Methods: HBsAg (+) KTR treated with antiviral agents were enrolled. Antiviral agents were withdrawn in KTR who met the following criteria: (i) normal liver biochemistry, (ii) HBV DNA (–) and HBeAg (–), (iii) at least 9 months antiviral treatment.

Results: Among a total of 424 KTR, 14 HBsAg (+) KTR were included. Antiviral therapy suppressed viral replication in 11 KTR (78.6%). Long-term graft and patient survival of HBsAg (+) KTR were comparable to those of HBsAg (–) KTR. Discontinuation of antiviral agent was attempted in 6 (42.9%) of 14 patients who satisfied the criteria. Four (66.7%) of six KTR were successfully withdrawn and remained negative for HBV DNA for 62.5 vs. 14.7 months.

Conclusion: Antiviral therapy can be successfully discontinued in selected KTR with chronic HBV infection.

P259

OLD-FOR-OLD KIDNEY TRANSPLANTATION WITHOUT PRETRANSPLANT CROSS-MATCH

Eytan Mor, Maya Mor, Rachel Michowiz, Sigal Eizner, Eviatar Neshet, Ezra Shaharabani, Evgeny Solomonov, Tiki Mashraki, Ruth Rahamimov
Rabin Medical Center

Allocation of kidneys from old donors to old recipients was launched in Israel in 2001. We reviewed our experience with old-for-old (OFO) transplantation.

Patients and Methods: We analyzed graft and patient survival, ATN and primary non-function rates in a cohort of 87 transplants performed between 2001 and 2011. All patients had 0% PRA and allocation was based on time on dialysis only. CDC cross-match results were reported at transplant. Survival analysis was done using Kaplan–Meier method on SPSS program.

Results: The mean age of the donor and recipient was 65.4 and 65.3 y, respectively. Mean cold ischemia was 8.1 h (4.3–12.4 h). ATN rate was 54%. Three grafts never functioned, one probably due to antibody-mediated rejection. Overall 33 grafts were lost with 15 (45.5%) of which for death with a functioning graft. Graft survival rates at 1, 5 and 10 years, were 81.7%, 62.6% and 23.8%. Patient survivals at 1, 5 and 10 years were 87.2%, 75.7% and 25.2%.

Conclusions: The use of kidneys from elderly donors in age matched recipients yields a relatively good graft survival for the short term. Omitting cross-match test before transplant in these low-risk group allows to keep a short cold ischemia.

P260

DIAGNOSTIC VALUE OF ENZYMEMIA AND ENZYMURIA IN RECIPIENTS WITH CHRONIC KIDNEY ALLOGRAFT DYSFUNCTION (CKAGD)

Alexander Nikonenko, Andrei Trailin, Nadezhda Yefimenko, Tamara Nikonenko, Tatiana Ostapenko, Marina Pleten

SI "Zaporizhzhia Medical Academy of Postgraduate Education Ministry of Health of Ukraine"

Introduction: The aim of the study was to investigate the diagnostic value of the enzymemia and enzymuria as markers of CKAGD.

Methods: Alkaline phosphatase (AP), γ -glutamyltransferase (γ -GGT), alanine-aminotransferase (ALT), aspartate-aminotransferase (AST) were measured in the serum and urine by standard laboratory methods using the spectrophotometry. N-acetyl- β -D-hexosaminidase (NAG) activity was measured in the urine by a colorimetric assay.

Results: Analysis of the results showed no significant differences in the activity of the enzymes in the blood, while it found significant increase in the urinary excretion of γ -GGT, AP, NAG and AST in patients with CKAGD (serum creatinine above 150 μ mol/l). Univariate logistic regression revealed that only the activities of AP (OR=1.13, $p = 0.04$) and NAG (OR=1.26, $p = 0.01$) were significantly associated with the CKAGD. Multivariate analysis showed that only the activity of NAG in urine had an independent predictive value (OR=1.38, $p = 0.01$).

Conclusion: Our findings demonstrate the inutility of enzymes studies in the serum in the monitoring of CKAGD. They confirmed the diagnostics value of urinary enzymes, especially, NAG, that indicates the ongoing damage of the tubules epithelium and requires prescribing of relevant therapy.

P261

GENETIC DIAGNOSIS OF RARE NEPHROPATHIES AFTER RENAL TRANSPLANT: AN UNMET CHALLENGE

Marco Quaglia¹, Roberta Fenoglio², Elisa Lazzarich², Andrea Airoldi², Cristina Izzo², Mara Giordano¹, Piero Stratta¹

¹Amedeo Avogadro University, Novara; ²Maggiore della Carità Hospital, Novara

Background: Several undiagnosed rare disorders could be recognized after renal transplant (Tx) through genetic analysis.

Material and Methods: We analysed a ten-year experience (2003–2012) of a genetic diagnosis of rare nephropathies after Tx. This was performed for: uromodulin or HNF1 β -associated nephropathy (chronic interstitial nephropathy and renal cysts, extrarenal involvement); Fabry disease; "Dense deposits disease" (DDD); adenine phosphoribosil-transferase (APRT) deficiency (intratubular 2,8 dihydroxyadenine crystals in acute renal failure); mutation of formin 2 (nephrotic syndrome).

Results: Six nephropathies were diagnosed in nine patients: 2 UMOD and 2 HNF1 β -associated nephropathies; one DDD; one FSGS from INF2 mutation; one Fabry and 2 APRT-deficiency nephropathies. The latter relapsed on the graft and diagnosis was crucial for management.

Conclusion: Genetic analysis has the potential to disclose rare nephropathies in Tx with heavy clinical implications.

P262

TERIPARATIDE IN RENAL TRANSPLANT PATIENTS WITH SEVERE HYPOPARATHYROIDISM

Luis Leon, Demian Curcio, Olga Guardia, Maria del C Rial, Domingo H. Casadei

Nephrology SA

Objective: To evaluate teriparatide subcutaneous (sc) treatment in renal transplant patients with symptomatic post-surgical hypoparathyroidism.

Materials and Methods: We reported the treatment of teriparatide 20 μ g/day (sc) in three patients who received a renal transplantation from deceased donor with post-surgical symptomatic hypoparathyroidism since January 2012. The following biochemical parameters were determined: (Basal time, 1°, 3° 6° y 12° months post treatment), ionic calcium (normal value: 1–1.30 mmol/l), phosphatemia (NV: 2.5–4.50 mg/dl), magnesemia (NV: 1.70–2.40 mg/dl), alkaline phosphatase (NV: 120–270 mU/l), Calciuria (NV 60–200 mg/day), uric acid (NV 3.3–7 mg/dl y 2.2–5.7 mg/dl in women), cholesterol (NV150–200 mg/dl), iPTH (NV 35–72 pg/ml), 25OHD (NV >40 ng/ml) and serum creatinine (0.8–1.2 mg/dl). All patients received in post transplantation thymoglobuline (6 mg/kg) and subsequent maintenance immunosuppression with calcineurin inhibitors (2 pts), sirolimus (1 pts), all associated with mycophenolate and methylprednisolone. Besides, all the patients were treated with ergocalciferol, calcium and calcitriol.

Results: Three pt received a renal transplantation from deceased donors (1 patient a 2°TX) 2 male, Mean age: 42, 6 \pm 6.02 years, CKD Etiology: obstructive uropathy, unknown, systemic lupus erythematosus. Time on dialysis (mean): 101.3 \pm 121, 7 m, Transplant follow up: 6 \pm 3, 46 years, Parathyroidectomy: one patient previous transplantation; two patients after 4 years of transplantation. All cases were due to severe secondary hypoparathyroidism with subtotal parathyroidectomy indication. Two pts showed convulsion due to hypocalcemia in the immediate parathyroidectomy surgery, one of them fell down and had a clavicle and scapula fracture. Patients continued with hypoparathyroidism in their follow up (PTH <5 ng/ml) with symptomatic hypocalcemia despite of required high doses of calcium and calcitriol (oral and intravenous administration) and ergocalciferol (oral administration; keeping levels of 25 OHD in 40 ng/ml) so in January 2012, all the patients started with synthetic human parathyroid hormone. Once teriparatide was administered, calcium and calcitriol requirements substantially diminished and were afterwards suspended (in 30 days). SIDE EFFECTS at initial time: only one patient experienced nausea, mild hypotension, numbness of the legs (due to hypomagnesemia) one patient presented chills episodes, tachycardia and dyspnea at 9° month of the treatment. Therefore, teriparatide was discontinued. She did not show any other symptoms within the subsequent days (As described in the literature have been detected antibodies with cross-reactivity with Teriparatide in 2.8% of women treated with this medication, usually after 12 months of treatment yielding the symptoms to suspend it). Non alterations

in creatinine levels and urinary calcium were observed but a slight increase in uric acid, cholesterol and alkaline phosphatase (PTH effect) were exhibited (Table).

Conclusion: The use of intermittent synthetic parathormone is a therapeutic option in those patients with hypoparathyroidism. It reduces their calcium and calcitriol requirements and remarkably improves their life standard.

References: Nogueira EL, y col, Teriparatide efficacy in the treatment of severe hypocalcemia after kidney transplantation in parathyroidectomized patients: a series of five case reports, Transplantation, 2011 Aug 15: 92(3): 316–20.

Mahajan A, Hypoparathyroidism associated with severe mineral bone disease postrenal transplantation, treated successfully with recombinant PTH, Hemodial Int, 2009.

P263

THE IMPACT OF ABCB1 SNP ON STEROID RESPONSIVENESS FOR ACUTE REJECTION IN KIDNEY TRANSPLANTATION

Yeon Ho Park¹, In Eui Bae¹, Woo Kyung Chung², Hyun Hee Lee², Jaeseok Yang³, Curie Ahn⁴

¹Department of Surgery, Gil Medical Center, Gachon University; ²Department of Internal Medicine, Gil Medical center, Gachon University; ³Transplantation Center, Seoul National University Hospital; ⁴Department of Internal Medicine, Seoul National University Hospital

Background: Steroid pulse therapy has been used for patients with acute rejection after kidney transplantation. The ABCB1 gene codes for P-glycoprotein, a transporter involved in the metabolism of steroid. However, role of ABCB1 polymorphisms have not yet been delineated in patients with acute rejection after kidney transplantation.

Methods: Among 763 patients performed kidney transplantation or simultaneous pancreas-kidney transplantation at Seoul National University Hospital between May 1996 and July 2009, 684 patients agreed genetic sampling for polymorphism.

Results: Steroid resistant group showed higher serum creatinine than steroid sensitive group. Frequency of ABCB1 gene polymorphism (C1236T and C3435T) did not show significant difference between steroid sensitive group and steroid resistant group.

Conclusions: ABCB1 gene polymorphism (C1236T and C3435T) did not associate with steroid resistance in patients with acute rejection after kidney transplantation.

P264

ANTI-INFLAMMATORY IL-10 AND PROFIBROTIC TGF- β 1 FAILED AS PREDICTORS OF KIDNEY ALLOGRAFT'S FATE

Oktawia Mazanowska¹, Dorota Kaminska¹, Magdalena Krajewska¹, Miroslaw Banasik¹, Marcelina Zabinska¹, Katarzyna Koùcielska-Kasprzak¹, Pawel Chudoba², Dariusz Patrzalek², Maria Boratynska¹, Marian Klinger¹

¹Department of Nephrology and Transplantation Medicine, Wrocław Medical University; ²Department of Vascular, General and Transplant Surgery, Wrocław Medical University

Background: The aim of the study was to assess IL-10 and TGF- β 1 in renal transplant recipients (RTR) as predictors of allograft failure.

Methods and Material: IL-10 and TGF- β 1 were assessed by ELISA in 150 RTR (aged 49A \pm 11 y., male 66%).

Results: Only plasma TGF- β 1 ($p = 0.05$) had a tendency to be increased in 105 RTR with eGFR < 60 ml/min/1.73 m² [IL-10: plasma ($p = 0.9$) and urine ($p = 0.7$); TGF- β 1: urine ($p = 0.4$)]. After 1 year no one factor correlated with eGFR (IL-10: plasma: $p = 0.1$; urine: $p = 0.8$; TGF- β 1: plasma: $p = 0.1$, urine: $p = 0.9$). Within 2-years 12 RTR lost graft function, but in regression analysis neither IL-10 (plasma: unavailable data; urine: $p = 0.99$) nor TGF- β 1 (plasma: $p = 0.4$, urine $p = 0.8$) had an independent impact on graft survival.

Conclusions: IL-10 and TGF- β 1 are not good predictors of kidney allograft fate in prospective analysis.

P265

PLASMA EXCHANGE FOR THE RECURRENCE OF PRIMARY FOCAL SEGMENTAL GLOMERULOSCLEROSIS IN RENAL TRANSPLANT RECIPIENTS: A META-ANALYSIS

Georgios Vlachopoulos¹, Argvrios Georgalis², Harikleia Gakiopoulou³

¹IATOS Dialysis and Nephrology Centre, Chania, Greece; ²Nephrology Department, Evangelismos Hospital, Athens, Greece; ³1st Department of Pathology, University of Athens, Athens, Greece

Background: Post renal transplantation recurrence of primary focal segmental glomerulosclerosis (rFSGS) in the form of massive proteinuria is not uncommon and has detrimental consequences on allograft survival. We

reviewed published studies for the role of plasma exchange (PLEX) and its variants on rFSGS in adults.

Methods and Materials: Eligible manuscripts compared PLEX with supportive care for inducing proteinuria remission (PR) in rFSGS and they were identified through MEDLINE and reference lists. Data were abstracted in parallel by two reviewers. No randomized controlled trial met the defined inclusion criteria.

Results: We identified four cohort trials which used historical control groups. A total of 93 patients were included in the analysis. In a random effects model, the pooled risk ratio for the composite end-point of partial or complete PR was 3.19 for patients treated with PLEX compared with controls (95% CI: 1.72–5.90, $p < 0.05$). No statistically significant heterogeneity was detected ($p = 0.33$, $I^2 = 13\%$).

Conclusion: Notwithstanding the inherent limitations of non randomized trials, PLEX appears to be efficacious for PR in rFSGS. Additional research is needed to further elucidate its impact on long-term allograft survival.

P266

PROGNOSTIC VALUE OF PRE-TRANSPLANT SERUM KYNURENINE LEVELS IN KIDNEY TRANSPLANTATION

Jürgen Kaden¹, Dietmar Abendroth², Andreas Völp³, Michael Marzinzig², Claus Wesslau¹

¹Municipal Friedrichshain Hospital Berlin; ²University of Ulm; ³Psy Consult Scientific Services

Background: The activation of indoleamine 2,3-dioxygenase leads to the formation of kynurenine (Kyn) and other metabolites which counter-regulates immune activation. But in chronic immune activation – as in hemodialyzed patients – the immunosuppressive feedback mechanisms continue as indicated by elevated Kyn concentrations. However their prognostic relevance is still a matter of debate.

Materials and Methods: This retrospective analysis presents the pre-transplant Kyn levels (quantified photometrically) of 307 kidney graft recipients in connection with some pre- and post-transplant variables and the type of immunosuppression (cyclosporine based triple drug therapy without/with ATG-[Fresenius]-induction). Statistics: analysis of variance, Scheffé's test for pairwise comparisons, Cox regression, extended CHAID segmentation analysis.

Results: The pre-transplant Kyn levels were significantly elevated in comparison to those of 257 healthy adults (14.1 ± 5.9 vs. 2.5 ± 0.4 nmol/ml). The magnitude of the pre-transplant Kyn levels was higher in Panel-Reactive-Antibody-positive ($\geq 5\%$, $n = 196$) than in PRA-negative ($< 5\%$, $n = 111$) patients (16.1 vs. 12.9 nmol/ml; $p = 0.0001$) but was neither related to underlying disease and time on dialysis nor to rejections and graft survival, however to a certain degree to post-transplant graft function (immediate versus non-immediate: $p = 0.053$). Post-transplant differences in graft outcome depended mainly on the type of immunosuppression.

Conclusions: The pre-transplant elevated serum Kyn levels did not predict graft outcome.

P267

NET TIME-DEPENDENT ROC CURVES: A NEW METHOD FOR EVALUATING THE ACCURACY OF A MARKER TO PREDICT MORTALITY RELATED TO END-STAGE RENAL DISEASE IN KIDNEY TRANSPLANT RECIPIENTS

Marine Lorent¹, Yohann Foucher¹, Magali Giral-Classe²

¹Department of Biostatistics EA 4275, University of Nantes; ²ITUN, Nantes Hospital and University, Inserm U1064,

Background: Identifying prognostic markers of mortality in transplantation is essential for determining patients at high-risk of death and optimizing medical management. Nevertheless, an important part of the mortality may not be due directly to end-stage renal disease and/or kidney transplantation. Moreover, it is often impossible to individually determine the death causality, for example a cancer can be related to the chronic disease and immunosuppressive drug exposure or this cancer would have an independent link.

Methods: In survival analysis, one solution is to distinguish between the expected mortality of one general population (estimated on the basis of mortality tables) and the excess mortality attributable to the pathology, by using an additive relative survival model. The main objective of such models is to estimate the "net survival", survival which would be observed if the only possible death is related to the transplantation. We have adapted this concept in order to evaluate the capacity of a marker to predict the mortality attributable specifically to transplantation.

Results: We illustrate this method of net time-dependent ROC curves with the analysis of kidney transplant recipients of the DIVAT (Nantes). From 1230 patients and by using the mortality tables of the general population, we have validated the score of Hernandez et al. (Transplantation 2009) to predict the all-cause mortality for a prognostic time at 10 years post transplantation (AUC=0.68, CI95%=[0.62, 0.74]). However, this score seems to not predict the mortality specifically related to end stage renal disease in the ten years post transplantation (AUC=0.65, CI95%=[0.56, 0.72]). We have modified this score by recalculating each variable weight. This modified score allows to do a better prognostic of the excess mortality (AUC=0.73, CI95%=[0.64, 0.80]).

Conclusion: This method is particularly useful when attribution of the deaths is impossible.

P268

CLINICAL SIGNIFICANCE OF THE FLOW CYTOMETRIC CROSSMATCH IN THE LUMINEX ERA OF KIDNEY TRANSPLANTATION

Jonathan Wong, Kamini Rao, Arun Gupta, Sarah Edwards, Daniel McCloskey, Raj Thuraisingham

Barts and the Royal London NHS Trust

Introduction: Flow cytometric crossmatch (FXCM) and solid phase assays are used to identify kidney transplant recipients at risk of rejection. The clinical significance of the FXCM in the presence or absence of Luminex donor specific antibodies (DSA) remains a contentious area.

Method: All kidney transplant patients at our centre between 2007 and 2011 were analysed and divided into four groups. Patients transplanted across a positive FXCM were compared with patients transplanted across a negative FXCM with and without detectable DSA.

Results: The incidence of rejection was highest in patients with detectable DSA transplanted across a positive FXCM. Patient and graft survival were lowest in this group. Patients without detectable DSA transplanted across a positive FXCM had similar rejection rates and graft survival to patients transplanted across a negative FXCM.

Conclusion: Patients transplanted with DSA- FXCM+ have similar outcomes to low risk antibody negative patients who are FXCM –ve.

P269

SUCCESSFUL TREATMENT OF RECURRENT FOCAL SEGMENTAL GLOMERULOSCLEROSIS WITH A LOW DOSE RITUXIMAB IN A KIDNEY TRANSPLANT RECIPIENT

Owen Kwon, Kyung-Hoon Kim, Seung-Chan Park, Hee-Yeon Jung, Jeong-Hoon Lim, Jang-Hee Cho, Ji-Young Choi, Sun-Hee Park, Yong-Lim Kim, Chan-Duck Kim

Kyungpook National University School of Medicine

Recurrent focal segmental glomerulosclerosis (FSGS) is a major therapeutic challenge in kidney transplant. However, the most effective dosage and regimen of rituximab have not been determined. Herein we reported the first case of successful treatment of recurrent FSGS with a low dose rituximab. The patient showed marked proteinuria (3.5 g/day) and oliguria two days after transplantation. Two courses of plasmapheresis and immunoglobulin treatment were applied for treatment of recurrent FSGS, however, nephrotic range proteinuria persisted and creatinine level increased to 3.56 mg/dl. Five months post-transplant, the patient received only one dose of rituximab 100 mg, without further plasmapheresis, which resulted in immediate reduction of serum creatinine and full remission of proteinuria during the following 10 months. This case suggested that recurrent FSGS, which relapses after plasmapheresis, could be treated successfully with a low dose rituximab even without plasmapheresis.

P270

INCIDENCE OF DEEP VEIN THROMBOSIS IN RENAL TRANSPLANT RECIPIENTS

Paola Todeschini, Dalmastris Vittorio, Giorgio Feliciangeli, Gaetano La Manna, Mara Montanari, Maria Cappuccilli, Maria Piera Scolari, Sergio Stefoni

University of Bologna

Introduction: Kidney transplant recipients (KTR) show an acquired hyper-coagulable state determining an increased incidence of deep vein thrombosis (DVT). A possible underlying mechanisms might be hemostasis imbalance, with a multifactorial rise of procoagulant factors, both traditional (diabetes, pregnancy, obesity, preexisting thrombophilias), and transplant-related factors (surgery, immunosuppression, primary nephropathy, pre-transplant dialysis mode, erythrocytosis, infections). We investigated KTR with DVT at least 6 months post-transplant.

Methods: We included 30 patients transplanted between 2008 and 2011 who experienced DVT (lower limbs, lower limbs complicated by pulmonary embolism, retinal) at least 6 months post-transplant. Primary nephropathy, immunosuppressive regimen, infections and erythrocytosis were recorded. LMWH was given as thrombolytic treatment in the first post-transplant week and thereafter aspirin. All patients underwent color duplex ultrasonography.

Results: Increased DVT incidence was observed in patients receiving cyclosporine or cyclosporine+mTOR inhibitors, in PCKD, LES, nephrotic syndrome, peritoneal dialysis and in those with rapid and excessive correction of hematocrit values after transplant. DVT was unrelated to acute infection and dialysis modality.

Conclusions: These study suggest that the prevention of DVT consist either in accurate pre-transplant thrombophilia screening or in identification of patients at higher DVT risk requiring long-term antiplatelet therapy.

P271

OUTCOME ON RENAL FUNCTION OF EVEROLIMUS CONVERSION IN MAINTENANCE KTX PATIENTS: 4 YEARS APOLLO TRIAL

Thomas Rhat¹, Claudia Sommerer¹, Hermann Haller¹, Petra Reinke¹, Oliver Witzke¹, Barbara Suwelack¹, Christoph May², Daniel Bäumer², Eva-Maria Paulus², Wolfgang Arns¹, Klemens M.D. Budde¹

¹APOLLO Study Group, Germany; ²Novartis Pharma, Nuremberg, Germany

Open-label, randomized, controlled, multi-center 12 months study assessing safety and efficacy of Everolimus (EVR) regimen after Calcineurin-Inhibitor (CNI) withdrawal in maintenance KTx patients (pts). 93 pts on stable CNI+Enteric-Coated MycophenolateSodium (ECMPS) regimen were randomized to either continued CNI/ECMPS (n47) or EVR/ECMPS conversion (n46). 72(77%) pts completed observational 48 months follow-up visit. Mean trough levels[ng/ml]: 84 ± 44 CsA, 5.9 ± 2.4 Tacrolimus, 6.7 ± 2.0 EVR. Mean adjustedGFR (Nankivell [ml/min/1.73 m²]) +5.6 ([-0.6; +11.8]) for EVR over CNI ITTpts and +8.7(+16.0;+1.4);p = 0.02) for EVR (n20) over CNI (n31) non-switcher pts. 2 deaths, 1 graft loss in CNI, 1 death, 3 graft losses in EVR, no BPAR in either group. Infections months 12 to 48: 23(50%) EVR vs. 20(43%) CNI pts, severe 3 (7%) EVR vs. 1(2%) CNI; none leading to hospitalization. Malignancies: EVR none versus 1(2%) CNI. Late conversion to EVR/ECMPS treatment in maintenance KTx pts after CNI withdrawal is safe with by trend better RF after 4 years.

P272

GRAFT INTERSTITIAL FIBROSIS IN RECIPIENTS OF LIVE DONOR KIDNEYS

Colin Wilson, Charlotte Crotty, Sarah Hosgood, Michael Nicholson
Leicester General Hospital

Background: Interstitial fibrosis (IF) and tubular atrophy in kidney transplant recipients have been associated with calcineurin inhibitors and ischaemia. This study aimed to evaluate IF in live donor (LD) biopsies.

Methods: Surveillance biopsies from recipients of LD kidneys were stained using Sirius Red and assessed using computer assisted scanning.

Results: Sixty-two LD recipients (1998–2005) were identified with both a pre-implantation and 12 month biopsy. The area fraction of IF at 6 months (25 ± 8%) and 1 year (25 ± 8%) was equivalent but significantly greater than pre-implantation (18 ± 6%, t-test, p < 0.0001). Recipient serum creatinine was correlated with the degree of fibrosis at 1 year (Pearson $r = -0.255$, p = 0.045). A subset of patients (n = 14) changed to rapamycin at 3 months also had equivalent levels of IF (27%). Previous studies at our institution have shown similar levels of IF at 1 year in recipients of cadaveric grafts (27%).

Conclusion: Interstitial fibrosis develops early after transplantation, irrespective of donor source and immunosuppression, and correlates with serum creatinine at 1 year.

P273

PRETRANSPLANT MALNUTRITION AND INFLAMMATION AFFECTS OUTCOME AFTER KIDNEY TRANSPLANTATION

Jin Ho Hwang¹, Yon Su Kim², Jung Pyo Lee¹, Chun Soo Lim¹, Yun Kyu Oh¹, In Mok Jung¹

¹Boramae Medical Center, Seoul National University; ²Seoul National University Hospital

Malnutrition, inflammation, and atherosclerosis (MIA) is associated with a high mortality rate in ESRD patients. However, the clinical relevance of MIA syndrome in kidney transplantation (KT) recipients remains unknown. A total of 394 adult recipients of KT were enrolled and analyzed by level of serum albumin and hs-CRP. Recipients were classified into four groups according to pretransplant albumin and hs-CRP levels. Recipients with lower pretransplant albumin showed higher occurrence of CVE, and composite of CVE with all-cause mortality. The lower albumin level was, the more CVE occur. The higher hs-CRP level tends to be associated with occurrence both of primary outcomes. In four groups analysis, cumulative CVE free survival was lower in low albumin + high hs-CRP group. The composite of CVE and all-cause mortality was high in low albumin + high hs-CRP group. In conclusion, the malnutrition and inflammation status before KT increases the risk of developing CVE and all-cause mortality.

P274

CONVERSION FROM TWICE-DAILY TO ONCE-DAILY TACROLIMUS FORMULATION DOES NOT REDUCE INTRA-PATIENT VARIABILITY IN TACROLIMUS EXPOSURE

Nauras Shuker, Teunvan Gelder, Cadogan Monique, Willem Weimar, Dennis A. Hesselink
Erasmus MC

Background: Intra-patient variability (IPV) in tacrolimus exposure was associated with rejection and graft failure (e.g. Borra, L.C.P et al. Nephrol

Dial Transplant 2010; 25: 2757–2763). The aim of this study was to investigate whether conversion from twice-daily tacrolimus formulation (Tac-TD) to a once-daily formulation (Tac-OD) leads to a lower IPV in tacrolimus exposure.

Methods: Two hundred and fifty two stable renal transplant recipients were converted from Tac-TD to Tac-OD. We analyzed tacrolimus trough blood concentrations (C₀), serum creatinine, estimated glomerular filtration rate (eGFR) and proteinuria over a period of 1 year before and after conversion.

Results: For the analysis we included only patients of whom three or more C₀ values were available (n = 220). After conversion, the mean tacrolimus C₀ fell from 6.10 ± 1.76 µg/l to 5.37 ± 1.29 µg/l, corresponding to a 12% reduction (p < 0.001). Both drugs exhibited similar IPV (Tac-TD: 18.88 ± 9.32% vs. Tac-OD: 18.85 ± 9.97%; p = 0.387). Renal function remained stable (eGFR prior conversion: 47.31 ± 15.47 ml/min versus eGFR 12 months after conversion: 47.54 ± 15.50 ml/min; p = 0.656), demonstrating the safety of switching to Tac-OD.

Conclusions: Conversion from Tac-TD to Tac-OD leads to a significantly lower tacrolimus exposure, however it does not lead to lower IPV in tacrolimus exposure.

P275

IS PLASMA NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN MEASUREMENTS A GOOD MARKER FOR DETERMINING CHRONIC KIDNEY ALLOGRAFT INJURY DUE TO ONGOING IMMUNE ACTIVATION?

Acar Tüzüner¹, Ernst Mamatov¹, Firat Kocaay¹, Cihangir Akyol¹, Zeynep Kendi Celebi², Sule Sengul², Kenan Keven², Huseyin Tutkak³

¹Department of General Surgery, Ankara University Faculty of Medicine;

²Department of Nephrology, Ankara University Faculty of Medicine;

³Department of Immunology, Ankara University Faculty of Medicine

Background: Neutrophil gelatinase-associated lipocalin (NGAL) is early biomarker which reflects acute renal injury. The aim of this study is to evaluate the NGAL as a kidney injury marker in donor specific antibody positive and negative renal transplant recipients (RTx) with functional graft.

Material and Methods: A total of 161 RTx between November 2006 and August 2010 were enrolled to the study. Pretransplant panel reactive antibody (PRA) positive patients (9), patients with graft failure and dialysis (14), patients died during follow up (5) and patients with failed follow up (42) were excluded from the study. Post-transplant DSA status was determined by Luminex. Plasma NGAL levels were measured with Lipocalin-2/NGAL Human ELISA immunoassay.

Results: Our results are a summarized at table 1. Conclusion: Plasma NGAL measurements might be a good marker for determining chronic kidney allograft injury due to ongoing immune activation.

P276

COMPREHENSIVE ANALYSES OF PARATHYROID FUNCTION IMMEDIATELY AFTER RENAL TRANSPLANTATION

Yuji Hidaka, Shigeyoshi Yamanaga, Umi Fukuda, Kouta Hori, Takashi Senba, Youei Miyabe, Kenichiro Tokunaga, Mariko Toyoda, Hiroshi Yokomizo, Seishi I, Sohichi Uekihara

Japanese Red Cross Kumamoto hospital

Background: Secondary hyperparathyroidism (SHPT) is one of the major complications among the dialysis patients. Although parathyroid function improves dramatically immediately after renal transplantation (RTx), there have been little regarding reports parathyroid function of perioperative period. We aimed to investigate the comprehensive analyses of perioperative parathyroid function in early post-RTx period.

Materials and Methods: From April 2011 to January 2013, 33 living-donor RTx were performed at our institution. Four patients were excluded (two patients received cinacalcet after RTx and two patients with parathyroidectomy before RTx), then a total of 29 patients were analysed (20 males, nine females; age, 43.3, 14.8 years; duration of dialysis, 26.1, 22.4 months). Changes of intact parathyroid hormone (i-PTH), serum calcium (sCa), serum phosphorus (sP) and sCa ~ sP, and alkaline phosphatase between pre-ope and about three weeks after RTx were analyzed.

Results: There were significant reduction in the values of i-PTH (p < 0.01), sP (p < 0.01), and sCa ~ sP (p < 0.01). The excretion of urinary calcium was increased immediately after RTx and transient hypocalcemia was seen in the very early phase of post-RTx. However, one patient had been oral administration of cinacalcet before RTx was more than 10.5 mg/dl in serum calcium level at 1 year after RTx.

Conclusions: Parathyroid function was improved in the phase of post-RTx. However, patients persistent HPT after RTx must be observed carefully. In SHPT patients with cinacalcet before RTx might be the candidates of pre-ope parathyroidectomy.

P277

IS UNPLANNED REOPERATION AFTER KIDNEY TRANSPLANTATION AN INDICATOR FOR ORGAN LOSS?

*Reinhold Fuegger, Kerstin Huber, Axel Krause, Odo Gangl
KH Elisabethinen Linz*

Background: Unplanned reoperation is used as indicator of quality control in surgery. For kidney transplantation no such data exists so far. The aim of this study was to find out if there is a correlation between reoperation, organ function, loss of organ and survival.

Methods: We retrospectively analysed all kidney transplantations performed from September 2002 until December 2010.

Results: Out of 320 transplanted organs 46 reoperations took place, 40 organs where lost in the time of surveillance. Organ loss occurred in 37% of all reoperated patients compared to 9% in the not reoperated group ($p < 0.001$). The main complications that led to reoperation were vascular (14/46, 64% organ loss), haematomas or abscesses (13/46, 31% organ loss), urological (12/46, 8% organ loss), abdominal (4/46, 50% organ loss) and lymphatic (3/46, 33% organ loss). In relation to immunosuppression no statistically significant correlation could be found.

Conclusions: Complications with the need of reoperation after kidney transplantation are related with early organ loss. Also the transplant function, measured in serum creatinine is worse in reoperated patients. Especially vascular complications predispose to early organ loss.

P288

ER-TACROLIMUS PLUS EVEROLIMUS VS ER-TACROLIMUS PLUS MMF IN PRIMARY DECEASED DONOR KIDNEY TRANSPLANTATION: 1-YEAR RESULTS OF SINGLE CENTER, OPEN LABEL, PROSPECTIVE, RANDOMIZED CLINICAL TRIAL

*Evaldo Favi, Nicola Silvestrini, Josè Alberto Pedrosa, Maria Paola Salerno,
Gionata Spagnoletti, Jacopo Romagnoli, Franco Citterio
Surgery, Renal Transplantation, Catholic University*

Background: Aim of this single center randomized, clinical trial in kidney transplantation was to compare an immunosuppressive regimen based on the association of low-dose ER-tacrolimus and everolimus to a standard-dose ER-tacrolimus and MMF regimen. Results after 1 year of follow up are presented.

Methods: Forty-two primary deceased donor kidney transplant recipients were randomly assigned before transplantation to receive ER-tacrolimus plus everolimus (EVE group: 21 patients) or ER-tacrolimus plus mycophenolate mofetil (MMF group: 21 patients). As induction therapy all patients received a combination of basiliximab (20 mg IV on day 0 and day 4), thymoglobulin (50 mg/day IV from day 0 to day 3) and steroids. EVE and MMF patients received study medications orally, once a day, starting on p.o. day 4. Three to six months after transplantation, steroids were selectively withdrawn in patients with no acute rejection episodes, serum creatinine < 2 mg/dL and proteinuria < 300 mg/l/24 h.

Results: Demographics were similar between groups. Efficacy and safety parameters after 1 year of follow up are summarized in the table.

Conclusion: Our data show that 1 year after transplantation the association of low-dose ER-tacrolimus and everolimus when compared to a standard-dose ER-tacrolimus and MMF regimen provides similar patient survival, graft survival, acute rejection rates and renal function with significantly lower tacrolimus exposure.

P279

SUCCESSFUL ABO-INCOMPATIBLE KIDNEY TRANSPLANTATION WITH LOW-DOSE OF ANTI-CD20 TREATMENT IN CHINA

*Yi Wang¹, Hongtao Jiang¹, Zhigang Luo¹, Peigang Gui¹
¹The second Affiliated Hospital, University of South China*

Purpose: Most successful protocols for ABO-incompatible (ABOi) renal transplantation have utilized anti-CD20 500–1000 mg/body monoclonal antibody as Standard Immunosuppression of the pre-conditioning process. Here, we described successful ABOi transplantation using only 200 mg/body of anti-CD20 Standard Immunosuppression in lieu of it in China.

Material and Methods: Nine cases of ABO-i kidney transplantations were performed at the Second Affiliated Hospital, University of South China between December 2006 and November 2012. The blood type incompatible patients who received live donor renal transplants are A1 to O (4 patients), A1 to B (1 patient), B to A (1 patient) and B to O (3patient). Antibody removed was scheduled according to baseline anti-ABO antibody titer (median 1:256, range 1:16–1:1024). Perioperative antibody remove, used only 200 mg/body of anti-CD20 antibody and receiving an identical tacrolimus-based immunosuppressive regimen to contemporaneous ABOcompatible (ABOo) recipients.

Results: All nine patients underwent successful transplantation and have a mean current serum creatinine of 97.3 (range: 78.4–134.4). There were no episodes of antibody mediated rejection. The elimination of the peripheral blood CD19 cells are effective in every recipient preoperative.

Conclusion: We conclude that ABOi transplantation can be performed successfully with perioperative antibody removal, low-dose of anti-CD20

antibody and conventional immunosuppression. This suggests that access to ABOi transplantation can include a broader range of end-stage kidney disease patients in China. Key words: ABO incompatible, low-dose of anti-CD20.

P280

ASSESSMENT OF LIVER DYSFUNCTION BEFORE AND 3-MONTH AFTER RENAL TRANSPLANTATION

*Krishan Lal Gupta¹, Harpal Singh², R K Ratho³, Mukut Minz⁴, Y.K. Chawla⁵
¹Department of Nephrology; ²Internal Medicine; ³Department of Virology;
⁴Department of Renal Transplant Surgery; ⁵Department of Hepatology,
Postgraduate Institute of Medical Education and Research, Chandigarh, India*

Background: Liver disease is an important cause of morbidity and mortality both before and after transplantation in patients with chronic kidney disease (CKD). Abnormal liver function tests (LFTs) is caused by hepatotropic viruses including HBV and HCV in 10–44% of CKD patients. In addition CMV infection occurs in 20–60% of all transplant recipients.

Methods: In a prospective study 70 patients of CKD taken up for renal transplantation at a northern tertiary hospital in India, PGIMER, Chandigarh were evaluated for deranged LFTs and viral markers (HBsAg, Anti-HCV, HCV-RNA (Qualitative), IgM CMV serology, pp65 antigen and PCR for CMV DNA (if required)). Liver dysfunction was defined as ALT > 1.5 times the upper limit of normal (i.e. 40 IU/ML) and/or total bilirubin ≥ 2 mg/dl. The standard immunosuppression protocol was tacrolimus, MMF and steroids. Cyclosporine was preferred over tacrolimus if the patient is HCV positive. Azathioprine was used in place of MMF in case of poor affordability or intolerance due to side-effects. For cellular rejection, Methylprednisolone \pm ATG and for humoral rejection, Methylprednisolone \pm IVIG was used.

Results: Pretransplant, deranged LFTs were found in 12 patients (17%). Of them, one each had HBV and HCV infection. Of the 58 patients with normal LFTs, two each were positive for HBV and HCV respectively whereas one had dual infection with HBV and HCV. At 3 months post-transplant, all 12 patients continued to have deranged LFTs with same HBV or HCV status. All 4 HCV positive cases were detected by HCV RNA. In addition one developed fever with deranged LFTs, pancytopenia and was positive for CMV-DNA on PCR, with negative IgM serology and pp65 antigenemia.

Conclusions: Pre-transplant liver dysfunction was noted in 17% of patients. HBV and HCV were incriminated in 8.3% (1/12) of these patients which persisted at 3 months post-transplant. CMV was found in 7.6% (1/13) of renal transplant recipients with deranged LFTs.

P281

A LOW TOXICITY IMMUNOSUPPRESSIVE PROTOCOL USING LOW-DOSE, EXTENDED-RELEASE TACROLIMUS AND STEROID IN COMBINATION WITH CONCENTRATION-CONTROLLED MYCOPHENOLATE MOFETIL

*Yoshio Kushida¹, Kazunori Yamaguchi¹, Yuushi Hayashida¹, Kanae Koyama²,
Yuichi Shibuya³, Hironobu Arai⁴, Nobufumi Ueda¹, Noriyasu Fukuoka¹, Reiji Haba¹, Yoshiyuki Kakehi¹, Jun Minakuchi⁴, Masashi Inui⁵
¹Kagawa University Hospital; ²Ehime Prefectural Central Hospital; ³Kochi Health Science Center; ⁴Kawashima Hospital; ⁵Tokyo Women's Medical University*

Background: There are no standard guidelines regarding the appropriate dose of mycophenolate acid (MPA) to be used in combination with extended-release tacrolimus (Tac-ER). In this study, we aimed to investigate the efficacy of a low toxicity immunosuppression protocol consisting of a reduced dose of Tac-ER and concentration-controlled (CC) mycophenolate mofetil (MMF).

Methods: A total of 31 adult de novo living donor kidney transplant recipients were treated with reduced doses of Tac-ER, MMF, and methyl prednisolone for basic immunosuppression. Basiliximab was administered during the induction phase of immunosuppression. The dose of MMF was adjusted to achieve MPA levels, as measured by the area under the curve, within a target range of 50–60 mg/h/l. The dose of Tac-ER was adjusted to achieve a target trough level of 8 ng/ml for the first 2 weeks, after which the dose was tapered to 5 ng/ml for 6 months.

Results: The patient survival rate was 100%. Graft loss resulting from BK virus nephropathy was observed in one patient. Acute rejection was noted in two patients in the early post-transplantation period. Leukocytosis and asymptomatic cytomegalovirus viremia were observed in six and 11 patients, respectively. The average estimated glomerular filtration rate 1 year post-transplantation was found to be 65.4 ml/min 1.73 m², and protocol biopsy performed 1 year after transplantation indicated no toxic tubulopathy.

Conclusion: We found that a low dose Tac-ER and CC MMF regimen was safe and less toxic in the short-term.

P282

CINACALCET FOR NORMO- AND HYPERCALCEMIC SECONDARY HYPERPARATHYROIDISM (SHPT) AFTER RENAL TRANSPLANT

José Vicente Torregrosa¹, Enrique Morales², Juan Manuel Díaz³, Josep Crespo⁴, Juan Bravo⁵, Gonzalo Gómez⁶, Miguel Ángel Gentil⁷, Alberto Rodríguez-Benot⁸, Minerva Rodríguez⁹, Verónica López¹⁰, Álex Gutiérrez¹¹, Luisa Jimeno¹², María José Perez-Saez¹³, Rafael Romero¹⁴, Carlos Gómez¹⁵
¹Hospital Clínic Barcelona, Spain; ²Hospital 12 de Octubre, Madrid, Spain; ³Fundación Puigvert, Barcelona, Spain; ⁴Hospital Dr. Peset, Valencia, Spain; ⁵Hospital Virgen de las Nieves, Granada, Spain; ⁶Hospital Son Espases, Mallorca, Spain; ⁷Hospital Virgen del Rocío, Sevilla, Spain; ⁸Hospital Reina Sofía, Córdoba, Spain; ⁹Hospital Central de Asturias, Oviedo, Spain; ¹⁰Hospital Carlos Haya, Málaga, Spain; ¹¹Hospital Miguel Servet, Zaragoza, Spain; ¹²Hospital Virgen de la Arrixaca, Murcia, Spain; ¹³Hospital del Mar, Barcelona, Spain; ¹⁴Hospital Clínico de Santiago de Compostela, Santiago de Compostela (A Coruña), Spain; ¹⁵Hospital Marqués de Valdecilla, Santander, Spain

Background: Long-term effect of cinacalcet in normo- and hypercalcemic SHPT after renal transplant (RT) is scarcely described.

Methods: Multicenter, retrospective, 3-year study in 32 patients with normo- and 193 with hypercalcemic SHPT.

Results: In normocalcemic SHPT, iPTH levels decreased by 48.6% at 6 months from initiation of cinacalcet (m; p = 0.001; n = 32), without changes in calcium (Ca) and phosphorus (P). In hypercalcemic SHPT, Ca decreased from a mean (SD) of 11.1(0.6) at baseline to 10.1(0.8) at 6 m (-9.0%, p < 0.001; n = 193). iPTH was reduced by 23.0% at 6 m (p < 0.001; n = 193) and P levels increased by 11.1% (p < 0.001; n = 193). The effects were maintained for 3 years (n = 6/44 normocalcemic/hypercalcemic). No changes were observed in renal function or anticalcineurin levels. 4.0% and 1.8% of patients discontinued drug due to intolerance and lack of efficacy, respectively.

Conclusions: After initiation of cinacalcet in RT patients with SHPT, long-term control of blood levels of iPTH without changes in Ca or P were observed in normocalcemic patients, and blood levels of Ca, iPTH and P were controlled in hypercalcemic patients.

P283

FEASIBILITY OF TWO INNOVATIVE ELISPOT-BASED ASSAYS TO ASSESS THE FUNCTIONALITY OF CMV- AND EBV-SPECIFIC CELL-MEDIATED IMMUNITY (CMI)

Bernhard Banas¹, Carsten Böger¹, Gerhard Lückhoff², Bernd Krüger³, Astrid Starke⁴, Julia Batzill⁴, Mathias Schemmerer⁴, Josef Köstler⁵, Ludwig Deml⁴, Joachim Leicht⁶, Bernhard K. Krämer³

¹Department of Internal Medicine II, University Medical Center Regensburg;

²Dialysis Center Landshut; ³5th Department of Medicine, University Medical Center Mannheim;

⁴Lophius Biosciences GmbH; ⁵Institute for Medical

Microbiology and Hygiene, University Medical Center Regensburg; ⁶Dialysis Center Schwandorf

Inadequate impairment of cell-mediated immunity (CMI) by immunosuppressive therapy is a major cause of severe clinical complications in solid organ transplantation. Assessment of CMI may help to predict the onset of complications, as well as to adjust immunosuppressive/antiviral therapy. The aim of this cross sectional multicenter study was to evaluate the feasibility of the novel tools [T-Track[®]] CMV and [T-Track[®]] EBV to assess the functionality of virus-specific CMI in a clinically relevant patient population. Applying activated viral stimulator antigens, [T-Track[®]] assays provide information about the functionality of a broad network of virus-reactive effector cells including CD4 + , CD8 + , NK and NKT cells. The test sensitivities of [T-Track[®]] CMV/EBV assays were examined in a cohort of 124 hemodialysis patients and compared with Quantiferon[®]-CMV and a panel of 6 preselected CMV tetramers. Herein, positive [T-Track[®]] CMV or [T-Track[®]] EBV results were obtained in 60/67 (89.6%) of CMV- and 104/118 (88.1%) of EBV-seropositive hemodialysis patients, respectively. In addition, also 12/57 (21.1%) of CMV-seronegative dialysis patients showed significant numbers of CMV-responsive cells. Quantiferon[®]-CMV and CMV tetramers revealed sensitivities of 72.6% (45/62) and 76.9% (40/52), respectively. [T-Track[®]] CMV/EBV assays can be used in a broad population of hemodialysis patients neglecting their HLA-type. Thus, T-Track[®] assays may also represent valuable tools to assess functionality of CMI in transplant recipients and help to guide personalized therapy.

P284

ISOLATED MICROCIRCULATION INFLAMMATION IS ASSOCIATED WITH IMPAIRED RENAL FUNCTION AND ENHANCED PROTEINURIA

Maxime Touzot¹, Agnes Debout¹, Anne Cesbron², Anne Moreau³, Karine Renaudin³, Magali Giral-Classe⁴

¹ITUN, CHU Nantes; ²EFS; ³Service anatomie pathologie, CHU Nantes;

⁴ITUN, INSERM 1064

Background: Microcirculation inflammation (MI) associated with Donor-Specific Antibody (DSA) with/without C4d deposits in peritubular capillaries currently defines humoral rejection with a poor graft survival. Outcome of isolated MI without C4d and DSA on graft function remains unclear.

Methods: Restrospective comparison of 40 patients diagnosed with isolated MI, with 46 controls with normal histology on one year surveillance biopsies. Anti-HLA DSA were identified by Luminex technique.

Results: Patients had mild MI (mean g+ptc = 1.75 ± 1). In patients with MI and controls, the estimated Glomerular Filtration Rate (eGFR, MDRD) dropped from 52.7 to 47 ml/min and 62.3 to 58.5 ml/min respectively (p < 0.05) between one to three years after transplantation. Daily proteinuria significantly increased at the time of diagnosis (0.59 vs. 0.20 g/24 h p < 0.001) and persisted during follow-up (0.47 vs. 0.27 g/24 h p < 0.05). Graft loss was observed only in the MI group (10%). One person in each group developed DSA at 3 years without renal impairment.

Conclusion: Isolated MI despite any evidence of humoral activity may worsens proteinuria and further impairs graft function.

P285

THE MOLECULAR COMPOSITION AND FUNCTION OF HIGH-DENSITY LIPOPROTEIN IS UNIQUELY ALTERED AFTER KIDNEY TRANSPLANTATION

Chantal Kopecky¹, Michael Haidinger¹, Christopher Kaltenecker¹, Marlies Antlanger¹, Gunther Marsche², Michael Holzer², Johannes Kovarik¹, Johannes Werzowa¹, Manfred Hecking¹, Marcus D. Säemann¹

¹Medical University of Vienna; ²Medical University of Graz

Background: Renal transplant recipients experience increased cardiovascular morbidity and mortality, largely unaffected by standard therapeutic measures such as statins: here we analyzed the molecular composition and functionality of High-Density Lipoprotein (HDL) to explore a potential mechanism of this excessive cardiovascular risk.

Methods: HDL was isolated from renal transplant recipients with excellent or poor graft function by one-step density gradient ultracentrifugation. Changes in protein composition were identified by immunoblot and ELISA. Functional HDL modifications were determined by measurement of cholesterol-efflux, the membrane cholesterol concentration in peripheral blood mononuclear cells and paraoxonase (PON)-1 activity.

Results: Distinct proteins including surfactant protein B and serum amyloid A were enriched in HDL of transplant patients in both groups compared to HDL from healthy controls indicating a disease-specific HDL proteome. Transplant HDL displayed decreased cholesterol acceptor capacity along with substantially increased free cholesterol within patient leukocytes. Impaired anti-oxidative HDL function was demonstrated by decreased PON-1 activity in all transplant groups.

Conclusion: We demonstrate unique alterations of HDL in renal transplant recipients at the molecular and functional level. Of note, HDL modifications were virtually identical between transplant patients with excellent and poor graft function and independent of transplant vintage. These data may therefore help to unravel the causality of the excessive cardiovascular risk after renal transplantation and could pave the way for novel diagnostic and therapeutic directions.

P286

RECURRENCE OF MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS TYPE I AFTER KIDNEY TRANSPLANTATION -17 YEARS' EXPERIENCE OF A SINGLE CENTER

Hefziba Green, Ruth Rahamimov, Uzi Gafter, Eytan Mor
 Rabin medical center

Background: The reported outcome of kidney transplantation in patients with membranoproliferative glomerulonephritis (MPGN) type 1 is relatively poor. We report our 17-years' experience with transplantation for MPGN type 1.

Patients and Methods: Between the years 1995-2012, forty-eight out of 1882 transplantations were done in forty-four patients with MPGN type 1. Twenty-eight (58%) transplantation were from living donors. Overall patient survival was 100%, 97.7% and 87.7% at 1, 5 and 10 years respectively. Overall graft survival was 95.6%, 75% and 50% at 1, 5 and 10 years, respectively. Graft survival for recipients of living-donor was 60% vs. 33.6% for recipients of deceased-donor (p = 0.25). There were eight graft losses in seven patients (16%) due to recurrent MPGN type 1; four in living-related transplants and four in deceased donor transplants. Five-year graft survival in patient who had

recurrence of MPGN type 1 was 25% vs. 90% in non-recurrence; mean graft survival was 40 ± 9 vs. 157.6 ± 9.6 months ($p < 0.0001$). Patients who lost their graft due to MPGN type 1 recurrence were younger; mean 23 ± 9.2 vs. 37.7 ± 12.5 years ($p = 0.004$), and had higher mean proteinuria: 7.2 ± 3.6 g/day vs. 1.5 ± 0.25 g/day ($p = 0.006$).

Conclusions: Graft survival for patients with MPGN type 1 in our cohort is better than previously reported. Graft loss as a result of disease recurrence was rather low. Patients with recurrent MPGN type 1 were younger and had a significantly shorter term graft survival. Transplant from living-donor was not associated with increased risk for recurrence.

P287

THE GABOIR-REGISTRY WILL HELP TO IMPROVE THE HEALTH AND RISK COMMUNICATION

Przemyslaw Pisarski¹, Silvia Hiis¹, Albrecht Kramer-Zucker¹, Bernd Jänigen¹, Marcel Geyer²

¹University Clinic Freiburg; ²Hegau Clinic Singen

Background: Transplant institutions in Germany are facing a persistent and severe shortage in organ donors. This forces Transplant-Centers to search for new ways to expand the donor pool and explore novel therapeutic options. Therefore the Transplant-Center Freiburg performed the first German ABO-incompatible Living-Kidney-Transplantation in 2004. Since than over 500 ABO-i-Living-Kidney-Transplantations were realized at 32 German Transplant Centers.

Method: The GABOIR-Registry is a data registry which offers the possibility to pool data gathered in all patients undergoing ABO-incompatible kidney transplantation in Germany. The registry is intended to allow for medical-scientific data analyses as well as economical analyses, with the intention of increasing the rate of living donor kidney transplantations in Germany and to improve the health and risk communication. The design and development of the registry for ABO-incompatible kidney transplantation patients provide important insights into success rates and safety issues concerning this novel therapeutic option in Germany and will help establish this procedure as being reliable and safe.

Results: The aims of this registry were to insure transparency with regards to economical factors involving the medical procedure, to establish the safety of the therapeutic measure by recording outcome data and adverse events and provide a foundation for continued documentation of medical long term outcome data of a novel therapeutic intervention.

Conclusion: The registry will allow to gather and access medical long term data for scientific analyses and will help to increase the rate of living donor kidney transplantations in Germany. Moreover the analysis of the registered data will help to establish that ABO-incompatible kidney transplantation in comparison to maintenance on dialysis is highly cost effective and carries a significant socioeconomic benefit-first model calculations have provided evidence for this hypothesis.

P288A

PREVALENCE OF METABOLIC ACIDOSIS IN KIDNEY TRANSPLANT PATIENTS

Katarzyna Skiba, Magdalena Szotowska, Aureliusz Kolonko, Marcin Adamczak, Andrzej Więcek

Department of Nephrology, Endocrinology and Metabolic Diseases, Medical University of Silesia, Katow

Background: Results of recent studies suggest that metabolic acidosis (MA), which often is present in chronic kidney disease (CKD) patients accelerate the CKD progression. The aim of this clinical, single-center, cross-sectional, case-control study was to assess the prevalence of metabolic acidosis in KTP in comparison to CKD patients.

Material and Methods: Venous blood bicarbonate [HCO_3^-] concentration was measured in 443 KTP (259 males, 184 females, age 50 ± 12 years; eGFR 50 ± 23 ml/min) and sex, age and eGFR matched CKD patients (259 males, 184 females, age 51 ± 14 years; eGFR 50 ± 26 ml/min). Metabolic acidosis was defined if [HCO_3^-] was lower than 22 mmol/l.

Results: KTP and CKD patients did not differ with respect to [HCO_3^-] (25.31 ± 3.38 vs. 24.87 ± 3.69 mmol/l) and to the prevalence of metabolic acidosis (12.4% vs. 10.6%). In both groups [HCO_3^-] significantly ($p < 0.001$) decreased, and prevalence of metabolic acidosis significantly ($p < 0.01$) increased with the advancing CKD stages. In KTP and CKD patients the significant positive correlations were found between [HCO_3^-] and eGFR ($R = 0.450$, $p < 0.001$; $R = 0.392$, $p < 0.001$, respectively)

Conclusion: In KTP the risk of metabolic acidosis is high and is related to the kidney graft function.

P289

THE PREVALENCE OF STEROID RESISTANCE LYMPHOID POPULATION ANT ITS IMPACT ON KIDNEY TRANSPLANT OUTCOME

Wael Nassar¹, Essam Harash², Malaka Fouad³, Mustafa Abdelaziz Mohamed⁴, Sahir El-Khashab³, Mohamad H. Hafez²

¹Sahel Teaching Hospital; ²Zagazig University; ³Cairo University; ⁴Six October University

Background and Aim of the work: Since 1980s many reports have been investigating for the steroid-resistant lymphoid population from many aspects. We studied the prevalence of steroid resistant lymphoid population among uremic patients and correlate it with the ten years outcome of kidney transplant as well as their predictive value regarding postoperative immunosuppressive protocols.

Patients and Methods: Three hundred and fifty five uremic patients, were included in this study. The stimulation Index (SI) of one-way Mixed Lymphocytic Culture (MLC) against a potential donor was done before and after *in vitro* treatment of recipient lymphocytes with 1.0 $\mu\text{g/ml}$ methyl prednisolone. The MLC response will be considered sensitive if the inhibition level (CH50) was 50% or greater or otherwise resistant. Morning plasma cortisol and morning serum ACTH levels were measured. Ten years follow up comparing the allograft outcome between steroid resistant and steroid sensitive groups.

Results: The incidence of steroid resistant lymphoid population was 56.36% at a dose of 1.0 $\mu\text{g/ml}$ and 34.18% at a dose of 2.0 $\mu\text{g/ml}$ methyl prednisolone. Age, sex and duration of dialysis showed no effect on lymphocytic sensitivity to steroids whereas pregnancy, blood transfusion, previous treatment with steroids, morning plasma cortisol and morning serum ACTH showed significant impact on the development of steroid resistant lymphocytes ($p < 0.0094$, 0.006, 0.001, 0.001 and 0.001) respectively. Steroid sensitive group has a significant ten years better outcome than the steroid resistant group ($p < 0.001$).

Conclusion: This study shows high incidence of steroid resistant lymphoid population and this resistance is dose dependent. The *in-vitro* steroid treatment one-way MLC test has a good predictive value to help clinicians to select the donor and the most appropriate immunosuppression on basis of pre-transplant assessment.

P290

THE NECESSITY OF LOW DOSE RITUXIMAB INDUCTION IN KIDNEY TRANSPLANTATION; SINGLE CENTER EXPERIENCE

Hiroki Shirakawa¹, Jumpei Hasegawa¹, Mariko Endo¹, Sachiko Wakai¹, Daishi Nozak², Tadahiko Tokumoto³, Kazunari Tanabe²

¹Ohkubo hospital; ²Tokyo Women's Medical University; ³Shonan Kamakura General Hospital

Background: A new protocol for ABO-incompatible (ABO-i) or highly sensitized kidney transplantation including rituximab was introduced in Tokyo Women's Medical University since 2005. However, ABO compatible recipients without DSA were thought to be low risk recipients and they underwent kidney transplantation without rituximab. We evaluated the necessity of rituximab induction in kidney transplantation.

Methods: Between April 2009 and December 2012, 76 kidney transplantations were performed at our hospital. The immunosuppressive protocol, consisting of tacrolimus, mycophenolate mofetil and methylprednisolone, was started 1 week prior to the operation. All the patients received induction with basiliximab. Only ABO-i recipients and DSA positive recipients underwent preconditioning including with plasmapheresis and a single dose of rituximab. The Group I was rituximab group ($n = 45$) and Group II was non-rituximab group ($n = 31$). We compared the Group I with Group II.

Results: Each one patient in each group lost the graft after one year later (one patient died of cerebral infarction with functioning graft and the other patient lost the graft due to nonadherence). Within 3 months, rejection rates were 15.6% (Group I) and 16.1% (Group II), respectively. After 1 year, rejection rates were 9.3% (Group I) and 4.5% (Group II), respectively. There were no adverse effects associated with rituximab in both groups.

Conclusions: ABO-i and highly sensitized recipients with DSA are thought to be high risk recipients, however their rejection rate was equal to the low risk recipients. Rituximab was safe and useful drug for ABO-i and highly sensitized recipients. In the future, induction therapy of rituximab may be expanded to all the recipients also including low risk recipients in order to prevent the acute or chronic antibody mediated rejection.

P291

EFFECT OF CYCLOSPORINE A ADMINISTRATION IN PREGNANT RATS ON KIDNEY MORPHOLOGY IN THEIR OFFSPRING

Natalia Słabiak-Blaz¹, Marcin Adamczak¹, Nadezda Koleganova², Jens Randel Nyengaard³, Eberhard Ritz⁴, Andrzej Więcek¹

¹Department of Nephrology, Endocrinology and Metabolic Diseases, Medical University of Silesia, Katow; ²Department of Pathology, University of Heidelberg, Germany; ³Stereology and Electron Microscopy Research Laboratory, Institute for Clinical Medicine, Aarhus University; ⁴Department of Internal Medicine, University of Heidelberg, Germany

Background: Cyclosporine A (CsA) crosses the placenta and therefore may interfere with fetal growth, causing different pathologies in adult life. The aim of this study in rats was to assess the effect of exposure to CsA during the gestation on kidney morphology in the offspring.

Materials and Methods: Eight pregnant Sprague-Dawley rats were randomly allocated to two groups received CsA (3 mg/kg/day) or the corresponding volume of solvent (0.9% NaCl). These substances were administered subcutaneously, from the 10th day after the fertilization till the 7th day after the delivery. 12 weeks after delivery kidneys were obtained using glutaraldehyde perfusion. The number and volume of glomeruli was assessed using unbiased stereological methods.

Results: The number of glomeruli was lower (19524 ± 758) and the glomerular volume was higher ($2.44 \pm 0.32 \times 106 \mu\text{m}^3$) in the kidneys of offspring from mothers treated with CsA ($n = 34$) compared to the offspring of mothers treated with the solvent ($n = 31$; 24017 ± 861 ; $1.68 \pm 0.19 \times 106 \mu\text{m}^3$, respectively).

Conclusions: 1. Treatment with CsA during pregnancy decreases the number of glomeruli and increases the volume of glomeruli in the offspring of rats. 2. Such effects of CsA may participate in the pathogenesis of kidney disease in the adult life.

P292

HAND-ASSISTED LAPAROSCOPIC NEPHRECTOMY FOR RENAL CELL CARCINOMA IN RENAL TRANSPLANT RECIPIENTS AND PATIENTS WITH END-STAGE RENAL DISEASE

Jacopo Romagnoli¹, Maria Paola Salerno¹, Roberto Iezz², Josè Alberto Pedroso¹, Gionata Spagnoletti¹, Evaldo Favi¹, Valentina Bianchi¹, Franco Citterio¹

¹U.O. Trapiantologia Renale, Università Cattolica del Sacro Cuore, Roma;

²Department of Biomedicine and Radiological Sciences, Institute of Radiology, Università Cattolica del

Background: The risk for developing Renal Cell Carcinoma (RCC) of the native kidneys in renal transplant recipients (RTR) and end-stage renal disease (ESRD) patients is higher compared to the general population. Hand assisted laparoscopic nephrectomy (HALN) offers the advantage of increased safety over conventional pure laparoscopic techniques. Since 2011 we adopted this technique for living kidney donation and small native kidney tumors. We report our experience with RTR and ESRD patients undergoing HALN for small RCC (<3 cm).

Methods: All RCC were incidentally detected during follow-up ultrasound screening of RTR and ESRD patients on the waiting list for renal transplant. From October 2011 to October 2012 five native kidneys were removed from four patients at our centre using a transperitoneal HALN technique. Three procedures were performed in RTR and two in ESRD patients. One RTR underwent bilateral HALN because of masses on both native kidneys.

Results: HALN was successfully completed in all patients with no intraoperative or postoperative complications. No blood transfusion were required. Histology of renal masses revealed 4 RCC in four patients (2 papillary, 1 clear cell and 1 chromophobe subtype) and a fibrotic nodule in one patient, this occurred in the patient with bilateral lesions where the nodule on the right kidney was a chromophobe renal cell carcinoma, while the left one, which had on CT scan the same appearance of the right one, resulted to be a fibrotic nodule. All patients were stage T1N0M0. There were no episodes of rejection or graft loss. Graft function was not affected by the surgical procedure. None of the transplant patients had immunosuppression withheld. One ESRD patient who was on peritoneal dialysis was safely restarted on peritoneal dialysis within 7 days of the operation. Mean follow-up was 7.6 months (range 2.6–11.8), mean interval between kidney transplant and nephrectomy for RCC was 2.8 years (range 1.6–5). The average length of stay.

P293

PREGNANCY AFTER KIDNEY TRANSPLANTATION – A SINGLE CENTRE EXPERIENCE

Alicja Dębska-Słizier¹, Joanna Galgowska¹, Bolesław Rutkowski¹
Medical University of Gdańsk, Clinic of Nephrology, Transplantology and Internal Medicine

Background: Successful pregnancy in hemodialysed women is rare. After kidney transplantation, pregnancy is possible, although the risk of maternal and fetal complications is higher than in general population. Material and

Methods: The outcome of 22 pregnancies in 17 patients transplanted in Gdańsk center in the period 1987–2010 was studied. None of patients suffered from diabetes or lupus nephritis. Mean: maternal age at pregnancy was 30 ± 5 (range 23–39) years, interval between transplantation and conception was 41 ± 30 (range 7–132) months. Mean creatinine concentration before conception was 1.34 ± 0.4 (range 0.9–2) mg/dl and was stable during one year preceding pregnancy (mean increase 0.05 mg/dl). 9/17 patients received 1, 4/17 received two or more anti-hypertensive drugs, 1/17 had proteinuria.

Results: At time of conception, 20pts received CNI (CsA-14, Tac-6), 15 anti-metabolites (MMF-3, Aza-12), 1 mTOR (Rapap) and all prednisone. MMF and mTOR were discontinued before or during first weeks of pregnancy. All mothers survived the pregnancy. No rejections or graft losses were observed as a result of pregnancy. Maternal complications included edema (5/17), worsening of blood pressure control (5/17) and worsening (1/17) or new onset of proteinuria (1/17). Mean creatinine decrease in pregnancy was 0.06 mg/dl. Mean creatinine 1 year after pregnancy was 1.49 mg/dl (± 0.53). Pregnancy complications included 1 imminent abortion, one cervical insufficiency, one anhydramnion. There were 12 cesarean sections. Fetal outcomes included: 17 alive births (2 with serious inborn defects), two spontaneous and one artificial abortion, two stillbirths. Mean: pregnancy age and neonate birth weight were 35 ± 4 (range 23–39) weeks and 2552 ± 629 (range 1480–3420) grams. During 8.5 (mean 1–25) year follow-up after pregnancy 4/17 patients lost grafts. **Conclusions:** Pregnancy does not exert negative influence on patient and graft survivals. 68% of all pregnancies resulted in delivering healthy neonates.

P294

PREGNANCY AFTER KIDNEY TRANSPLANT IN ITALY

Pierluigi Di Loreto¹, Linda De Silvestro¹, Francesca Martino², Gianfranco Cabiddu³, Silvio Sandrini⁴, Enrico Minetti⁵, Domenico Miontano⁶

¹Nephrology Unit San Martino Hospital Belluno; ²Nephrology Dialysis

Transplantation Unit San Bortolo Hospital Vicenza; ³Nephrology Unit Brotzu

Hospital Cagliari; ⁴Nephrology Dialysis Transplantation Unit Brescia;

⁵Nephrology Unit Firenze; ⁶Nephrology Dialysis Transplantation Unit Udine

Introduction: Fertility is restored in women undergoing kidney transplantation.

Objective: Evaluate the gestations of transplant patients, analyzing outcomes and complications.

Methods: Retrospective study investigating the outcome of 101 pregnancies in 89 renal transplant recipients. variables analyzed: Type of nephropathy, patient age when dialysis started, at transplantation, at pregnancy, time between dialysis and transplantation, and between transplantation and baby birth. Immunosuppressive therapy, type of delivery, baby weight, Apgar score and mother and baby follow up were also considered.

Results: In nine patients were diagnosed: chronic pyelonephritis, post partum cortical necrosis (1 pt), IgA GN (11 pt), diabetic nephropathy (5 pt), unknown nephropathy (35 pt), ADPKD 1, 5 Nephroangiosclerosis, 26 Glomerulonephritis, two cystic Kidney disease, one Nephronoptosis, one Tubulo interstitial Nephropathy, one Obstructive Nephropathy, one Alport syndrome, one Renal displasia. The patients' age at start of hemodialysis (3 times/week) was 28.05 ± 2.35 years, the patients' age at transplantation was 30.25 ± 2.52 years, the patients' age at pregnancy was 33.9 ± 3.1 years, the interval between the start of hemodialysis and transplantation was 16 ± 22.3 months, the time between transplantation and childbirth was 4.45 ± 3.15 years. Immunosuppressive therapy included Prednisone, Azathioprine and CyA in 39 pt, Prednisone and Tacrolimus in 1, Prednisone e CyA in 16 pt, Aza e Prednisone in 3 pt, Prednisone, Aza, CyA, Fkin 1 pt., Aza, Prednisone, Fk in 5 pt, CyA (2 pt), 5 FK (5 pt), Aza (1 pt) e CyA 7 pt. The renal function was normal before (serum creatinine 1.1 ± 0.115 mg/dl), during (0.9 ± 0.10 mg/dl) and after pregnancy (1.09 ± 0.125 mg/dl). The mode of delivery was Caesarean section in 99% cases, 1% vaginal delivery. The mothers' complications during pregnancy) were: Non Nephrotic Proteinuria ($n = 6$), Urinary Tract Infect.

P295

RENAL REPLACEMENT LIPOMATOSIS MIMICKING MALIGNANCY AFTER RENAL TRANSPLANTATION

Marco Bonani¹, Thomas Fehr¹, Simone Brandt², Dorothee Rita Fischer³, Beate Bode-Lesniewska², Rudolf P. Wüthrich¹, Ariana Gasper²

¹Division of Nephrology, University Hospital of Zurich; ²Institute of Surgical Pathology; ³Division of Radiology

Background: We present two patients who underwent nephrectomy due to suspicion of malignant renal tumors.

Methods: The nephrectomies were examined grossly, on microscopy, by immunohistochemistry and fluorescence in-situ-hybridization (FISH). The findings were correlated with clinical data and CT-findings.

Results: Case 1: A 63y old man was on dialysis for 9 years due to chronic GN, until he was 1st transplanted in 1984. After 1 year, a cellular rejection occurred and a therapy with PDN, ATG and irradiation of the graft was initiated. Due to graft failure, a 2nd transplantation followed in 1996. 16 years after the 2nd transplantation, a CT scan showed a tumorous growth in both native

kidneys. At this time GFR was 66 ml/min. Immunosuppression consisted of CyA, Aza and PDN. Grossly, the kidneys were shrunken, but the perirenal fat was massively hypertrophic (Fig. 1). Histology revealed renal replacement lipomatosis (RRL) with end-stage kidneys and massively increased perirenal fatty tissue with focal inflammation; no malignant cells. Case 2: A 62y old man was 1st transplanted in 1983 due to a MPGN. In 1984, cellular rejection occurred and was treated with PDN, ATG and graft irradiation. Due to graft failure, a 2nd transplant was realized in 1986. Twenty-eight years after the 1st transplantation, a tumor in the 1st graft was detected by MRI and nephrectomy was performed. At this time GFR was 25 ml/min. Immunosuppression consisted of CyA and PDN. Grossly, the kidney was shrunken and surrounded by predominantly myxoid tissue. Histology showed RRL with end-stage kidney and increased perirenal fatty tissue with extensive myxoid areas and fibrosis; no malignant cells.

Conclusion: RRL is a rare condition described in renal allografts and native kidneys. RRL has been associated with kidney stones, recurring infections and rejection episodes. In immunosuppressed patients, the differential diagnosis between RRL and renal tumors or PTLD is crucial and can avoid unnecessary nephrectomies.

P296

CORRELATION BETWEEN SERUM YKL-40 (CHITINASE-3-LIKE PROTEIN 1) LEVEL AND PROTEINURIA IN RENAL TRANSPLANT RECIPIENTS

Erhan Tatar¹, Ozkan Gungor², Aygul Celtik², Ali Rýza Sisman³, Mustafa Yaprak², Gulay Asc², Mehmet Ozkahya Ozkahya², Hüseyin Töz²
¹Izmir Training and Research Hospital, Department of Nephrology and Transplantation Center, Izmir, Tu; ²Ege University, School of Medicine, Division of Nephrology, Izmir, Turkey; ³Dokuz Eylul University, School of Medicine, Department of Biochemistry, Izmir, Turkey

YKL-40 (chitinase-3-like protein 1) is a novel inflammation and endothelial dysfunction biomarker. Although YKL-40 is associated with albuminuria and predicts cardiovascular morbidity and mortality in a nonuremic population, its status is not known in renal transplant patients. The aim of this study was to investigate plausible links between serum YKL-40, proteinuria and graft dysfunction.

Methods: A total of 110 renal transplant recipients were included in this study. The level of proteinuria was calculated from spot urine using the protein/creatinine ratio. The estimated glomerular filtration rate (GFR) was calculated using the Modification of Diet in Renal Disease (MDRD) formulae. Serum YKL-40 was determined by an ELISA (R&D Systems, USA).

Results: The mean patient age was 40.5 ± 10 years. The mean YKL-40, GFR and proteinuria levels were 66 ± 46 ng/ml, 49 ± 24 ml/min/1.73 m² and 0.77 ± 1.15 g/day, respectively. Increases in the YKL-40 tertiles were correlated with increases in proteinuria and C-reactive protein and decreases in the GFR and serum albumin. The mean YKL-40 level was higher in patients with proteinuria higher than 1 g/day compared to patients with proteinuria less than 1 g/day (p < 0.001; Figure). An adjusted linear regression analysis demonstrated that the YKL-40 level (t = 3.28, P = 0.001), GFR (t = -3.00, P = 0.003) and systolic blood pressure (t = 2.51, P = 0.01) were independently associated with proteinuria.

Conclusions: We are the first to show that increased serum YKL-40 is independently associated with proteinuria in renal transplant patients. YKL-40 may be responsible for the pathogenesis of cardiovascular injury.

P297

THE LINK BETWEEN KIDNEY VOLUME DETERMINED BY TOMOGRAPHY AND KIDNEY HISTOLOGY IN RENAL TRANSPLANT DONORS

Erhan Tatar¹, Sait Sen², Mustafa Harman³, Fatih Kircelli⁴, Ozkan Gungor⁴, Banu Sarsik², Cuneyt Hoscokun², Ali Basci⁴, Hüseyin Töz⁴
¹Izmir Training and Research Hospital, Department of Nephrology and Transplantation Center, Izmir, Tu; ²Division of Patology, Ege University School of Medicine, Izmir, Turkey; ³Division of Radiology, Ege University School of Medicine, Izmir, Turkey; ⁴Division of Nephrology, Ege University School of Medicine, Izmir, Turkey; ⁵Division of General Surgery, Ege University School of Medicine, Izmir, Turkey

Background: Multi-detector computerized tomography (CT) is suggested to provide reliable estimation of nephron mass and renal functions. On the other hand, the significance of this method in predicting renal histology is lacking. In this study, we tried to explore the link between renal volume (RV) determined by CT and renal histology along with functional parameters in a healthy cohort; namely, renal transplant donors.

Methods and Results: Of the 82 cases enrolled in the study, 62% were male and the mean age was 50.4 ± 12 years. Mean body mass index (BMI) was 28 ± 4.2 kg/m²; of whom 32.9% were obese. Mean serum creatinine level and creatinine clearance were 0.79 ± 0.15 mg/dl and 122 ± 33 ml/min/1.73 m², respectively. Mean RV was 196 ± 36 cm³ and was positively correlated with BMI and surface area, proteinuria and creatinine clearance; negatively with HDL-cholesterol. In the biopsy samples, 4.6 ± 5.7% of the glomeruli was sclerotic and chronicity index was 2.4 ± 1.8. In the whole population, chronicity

index was significantly associated with age but not with RV. However, in obese cases corrected RV was positively correlated with glomerular filtration rate (r = 0.46, p = 0.01) and negatively with sclerotic glomeruli (r = -0.38, p = 0.04) and chronicity index (r = -0.43, p = 0.02). In adjusted ordinal logistic regression analysis, corrected RV was significantly associated with chronicity index.

Conclusions: In obese cases, decreased RV determined by CT is associated with worse renal histology.

P298

IMPACT OF EVEROLIMUS ON DE NOVO DONOR-SPECIFIC ANTI-HLA ANTIBODIES IN RENAL TRANSPLANT RECIPIENTS

Kumiko Kitajima, Ichiro Nakajima, Shohei Fuchinoue
 Kidney Center Surgery, Tokyo Women's Medical University Hospital

Background: The presence of donor-specific antibodies (DSA) is a leading cause of renal allograft failure. Although various attempts to remove DSA have been made, complete success has not yet been achieved.

Methods: In nine renal transplant recipients with de novo DSA treated with tacrolimus and mycophenolate mofetil, we attempted to add everolimus on the basal immunosuppressant therapy. We then investigated the evolution of DSA using the mean fluorescence intensity (MFI), and the estimated glomerular filtration ratio (eGFR).

Results: All but one patient exhibited donor-specific anti-HLA class II antibodies. Mean follow-up period was 9.9 months (range: 6.4–12.7). The MFI of five of the nine patients decreased after modification of immunosuppressants, and particularly, the DSA intensity of two patients in these five patients with DSA against DQ4 and DQ5, respectively, completely disappeared. The MFI in two patients continued to increase; no change was observed in the remaining two. The declines in the eGFR in the five patients with a reduced or undetectable MFI and remaining four patients were 5.0% and 19.7%, respectively.

Conclusion: Although the DSA intensity reduced in more than half of patients in this study, the exact effect of everolimus on anti-HLA antibody-producing cells was not sufficiently elucidated. Further studies are needed to evaluate the ability of everolimus to prevent chronic rejection resulting in allograft failure.

P299

EXPANSION TREGS AND INHIBITION TH17/TH1 BY SIROLIMUS-BASED REGIMEN IS DEPENDENT ON STAT-SIGNALING IN RENAL TRANSPLANT RECIPIENTS

Yi Li¹, Yuning Shi², Yangjuan Bai¹, Jiangtao Tang¹, Junlong Zhang¹, Lanlan Wang¹
¹Department of Laboratory Medicine, West China Hospital of Sichuan University; ²Department of Nephrology, West China Hospital, Sichuan University

Background: mTOR inhibitors (Sirolimus) has been used as de novo base therapy in an effort to completely avoid the use of CNi. Recent studies found the kinase mTOR has emerged as an important regulator of the differentiation of helper T cells. So we focus on the changes of Th cells in recipients treated by sirolimus.

Methods: We included 48 renal transplantation recipient (24 used sirolimus and 24 used tacrolimus) and 24 healthy controls. Of all these subjects, Th cells and the STAT proteins frequencies in the peripheral blood were analyzed by flow cytometry (FCM). Plasma levels of cytokines were analyzed by Bio-Plex[®] suspension array system.

Results: We found that the recipients used sirolimus based regimen had better renal function after conversion. The recipients used SRL based regimen can increase Treg cell (3.9[2.5–5.5]%), decrease Th17, Th1 cells, Th1 related cytokine (IL-1 α and IFN- γ) and Th17 related cytokine (IL-17, IL-6) compared with tacrolimus group Treg (1.5[1.2–1.8]%; p < 0.05). The Th17/Treg ratio in TAC group (1.2[0.6–1.6]) decreased significantly when compared with SRL group (0.5[0.3–1.6]) and healthy control group (0.6[0.2–1.2]; p < 0.05). Furthermore, the recipients used sirolimus showed increased STAT5 activation and decreased STAT3 activation.

Conclusion: Our results indicated that conversion to SRL may both minimize CNi toxicity and facilitate CNi withdrawal by promoting immunoregulation.

P300

PREVALENCE OF METABOLIC SYNDROME AND RELATED FACTORS IN THAI RENAL TRANSPLANT RECIPIENTS: A MULTI-CENTER STUDY

Prajej Ruangchanaset¹, Bancha Satirapoj¹, Sakam Bunnag², Attapong Vongwiwatana³, Nalinee Premasathian³, Yingyos Avihingsanon⁴
¹Phramongkutklao Hospital; ²Rajavithi hospital; ³Siriraj hospital; ⁴King Chulalongkorn Memorial hospital

Background: Metabolic syndrome (MS) is a risk factor for atherosclerotic cardiovascular disease as well as graft dysfunction, graft loss and patient death in renal transplant recipients (RTR). There have been limited studies of MS in

Asian kidney transplant (KT) population. Our aim was to assess the prevalence and associated factors of MS in Thai RTR.

Methods: A cross-sectional study was conducted in 263 RTR during March and December 2012 in 4 kidney transplant centers in Bangkok, Thailand. MS was diagnosed based on the National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATPIII; modified Asia and original) and the International Diabetes Federation (IDF) criteria.

Results: Of 263 recipients studied, 76(28.9%), 58(22.1%) and 48(18.3%) had MS according to modified Asia-NCEP-ATPIII, NCEP-ATPIII and IDF criteria, respectively. Based on modified Asia-NCEP-ATPIII criteria, 36 female (47.4%) and 40 male (52.6%) had MS. Age (Odds ratio [OR], 1.03; 95% confidence interval [CI] 1.01–1.06), body mass index (OR, 1.29; 95% CI 1.18–1.4) and systolic blood pressure (OR, 1.03; 95% CI 1.01–1.04) were associated with the development of MS. Compared to 187 patients who did not meet the criteria of MS, patients with MS had lower estimated GFR by using CKD-EPI formula (54.04 + 17.99 vs. 62.45 + 22.32 ml/min/1.73 m²; p = 0.004) and higher urine protein-creatinine index [0.21 (IQR 0.08–0.78) vs. 0.11 (IQR 0.07–0.18); p = 0.001] despite the time of follow up was not significantly different (68 vs. 66 months; p = 0.476). There was a significant graded relationship between the number of antihypertensive medications and MS. The prevalence of MS was 19.2% in the first 12 months, 17.8% between 13 and 36 months and rose up to 32.8% after 3 years post transplantation.

Conclusions: The study demonstrated the high prevalence of MS in Thai RTR especially after 3 years post transplantation. MS is associated with lower renal function, higher proteinuria and requirement of more number of antihypertensive medications in KT population.

P301

NEW ONSET DIABETES AFTER TRANSPLANTATION IN THAI RENAL TRANSPLANT RECIPIENTS: A MULTI-CENTER STUDY

Prajei Ruangkanhanaset¹, Bancha Satirapoj¹, Sakarn Bunna², Attapong Vongwiwatana³, Naline Premasathian³, Yingyos Avihingsanon⁴

¹Phramongkutklao Hospital; ²Rajavithi hospital; ³Siriraj hospital; ⁴King Chulalongkorn Memorial hospital

Background: New onset diabetes after transplantation (NODAT) is a risk factor for cardiovascular disease, infection, reducing graft and patient survival. Our aim was to determine the prevalence and associated factors of NODAT in Thai renal transplant recipients (RTR).

Materials and Methods: A cross-sectional study was conducted in 263 RTR during March and December 2012 in four kidney transplant centers in Bangkok, Thailand. NODAT was diagnosed based on the American Diabetes Association criteria for type 2 diabetes.

Results: The data of 263 recipients were collected. After the exclusion of 15 pretransplant diabetes patients, 248 patients were studied. NODAT was diagnosed in 27 patients (10.9%) after the median follow-up time of 67 (IQR 35–122) months. Advanced age (Odds ratio (OR), 1.05; 95% confidence interval (CI) 1.01–1.09; p = 0.014) and the presence of metabolic syndrome (MS) based on modified Asia-NCEP-ATPIII criteria (OR, 5.24; 95%CI 2.28–12.04; p < 0.001) but not body mass index (OR, 1.08; 95%CI 0.98–1.18; p = 0.111) were associated with the development of NODAT. Compared to 221 patients who did not meet the criteria of NODAT, patients with NODAT had non-significantly lower estimated GFR by using CKD-EPI formula (56.62 + 19.20 vs. 60.65 + 21.61 ml/min/1.73 m², p = 0.354) but higher HbA1C levels (6.98 + 1.24 vs. 5.10 + 1.80%, p < 0.001). Regarding immunosuppressive medications, use of sirolimus (OR, 4.09; 95%CI 1.16–14.36; p = 0.028) but not with tacrolimus use (OR, 2.04; 95%CI 0.91–4.59; p = 0.086) nor steroid use (OR, 0.77; 95%CI 0.29–2.04; p = 0.604) was associated with the development of NODAT. Cyclosporine use seemed to be protective in the development of NODAT (OR, 0.294; 95%CI 0.11–0.76; p = 0.011) in our study.

Conclusions: Our study demonstrates a low burden of NODAT at the median follow-up time of 67 months in Thai RTR when compared to the western population. Similarly, NODAT was more prevalent in advanced age group, the presence of MS and the use of sirolimus.

P302

SERUM CHEMOKINE CXCL10 PREDICTS T CELL-MEDIATED REJECTION AFTER KIDNEY TRANSPLANTATION

Koichi Tsutahara¹, Masayoshi Okumi², Kazuaki Yamanaka², Taigo Kato², Yoichi Kakuta², Koji Yazawa², Ryoichi Imamura¹, Seiji Yamaguchi¹, Norio Nonomura²

¹Department of Urology, Osaka General Medical Center; ²Department of Urology, Osaka University Graduate School of Medicine

Background: Acute rejection (AR) is the main causes leading to kidney allograft dysfunction. Kidney allograft biopsies are the most useful means of diagnosing allograft pathology. However, kidney allograft biopsies are expensive and invasive, and are associated with potential complications. Therefore, a rapid, noninvasive test that accurately reflects kidney allograft pathology is needed to avoid the number of unnecessary allograft biopsies and enable more frequent monitoring. The aim of this study was to investigate whether CXCL9,

CXCL10, CCL2, and CCL5 can be used as biomarkers to distinguish kidney allograft pathology.

Materials and Methods: Serum chemokine levels were evaluated, using a cytometric bead array, in recipients who underwent kidney allograft biopsies. Serum chemokines were measured in kidney transplant patients with AR (n = 19) and other pathological findings (n = 69). Result Serum CXCL9, CXCL10, CCL5 levels in patients with AR were significantly higher than those without AR (p < 0.01). The area under the ROC curve (AUC) of serum CXCL9, CXCL10, CCL5 for AR vs. non-AR was respectively 0.74, 0.89, 0.68. Serum CXCL10 levels, with a cut-off value of 180.3 pg/ml, had a sensitivity of 89.5% and a specificity of 79.8% for detecting patients with AR from those without AR.

Conclusion: These results demonstrate that serum CXCL10 concentration may be a highly accurate biomarker for predicting AR.

P303

THERAPEUTIC DRUG MONITORING OF MYCOPHENOLIC ACID DURING COMBINED IMMUNOSUPPRESSIVE THERAPY

Yuangao Zou¹, Yunying Shi², Yangjuan Bai¹, Yi Li¹, Shu Wang¹, Lanlan Wang¹

¹Department of Laboratory Medicine, West China Hospital of Sichuan University; ²Department of Nephrology, West China Hospital of Sichuan University

Background: Therapeutic drug monitoring (TDM) of Mycophenolic acid (MPA) is recommended to include full area under the concentration–time curve (AUC), but full AUC estimates are not practical for routine monitoring, so limited sampling strategy (LSS) have been suggested.

Methods: Plasma MPA was measured by EMIT, the AUC_{0–4} was calculated, completing 1216 MPA concentration-time points from 304 adult kidney transplant recipients. Besides MPA, patients received tacrolimus (Group A, n = 231) or cyclosporine (Group B, n = 73).

Results: The mean AUC_{0–4} level was 72.78; Å27.01 µg/h/ml. The LSS AUC_{0–4} level was above the therapeutic range in 40.3% (Group A) and 46.3% (Group B) of patients, respectively. The mean values for C₀ was 3.93; Å2.65 mg/l in Group A, and 3.23; Å2.34 mg/l in Group B, but C₀ showed a low correlation with AUC_{0–4} h (r² = 0.36).

Conclusions: MPA TDM will be a useful tool to cope with the wide pharmacokinetic variability of MMF after kidney transplantation.

P304

FLEXIBLE IMMUNOSUPPRESSIVE PROTOCOL FOR ABO-INCOMPATIBLE KIDNEY TRANSPLANTATION

Alexander Sushkov, Yan Moysyuk

Academician V I Shumakov Federal Research Center of Transplantation and Artificial Organs

ABO-incompatible kidney transplantation (iABO Ktx) is effective and well-known option for increasing living donation. Since the end of 1980-s a lot of different immunosuppressive protocols for iABO KTx were established. The iABO KTx program was started in our institution in 2011. For pre-transplant preparation we use combination: rituximab (Rtx) + plasmapheresis (PP) or anti-A/B immunoabsorption (IA) + high-dose IVIG and three-component maintenance immunosuppression: tacrolimus + MMF + steroids that continued after Tx. We modify original "Stockholm protocol": the duration of pre-transplant preparation, number pre- and post-transplant PP or IA sessions, doses of immunosuppressive medications depends on initial anti-A/B titers. 12 patients were transplanted. Mean follow-up period – 18 months (range: 24–6). The initial anti-A/B titer range from 1:1024 to 1:2. All recipients are still alive. One transplant was lost 3 months after surgery because of atypical hemolytic uremic syndrome recurrence. We can't find any significant differences in patient and graft survival rates, glomerular filtration rate and frequency of infection complications between ABO-incompatible (n = 12) and ABO-compatible (n = 51) groups of our live-donor kidney recipients.

P305

OUTCOME OF UROLOGIC COMPLICATIONS AFTER RENAL TRANSPLANTATION

Hakan Sozen, Kibriya Fidan, Sükrü Sinder, Metin Onaran, Aydın Dalgic Gazi University

Urologic complications after kidney transplantation are associated with significant morbidity, mortality and prolonged hospital stay. An intervention or second surgical procedure is frequently required. Here we report urologic complications in adult renal recipients.

Material and Methods: Totally 98 adult kidney transplantations were performed since Jan 2006 at Gazi University Transplantation Center, Ankara, Turkey. Among 98 adult kidney transplantations, there were 40 (40%) female and 58 (60%) male recipients. Source of the donor was in 47(48%) deceased and 51 (52%) living related. The Haberal's corner saving technique was used for ureteroneocystostomy anastomosis. We routinely use double J stent (DJS)

during surgery. All patients received antibiotic treatment with seftriaxone (1 g every 12 hours) until the removal of surgical drain. The DJS was removed with cystoscopy by Urology in an out-patient clinic under sedation by postoperative 3rd week. All recipients received calcineurine based triple immunosuppression. Also, all recipients have received trimetoprim-sulphametoksazol prophylaxis for 3 months after transplantation.

Results: We retrospectively analyzed 98 adult recipients for urologic complications. Source of the donor was in 47(48%) deceased and 51 (52%) living related. The mean age of the recipients were 36.6 ± 12.1 years old (median: 34 years old; range 18–67). Mean donor age was 44.1 ± 14.4 , and median age was 46 years old. We focused on 4 specific urologic complications: urine leak, ureteric stenosis, hematuria, and symptomatic vesicoureteral reflux (SVUR) in this study. Totally 3 (3%) urologic complications were encountered. Two out of three were urine leak early after transplantation and one was distal ureter necrosis. We have not seen any hematuria, stenosis or SVUR in this group. Two urine leaks were treated successfully by conventional radiology. For patient with distal ureter necrosis, conventional radiology did not succeed in treatment, thus surgical revision was done successfully. We haven't lost neither patient nor graft due to urologic complications.

Conclusion: In this study, the Haberal's corner saving suture technique with DJS seemed to protect against the development of urologic complications.

P306

PLASMA LEPTIN IN KIDNEY TRANSPLANTED PATIENTS DURING THE EARLY POST TRANSPLANT PERIOD

Ayman Elsayed¹, Nadia Marie², Walaa Elbazz², Laila Fawzy²

¹OTC; ²Faculty of medicine for girls Al-Azhar University

Leptin is a 16 KD protein that is encoded by the ob gene and secreted by adipocytes. Leptin is important in regulation of appetite, food intakes and energy expenditure, sexual maturation and fertility, hematopoiesis and activity of the hypothalamic-pituitary-gonadal axis. Leptin is primarily cleared from the circulation by the kidney and elevated plasma leptin are reported in uremic patients. The present study aimed to assess plasma leptin concentrations in patients with kidney transplant during the early post renal transplant period. Serum leptin were measured in 30 ESRD patients undergoing renal transplant (22 males & 8 females), 20 subjects as a control (17 males & 3 females). This study showed hemodialysis patients (pre-transplant patients) had significantly lower mean BMI than the control subjects. The study showed the mean serum leptin concentration in hemodialysis patients was higher than the control subjects. Our study showed that post-transplant patients had mean serum leptin concentration similar to the control subjects and significantly lower than the hemodialysis patients. This study showed serum leptin levels are correlated positively with BMI in all groups and significantly decreased in post-transplant than pre-transplant. This work showed that there were no correlation between serum leptin and parameters commonly used to assess the extent of renal function. Our data revealed higher serum leptin levels in females than males' inspite of similar BMI.

Conclusions: Successful renal transplant is followed by a significant decrease of leptin concentration. Successful renal transplant is followed by a significant increase of BMI *Significant correlation between serum leptin and BMI. Thus, leptin may play an important role in improvement of anorexia, weight gain after normalization of renal function after renal transplantation. Factors other than excretory capacity of the transplanted kidney are apparently in the post transplant decrease of leptin.

P307

NEW ONSET DIABETES AFTER ORGAN TRANSPLANT

Ahmed Daoud¹, Amany Shoulqamy²

¹Faculty of Medicine, Cairo University; ²Cairo University

New onset diabetes mellitus after transplantation has been reported to occur in 4% to 25% of renal transplant recipients, 2.5% to 25% of liver transplant recipients, 4% to 40% of heart transplant recipients, and 30% to 35% of lung transplant recipients. Risk factors for the development of NODAT can be categorized as non-modifiable, modifiable or potentially modifiable, the former category facilitates the identification of high risk individuals, and the latter two categories to optimize the management of NODAT. Diabetes leads to various medical complications in the post-transplant population. Diabetic patients suffer from an increased risk of cardiovascular complications, graft failure and death. Management of NODAT includes lifestyle modification, oral medications and insulin.

P308

TRANSFORM TRIAL DESIGN: EFFECT OF EVEROLIMUS ON LONG-TERM OUTCOMES AFTER KIDNEY TRANSPLANTATION

Julio Pascual¹, Steve Chadban², Franco Citterio³, Mitchell Henry⁴, Christophe Legendre⁵, Federico Oppenheimer⁶, Titte R. Srinivas⁷, Hélio Tedesco-Silva⁸, Flavio Vincent⁹, Yoshihiko Watarai¹⁰, Peter Bernhardt¹¹, Martin Zeier¹²

¹Hospital del Mar, Barcelona, Spain; ²Royal Prince Alfred Hospital, Australia; ³Catholic University of Rome, Rome, Italy; ⁴Wexner Medical Center, Columbus, OH, USA; ⁵Hôpital Necker, Paris, France; ⁶Chief, Renal Transplant Unit; ⁷Director, Transplant Nephrology Section; ⁸Hospital do Rim e Hipertensão, Sao Paulo, Brazil; ⁹University of California, San Francisco, California, USA; ¹⁰Nagoya Daini Red Cross Hospital, Nagoya, Japan; ¹¹Novartis Pharma AG, Basel, Switzerland; ¹²University of Heidelberg, Heidelberg, Germany

Background: There is an unmet need in kidney transplant recipients (KTxR) for an immunosuppressive regimen that improves long-term outcomes.

Methods: In this 24-month (mo), multicentre, open-label study with a 36-mo extension, approximately 2000 *de novo* KTxR will be randomised (1:1) to receive either everolimus (EVR; C0: 3–8 mg/ml) with reduced calcineurin inhibitor (CNI) exposure or mycophenolic acid with standard CNI exposure, all with basiliximab and steroids (Figure). The primary objective is to demonstrate superiority of the EVR arm on the composite rate of treated biopsy-proven acute rejection or eGFR<50 ml/min/1.72 m² at 12 months. The trial will also evaluate long-term outcomes up to 5 years, including renal function, patient and graft survival, and incidences of cardiovascular disease, malignancies and infections.

Conclusion: TRANSFORM is a large study that will evaluate short- and long-term benefits of EVR-based regimen, and has the potential to change the treatment paradigm in *de novo* KTxR.

P309

LIVING DONOR NEPHRECTOMY – A SINGLE-CENTER EXPERIENCE WITH OPEN AND LAPAROSCOPIC APPROACHES

Juliane Liese¹, Markus Wortmann¹, Andreas A. Schnitzbauer¹, Guido Woeste¹, Ingeborg Hauser², Wolf Otto Bechstein¹, Frank Ulrich¹

¹General and Visceral Surgery, Goethe University, Frankfurt; ²Nephrology, Goethe University, Frankfurt

Introduction: Kidney transplantation is the treatment of choice for patients with end stage kidney diseases, but the average time on the waiting list is up to 6 years. Offering a standard laparoscopic donor nephrectomy technique, the number of living kidney donations increased in our institution.

Methods: In 2010 our institution introduced a fully laparoscopic donor nephrectomy technique. The aim of our study was the comparison with the open donor nephrectomy approach used before. Therefore, we analyzed all patients (01/2007–12/2012), who underwent a donor nephrectomy and compared the operation and warm ischemia times, complication rates, the length of hospitalisation and other parameters.

Results: We performed 88 donor nephrectomies (51 women, 37 men). The mean age was 51.1 years. 62.5% (56) of the procedures were performed as open and 37.5% (33) as laparoscopic nephrectomy. The mean operation time was longer in the laparoscopic group with 196.4 min compared to 185.1 min (p = 0.007). The warm ischemia time in the laparoscopic group was 22 s longer than in the open nephrectomy group (p = 0.001). No conversion to open surgery was necessary. In contrast to other studies the complication rate was not higher in the laparoscopic group. We had to perform two reoperations in the group of open nephrectomy (bleeding, ureter complications) and one reoperation in the laparoscopic group (wound infection). Donor creatinine 1 year after donation did not differ between the two groups.

Conclusion: We were able to show that our fully laparoscopic donor nephrectomy technique is a safe approach with favourable donor acceptance. Operation and warm ischemia times were slightly longer. Although we had a complete change of our approach and an unavoidable learning curve, no higher rates of complications and no conversion to open surgery were observed. Laparoscopic donor nephrectomy might be the new standard for living kidney donation.

P310

FIRST EUROPEAN CLINICAL EXPERIENCE WITH CONVERSION FROM TWICE-DAILY TO ONCE-DAILY TACROLIMUS FORMULATION IN RENAL TRANSPLANT PATIENTS: TEN YEARS DATA

J.P. van Hooff, Frank Stifft, M.J.H. Mullens, Maarten Christiaans
MUMC

Our center participated 10 years ago with 39 patients in a multicenter study. The pharmacokinetics of tacrolimus before and after conversion from twice-

daily (Prograf) to once-daily (Advagraf) was investigated. This was the first European clinical experience with Advagraf in renal transplant patients. We were interested in the long-term outcome of these patients.

Methods: Tacrolimus based immunosuppression was prescribed according to local protocol. No induction therapy, withdrawal of concomitant immunosuppressive agents in uncomplicated cases. Selection criteria for conversion: Informed consent, >6 months after transplantation and stable. The data were collected retrospectively.

Results: Demographics: Median age at the time of conversion, 54 years (21–64); Male 25, female 14: Donor, cadaveric 27, living 12. Immunosuppression Tacrolimus monotherapy 80%, Tacrolimus+ MMF 12.5% and Tacrolimus+steroids 7.5%. Four patients were converted back to Prograf (dizziness, withdrawal of consent, decision by local physician, non-compliant to scheduled outdoor visits; respect. Month 3, 6, 48 and 54). These patients were excluded from further analyses. There were four deaths with a functioning graft (pneumonia, lung cancer, heart surgery and heart infarction respect. month 28, 30, 48 and 94). Two patients returned to hemodialysis, both because of recurrence of IgA nephropathy (respect Month 96 and 108). Ten year patient and graft survival was respect 89% and 83%. Graft survival censored for death and recurrence of IgA nephropathy was 100%. Of the 29 patients with a functioning graft, 21 showed a stable creatinin (<20% increase). Three of the eight patients with an increase of creatinin >20% had recurrence of IgA nephropathy.

Conclusion: In this small but unique cohort of renal transplant patients converted from Prograf to Advagraf 10 year patient and graft survival was excellent notwithstanding (or due to) the fact that 80% were on monotherapy Advagraf.

P311

CONVERSION OF STABLE ABO-INCOMPATIBLE KIDNEY TRANSPLANT RECIPIENTS FROM MYCOPHENOLATE MOFETIL WITH STANDARD EXPOSURE CALCINEURIN INHIBITOR TO EVEROLIMUS WITH VERY LOW EXPOSURE CALCINEURIN INHIBITOR

*Junji Uchida, Yuichi Machida, Kazuya Kabei, Tomoaki Iwai, Nobuyuki Kuwabara, Toshihide Naganuma, Norihiko Kumada, Tatsuya Nakatani
Osaka City University Graduate School of Medicine*

Background: Although ABO-incompatible kidney transplantation is an immunologically high-risk procedure, the development of powerful immunosuppressant drug combinations including rituximab has resulted in excellent graft and patient survival. However, the intensity of immunosuppression may be linked to a higher risk of tumor development and viral infection. Everolimus provides safe and effective immunosuppression after kidney transplantation and has been suggested to have anti-tumor and anti-viral activities.

Methods: An open-label design was used to examine the efficacy and safety of conversion of stable ABO-incompatible kidney transplant recipients from mycophenolate mofetil (MMF) with standard exposure calcineurin inhibitor (CNI) to everolimus with very low exposure CNI. A total of 16 recipients of ABO-incompatible kidney transplantation at our institution were enrolled. The patients without acute rejection by graft biopsy were switched from MMF to everolimus with dose adjustments to target an everolimus trough level of 3–8 ng/ml. The CNI dose was reduced to a target trough level of 2–4 ng/ml (tacrolimus) or 25–50 ng/ml (cyclosporin). At 3 months after conversion, graft biopsies were performed to check acute rejection. At baseline and at 1, 2 and 3 months after conversion, the peripheral CD19 + cells and CD20 + cells and anti-A/B antibody titers were monitored.

Results: Conversion to everolimus with CNI minimization did not induce acute rejection in the ABO-incompatible kidney transplant recipients. There were no significant changes in CD19 + cells and CD20 + cells during the study period, but a slight elevation in anti-A/B antibody titer (IgG; less than 2 times) occurred.

Conclusion: Everolimus elicited no acute rejection and suppressed B cell function and activation in ABO-incompatible kidney transplantation recipients. Everolimus may therefore be a potential immunosuppressant for ABO-incompatible kidney transplantation.

P312

SEARCH FOR NEW ENDPOINTS FOR CLINICAL TRIALS OF IMMUNOSUPPRESSIVE DRUGS IN KIDNEY TRANSPLANTATION

*Hélio Tedesco-Silva¹, Peter Bernhardt², Gaohong Dong³, Cesar Escrig²
¹Division of Nephrology, Hospital do Rim e Hipertensão – UNIFESP; ²Novartis Pharma AG, Basel, Switzerland; ³Novartis Pharmaceutical, East Hanover, United States*

Introduction: To gain information on new clinically relevant endpoints in kidney transplantation (KTx) for use in future trials, we retrospectively examined different endpoints in study A2309.

Methods: This 24-month (mo), multicentre, study randomised 833 *de novo* KTx patients to compare 2 regimens of everolimus (EVR; 1.5 mg/day or 3.0 mg/day) + reduced cyclosporine A (CsA) vs. enteric-coated mycophenolate sodium (EC-MPS; 1.44 g/day) + standard CsA. Renal function (RF) was measured by estimated GFR (MDRD).

Results: Analyses of RF at month 12 showed a benefit for EVR 1.5 mg vs. EC-MPS group across different cut-off points. Fewer patients in the EVR group experienced the composite endpoint of impaired RF or treated biopsy proven

acute rejection (tBPAR) or a composite of RF event, tBPAR, graft loss, or death (Table).

Conclusion: Study endpoints that consider RF and various composites are a novel approach to clinically relevant graft outcomes. These endpoints need to be further explored in prospective trials.

P313

FORBIDDEN HLA ANTIGENS IN PATIENTS WAITING FOR KIDNEY RE-TRANSPLANTATION – A SINGLE CENTRE EXPERIENCE

*Eva Slimackova, Alena Verflava, Janka Slatinská, Eva Pokorna,
Antonij Slavcev, Ondřej Viklický
IKEM*

A possible approach to decrease the risk for development of antibody-mediated rejection (AMR) in patients waiting for transplantation is to avoid the same HLA mismatches from previous transplantation (s). However, there are no guidelines about how and which HLA mismatches to exclude in order not to unjustifiably limit the chance of patients to receive another transplant.

Objective: The aim of our study was to find an optimal way of forbidding HLA antigens for the next transplantation, so that patients would have a good chance to receive a new graft, while diminishing the risk for development of AMR.

Methods: In our center, testing for specificity of HLA antibodies by Luminex was introduced for all patients waiting for re-transplantation. In case antibodies specific to mismatched HLA antigens to the previous donor (s) were detected, these antigens were “forbidden” in the organ allocation algorithm for the next transplantation.

Results: Out of 121 patients, 107 (88%) had HLA antibodies (65% class I and II, 11% class I and 12% class II). In 76 (63%) patients were forbidden both class I and II antigens, 11 (9%) class I and 3 (2%) only class II antigens. Twenty-six re-transplantations were performed in the study group in 2011 and the incidence of AMR and other complications were compared with a control group (62 in which forbidden antigens were not taken into account during the organ allocation). Lower incidence of delayed graft function in the study group was observed as compared with the control group (23% vs. 53%; $p = 0.01$), however the incidence of AMR was similar (19% vs. 26%; $p = 0.5$). There was a tendency towards better 6 months graft survival in the study group (96% vs. 82%; $p = 0.1005$).

Conclusions: The implementation of forbidden HLA antigens based on Luminex technology in the allocation system might improve the outcome of kidney re-transplantation, however these results have to be confirmed in larger prospective studies.

P314

CONNECTION BETWEEN ARTERIAL STIFFNESS AND LIPID PEROXIDATION CHANGE IN RENAL TRANSPLANTED PATIENTS

Lajos Lőcsey¹, Ildikó Seres², Dávid Kovács¹, László Asztalos¹, György Paragh²

¹Institute for Surgery, Center of Transplan, University of Debrecen Medical and Health Science Center; ²Institute for Internal Medicine, University of Debrecen Medical and Health Science Center

Background: Lipid peroxidation and atherosclerosis development remain accelerated in patients with chronic renal failure even after renal transplantation. Oxidative stress and inflammation facilitate atherosclerosis development all over the peripheral, central and coronary arteries. We investigated the connection between lipid peroxidation and arterial stiffness parameters after renal transplantation.

Methods: One hundred and thirty one renal transplanted patients (46.40 ± 14.20 years) and 63 healthy controls (48.20 ± 9.80 years) were involved in this study. Fasting serum creatinine, urea, cystatin-C, homocysteine, lipids, glucose, C-reactive protein (CRP), asymmetric-dimethyl arginine (ADMA), adiponectin (ADPN), leptin (LEP) concentrations were measured with ELISA and paraoxonase (PON1), arylesterase activities were measured spectrophotometrically. Arterial stiffness parameters (PWV-pulse wave velocity, Alx-augmentation index, PP-pulse pressure, SIA-systolic area index, DIA-diastolic area index, systolic and diastolic blood pressure, and MAP-mean arterial pressure) were measured with Arteriograph.

Results: In case of kidney transplanted patients with dyslipidaemia we found significant lower PON1 activity (101.71 ± 52.31 U/l) compared to controls ($p < 0.01$). Significant negative correlation were found between serum cystatin-C level, homocysteine ($p < 0.05$), and ADMA ($p < 0.05$), and there was significant positive correlation in case of cystatin-C and ADPN ($p < 0.03$) concentrations. Significant negative correlation were found in case of PON1 activity and PWV ($r = -0.2315$, $p < 0.0488$); DAI, LDL ($p < 0.0452$), and total cholesterol ($p < 0.0301$); MAP ($p < 0.0057$) and ADMA concentrations. There was positive correlation between PWV and CRP ($p < 0.03$); PWV and total cholesterol ($p < 0.0215$); PWV and LDL ($p < 0.045$). In obese transplanted patients we measured significant higher LDL and leptin levels ($p < 0.05$). Positive correlation was found between PWV and Alx; systolic, diastolic blood pressure and MAP ($p < 0.01$).

P315

EVALUATING EFFICACY AND SAFETY OF TWO IMMUNOSUPPRESSIVE REGIMENS IN KIDNEY TRANSPLANT PATIENTS – SIX YEARS RESULTSMilan Kuman¹, Vladimír Mejzlík¹, Sona Stepankova¹, Liba Husova¹, Jiri Ondrasek¹, Petr Nemeč¹¹Center of Cardiovascular Surgery and Transplantation Brno

End Points: PRIMARY: To determine the biopsy-confirmed acute rejection = AR rate at month 12, 36 and 72. SECONDARY: to determine the renal function, as expressed by serum creatinin and the glomerular filtration rate over the course of study and at month 12, 36 and 72. To determine patient and graft survival rates at month 12, 36 and 72.

Study Design: Group A – daclizumab, tacrolimus, mycophenolate and corticosteroids, group B- control group tacrolimus, mycophenolate and corticosteroids Number of patients

Forty patients, 20 for each treatment arm.

Results: AR rate at 12 months- group A one corticoid sensitive rejection,-group B two corticoid sensitive rejections – statistically not significant = sns. There was no rejection between month 12–36 in both groups. Between month 36–72 was 1 chronic rejection in groupe B. SERUM CREATININ at month 1 was: group A 142 ± 44.2 µmol/l group B 154 ± 42.7 µmol/l, at month 12 group A 133.4 ± 32.2 µmol/l, group B 148.9 ± 44.3 µmol/l (sns), at month 36 group A 120.8 ± 31.9 µmol/l, group B 165.3 ± 68.5 µmol/l (sns), at month 72 group A 124.9 ± 41.1 µmol/l, group B 148.9 ± 68.8 µmol/l (sns). GLOMERULAR FILTRATION at month 1 was: group A 1.058 ± 0.385 ml/s group B 0.95 ± 0.280 ml/s, at month 12 group A 1.136 ± 0.389 ml/s group B 1.099 ± 0.256 ml/s (sns), at month 36 group A 1.175 ± 0.358 ml/s group B 0.983 ± 0.422 ml/s (sns), at month 72 group A 1.124 ± 0.37 ml/s group B 1.143 ± 0.45 ml/s (sns). PATIENT SURVIVAL RATES at 12 months were 100% in both groups. At 36 months group A 100% group B 90%. At month 72, group A 90% group B 85% (sns). GRAFT SURVIVAL RATES at 12 months was: group A 95%, group B 100% (sns), at month 36 group A 90%, group B 90% (sns). At month 72 group A 90%, group B 85% (sns). Censored to patients died with functional graft.

Conclusion: The follow up has not documented beneficial effect of daclizumab use to the existing standard regimen.

P316

UROLOGICAL COMPLICATIONS AFTER KIDNEY TRANSPLANTATION: A COMPARISON BETWEEN TRANSVESICAL LEADBETTER-POLITANO VERSUS EXTRAVESICAL LICH-GREGOIR TECHNIQUEMihai Harza, Catalin Baston, Adrian Preda, Bogdan Stefan, Ioan Manea, Bogdan Haineala, Bogdan Badescu, Silviu Guler-Margaritis, Ioanel Sinescu
Center of Urology and Renal Transplantation, Fundeni Clinical Institute

Background: Incidence of urological complications after kidney transplantation remains high despite improvements in diagnosis and surgical techniques. Urinary tract reconstruction is usually done by ureteroneocystostomy, of which there are several techniques. In this study we evaluate the outcomes of two different techniques of ureteroneocystostomy performed in our department, the transvesical Leadbetter-Politano (L-P) and the extravasical Lich-Gregoire (L-G) technique. **Methods:** During 1st of July 2006 and 31st of December 2011 we performed 524 consecutive renal transplants, 264 cases using L-P technique (50.3%) and 260 cases with L-G technique (49.7%). Renal grafts were obtained from cadaveric donors in 146 cases (27.86%) and from living-related donors in 378 cases (72.14%). Ureteral stenting was performed in 103 cases (19.6%).

Results: Urological complications after kidney transplantation occurred in 22 cases in the L-P ureteroneocystostomy group (8.33%). The most common complications were ureteral stenosis (3.41%) and leakage (2.65%). Compared with the L-P ureteroneocystostomy technique, the L-G technique was associated with fewer overall complications (6.15% vs. 8.33%; $p = 0.06$), a lower rate of ureteral stenosis (2.31% vs. 3.41%; $p = 0.08$) and a similar rate of leakage. However, statistical analysis revealed no significant differences between the two techniques ($p = 0.06$). In addition, we did not notice any differences in graft and patient survival between two groups.

Conclusions: In our study, the extravasical L-G technique has a lower urological complications rate compared to transvesical L-P procedure but without statistical significant differences. Furthermore, Lich-Gregoire technique is easier to perform, faster, avoids a separate cystostomy and requires a shorter ureteral length. In conclusion, we recommend L-G technique as the technique of choice in kidney transplantation.

P317

DOES TECHNIQUE OF LIVING DONOR NEPHRECTOMY INFLUENCE ON SAFETY?Alexey Sharshatkin, Andrey Efimkin, Alexander Sushkov, Yan Moysyuk
Academician V I Shumakov Federal Research Center of Transplantology and Artificial Organs

Preferences and disadvantages of laparoscopic hand-assisted donor nephrectomy (LHADN) are well-known. The corner stone of living donation is donor

guaranteed safety. Since 1999 more than 500 consecutive living donor kidney transplantations were performed. During the last 4 years we exclusively used LHADN. We have analyzed the frequency of complication incidences (Fisher exact criteria) in groups of open donor nephrectomy (ODN, $n = 250$) and LHADN ($n = 170$). There are no significant differences between groups in bleeding frequency. Two LHADNs (1.2%) were converted to open approach because of serious abdominal bleeding; one splenectomy has been performed. Another splenectomy was done in one case of LHADN reoperative donors. LHADN has significant advantages in wound complications. All donors have excellent renal function after surgery. Short hospital staying, excellent cosmetic effect, minimal postnephrectomy pain have positive impact on increasing living donor pool. Despite of existing minimal risk of severe surgical complications we consider LHADN as the most safety approach for living kidney donation. However, there is a long learning curve and experienced surgeons are required.

P318

GENERIC TACROLIMUS AND BRANDED TACROLIMUS HAVE SIMILAR BIOAVAILABILITY IN GENETICALLY MATCHED PATIENTSArmando Gennazani¹, Piero Stratta², Elisabetta Radin², Claudio Musetti², Roberta Fenoglio², Elisa Lazzarich², Guido Merlotti², Daniele Cagna², Marco Quaglia²¹Interdepartmental Research Center of Pharmacology and Pharmacogenomics (CRIFF), "Amedeo Avogadro" Un; ²Department of Translational Medicine, University

Background: The recent introduction in Italy of generic tacrolimus has created concerns in the transplant community about the risk of possible changes in drug blood through level (BTL). Since 2011 in Piedmont (Italy) generic tacrolimus has replaced branded tacrolimus, so we realized a retrospective analysis comparing the generic and branded tacrolimus metabolism in two groups of kidney transplant recipients in one Center.

Methods: Twenty-eight kidney transplant recipients (KTR, age 60.7 ± 7.2 years, male 18/28 = 64.3%) started generic tacrolimus ([Tacrini[®]] by Teva Pharmaceutical Industries LTD) in 2012 (group Gen): clinical data and drug dosage were recorded at the time of hospital discharge and they were screened for CYP3A4 and MDR1 C3435T alleles. For each patient one age and sex-matched control with the same genotype of tacrolimus-metabolizing enzymes receiving branded tacrolimus ([Prograf[®]] by Astellas Pharma, US) was selected from a historical cohort from the same Center (group Brand).

Results: In the Brand group the mean tacrolimus BTL was 12.1 ± 3.4 ng/ml, with a mean daily dose of 0.119 ± 0.068 mg/Kg (BTL/dose ratio: 135 ± 90), while in the Gen group the mean tacrolimus BTL was 11.3 ± 4.5 ng/ml ($p = 0.45$ vs. Brand group), with a mean daily dose of 0.125 ± 0.049 mg/Kg (BTL/dose ratio: 101 ± 49; $p = 0.08$ vs. Brand group). Moreover even if the patients are divided in classes according to the BTL/dose ratio in very fast (<90), fast (90–140), slow (141–210) and very slow (>210) there is no difference between Gen and Brand groups by Fisher exact test ($p > 0.1$). Lastly the incidence of new onset diabetes after transplant (NODAT) was 7/28 (58%) and 5/28 (48%) in the Gen and Brand groups respectively.

Conclusions: Since the BTL/dose ratio is the best available indicator of tacrolimus AUC, we conclude that patients receiving generic tacrolimus have the same drug bioavailability and NODAT incidence as age, sex and genotype matched controls receiving branded tacrolimus.

P319

HOW FRANCE LAUNCHED ITS NATIONAL KIDNEY MACHINE PERFUSION PROGRAMMEMarina Roche, Yoel Sainsaulieu, Christian Lamotte, Benoit Averland, Corinne Antoine, Karim Laouabdia, Helene Logerot
Agence de la biomédecine

Background: Kidney transplantation is known to be much more cost effective than dialysis in the treatment of End Stage Renal Disease.

Methods: Since the use of Machine perfusion (MP) has proven efficient for extended criteria deceased (ECD) donor, cost-benefit arguments have been used to get the support of policy makers from the Ministry of Health. In France, procurement and transplant activities are financed via a Diagnosis Related Groups-like system as for hospital coordination, organ surgical recovery, transplantation and all transversal activities related to transplant activities.

Results: Since March 2012, two lump sums, paid to hospitals, have been designed by the Agence de la biomédecine (ABM) to finance the use of MP. One for the cost of the surgical recovery of kidneys connected to a MP (808€, twice the amount of a standard recovery with cold storage) and one for the cost of the MP, maintenance, storage, return transport, and disposables (8814€ every 6 perfused kidneys). The rules for allocating lump sums have been validated by the ABM's Medical and Scientific committee: conditions are i) both kidneys retrieved from an ECD donor are connected to the MP at the end of the procurement process (exceptions will be examined case by case), ii) should a perfused kidney allograft be refused, the perfused organ will be proposed to the next patient on the national waiting list. The MP programme is progressing steadily: at month nine, the number of ECD kidney donors put under MP has

almost doubled (137 in 2012 vs. 75 in 2011). MP will be bought through a national tender procedure. As a mandatory complement, a procedure for adverse events notification has been implemented.

Conclusion: France is the first country to finance the use and the roll out of MP in ECD kidney transplantation. This activity should develop in 2013 and allow assessing the impact of our funding strategy, reported adverse events and transplantation outcomes.

P320

CARDIOVASCULAR DISEASE AFTER RENAL TRANSPLANTATION: PREVALENCE AND IMPACT ON GRAFT FUNCTION

Pasan Perera¹, Elizabete Folkmane², Inese Folkmane³

¹P. Stradins University Hospital, University of Latvia; ²Medical faculty of University of Latvia; ³Pauls Stradins University hospital. August Kirchenstein Institute of microbiology and virology, Riga

Background: Cardiovascular disease (CVD) is the leading cause of mortality following renal transplantation (RT). The aim was to evaluate the prevalence of CVD as well as to identify risk factors for CVD and to assess their impact on graft function.

Material and method: Retrospective analysis of 131 recipients transplanted between 2007 and 2009 was performed. Laboratory data, relevant history and cardiovascular risk factors (traditional and nontraditional), including the 1st, 2nd and 3rd year after RT, were analysed. Patients were classified into two groups (with CVD and without CVD) to evaluate the graft function. Cardiac risk factors were analyzed to determine their significance and correlation with graft function.

Results: Left ventricular hypertrophy was the most prevalent cardiac abnormality (61.83%) while bundle branch block (23.66%), valvular heart disease (14.5%), congestive heart failure (12.21%), myocardial infarction (10.68%), dysrhythmia (7.63%), cardiomyopathy (4.58%), atrioventricular block (3.81%), cerebrovascular disease (3.05%), peripheral arterial disease (2.29%) and hypertensive heart disease (0.76%) showed lower prevalence's. CVD had a significant impact on graft function as observed with a statistical significance; $p = 2.85061E-05$, 0.000465505 , 0.001161979 for each respective year. Traditional risk factors (increasing age, cholesterol, systolic and diastolic BP etc.) inversely affected GFR with negative correlations for each risk factor. The prevalence of non-traditional risk factors was highest for hyperuricemia (54.20%). Cholesterol ($r = 0.93102018$), triglyceride ($r = 0.885437745$), blood sugar levels ($r = 0.734733844$), age ($r = 0.662266179$), body mass index ($r = 0.668896737$), uric acid ($r = 0.687547085$) correlation to CVD was strong positive.

Conclusion: CVD is commonly observed after RT (82%). CVD has a negative impact on graft function.

P321

OUTCOME OF HEPATITIS B AND C VIRUS ASSOCIATED HEPATOCELLULAR CARCINOMAS OCCURRING AFTER RENAL TRANSPLANTATION

Nada Kanaan, Claudia Raggi, Eric Goffin, Ziad Hassoun

Cliniques universitaires Saint-Luc, Université Catholique de Louvain

Background: Chronic hepatitis B (HBV) and C (HCV) virus infections are causes of morbidity and mortality in kidney transplant recipients (KTR). The aim of this study was to assess the incidence and outcome of HBV- and HCV-related hepatocellular carcinoma (HCC) in KTR.

Methods: We performed a case-control study in patients with chronic HBV and/or HCV infection who underwent kidney transplantation (KT) between 1976 and 2011 and subsequently developed HCC. Patients' characteristics and outcomes were compared to a control group of HBV and/or HCV positive patients with HCC matched for age and gender who did not have KT.

Results: Among 2944 KTR, 330 had hepatitis B and/or C. Fourteen developed HCC, an incidence of 4.24%. All patients were Caucasian, and 86% were male. Mean age at HCC diagnosis was 52.6 ± 2 years (53.2 ± 1.5 in controls, $p = ns$). Mean time between transplantation and HCC diagnosis was 16.7 ± 2.7 years. Six HCCs were related to HBV, 6 to HCV, and 2 to co-infection with HBV and HCV. Immunosuppressive therapy was comparable in HBV, HCV and HBV+HCV patients. All patients had corticosteroids. Sixty-four percent of patients received induction treatment and were on triple therapy. At diagnosis, 71% of patients met Milan criteria (65% in the control group, $p = ns$). Tumour characteristics and treatment modalities including surgical resection, chemoembolization, radiofrequency ablation, or liver transplantation were comparable between the two groups. Patient survival 2 years after HCC diagnosis was 43% in KTR, compared to 76% in the control group ($p = 0.03$). There was no significant difference in overall survival between HBV- and HCV-infected KTR with HCC.

Conclusion: HCC occurs with an incidence of 4.24% in HBV and/or HCV infected patients after KT. Survival after HCC diagnosis is significantly worse compared to a control group of non-transplanted patients with HBV and/or HCV, matched for age and gender, and with similar tumour characteristics.

P322

NGAL PREDICTS THE DEVELOPMENT OF DELAYED GRAFT FUNCTION AFTER DCD KIDNEY TRANSPLANTATION

Elinevan den Akker, Dennis Hesselink, Olivier Manintveld, Jan Ijzermans, Ronde Bruin, Frank Dor
Erasmus MC

Background: To date, no specific biomarker is available to measure kidney damage and predict delayed graft function (DGF) after kidney transplantation (KT). Since NGAL and KIM-1 are sensitive and early biomarkers for acute kidney injury, we studied their potential as damage markers after KT. Kidneys donated after cardiac death (DCD) have extensive damage due to prolonged warm ischemia time with a high risk for DGF. We studied NGAL and KIM-1 in perfusate and early serum samples of 20 DCD KT recipients and correlated those with the occurrence of DGF, risk factors in donor characteristics and graft function.

Methods: Perfusate was collected by flushing the kidney with HTK during bench surgery before transplantation. Serum samples of the recipients were collected 30 min before and after reperfusion and 1, 4 and 7 days after transplantation. NGAL and KIM-1 were measured with an ELISA-assay.

Results: Seventeen of 20 patients experienced DGF. In perfusate, NGAL was detectable in 19 of 20 cases, whereas KIM-1 was detectable in 20%. No correlations between NGAL- or KIM-1-levels and risk factors or DGF were found. In pre-transplantation sera, NGAL-levels were high in all patients (730 ng/ml [355–1648]). 19 of 20 patients were on dialysis (1–5 years). There was no correlation between serum creatinine, last dialysis and NGAL levels. One day after transplantation, NGAL-levels strongly discriminated between immediate graft function and DGF; 417 ng/ml [232–481] vs. 716 ng/ml [490–1999] resp. ($p < 0.01$). There seems to be a cut off point between 480 and 490 ng/ml. KIM-1 levels in serum remained negative until 1–4 days after transplantation and no correlations could be found.

Conclusion: Despite the small number of patients without DGF ($n = 3$), these data strongly suggest that NGAL is a suitable biomarker to identify patients that will develop DGF after DCD KT. This warrants further study to determine the value of NGAL as biomarker for DGF.

P323

LONG TERM PROGNOSTIC IMPACT OF CEUS AND ECODOPPLER IN RENAL TRANSPLANTATION

Giacomo Mori, Maria Granito, Davide Favali, Decenzio Bonucchi, Pietro Torricelli, Gianni Cappelli
AOU Policlinico di Modena

Background: Contrast-enhanced sonography (CEUS) and power doppler ultrasound (US) are established tools in the study of renal allograft (RA) dysfunction, the aim of this study is to investigate their long term prognostic impact

Materials and Methods: Nine kidney recipients underwent CEUS and US at 5, 15 days and 1, 3, 6, 12 months after grafting, with yearly clinical, laboratory and US follow up for a total of four years. CEUS analysis according to gamma-variate model was performed on cortical and medullary regions (evaluating also cortical to medullary ratio). Patients were divided in two subsets: death and graft failure versus patients with functioning grafts; higher versus lower than 50% GFR reduction from first month to fourth year after grafting. Independent samples t-test was used to compare means. Bivariate correlation (Pearson) was performed between GFR at different times of follow up and CEUS/US findings. ROC analysis for death/graft failure and 50% GFR loss events was performed for variables with significant differences between groups or with significant correlation to GFR. The predictive value of different covariates over these endpoints was estimated with Cox regression.

Results: Several CEUS and US parameters show significant differences between the groups, with positive Pearson Coefficient (PC) ranging from 0.312 to 0.932 or negative (PC-0.384/-0.447) correlation to GFR in different stages of follow up. ROC analysis confirms the reliability of some of these variables as a test for long term graft survival or GFR loss, with high sensitivity (62–100%, ROC Area 0.748–0.938 for Resistive Index) or specificity (93–100%, ROC Area 0.008–0.247 for GFR, medullary Peak and Region Blood Flow [RBF]). Cox regression indicates as significant predictors of long term GFR loss not only clinical data as months in waiting list, diabetes or GFR but also Mean Transit Time, RBF and PEAK.

Conclusion: CEUS and US can be sensitive and specific tools in the early evaluation of long term evolution of RA function.

P324

OUTCOME OF ARISTOLOCHIC ACID NEPHROPATHY AFTER RENAL TRANSPLANTATION

Nada Kanaan, Claudia Raggi, Ziad Hassoun, MartineDe Meyer, Michel Mourad, Jean-Pierre Cosyns, Eric Goffin
Cliniques universitaires Saint-Luc, Université Catholique de Louvain

Background: In the early 1990s, intake of slimming pills containing Aristolochic Acids (AA) led to a rapidly progressive kidney failure. AA are nephrotoxins and a significant proportion of patients developed urothelial carcinoma. The aim of this study was to assess the outcome of patients with AA nephropathy (AAN) after kidney transplantation.

Methods: A case-control study in patients with AAN who underwent kidney transplantation. Patients' characteristics and outcomes were compared to a control group of patients with interstitial chronic nephropathy matched for gender and age at transplantation.

Results: Twenty patients were transplanted since 1992 for AAN. Nineteen were female. All but one were Caucasian. Mean age at diagnosis was 45 ± 2 years (39 ± 2 in controls, $p = ns$). Time on dialysis was 19 ± 4 months (28 ± 3 in controls, $p = ns$). Time from diagnosis to transplantation was significantly shorter in AAN patients (5 ± 0.7 vs. 11 ± 1 year). Mean age at transplantation was 50 ± 3 years (49 ± 2 in controls, $p = ns$). Mean time of follow-up was 13 ± 1 year. Immunosuppressive therapy was comparable in both groups. Seven patients presented with urothelial carcinomas of the upper-tract; two of them with additional bladder urothelial carcinomas. Of these two patients, one required radical cystectomy. In the control group, none suffered from urological complications. Cardiovascular complications were comparable in both groups. Patient survival was 100% in AAN patients compared to 100, 92 and 92% in the control group ($p = ns$) at 5, 10 and 15 years respectively after transplantation. Graft survival at 5, 10, and 15 years was 95, 83, and 75% in the AAN group compared to 100, 92, and 92% in the control group ($p = ns$).

Conclusion: AAN leads rapidly to end-stage renal disease requiring transplantation. Although 35% of patients presented urothelial carcinomas of the upper-tract and bladder, patients' survival is excellent and graft survival is not affected.

P326

ADOPTING THE RETROPERITONEAL APPROACH TO LIVE DONOR NEPHRECTOMY – CONFESSIONS OF A CONVERTED SURGEON!

*Nicos Kassaris¹, Sarah Heap²
¹Guy's & St Thomas's Hospital; ²St George's Hospital*

Background: Becoming trained and established in laparoscopic donor nephrectomy can be challenging as there have been few fellowships in the UK. This study was to review the development of a Live Donor BTS fellow who had been trained in transperitoneal techniques to adopt a retroperitoneal approach to donor nephrectomy at a single centre as a newly appointed consultant.

Method: A prospectively maintained donor database and operative logbook was reviewed from August 2011 to November 2012. There was a single senior surgeon training the new consultant in the Hand Assisted Retroperitoneal Donor Nephrectomy technique.

Results: There were a total of 57 donations. The mean age was 50 years (range 24–71) with a mean BMI of 29 kg/m^2 (range $18\text{--}33.8 \text{ kg/m}^2$). The training surgeon assisted in three full procedures and a further three to mobilise the vessels. In a further eight procedures the training consultant required minimal help with either mobilisation or vessels dissection. From the 15th case no further assistance was required. The decision to remove a kidney was decided in a multidisciplinary team meeting. Fifty were left sided, and 33 had simple anatomy. Thirteen cases there were two arteries, two cases three arteries and one case four arteries. The mean operating time was 199 mins (range 129–358 min). Mean blood loss was recorded as 115 ml. One right sided procedure required a further incision to accommodate a gel port to help mobilise the upper pole of an adherent kidney. Post operatively the mean length of post-operative stay was 2 days. There were two recorded chest infections requiring antibiotics and one prolonged wound discharge. Two patients required a post-operative CT scan to investigate unexplained abdominal discomfort and an elevated CRP > 250 . The scans showed no abnormal features and these donors were discharged on day 4.

Conclusion: Retroperitoneal approach to donor nephrectomy is a safe technique to train a surgeon with previous live donor nephrectomy experience.

P327

EXPLORATORY IMMUNOSUPPRESSIVE REGIMENS FOR RECIPIENTS OF KIDNEY TRANSPLANTS FROM EXPANDED CRITERIA DONORS

*Tainá Sandes-Freitas¹, Fernanda Costa², Alexandra Ferreira², Elisa Conceição², Hélio Tedesco-Silva², José Osmar Medina-Pestana²
¹Physician; ²Hospital do Rim e Hipertensão*

Background: the use of kidneys from expanded criteria donors (ECD) is increasing but the ideal immunosuppressive strategy for these recipients has yet to be established.

Materials and Methods: This study was an exploratory sequential investigation in 203 consecutive low risk recipients of kidneys from ECD. The first cohort (BSL-MPS, $n = 43$) received basiliximab, mycophenolate (MPS, 1080–1440 mg BID) and tacrolimus (TAC, 0.1 mg/Kg BID initiated at day 4). The second cohort (Thymo-SRL, $n = 49$) received thymoglobuline (Thymo, single 3 mg/Kg dose at day 1), TAC (0.1 mg/Kg BID) and azathioprine (2 mg/Kg/day) with conversion to sirolimus (SRL, 2 mg/day targeting blood concentrations of 5–15 ng/ml) 10 days after the transplant surgery. The third cohort (Thymo-EVL, $n = 26$) received Thymo (4 doses of 1.5 mg/Kg every other day), MPS (720 mg BID) and everolimus (EVR, 1.5 mg BID initiated at day 7 targeting blood concentration of 5–8 ng/ml). The fourth cohort (Thymo-MPS, $n = 85$) received Thymo (4 doses of 1.5 mg/kg every other day), MPS (720 mg BID) and TAC (0.05 mg/kg BID initiated at day 7). The TAC trough concentration

was maintained around 3–8 ng/ml and all patients also received prednisone. None patient received prophylaxis for cytomegalovirus (CMV) infection.

Results: There were no differences in main demographic characteristics. The mean recipient and donor age were 50 and 60 years, respectively. Mean cold ischemia time was 25 h and mean time on dialysis was 53 months. The main outcomes are presented in the table below.

Conclusion: BSL-MPS regimen was associated with highest incidence of acute rejection (AR). Thymo-SRL was associated with high AR incidence, treatment discontinuation, and inferior renal function. Thymo-EVL regimen was associated with high incidence of AR, CMV infection and treatment discontinuation. Thymo-MPS was associated with lowest incidence of AR and highest incidence of CMV infection. None of these strategies showed superior survival outcomes.

P328

DE NOVO IGA GLOMERULONEPHRITIS AND STEROID WITHDRAWAL IN RENAL TRANSPLANTED PATIENTS (RTRS)

*Maria Messina, Maria Cristina Di Vico, Manuel Burdese, Elisabetta Mezza, Roberta Giraudi, Fabrizio Fop, Alberto Mella, Angelo Nappo, Giuseppe Paolo Segoloni, Luigi Biancone
 Nephrology, Dialysis and Transplantation Center, Molinette Hospital and University of Turin- Italy*

Background: The role of steroids on the risk of recurrent (R) or de novo (DeN) glomerulonephritis (Gn) is poorly investigated in RTRs Materials: We analyzed the association between steroid withdrawal (SW) and DeNlgAGn and RlgAGn in 1268 RTRs in our Center (1995–2007). In 484/1268 grafts (38.1%) a for cause biopsy was performed: $> 20\%$ increase in serum creatinine or $> 500 \text{ mg/}$ day proteinuria. Overall 87 Gn were found.

Results: In 32/87 cases (36.7%) IgAGn was diagnosed (7/32 RlgAGn and 25/32 DeNlgAGn); 17/25 DeNlgAGn (68%) occurred after SW ($p = 0.006$). Median time to DeNlgAGn was 25.3 months (5.1–93) after SW. As for R+ DeNlgAGn altogether the association with SW was a tendency, but not significant. Compared to the other R+DeNGn, ($n = 62$), DeNlgAGn carried a statistically greater risk of developing after SW (OR 6.7). No other immunosuppressant showed a correlation with DeNlgAGn.

Conclusion: We found a strong association (OR 6.7) between SW and DeNlgAGn. Further studies are needed to confirm our preliminary data. The balance between SW and maintenance of steroids to reduce IgAGn should be tailored on the basis of the recipient risk profile.

P329

PULMONARY SYNERGISTIC TOXICITY IN A RENAL TRANSPLANT RECIPIENT (RTR) TREATED WITH AMIODARONE AND EVEROLIMUS: A CASE REPORT

*Maria Messina¹, Alberto Mella¹, Andrea Ranghino¹, Maura Rossetti¹, Maria Cristina Di Vico¹, Francesca Simonato¹, Gloria Giovinazzo¹, Giuseppe Paolo Segoloni¹, Luigi Biancone¹
¹Nephrology, Dialysis and Transplantation Center, Molinette Hospital and University of Turin, Italy*

Background: Several pneumotoxic drugs as amiodarone and m-TOR inhibitors (m-TORi) can be found associated in therapy of RTR. Differential diagnosis may promptly request invasive tests. We present a case of amiodarone pulmonary toxicity (APT) in a RTR treated with amiodarone and everolimus. Case Report A 57 year-old caucasian male in treatment both with everolimus-since 3 years- and amiodarone-since 2 months- for his second kidney transplant with suboptimal serum creatinine (3 mg/dl) presented with fever and dyspnoea, normal physical examination and negative chest X-Ray. A non-contrast high resolution computed tomography (HRCT) scan showed bilateral interstitial lung disease with associated reduction in carbon monoxide diffusing capacity (DLCO). Bronchoalveolar lavage (BAL) was negative for infection but BAL cytology was suitable for APT (50% of "foamy" macrophages). Complete recovery was obtained after amiodarone interruption and oral steroid therapy increase. Everolimus was not discontinued. The kidney function remained unchanged in the following months.

Conclusion: We suggest a possible synergistic effect between m-TORi and amiodarone (as seen in the image below) and we recommend promptly performed tests as HRCT and BAL for the differential diagnosis in case of suspected lung toxicity.

P330

EVALUATION OF STEADY-STATE PHARMACOKINETIC PARAMETERS OF LCP-TACROAND ADVAGRAF IN HEALTHY VOLUNTEERS USING A SYSTEMS DYNAMIC MODEL

*Steven Gabardi¹, Vincenza Nigro², Mary Johnson², Robert Nachtrieb³, John Weinberg²
¹Brigham and Women's Hospital; ²Veloxis Pharmaceuticals; ³Massachusetts Institute of Technology*

Background: Pharmacokinetic (PK) profiles of a medication with controlled or modified release formulations may differ depending on the delivery technology.

An extended-release formulation of tacrolimus designed for once-daily administration (LCP-Tacro, Veloxis Pharmaceuticals) utilizes proprietary MeltDose® technology and another extended-release once-daily formulation (Advagraf, Astellas Pharmaceuticals) is available and formulated utilizing technologies to prolong release of tacrolimus. By utilizing system dynamics modeling technique, PK parameters previously studied can be manipulated to predict dose.

Methods: Developed model using data from cross-over study of healthy volunteers who received 1 LCP-Tacro 2 mg tablet or 2 Advagraf® 1 mg capsules. PK was measured on Day 1 and 10 over 24 h, Day 5–9 pre-dose and 24, 48, 72, 96 and 120 h post last dose. The model utilizes blood concentration data and predicts same baseline trough levels or AUC exposure for both formulations and allows observation of the dose at steady state. Simulation was based on 19 subjects and calibrated for both formulations by fitting the experimental data while adjusting Advagraf dose to achieve equivalent trough and AUC levels as LCP-Tacro.

Results: Data from the Phase one study suggest, the systemic exposure (AUC₂₄ and C_{min}) of LCP-Tacro was ~49% and ~66% higher than that of Advagraf ($p < 0.05$) when comparing equivalent doses of 2 mg. In this model, however, when simulating similar C_{min} or AUC levels for Advagraf and LCP-Tacro at steady state, the data suggest that Advagraf may require a significant upward dose adjustment of a factor of at least 1.5 when compared to an equivalent dose of LCP-Tacro.

Conclusions: LCP-Tacro's MELTDOSE technology differs in the PK characteristics of tacrolimus from those of Advagraf. LCP-Tacro has shown increased bioavailability compared to Advagraf yet more studies are warranted in kidney transplant patients to compare the two formulations.

P331

A MULTIPLICATIVE-REGRESSION MODEL FOR RELATIVE SURVIVAL TO COMPARE THE EFFECT OF FACTORS ASSOCIATED WITH THE TIME TO GRAFT FAILURE BETWEEN FIRST AND SECOND RENAL TRANSPLANT

Katy Trebern Launay¹, Magali Giral-Classe¹, Jacques Dantal¹, Yohann Foucher²

¹Institut de Transplantation Urologie Néphrologie, Inserm U643; ²EA4275 Biostatistique, Recherche Clinique et Mesures Subjectives en Santé

Background: Whereas the prognosis of second kidney transplant recipients (STR) compared to first renal transplant recipients (FTR) has been frequently analyzed, no study has addressed the issue of comparing the risk factors effects on graft failure between both groups.

Materials and Methods: We propose a multiplicative-regression model for relative survival (MRS model) to study the factors associated with the time to graft failure (return-to-dialysis or patient death) of STR compared to a matched population of FTR. We performed an observational prospective study based on 641 STR from the multicentric French DIVAT database transplanted between 1996 and 2010. The expected graft failure hazard was estimated using a proportional hazard model based on 2462 FTR performed over the same period.

Results: We demonstrated for the first time in renal transplantation that: (i) male donor is a specific risk factor for STR, (ii) the adverse effect of recipient age is enhanced for STR (1.6-fold higher) and (iii) the graft failure risk related to donor age is attenuated for STR (1.7-fold lower).

Conclusions: While the traditional Cox model did not provide original results based on the renal transplantation literature, the proposed MRS model revealed new perspectives that may be useful for clinicians. This methodology may be of interest in other medical fields when the principal objective is the comparison of risk factors between two populations.

P332

ASSOCIATION BETWEEN CYP3A5*3 AND PPARA GENE VARIANTS ON TACROLIMUS CONCENTRATIONS IN RENAL TRANSPLANT RECIPIENTS

Ingrid Lunde¹, Karsten Midtved², Beata Mohebi¹, Miriam Dahl¹, Stein Bergan³, Anders Åsberg¹, Hege Christensen¹, Sara Bremer⁴

¹School of Pharmacy, University of Oslo; ²Laboratory for Renal Physiology, Medical Department, Oslo University Hospital, Rikshospitalet; ³School of Pharmacy, University of Oslo and Oslo University Hospital, Rikshospitalet; ⁴Oslo University Hospital, Rikshospitalet

Background: Tacrolimus (Tac), a narrow therapeutic index drug is metabolized by CYP3A enzymes. Variants in several genes have been reported to impact the CYP3A activity. Recently a single-nucleotide polymorphism in the nuclear receptor peroxisome proliferator-activated receptor gene (*PPARA*) has been identified as a regulator of CYP3A4 expression and activity, but the effect of *PPARA* on Tac metabolism in renal transplant recipients (RTR) remains unknown.

Methods: Hundred RTR were genotyped for *CYP3A53* and *PPARA*. The potential association with steady state dose adjusted trough Tac concentration (C₀/dose, µg/l/mg) 2–3 weeks post Tx was investigated.

Results: CYP3A5 non-expressers (*3/*3) had significantly higher mean C₀/dose, 2.5 ± 1.0 vs. 1.5 ± 0.7 ($p < 0.001$). CYP3A5 expressers (*1/*3), carriers of at least one variant *PPARA* allele showed significantly higher C₀/dose, 1.9 ± 0.8 vs. 1.2 ± 0.3 ($p = 0.009$).

Conclusion: Assessing both *PPARA* and *CYP3A5* genotype may improve the individualized dosing of Tac.

P333

URINARY TRACT RECONSTRUCTION BY URETERO-URETERAL END-TO-SIDE ANASTOMOSIS IN KIDNEY TRANSPLANT RECIPIENTS WITH DISUSED ATROPHIC BLADDER

Hideo Sasaki¹, Eriko Matsushashi¹, Tomohiro Nishi¹, Satoshi Hachisuka¹, Yuichi Katusoka¹, Maki Yoshioka¹, Ryuto Nakazawa¹, Takeshi Udagawa¹, Satetsu Miyano¹, Yuichi Sato¹, Masahiko Yazawa², Naohiko Ima², Hiroo Kawarazaki², Yugo Shibagaki², Kenjiro Kimura², Tatsuya Chikarashi¹

¹Department of Urology, St. Marianna University School of Medicine;

²Department of Nephrology and Hypertension, St. Marianna university school of medicine

Background: Although kidney transplantation has become a standard treatment for end-stage renal disease, complications associated with surgery compromise clinical outcomes. Because kidney transplant recipients have usually been on dialysis for a long time in Japan, post-operative urologic complications related to disused bladder are common.

Methods: Uretero-ureterostomy technique was employed in five kidney transplant recipients with disused atrophic bladder (bladder capacity <50 ml).

Results: The average dialysis was 11.8, 4.3(6.2–18.2) years. In three patients, the native ureter was ligated at the upper part of anastomotic site, leaving the native kidney *in situ*. A ureteral stent was placed in four patients, and then removed endoscopically removed after about 2 weeks. Two hydro-nephrosis in the native kidney were observed in patients with ligated ureter, both of which required no treatment.

Conclusion: End-to-side uretero-ureterostomy was safely performed and may be a treatment option for reconstruction of the urinary tract in renal transplant recipients especially with disused atrophic bladder due to long-term dialysis.

P334

THE IMPORTANCE OF EARLY DETECTION AND APPROPRIATE TREATMENT IN THE SUCCESSFUL TREATMENT OF POST-TRANSPLANT LYMPHOPROLIFERATIVE DISORDER AFTER KIDNEY TRANSPLANTATION-CASE REPORT

Lada Petrovic¹, Tatjana Djurdjevic-Mirkovic¹, Dejan Celic¹, Dusan Bozic¹, Igor Mitic¹, Ivana Urošević²

¹Clinic of Nephrology and Clinical Immunology, Clinical Center of Vojvodina,

University of Novi Sad; ²Clinic of Haematology, Clinical Center of Vojvodina,

University of Novi Sad

Introduction: Post-transplant lymphoproliferative disorder (PTLD) is one of the most severe and often fatal complications observed after solid organ and bone marrow transplantations. The histological subtypes of PTLD range from the early Epstein-Barr virus (EBV)-associated polymorphic lymphoid proliferation resembling infectious mononucleosis, to more aggressive EBV-positive or -negative monomorphic lymphomas of B-cell or less often T-cell origin. Case report: We presented a case of a patient HA, born 1989, who underwent live-related donor renal transplantation at the age of 16. Induction therapy implicated administration of ATG and corticosteroids, and maintenance dose encompassed combination of three immunosuppressive agents: tacrolimus, mycophenolate mofetil and corticosteroid. The patient experienced first complications six months after transplantation, manifested as lacunar angina and subsequent dysphagic problems. Upon recommendation of ENT-specialist, tonsillectomy was performed in April 2006. Histopathological and immunohistochemical analysis of tonsillectomy specimens revealed a polymorphic PTLD (with high expression of EBV LMP antigen). Definitive diagnosis of diffuse large B-cell lymphoma (CD20+) was established upon analysis of oesophageal biopsate. Antiviral therapy was applied, along with rituximab and CHOP therapy, whilst the dosage of basic immunosuppressive drugs was reduced. Complex diagnostic procedures confirmed the absence of disease recurrence and stable graft function five years after completing PTLD therapy.

Conclusion: The presented case of our patient, who developed PTLD after renal transplantation, demonstrated that an appropriate early diagnosis, reduction of immunosuppressive regimens and vigilant application of immunomodulatory and chemotherapy could result in complete disease remission, yet preserving and maintaining the stable function of the transplant.

P335

ABO BLOOD TYPE INCOMPATIBLE KIDNEY TRANSPLANTATION (ABOIKTX) WITHOUT SPLENECTOMY

Tatsuya Chikaraishi¹, Hideo Sasaki¹, Yuichi Sato¹, Ryuto Nakazawa¹, Naohiko Ima², Hlroo Kawarazaki¹, Yugo Shibagaki², Kenjiro Kimura²

¹Department of Urology, St. Marianna University, School of Medicine;

²Department of Nephrology, St. Marianna University, School of Medicine

Background: We reported our initial experience performing ABOikTx with a low dose of rituximab instead of splenectomy at ESOT 2009. Here, we aim to review

- 1. The extended outcomes of our earlier ABOikTx studies and
- 2. The early outcomes of recent studies involving ABOikTx, where patients were pre-treated with either reduced antibody removal or no antibody depletion.

Methods: Immunosuppression was induced by treatment with the following drugs: tacrolimus, mycophenolate mofetil, basiliximab, steroids, and rituximab.

- 1. Eight transplant recipients followed for more than five years were reviewed. Special emphasis was placed on graft function, infection rates, and malignancies.
- 2. Since 2010, antibody removal was not performed if the titre of anti-blood type antibodies was $\times 32$. The rate of antibody-mediated acute rejection (AMR) was examined for eight recipients treated with these guidelines.

Results:

- 1. All recipients had stable graft function with serum creatinine levels of 0.9–1.7 mg/dl. One case of pneumonia and one case of colon cancer occurred during the observation period.
- 2. No AMR occurred in the recipients with reduced or no antibody removal.

Conclusions:

- 1. ABOikTx can be successfully performed with low dose rituximab with excellent graft function for more than 5 years. Care must be taken to avoid late onset infections and malignancies.
- 2. Candidates for ABOikTx with anti-ABO antibody titres below $\times 32$ do not need antibody elimination prior to transplant to avoid AMR.

Reference: T. Chikaraishi et al. ABO Blood Type Incompatible Kidney Transplantation Without Splenectomy Prepared With Plasma Exchange and Rituximab. *Transplant Proc* 2008, 40, 3445–3447.

P336

FAVORABLE RESULT OF PREVENT OF POST-TRANSPLANT LYMPHOCELE BY USE OF ULTRASONIC SCALPEL FOR ILIAC LYMPHATICS DISSECTION

Man Ki Ju, Kyu Ha Huh, Myoung Soo Kim, Yu Seon Kim, Soon Il Kim
YUHS

A lymphocele is a common surgical complication after renal transplantation thought be due to disrupted lymphatic channels of the iliac vessels. Preventing lymphocele occurrence by ligation of lymphatic channels running along the iliac vessels using multiple surgical ties has been the standard treatment approach, but this requires significant time and can be tedious, labor intensive, and frustrating due to the friable nature of the tissue ligated. An alternative to control lymphatics is the use of ultrasonic scalpel for dissection, which has the advantage of quickly and reliably cutting and coagulating small bleeding sites and lymphatics during dissection around the iliac vessels and has been applied in many types of surgery to safely divide tissues while also achieving hemostasis. Since March 2010, we used ultrasonic scalpel for iliac lymphatic channels. Of 47 consecutive renal transplant recipients, there was no lymphocele. 31 recipients did not need drainage catheter. In addition, we have shortened the operation time about 30 min. A controlled comparative study should be required. However, the use of ultrasonic scalpel ensures total control of lymphatic compartment coagulation, alongside a reduction in time of surgical dissection.

P337

CLINICAL OUTCOME OF LIVING UNRELATED KIDNEY TRANSPLANTATION BETWEEN SPOUSES -A SINGLE CENTER EXPERIENCE

Yuichi Machida, Junji Uchida, Tomoaki Iwai, Kazuya Kabei, Nobuyuki Kuwabara, Toshihide Naganuma, Norihiko Kumada, Tatsuya Nakatani
Osaka City University Graduate School of Medicine

Background: Due to the severe shortage of deceased donors in Japan, living donor kidney transplantation is mainly performed in Japan. According to the Japanese renal transplant registry of 2011, there were 1389 living kidney transplantations including 32.3% from spouses. We summarized our experience with living unrelated kidney transplantation between spouses.

Patients and Methods: A total of 149 patients with end-stage renal disease underwent living donor kidney transplantation at Osaka City University Hospital between January 2000 and February 2013, of which 63 cases were kidney transplantation between spouses. ABO-incompatible kidney transplantation was performed in 20 of the 63 cases. We analyzed these recipients, focusing on the immunosuppressive protocols, complications, and patient/graft survivals.

Results: Patient and graft survival rates were 100%. Thirty-six patients received cyclosporine, and 27 received tacrolimus, as calcineurin inhibitor. One patient experienced antibody-mediated rejection and intractable acute cellular rejection, one had antibody-mediated rejection, and one had an intractable acute cellular rejection episode that was treated using OKT-3. The incidence of acute rejection was 14.3%. There were no severe complications among the recipients.

Conclusions: Previously, living unrelated kidney transplantation between spouses has met with some opposition due to poor tissue antigen compatibility. Recent significant improvements in immunosuppression and recipient care indicate that it has become a viable treatment option in Japan, which lacks deceased donors.

P338

CAN SHEAR WAVE VELOCITY OF DONOR KIDNEY PREDICT GRAFT FUNCTION AFTER TRANSPLANTATION?: A PRELIMINARY REPORT

A-Lan Lee¹, Dong Jin Joo¹, Young Taek Oh¹, Hyeon Joo Jeong¹, Su Hyung Lee¹, Jung Jun Lee¹, Beom Seok Kim¹, Kyu Ha Huh¹, Myoung Soo Kim¹, Yu Seun Kim¹, Soon Il Kim¹, Kiil Park²

¹Yonsei University College of Medicine; ²CHA University

Background: Interstitial fibrosis (IF) and tubular atrophy (TA) is well known predictor of poor graft function in renal allograft histology. Donor kidney can have IFTA and it could be a source of poor graft function after transplantation. However, kidney biopsy of donor can be a dangerous procedure. Thus, this study was prospectively designed to evaluate correlation between the value of "Acoustic Radiation Force Impulse (ARFI)" and IFTA score of donor kidney, and validation of ARFI quantification to predict graft function after transplantation.

Patients and Methods: Fifty seven adult living renal transplantation donors between June 2010 and October 2012 in our center were enrolled. Before transplantation, all donors were evaluated by ARFI-quantification to measure shear wave velocity (SWV, m/s) in graft kidney. Time-zero biopsies were performed in all graft kidneys before implantation. IFTA score was defined as "interstitial fibrosis (CI)" + "Tubular atrophy (CT)" score in Banff 07/criteria.

Results: Of the 57 donors, seven donors (12.3%) presented IFTA score 1. The mean value of SWV was 2.23 ± 0.55 m/s. The values of SWV was significantly associated with IFTA score (2.29 ± 0.55, 1.83 ± 0.41 in IFTA score 0, 1, respectively, p = 0.04, Table 1). The clinical parameters of donor except to cholesterol level did not showed difference from IFTA score. The IFTA score have significantly association with cholesterol level of donors (p = 0.03, Table 1).

Conclusion: These preliminary data showed that values of SWV were significantly associated with IFTA score. Thus, ARFI can be considered as a useful noninvasive method to predict pathologic abnormality of the donor kidney.

P339

FACTORS AFFECTING THE SUCCESS OF TRANSPLANTATION OF THE VERY SMALL PEDIATRIC DONORS KIDNEYS (VSPDK) WITH CARDIAC VERSUS BRAIN DEATH

Dai Nghiem, Angelo Demattos, Christoph Troppmann, John McVicar, Richard Perez

University of California Davis Medical Center, Sacramento

VSPDK are not widely performed. We have developed a protocol to procure, preserve and transplant these organs successfully.

Methods: Eighty-four en bloc kidneys from 2000 to 2012 donors (21 with Cardiac Death and 63 with Brain Death) were reviewed. Kidneys were removed en bloc with full aorta and cava bifurcation, placed on pulsatile perfusion and transplanted under thymoglobuline, short course of methylprednisolone, tacrolimus and mycophenolate.

Results: All donors aged 0.9 ± 1.2 year, weighed 8.3 ± 4.7 kg, had terminal CR 0.5 ± 0.45 ml, and ischemic time 21.6 ± 7.82 h. Pulsatile perfusion was maintained for 7 ± 3.9 h. 19 patients experienced DGF (23%) vs. 65% Immediate graft function (p = 0.7). CR at day 7, 30, 90, 1 year were 4.5 ± 3.01 ml, 2.4 ± 1.57, 1.5 ± 0.86 and 0.9 ± 0.26, respectively. DCD donors were younger 0.6 ± 0.6 years vs. 1.2 ± 1.3 (p = 0.012), smaller 6.4 ± 3.69 kg vs. 9.4 ± 4.92 (p = 0.005), had lower CR 0.4 ± 0.27 ml vs. 0.7 ± 0.64 (p = 0.002), and kidneys transplanted to older recipients 55 ± 11.9 years vs. 47 ± 15.6 (p = 0.028). CIT was 20.8 ± 6.37 h vs. 21.4 ± 8.26 (p = 0.7) and CR were 5.2 ± 3.07 ml vs. 4 ± 2.9 @day 7, 2.8 ± 1.93 vs. 2.1 ± 1.34 @ day 30, 1.6 ± 0.91 vs. 1.4 ± 0.7 @ day 60, 1.1 ± 0.47 vs 1.1 ± 0.46 @ day 90, 1.6 ± 0.91 ml vs. 1.4 ± 0.46 @ 6 months

and 0.9 ± 0.12 vs. 0.9 ± 0.33 @ 1 year, respectively. Perfusion time was similar 6.8 ± 3.53 h vs. 7.1 ± 4.17 . At 7 and 8 h the DCD group had lower flow 34 ± 14 ml/mn vs. 51 ± 24.3 ($p = 0.043$) and 31 ± 13.9 vs. 51 ± 22.6 ($p = 0.043$), respectively and lower resistance 1.05 ± 0.66 vs. 0.51 ± 0.25 ($p = 0.006$) and 1.12 ± 0.69 vs. 0.52 ± 0.25 ($p = 0.01$), respectively. But at transplantation flows were similar 42 ± 18.3 ml/mn vs. 49 ± 22.1 ($p = 0.1$) and pump resistance values were 0.69 ± 0.45 vs. 0.59 ± 0.41 ($p = 0.3$). Graft survival was 100% for DCD and 98% for DBD @ 1 year.

Conclusion: Under our protocol DCD and DBD kidneys provide similar excellent graft survival and function. The VSPD is an important source of organs.

P341

RELAPSE OF MONOCLONAL GLOMERULOPATHY AFTER LIVING RELATED KIDNEY TRANSPLANTATION IN A PATIENT WITH MONOCLONAL GAMMOPATHY OF UNDETERMINED SIGNIFICANCE (MGUS) – A CASE REPORT

*Jolanta Gozdowska**Institute OD Transplantology*

Monoclonal gammopathies are rare cause of end-stage renal disease (ESRD). MGUS is asymptomatic premalignant single-clone plasma cell proliferation, resulting in secretion of excessive homogeneous monoclonal light/heavy or light chains only. Abnormal protein is deposited in all renal structures resulting in their damage. Male aged 57, with ESRD due to MGUS, underwent a pre-emptive living related donor kidney transplantation. Maintenance immunosuppression consisted of tacrolimus, mycophenolate mofetil, and steroids. The first post-transplant 18 months were free of proteinuria, with good kidney function, thereafter the patient started to have proteinuria. Graft biopsy revealed no signs of cellular rejection, a suspicion of transplant glomerulopathy, recurrence of MGUS related glomerulopathy, and IF/TA grade I. On FREELITE test kappa/lambda serum and urine ratio were 3.6 (reference ranges: 0.4–3.1) and 147 (reference ranges: 2–10.4), respectively. Bone marrow biopsy was negative and diagnosis of recurrent monoclonal glomerulopathy was established. In order to treat MGUS and halt progression of glomerulopathy the administration of bortezomib/dexamethasone is now considered.

Conclusions: Definitive treatment of MGUS recurring in kidney graft has not been determined. To account for possible rapid recurrence of gammopathy in transplanted kidney transplantation from deceased donor should be preferred over living donation in ESRD patient due to MGUS.

P342

HYPERHOMOCYSTEINEMIA AND ASSESSMENT OF ITS PREDICTIVE FACTORS IN RENAL TRANSPLANT RECIPIENTS: A SINGLE CENTRE STUDY

*Ali Monfared¹, Seyyede Zeinab Azimi¹, Ehsan Kazemnezhad¹, Masoud Khosravi¹, Mohammadkazem Lebad¹, Ebrahim Mirzajani², Mohammad Kazemnezhad²**¹Urology Research Center, School of Medicine, Guilan University of Medical Sciences; ²School of Medicine, Guilan University of Medical Sciences*

Background: Hyperhomocysteinemia (hyperHcy) is an important risk factor for atherosclerosis, which is currently a major cause of death in renal transplant patients (RTRs). The aim of this study was to determine the predicting factors of hyperHcy in RTRs.

Methods: In 148 stable RTRs, total serum homocysteine (tHcy) level, folate, serum albumin and creatinine, creatinine clearance, lipid status, body mass index (BMI) and blood cyclosporine levels (C0 & C2) were determined. The mean doses of cyclosporine A (mg/kg/day) were recorded.

Results: The mean serum tHcy level was significantly higher in RTRs than in controls (16.26 ± 8.32 vs. 62 ± 4.26 $\mu\text{mol/l}$; $p = 0.0001$), and the prevalence of hyperHcy was 70.3%. Comparison of the group of 44 patients with tHcy level <12 $\mu\text{mol/l}$ and the group of 104 patients with tHcy level >12 $\mu\text{mol/l}$ revealed that those subjects with hyperHcy were mostly younger, male, with lower BMI, history of glomerulonephritis, higher serum level of uric acid and blood cyclosporine trough level (C0) and used higher doses of cyclosporine A. Significant correlation was found between tHcy level and recipients age, serum creatinine, BUN, folate concentrations and creatinine clearance. However, multivariate analysis indicated that serum folate ($p = 0.01$), vitamin B12 ($p = 0.05$), creatinine ($p = 0.03$) and BUN ($p = 0.05$), and blood cyclosporine trough level (C0, $p = 0.005$) were independently associated with tHcy levels.

Conclusion: HyperHcy persists after successful kidney transplantation in the majority of RTRs. Serum creatinine, BUN, folate and vitamin B12, and blood cyclosporine trough level (C0) are independent determinants of tHcy levels.

P343

MALE DONOR INTO FEMALE RECIPIENT INCREASES THE RISK OF KIDNEY GRAFT LOSS ONLY IN YOUNG FOR YOUNG TRANSPLANT

*Marco Quaglia¹, Roberta Fenoglio², Tiziana Cena¹, Andrea Airoldi², Piero Stratta¹**¹Amedeo Avogadro University; ²Maggiore Della Carità University Hospital, Novara*

Background: It is known that the Eichwald-Silmser effect, first demonstrated in female mice rejecting skin graft from male donors of the same strain, depends on the loci controlling weak transplantation antigens on the Y chromosome, responsible for H-Y incompatibility in transplants across a sex difference. This has been shown to have an impact on female recipients of male bone marrow transplant in humans, whereas conflicting results were reported in renal transplant. Aim of this study was to assess the clinical impact of the Eichwald-Silmser effect on a population of renal transplanted patients.

Materials and Methods: We performed a retrospective cohort study (1998–2010) at our Transplant Center. Overall, 289 women (mean age 50 ± 12 years, min 20 max 75) received single allografts from deceased donors (mean age 50 ± 17 years, min 15 max 83), 134 from male donors and 135 from female donors.

Results: Graft loss was more common in female patients receiving kidneys from male donors than in the opposite situation ($p < 0.04$) only in the subgroup of patients receiving donors aged below 50 years, but not in other subgroups with older age. Furthermore, women recipients from donors <50 years had significantly lower age than in other subgroups (42 ± 10 years versus 51 ± 10 years and 60 ± 9 years, $p < 0.001$). Therefore an increased risk of kidney graft loss was only demonstrated in young female recipients being transplanted from young male donors. In this subset of patients graft loss occurred for immunological causes in all cases (chronic and acute rejection).

Conclusions: Our results suggest that a role for H-Y minor histocompatibility in affecting human kidney transplantation has to be looked for in the setting of young-for-young transplant, and this could explain previous conflicting results.

P344

MAIN FACTORS INFLUENCING LONG TERM RENAL FUNCTION AND SURVIVAL OF KIDNEY TRANSPLANT. LATE REJECTION IS STILL AN IMPORTANT NEGATIVE FACTOR DESPITE NEW IMMUNOSUPPRESSANTS. A SINGLE CENTER STUDY

*Florentina Rosique Lopez¹, Luisa Jimeno¹, Matilde Campos², Santiago Llorente¹, Isabel Saura¹, Maria Jose Gonzalez Navarro¹, Mercedes Gil¹**¹Hospital Virgen De La Arrixaca; ²Universidad De Murcia*

Aim: To analyze which factors have a significant influence on long term (10 years) renal function and survival of kidney transplants in our Center.

Methods: All kidney-only recipients from deceased donors, transplanted in our Hospital from 30 July 1985 to 31 December 2005 and, functioning after 6 months, were included. Graft survival and renal function at 120 months were recorded. The following factors were analyzed: donor and receptor demographics, cause of death, early and late rejection (during or after the first year), delayed graft function (DGF), panel reactive antibodies (PRA), HLA compatibilities and cold ischemia time (CIT).

Results: 413 kidney recipients followed for 10 years were studied. The mean survival rate was 95.6% at 60 months and 82.7% at 120 months (60–300 m). Cerebrovascular death, donor age > 60 years, late acute rejection, DGF and immunized receptors had worse survival rate ($p < 0.05$). CIT >12 h. was significant only when the donor was > 60 years. Although renal function was worse from the beginning in patients with these negative factors, it kept steady along the 10 years except in those patients who had a late rejection as can be seen in figure 1 and 2.

Conclusions: 1. Our survival rate was 82% at 120 months. 2. Factors that influence this survival in the long term coincide with most authors. 3. Cold ischemia time < 12 h is especially important when donor age is >60 y. 4. Patients with negative factors and worse renal function from the beginning can have a kidney functioning for more than 10 years. 5. Late rejection was the worst prognostic factor.

P345

EXPANDING THE USE OF EXPANDED CRITERIA DONORS IN KIDNEY TRANSPLANTATION

*Tainá Sandes-Freitas, Marina Cristelli, Luciana Assis-Borba, Marcello Franco, Hélio Tedesco-Silva, José Osmar Medina-Pestana**UNIFESP, Hospital Do Rim E Hipertensão*

Background: Use of grafts from expanded criteria donors (ECD) has increased significantly in recent years. Little data is available to determine if results reported elsewhere are equivalent in other populations.

Methods: Retrospective cohort study analyzed 372 recipients from 272 ECDs, transplanted between 1998 and 2009. All recipients received single kidney transplants. Findings of preimplantation biopsy, done in 233 (62%) of

the kidneys, were reclassified according to a severity-based score. Primary endpoints were recipient and graft survivals at 36 months posttransplant.

Results: ECD had a mean age of 58 years old, 70% hypertensive, stroke being the main cause of death, and the final creatinine 1.7 mg/dl. Of the histological evaluated kidneys, 38% had a final ranking of "moderate changes" and 17% of "severe changes". Recipients had a mean age of 49 years, hypertension (17%) and diabetes mellitus (16%) the main cause of chronic renal failure, mean time on dialysis of 56 months, PRA < 50% in 94%. Mean cold ischemia time was 25 h. Global recipient and graft survival rates at 3 years were 81% and 69%. Improvement of outcome was noted: graft survival at 3 years was 61.4% for transplants between 1998 and 2006, and 70.4% for those between 2007 and 2009 ($p = 0.18$). Graft survival at 3-years was negatively associated to the severity of histological change: 78% for mild changes, 72% for moderate changes and 60% for severe changes ($p = 0.10$). Multivariable analysis, however, found recipient history of Diabetes Mellitus the only independent risk factor for graft loss (OR 2.1, CI 1.3–3.3, $p = 0.003$) and recipient death (OR 3.1, CI 1.6–5.8, $p < 0.001$).

Conclusions: There was a reasonable long-term survival for ECD single kidneys transplants, pointing to improvement over time. Histological analysis was not an independent risk factor for worse outcomes. Diabetic recipient presented the worst outcomes independently, and subsequent studies are needed for this subgroup.

P346

TRANSPLANTED KIDNEY FUNCTION AFTER ENDOVASCULAR ABDOMINAL AORTIC ANEURYSM REPAIR (EVAR)

Lukasz Romanowski, Tadeusz Grochowicki, Jacek Szmidi
Department of General, Vascular and Transplant Surgery, Medical University of Warsaw, Poland

Background: The increasing number of kidney recipients with abdominal aortic aneurysm is endovascularly treated with stent grafts. The aim of the study is to evaluate the impact of EVAR on kidney graft function.

Materials and Methods: Among 12 recipients after EVAR serum creatinine (sCr), glomerular filtration rate (GFR) and development of contrast induced nephropathy (CIN) was assessed. The impact of stent graft main body introduction side on graft function was analysed.

Results: Average serum creatinine levels before and after EVAR were 2.02 ± 0.8 mg/dl and 2.56 ± 1.3 mg/dl (ns) and GRF was 50.3 ± 18 ml/min and 45.6 ± 26.6 (ns), respectively. There was no impact of stent graft main body side introduction on kidney graft function. 50% of recipients met the criteria of CIN. Two patients required temporary hemodialysis and one of them died due to multiorgan failure. None of recipients returned to chronic hemodialysis during 48 \pm 35 months follow-up.

Conclusions: EVAR seems to be the optimal management for kidney transplant recipients and the deterioration of kidney graft function after intervention is transient.

P347

INITIAL EXPERIENCES OF POST TRANSPLANTATION URETERAL STENOSIS OF SINGLE TRANSPLANTATION CENTER

Bulent Unal¹, Turgut Piskin¹, Ruslan Mamedov¹, Idris Sahin², Sezai Yilmaz¹
¹Medical Faculty, Liver Transplantation Institute, Inonu University, Malatya;
²Medical Faculty, Internal Medicine Unit, Inonu University, Malatya

Background: We wanted to evaluate our surgical and non-surgical experiences about ureteral stenosis developed after renal transplantation as a center with initial experiences with renal transplantation in Turkey.

Material and Method: We performed total 76 renal transplantations (with 23 cadaveric and 53 living donor kidney transplantation) between November 2010 and December 2012 at our center. Patients with ureteral stenosis after renal transplantation were evaluated. Result: the ureteral stenosis was observed at three of our patients during post-transplantation period: at 3rd week after cadaveric transplantation (after removal of double J catheter), at 8 months after cadaveric transplantation and at 10 months after living donor kidney transplantation. We primarily applied by nonsurgical procedures (percutaneous nephrostomy, dilatation, percutaneous catheterization). End to side uretero-pelvic anastomosis was performed between transplanted renal pelvis and native ureter at two patients (Figure 1). New ureteroneocystostomy was performed after resection of fibrotic urethral segment at third patient. After reconstruction surgery, renal functions of all patients were normal and there is no problem was observed at their follow up period.

Conclusion: Non surgical interventions might be insufficient in patients with ureteral strictures seen after renal transplantation. In these patients surgical treatments should be applied before deterioration of graft functions. During surgical interventions, one should not insist on single procedures and the interventions with minimum harm to transplanted kidney should be preferred.

P348

STUDY OF EVEROLIMUS ADMINISTRATION IN RENAL TRANSPLANT PATIENTS DURING THE MAINTENANCE PHASE

Yuki Nakamura, Hitoshi Iwamoto, Osamu Konno, Takayoshi Yokoyama, Yu Kihara, Shigeyuki Kawachi, Motohide Shimazu
Tokyo Medical University Hachioji Medical Center

Background: Calcineurin inhibitors (CNIs), which are standard immunosuppressive drugs in kidney transplantation, are a risk factor for cardiovascular disease (CVD), and affect the long-term prognosis. Efforts to establish an immunosuppressive therapy free of renal toxicity has been an enduring theme. [Objective] To study safe and useful methods for administering everolimus (EVL), to renal transplant patients during the maintenance phase, and lowering the dosage of CNIs and other immunosuppressive drugs.

Methods: Immunosuppression was altered by a regimen comprising the addition of 1.5 mg/day EVL, lowering the CNI dosage to 50%, and either discontinuing or lowering the mycophenolate mofetil (MMF) dosage.

Results: There were 13 subjects (five men and eight women; average age 49.1 years) with an average of 5.3 years after transplantation. Eight of the subjects were tacrolimus (TAC) patients, whereas the remaining five were cyclosporine (CYA) patients. Reasons for inclusion were eight cases of CNI dose reduction, two cases of CMV infection, one case of malignant neoplasm, and three cases of CVD. Four of the eight TAC patients (50%) and one of the five CYA patients (20%) required an increased dosage to control the everolimus Cmin. Six patients (46.2%) showed exacerbated proteinuria, and four patients (30.8%) were started on oral administration and received increased dosages. Elevated total cholesterol and neutral lipids were observed in eight patients (61.5%), and two patients (15.3%) were started on oral administration and had increased dosages. Improved renal function was observed in four out of the 13 patients. In seven patients, renal function essentially did not change when the MMF dose or CNI dose was lowered. Rejection was not observed in any of the patients.

Conclusion: Although there were diverse reasons for eligibility, an effect was observed with administration aimed at lowering the CNI dosage, lowering the MMF dosage. Control of side effects is the key to continued administration.

P349

EASY AND FAST TECHNIQUE FOR FASCIA CLOSURE IN RENAL TRANSPLANT RECIPIENT PATIENTS

Taylan Özgür Sezer, Hayrullah Yıldırym, Alper Uđuz, Ömer Vedat Ünalp, Özgür Fýrat, Ýlhami Solak, Murat Sözbilen, Cüneyt Hocokun
Ege University School of Medicine

Background: Even if it seems simple to close the fascia after surgery of renal transplant recipients patients, in case of carelessness post-operative morbidity may increase and quality of life decreases. In this study, we aimed to show details that should be considered in the fascia closure

Methods: From January 2011 to December 2011, a total of 123 kidney transplants were performed in our Kidney Transplant Unit. Two patients developed eventrations in the incision; this represents an incidence of 1.62%. After Gibson incision made in the right or left lower quadrant, retroperitoneum is reached. After creating adequate space for the kidney in the retroperitoneal area, adhesions between the peritoneum and the transverse muscle are divided medially with cautery. This process eliminates hesitation whether suture has passed through peritoneum or not during fascia closure. Starting from distal (pubic region), closure is proceeded proximally. Full-thickened layer transition, comprising the abdominal internal and external oblique muscles, transverse muscle and fascia, is made over three sutures, then closure is continued in the same layer with internal and transverse muscle. Then the external fascia is closed with the same suture material on a second layer.

Results: Two patients developed eventrations in the incision; this represents an incidence of 1.62%. There were 78 living (63.4%) while 45 (36.6%) were cadaveric renal transplantation. All the patients were under triple immunosuppressive therapy with prednisolone, calcineurin inhibitors and antiproliferatif agents. The mean recipient age was 40.5 ± 10 years and mean donor age was 48 ± 14 . Cold ischemia time was 14.8 ± 6 h for deceased kidneys. There were 4 (3.2%) mortalities and 3 (2.4%) graft losses during the first year.

Discussion: Different closure techniques have been reported in renal transplantation. Fascia closure process we have described seems to be shorter and more reliable.

P350

ADRENOCORTICAL CARCINOMA FOLLOWING RENAL TRANSPLANTATION; THE FIRST DOCUMENTED CASE REPORT

Bruna Brunetta Gavranic, Ljubica Bubić Filipi, Darko Kaštelan
UHC Zagreb

The chronic use of immunosuppressive agents to prevent allograft rejection increases the long-term risk of malignancy compared with that of the general population. Adrenocortical carcinomas are rare, aggressive tumors, even at early stage, with incidence of approximately one to two per million population

per year. We present the case of a 33-year-old Caucasian patient with IgA nephropathy that was transplanted a cadaveric kidney eight years ago. Four years later he developed recurrence of IgA nephropathy and acute humoral rejection. During hospitalization a mass lesion of 5 cm was incidentally discovered in a right suprarenal gland. The mass was taken out surgically and pathohistology revealed adrenocortical carcinoma. Therapy with mitotane was tried but quickly withdrawn due to serious side effects. Eight months later patient developed another humoral and cellular rejection. Our decision was not to intensify immunosuppression because of already gravely damaged kidney and prior adrenocortical carcinoma, therefore patient started hemodialysis. A fluorodeoxyglucose-PET/CT scan was performed every 6 months and as the patient is now disease free for four years we decided to put him again on a kidney transplant waiting list. Despite poor prognosis that was attributed in the past to patients with adrenocortical carcinoma, contemporary series suggest that these patients are living longer; especially patients who present with early stage and have complete primary resection. To best of our knowledge, this is first case of a transplanted patient developing an adrenocortical carcinoma reported in the literature.

P351

GADOLINIUM-FREE MAGNETIC RESONANCE IMAGING IN THE DIAGNOSIS OF URETERAL STENOSIS OF RENAL TRANSPLANT RECIPIENTS

Elisa Lazzarich¹, Alessandro Stecco², Alessandro Volpe³, Roberta Fenoglio¹, Cristina Izzo¹, Claudio Musetti¹, Elisabetta Radin¹, Piero Stratta¹, Carlo Terrone⁴, Alessandro Carriero²

¹Department of Translational Medicine, University; ²Imaging Department; ³Surgery Department; ⁴Surgical Department

Introduction: Reteral obstructive disease is a frequent complication of renal transplantation and its diagnosis relies on Ultrasound (US), Computed Tomography (CT) or Magnetic Resonance (MRI). However TC and MRI require the use of iodinated contrast agents or gadolinium, which may be toxic for patients with renal disease. Aim of the study was to evaluate the usefulness of MRI without contrast agent (UroMRI) in the diagnosis of ureteral obstructive disease in kidney transplant recipients (KTRs).

Materials and Methods: From September 2011 to November 2012, KTRs with a suspected obstructive ureteral disease (worsening renal function and hydronephrosis), underwent a MRI without any contrast agent, with evaluation of T2-weighted sequences and signal suppression of adipose tissue and images were used to plan the surgical or endoscopic therapy.

Results: Out of 14 enrolled patients, 11 (78.6%) had an ureteral stenosis arising within 3 months from surgery, while the other 3 (21.4%) more than 3 months after. In all the cases, Uro-MRI confirmed the ureteral stenosis: 11 were intrinsic ureteral stenosis (2 proximal, 1 medium, 5 distal and 2 multiple) and three were due to external compression of the urether (2 proximal and 1 distal). On uro-MRI images indication 13/14 (92.9%) patients underwent surgical or endoscopic correction of the stenosis (7 endourethral stenting (54.8%), 4 pyelostomy (30.8%), two lymphocele drainage (15.4%). The other patient was not treated because he had only a mild obstruction and a small rise of creatinine (1.5 mg/dl). In 10/13 of the treated cases hydronephrosis resolved together with a reduction of serum creatinine from 3.87 ± 0.98 to 2.04 ± 0.37 mg/dl.

Conclusion: Uro-MR has a leading role in the study of KTRs: it is able to give good information on the location and nature of ureteral obstructions and may help a correct surgical planning. Moreover this method is well tolerated, not invasive and not nephrotoxic for KTRs with acute kidney injury.

P352

SURVEY OF CHRONIC PAIN FOLLOWING LAPAROSCOPIC-ASSISTED DONOR NEPHRECTOMY

Emma Griffin, George Tse, Marc Clancy, Mick Serpell
Renal Transplant Unit, Western Infirmary, Glasgow

Introduction: Several trials have shown superiority of laparoscopic nephrectomy when compared to open donor nephrectomy in terms of acute post-operative pain, hospital stay, patient satisfaction, cost-benefit ratio and early return to work. Previous investigations have quantified the incidence of chronic pain following open donor nephrectomy. We wished to ascertain if laparoscopic surgery conveys an advantage on chronic post-operative pain in donor nephrectomy.

Methods: Patients that were at least 6 months post surgery who underwent laparoscopic donor nephrectomy from 2008 to 2011 were surveyed. Anonymous, validated pain assessment questionnaires (sf-BPI, EQ-5D and s-LANSS) were sent out asking patients whether they'd experienced any chronic pain following their operation, these were used to quantify pain severity, type of pain and how it was managed.

Results: A total of 49 patients were identified as having undergone laparoscopic nephrectomy. Thirty-two of these responded but only 29 met the criteria to be entered in to our study. 16.7% reported to having chronic pain following the procedure with 7.9% of the group stating that they had pain affecting daily living. Of these only 3.7% of patients were classified as having neuropathic pain. When compared to previous open-nephrectomy studies no patients in our cohort reported having extreme pain. The incidence of chronic pain following open donor nephrectomy was found to be 26% and there was no significant

difference compared to laparoscopic-assisted surgery (Fishers exact test $p = 0.3654$).

Conclusion: We have previously found the incidence of chronic pain after open nephrectomy was higher than often quoted, though pain can be influenced by bio-socio-economic factors. We have studied the same socio-demographic population and found laparoscopic-assisted kidney donation to be associated with lower incidence of chronic pain markers following open nephrectomy however this did not reach statistical significance.

P354

NON INVASIVE EVALUATION OF RENAL ALLOGRAFT HYDRONEPHROSIS

Tarek Fathi, M Samhan, N Ahmad
Hamed Alessa Organ Transplantation Centre

Introduction: Renal allograft dysfunction with hydronephrosis is a clinical situation that requires exploring the possibility of surgically correctable underlying cause. This study aims to evaluate the significance of output efficiency (O/E) as a diagnostic tool.

Patients & Methods: ultrasound scanning and diuresis renogram, including calculated O/E were performed in recipients with impaired renal function. Results were compared with the base line findings. In suspected cases of ureteric obstruction, percutaneous (p/c) nephrostomy and nephrostography were done, and management was according to findings.

Results: In 16 recipients who developed graft dysfunction with hydronephrotic changes, diuresis renogram was done. [A] In 11 cases O/E dropped from >85% to <79%. Antegrade nephrostogram findings were suggestive of obstruction in nine cases. Recipients were managed by stenting (5 cases), ureteric surgical reimplantation (4 cases), lymphocele drainage (1 case) and lithotripsy (1 case). All 11 cases (100%) showed improved O/E and kidney function. [5] In five cases there was no change in O/E, but antegrade nephrostogram was suggestive of ureteric obstruction, they were treated by ureteric stenting, with no improvement in O/E. But two of recipients (40%) showed improved renal function. Discussion: Renal allograft ureteric stricture is a rare but serious complication, if not treated properly it may lead to graft loss. O/E was introduced recently as a non invasive diagnostic tool. In the present study it was observed that correction of ureteric obstruction was associated with improved O/E and kidney function in all recipients with positive O/E findings and in 40% of patients with negative O/E findings.

Conclusion: Diuresis renogram with O/E measurement is a simple, non invasive and safe procedure. While positive O/E test is a reliable indication of ureteric obstruction, negative O/E test does not rule out uretic obstruction and has to be correlated with other diagnostic methods.

P355

CHARACTERISTICS AND EVOLUTION OF NON SKIN TUMORS IN RENAL TRANSPLANT RECIPIENTS AT SALAMANCA UNIVERSITY HOSPITAL (SUH), SPAIN

Josepa Sebastiá Morant¹, Roberto D. Tabernerico², Marc H. Blanc¹, Pilar Fraile Gómez¹, Guadalupe Tabernerico Fernández¹, Pedro García Cosmes¹, José M. Tabernerico Romo¹

¹Hospital Clínico Universitario de Salamanca; ²Hospital Virgen de la Concha de Zamora

Background: It is known that in transplanted recipients, as a result of immunosuppression, we find a high incidence of cancer, being this more aggressive than in the general population.

Aims: To define the characteristics of kidney transplant recipients who develop a non skin cancer along their post-transplant control at SUH. – To identify the most common non skin cancers between kidney transplant recipients and their behavior.

Material and Methods: Once reviewed the Nephrology's date base, we selected those patients who had had non skin cancer along their post-transplant control (37 patients) from 1983 to 2012, both included. Four patients who did not have a periodic control at SUH and one patient with a pathology of adenoma were excluded from the survey. Later, the clinical histories of these patients were reviewed. Data analysis was done with SPSS (v15.0). Quantitative data with normal distribution are expressed as mean ± SD.

Results: Cancer was observed in 32 transplanted and controlled patients at SUH. 50% were males, 75% suffered from Hypertension (HTA), 9.37% from Diabetes Mellitus and 15.63% from dyslipidemia. The most important cause of End stage renal disease in these patients was nephrosclerosis. The neoplasias seen in our patients are reflected in graphic 1. Most of the tumors were local or with lymphadenopathy extension. The mean age at kidney transplantation was of 54.38 ± 11.43 years. The mean age at cancer diagnostic was of 59.5 ± 9.06 years. Then, the mean time between transplantation and cancer diagnostic was of 5.57 ± 4.68 years. The mean age of death was of 62.29 ± 9.16 years. Eight patients were still alive at the moment of the study.

Conclusions: We found 32 renal transplant recipients with cancer at our hospital. Most of them had HTA. 50% were male. The most common tumor was lung cancer. The mean age of cancer diagnostic was of 60 years and the mean age of death 62.3 years, and just eight patients are still alive.

P356

TACROLIMUS BRAND AND GENERIC DRUG: COMPARISON IN DE NOVO KIDNEY TRANSPLANT (KT) IN A MONOCENTRIC ANALYSIS

Maria Messina, Elisa Basso, Claudia Ariaudo, Ester Gallo, Ana Maria Manzione, Fabrizio Fop, Francesca Simonato, Luigi Biancone, Giuseppe Paolo Segoloni
Nephrology, Dialysis and Transplantation Center, Molinette Hospital and University of Turin- Italy

Background: Generic tacrolimus [with Prograf®-Astellas (P) as the brand drug], seems to of provide reduction with comparable efficacy, as reported in literature. We present results with generic tacrolimus formulation [Tacni®-Teva (T)] in KT in our Center.

Material and Methods: We compared 33 patients de novo treated with T and 67 P treated in case-control study, evaluating donors/recipients/KT characteristics, adverse events (AE), tacrolimus blood levels (TBL – HPLC assay) and doses in short (during hospitalization) and medium (at least 3 months) follow-up.

Results: Donor age was greater in T patients (T 64 years–P 56 years; $p = 0.003$). Comparable parameters are: percentage target TBL, time to reach target levels in short-term follow-up, percentage acute rejections and percentage drop-out in medium-term follow-up. For a target TBL 12–15 ng/ml in the first month and for the daily same dose, we found initially in T lower TBL (T 12 ng/ml–P 13.2, $p < 0.001$). After 3 months no difference for doses or TBL were reported.

Conclusion: In our experience T and P, as in most literature results, show similar safety and efficacy. Starting with the same dose, T TBL are lower only initially, without an increase of AE.

P357

LATE-ONSET NEUTROPENIA IN ABO-INCOMPATIBLE RENAL TRANSPLANT RECIPIENTS RECEIVING RITUXIMAB

Kazuya Kabei, Junji Uchida, Yuichi Machida, Tomoaki Iwai, Nobuyuki Kuwabara, Toshihide Naganuma, Norihiko Kumada, Tatsuya Nakatani
Osaka City University Graduate School of Medicine

Background: Due to the severe shortage of deceased donors in Japan, ABO-incompatible kidney transplantation has been performed since the late 1980's. Recently, it is demonstrated the new avenue in the management of ABO-incompatible kidney transplantation by introducing an anti-CD20 monoclonal antibody, rituximab. Using rituximab, we have reported successful ABO-incompatible renal transplantations without splenectomy as well as with high anti-A/B antibody titer in pre-transplant status. However, occasional episodes of late-onset neutropenia (LON) also have been reported during the administration of rituximab.

Methods: Twenty-five patients underwent ABO-incompatible kidney transplantation with rituximab induction at Osaka City University Hospital. In our institution, rituximab (150 mg/m²) was administered twice at 2 weeks prior to and on the day of transplantation except for elderly recipients. The recipients aged 65 years and older received consisting of only a single dose of rituximab 150 mg/m² at 2 weeks prior to the transplantation. The patients with high anti-A/B antibody titers ($\geq 1:512$) received splenectomy and administration of two doses of rituximab.

Results: Fourteen patients received two doses of rituximab administration and three elderly patients received single dose of rituximab without splenectomy. Eight with high titer received both two doses of rituximab and splenectomy. Twelve recipients experienced LON 3–12 months after transplantation. The primary causes of neutropenia, such as viral and/or bacterial infection did not occur. Other drugs which could induce myelosuppression were not given to these patients. After administration of granulocyte colony stimulating factor, neutropenia improved.

Conclusion: In our study, 48% of the recipients using rituximab experienced LON. Our desensitization protocol may induce over-immunosuppression. The effort to estimate the lowest effective dose of rituximab for transplant recipients is necessary.

P358

THE USE OF INTRAOPERATIVE URETERIC DOUBLE J STENT FOR PREVENTION OF UROLOGICAL COMPLICATIONS IN KIDNEY TRANSPLANT RECIPIENTS

Nam Kyu Choi
Department of Surgery, Division of Hepatobiliary Surgery and Transplantation, Chosun University Hosp

Objective: To evaluate the impact of the use of the double J stent in kidney transplant recipients with or without ureteric double J stent. To examine the benefits and harms of routine ureteric double J stenting to prevent urological complications in kidney transplant recipients.

Materials and Methods: Between March 2011 and February 2012, 30 adult recipients underwent renal transplant at a single center and one surgeon. A

retrospective study was conducted on two groups of patients: Group A undergo Double-J stent and group B no-stent ureterovesical anastomosis. We reviewed the urological complications: fistula, ureteral obstruction, urinary leakage and urinary tract infection. The patients were scheduled for stent removal after 2 weeks.

Results: A total of 30 patients were randomized to a stent (15) and a no-stent (15) group. Group A: No ureteral obstruction and urinary leakage were developed in this group. Three patients (20%) had a positive urinary culture. Group B: Two patients (13%) developed ureteral obstruction and another four (26.7%) developed urinary leakage. Four patients (26.7%) had a positive urinary culture.

Conclusion: The routine insertion of a double J stent in kidney transplants reduces the number of early complications urinary fistula and ureteral obstructions. Using a ureteral stent at renal transplantation significantly decreases the early urinary complications of urine leakage and obstruction. However, stent removal within 4 weeks of insertion appears advisable.

P359

URINARY UROMODULIN AS A MARKER OF PHOSPHATE INDUCED RENAL ALLOGRAFT INJURY

Carlos Franco Palacios, John C. Lieske, Andrew D. Rule, Nick Voskoboiev, Fernando G. Cosio, Hatem Amer
Mayo Clinic

Background: Recently, pre transplant phosphorus was shown to be associated with increased risk of renal allograft loss and patient death. Finding markers of renal allograft injury that relate to pre transplant phosphorus could provide a means of assessing therapeutic interventions aimed at mitigating this risk.

Methods: We studied the relationship between pre transplant phosphorus; one-year renal allograft histology and six urinary proteins (Total protein, Albumin, uromodulin, NGAL, Retinol Binding Protein (RBP), and alpha one microglobulin) in 207 renal allograft recipients. Patients receiving sirolimus were excluded.

Results: Mean recipient age 52 (± 13) years; 110 (55%) males; 189 (94%) Caucasian; 170 (85%) living Donor. Follow-up was 67 (± 14 , 19–86) months. Pre-transplant phosphorus was 5.4 (± 1.4 , 2.8–11.4) mg/dl. During follow-up 28 grafts were lost (ACGL), 16 not due to patient death (DCGL) beyond one year. Pre-transplant phosphorus was associated with ACGL (HR 1.3, $p = 0.018$) and DCGL (1.5, $p = 0.001$). There was no association between pre-transplant phosphorus and one year graft interstitial fibrosis. Of the urinary markers studied at one-year post transplant, only uromodulin was associated with pre-transplant phosphorus $r = -0.17$, $p = 0.046$ (Spearman's ρ).

Conclusions: Pre-transplant phosphorus has a negative impact on ACGL and DCGL beyond one-year from transplant. We speculate that patients with severe hyperphosphatemia pre-transplant may have high urinary phosphorus excretion post-transplant that may cause distal tubular injury, as suggested by reduced uromodulin production. Urinary uromodulin levels may reflect ongoing distal tubular injury.

P360

CORRELATIONS BETWEEN ARGININE VASOPRESSIN AND AQUAPORIN-2 IN EARLY POSTOPERATIVE KIDNEY TRANSPLANTATION PATIENTS

Yang Wook Kim¹, Bongsoo Park¹, Kyubok Jin², Seok Ju Park³
¹Haeundae Paik hospital Inje medical school, ²Haeundae Paik Hospital1, Inje medical college, ³Busan Paik Hospital, Inje medical college

Background: Aquaporins (AQP) are proteins that are responsible for the water permeability in cell membrane. Especially, AQP2 which mainly distributed in renal principle cells is related to water reabsorption in collecting duct under the control of arginine vasopressin (AVP). AVP level abnormally increases in chronic kidney disease (CKD) patients, but its mechanism has not been clear and studies on kidney transplant patients have rarely been reported. This report allows us to assess the changes in AVP and urine AQP2 (uAQP2) expression in kidney transplant patients.

Method and Material: We enrolled 14 kidney transplant patients prospectively. We measured the serum AVP, serum osmolality, urine osmolality and urine AQP2 expression by western blot method before and until serum creatinine is normalized after transplantation.

Result: The average age of the overall patients was 43.1 \pm 13.7 years (range: 22–62 years) and the male to female ratio of the patients was 2.5:1. The frequency of patients with diabetes was 14.3%. Dialysis duration of pre-transplant period was 78.2 \pm 63.3 months (range: 2–180 months). Pre-transplant AVP was elevated (21.42 \pm 5.03 pg/ml), and the level was normalized (3.76 \pm 0.6 pg/ml) relatively to sCr level after the transplantation. Contrary to the expectations, however, the pre-transplant uAQP2 expression was 5.63 and post transplant uAQP2 expression was elevated to 15.73. Post-transplant uAQP2 expression was significantly higher than pre-transplantation ($p = 0.021$). However, uAQP2 did not significantly correlated with plasma AVP, serum creatinine, serum sodium, serum potassium, FENa, serum and urine osmolality including urine volume.

Conclusion: The urine concentration ability and serum AVP level were normalized after kidney transplantation. However, the uAQP2 expression did not correlated with the serum AVP level. These results may be related with dysregulation of AQP2 receptor in early kidney transplantation period.

P361

PROTEINURIA AND HISTOPATHOLOGICAL CHANGE OF EVEROLIMUS BASED IMMUNOSUPPRESSION ON DE NOVO KIDNEY TRANSPLANTATION WITH 4 YEARS FOLLOW-UP IN ALLOGRAFT BIOPSIES

Asami Takeda, Yoshihiko Watarai, Shunji Narumi, Takayuki Yamamoto, Makoto Tsujita, Takahisa Hitamitsu, Norihiko Goto, Keiji Horike, Kunio Morozumi

Japanese Red Cross Nagoya Daini Hospital

Purpose: The impact of everolimus (EVR) based immunosuppression in de novo kidney transplantation was evaluated in safety profile, focusing proteinuria and histopathological change through the allograft biopsy findings.

Methods: During 2008 and 2009, twenty-six living donor kidney transplant patients were enrolled to compare the safety and efficacy between EVR based and mycophenolate mofetile (MMF) based immunosuppression. EVR group received reduced-exposure cyclosporine (CsA; target C0 25-50 ng/ml after 6 months) + steroid, and EVR-C0 were adjusted 3-12 ng/ml. MMF group received standard-exposure cyclosporine (CsA; target C0 100-250 ng/ml after 6 months) + steroid. Both group received basiliximab induction. Allograft biopsies were performed as protocol at 1 h, 3 weeks, 6 and 12 months after kidney transplantation and episode biopsies.

Results: With a mean observation period of 49 (49-57) months, current patient and graft survival is 100% in both groups (EVR; $n = 13$, MMF; $n = 13$). Renal function expressed as eGFR was similar 41.6, 14.3 in EVR group and 37.2, 7.0 in MMF group. None of EVR and MMF group was treated for clinical T cell mediated rejection, similar incidence of Banff borderline change on 6 or 12 months protocol biopsies were observed in 7.7% of EVR group and 15.4% of MMF group, but none of both groups revealed peritubular capillaritis. Proteinuria, more than 300 mg/day, were observed more in EVR group (69%) than in MMF group (27%) respectively. There were two patients whose proteinuria developed over 2 g/day at 12 months or later in EVR group. We could not find any particular glomerular lesion in the graft biopsies, however neovascular hyalinosis at glomerular vascular pole was noticeable. The significant proteinuria in EVR group was successfully treated with angiotensin-II receptor blockade.

Conclusions: EVR based immunosuppression does not provide particular histological change of glomeruli though significant proteinuria was frequently observed.

P362

INTRACELLULAR ATP SYNTHESIS ASSAY AS A USEFUL TOOL TO PREDICT EARLY ACUTE REJECTION AND GRAFT OUTCOME IN KIDNEY TRANSPLANTATION

Andrea Ranghino¹, Cristiana Caors², Antonio Lavacca³, Alberto Giordano⁴, Franco Novelli⁵, Giuseppe Paolo Segoloni⁵, Stefano Roggero⁶, Luigi Biancone³

¹Nephrology, Dialysis and Transplantation Center, Molinette Hospital and Dep. of Medical Sciences Un; ²Medicine and Experimental Oncology, University of Turin, Italy; ³Nephrology, Dialysis and Transplantation Center, Molinette Hospital and University of Turin, Italy; ⁴Medicine and Experimental Oncology, University of Turin, Italy; ⁵Department of Molecular Biotechnology and Health Science, University of Turin, Italy; ⁶Genetics, Biology, and Biochemistry, University of Turin, Italy

Background: Post-transplant immunosuppressive drugs monitoring cannot predict the effect on immune cells. Thus, different biomarkers are been investigated to identify patients at risk for acute rejection (AR). The aim of our study was to evaluate whether immune parameters were associated with early AR and poor outcome.

Material and Methods: Immune parameters, including HLA-specific antibodies, circulating Tregs, Th17 and T-cell reactivity tests including intracellular ATP synthesis assay (ImmunoKnow, IK) and IFN- γ ELISPOT were determined for 27 kidney recipients prior to transplantation and at day 4, 15, 30, 90, 180 360 after.

Results: 3/27 developed AR (2/3 within 2 weeks). Mean IK value at day 4 in pts with AR was 726; Δ 152 vs. 449.6; Δ 131.4 ng/ml in pts without AR, $p < 0.011$. Specifically, IK value > 600 ng/ml at day 4 has sensitivity of 100% and specificity of 87.5% in predicting AR (AUC 0.96 in the ROC curve, $p = 0.007$). Patients with better outcome at 1 year (GFR; \bar{Y} 40 ml/min) had a mean basal IK lower than pts with GFR < 40 ml/min (434.9; Δ 184.4 vs 583.8; Δ 137.9 ng/ml, $p < 0.002$).

Conclusion: Our results indicate that IK is useful to predict AR in the early post-transplant time and the recipients outcome at 1 year.

P363

ANGIOTENSINOGEN POLYMORPHISMS AND POST-TRANSPLANTATION DIABETES MELLITUS IN KOREAN RENAL TRANSPLANT SUBJECTS

Joo Hee Cho¹, Hwa young Seok¹, Ji Yun Park¹, Seulki Kim¹, Sul ra Lee¹, Joo Young Moon¹, Sang Ho Lee¹, Chun Gyoo Ihm¹, Tae Won Lee¹, Joo-Ho Chung², Sun Woo Kang³, Yeong Hoon Kim³, Kyung Hwan Jeong¹

¹Division of Nephrology, School of Medicine, Kyung Hee University, Seoul, Korea; ²Kohwang Medical Research Institute, School of Medicine, Kyung Hee University, Seoul, Korea; ³Division of Nephrology, School of Medicine, Inje University, Busan, Korea

Background: Post-transplant diabetes mellitus (PTDM) is a common and serious metabolic complication. Genetic polymorphisms of angiotensin-converting enzyme (ACE) and angiotensinogen (AGT) genes have been reported to be related to diabetes mellitus and insulin sensitivity; however, the role of these genes in the development of PTDM is not known. For this purpose, we investigated the association of ACE and AGT genetic polymorphisms with PTDM.

Methods: A total of 302 subjects without previously diagnosed diabetes who had received kidney transplants were included. One ACE single nucleotide polymorphism (SNP; rs4291) and two AGT SNPs (rs 699 and rs 4762) were genotyped from genomic DNA with direct sequencing.

Results: PTDM developed in 49 (16.2%) of 302 subjects. Subjects in the PTDM were older than those in the non-PTDM. There was a significant difference between the two groups in tacrolimus use ($p = 0.03$). Of the three SNPs, the rs4762 of the AGT gene was significantly associated with the development of PTDM in the dominant models ($p = 0.03$) after adjusting for age and tacrolimus usage. The function and protein structure of AGT was significantly affected by the Thr207Met missense SNP (rs4762).

Conclusions: AGT gene rs4762 polymorphisms may serve as genetic markers for the development of PTDM. Additional genetic studies are needed to provide an understanding of the precise mechanisms underlying the pathogenesis of PTDM in kidney transplantation patients.

P364

DE NOVO THROMBOTIC MICROANGIOPATHY IN RENAL ALLOGRAFT RECIPIENTS: ROLE OF MTOR INHIBITORS

Fabio Nava, Giacomo Mori, Antonio Ciaravello, Giacomo Magnoni, Francesca Facchini, Marco Leonelli, Gianni Cappelli, Decenzio Bonucchi
AOU Policlinico di Modena

Background: Thrombotic Microangiopathy (TMA) is characterized by endothelial cells injury and formation of fibrin thrombi within capillary-arterioles. TMA mainly presents in renal allograft recipients as Hemolytic Uremic Syndrome (HUS), a rare and life-threatening condition, which requires early diagnosis and treatment. Drug toxicity, in particular from Calcineurin Inhibitors (CNIs) and mTORi, is TMA's most common cause after transplantation. The aim of the study was to investigate the role of mTORi as an added risk factor in the development of TMA, in order to develop strategies for modulation of the immunosuppressive therapy.

Materials and Methods: From a database of 496 renal graft recipients we analyzed 350 renal graft biopsies performed at our Center from 1998 to 2012. Histological features of TMA were found in 36 patients (prevalence of 7.3%). We divided the cases in two groups: not drug-related TMA (n 19) and drug-related TMA (n 17). In patients exposed to mTORi (alone or combined to CNIs) we measured mean immunosuppressants levels comparing TMA and TMA free groups

Results: The prevalence of TMA in patients exposed to mTORi in our study was greater (5.3%) than exposed to other therapy (2.8%), but not statistically significant. However drugs blood levels resulted significantly higher in patients with TMA

Discussion: The frequent lack of TMA systemic signs underscores the importance of graft biopsy in the differential diagnosis between TMA, rejection and viral infection. Our results confirm the pivotal role of immunosuppressive drugs in the onset of de novo TMA. Endothelial damage by CNI, followed by Everolimus induced delayed repair of endothelial injury, seem to predispose patients to post-transplantation HUS, with higher drugs levels relating to higher risk of TMA. Thus combined monitoring of these drugs may be used to prevent TMA. Our results suggest to keep blood levels of Everolimus TLC + (Cyclosporine 2nd hour/100) under a cut off of 11 ± 2 ng/ml.

P365

CORRELATION OF PLATELET FUNCTION ANALYZER AND BLEEDING TIME IN PREDICTION OF BLEEDING EVENTS AFTER PERCUTANEOUS RENAL BIOPSY IN KIDNEY TRANSPLANTATION

Andrea Ranghino, Alberto Mella, Ana Maria Manzione, Angelo Nappo, Ester Gallo, Gloria Giovinnazzo, Elisabetta Mezza, Caterina Dolla, Giuseppe Paolo Segoloni, Luigi Biancone

Nephrology, Dialysis and Transplantation Center, Molinette Hospital and Department Medical Sciences, Uni

Background: Kidney biopsy (KB) is the gold standard for diagnostic information after kidney transplantation. Nevertheless, KB is associated with risk of bleeding complications (BCs). Bleeding time (BT) is an established predictor of BCs. The aim of our prospective study was to evaluate the association of platelet function analyzer (PFA-100) with BT in predicting the risk of BCs.

Material and Methods: One hundred and nineteen transplanted patients undergoing KB were screened for PFA-100, BT, PT/PTT, Hb, PLT count, GFR and blood pressure. Our protocol is designed to perform KB with a BT \leq 8 min regardless of PFA-100 values, with BT $>$ 8 min in presence of normal PFA-100, with BT $>$ 8 min and abnormal PFA-100 desmopressin is administered prior KB.

Results: PFA-100 was abnormal in 56/119 pts. BT $>$ 8 min in 9/119 pts with 1 having abnormal PFA-100. 9/119 pts developed BCs. 2/9 pts with BCs displayed BT \leq 8 min and abnormal PFA-100. 1/9 with BCs had BT $>$ 8 min and normal PFA-100. No correlation between PFA-100 and BT was observed. No significant differences in any clinical and hematological parameters and in the number of biopsy passes were observed regardless of BCs.

Conclusion: PFA-100 does not provide any additional value to BT in predicting BCs in kidney recipients undergoing KB.

P366

CONCURRENT UNILATERAL OR BILATERAL NATIVE NEPHRECTOMY IN KIDNEY TRANSPLANT RECIPIENTS

Ayhan Dinckan, Huseyin Kocak, Ayhan Mesci, Ibrahim Aliosmanoglu, Selcuk Yucel, Filiz Gunseren, Ahmet Tekin, Serdar Turkyilmaz, Necmiye Hadimioglu, Erhan Ari, Zeki Ertug

Akdeniz University Organ Transplantation Institute

When native nephrectomy is scheduled in potential kidney recipients, it is still not clear whether the operation should be performed before, after or during the transplantation the aim of the study is to evaluate the results of the patients who have undergone kidney transplantation concurrent with bilateral or unilateral native nephrectomy. The data of 1980 patients with end-stage renal disease who had undergone renal transplantation between June 2000 and December 2009 in the Organ Transplantation Institute at Akdeniz University were evaluated. We evaluated the outcome of kidney transplant patients who have undergone native nephrectomy unilaterally ($n = 38$) and bilaterally (125). Graft survivals at 1st, 3rd and 5th years were 93%, 90% and 89%, patient survival in the 1st, 3rd and 5th years were 97%, 94% and 94%, respectively. Surgical complications were significantly more frequent in nephrectomy patients due to higher complication rate in the polycystic kidney disease subgroup of nephrectomized patients. Despite additional surgery, the long term results of patients with complications were not affected negatively due to the early diagnosis and treatment. We believe that, native nephrectomy concurrent with transplantation can be performed when indicated in selected patients at experienced centers with large patient volume and with well-complication management.

P367

KIDNEY TRANSPLANTATION FROM NON-HEAT BEATING DONORS: IMPACT OF DELAYED GRAFT FUNCTION

Claire Billault¹, Rodolphe Thuret², Emmanuelvan Glabeke³, Karim Fehri⁴, Stephane Bart⁵, Frédéric Thibaut⁶, Nadia Arzouk⁶, Victor Gueutin⁶, Jérôme Turrel⁶, Saida Ourahma⁶, Armelle Nicolas-Robin⁶, Benoit Barrou⁶

¹Hôpital de la Pitié Salpêtrière; ²Hôpital Lapeyronie, Montpellier, France; ³CH André Grégoire, Montreuil; ⁴Ch Robert Ballanger, Aulnay sous Bois; ⁵CH René Dubos, Pontoise; ⁶Service d'Urologie et Transplantation Rénale, Hôpital de la Pitié Salpêtrière

Introduction: Transplantation of kidneys from uncontrolled non-heart beating donors (NHBD) in France was first started in 2006. Several questions arose: how to minimize the primary non-function (PNF) rate, what would be the delayed graft function (DGF) rate, how well would these kidneys perform, what would be their long-term survival. DGF is especially common in NHBD transplantation, and is known in HBD transplantation to have a negative impact on long-term graft survival. We analysed whether the same impact existed on NHBD grafts.

Material and Methods: Between 2008 and 2011, 205 transplantations from uncontrolled heart-beating deceased donors (HBD) and 53 NHBD trans-

plantations were performed at our institution. Criteria for NHBD selection were established by the Agence de la Biomédecine. We used normothermic recirculation (NRC) over double-lumen catheter (DLC) perfusion prior to procurement whenever possible. Kidneys were preserved using the Life-port[®] perfusion machine and transplanted within the shortest possible timeframe.

Results: NRC was used in 33 and DLC in 20 cases. We did not observe any case of PNF. DGF occurred in 63.5% of all NHBD transplantations, and 21% on HBD transplantations ($p < 0.0001$). There was no difference in the number of dialysis treatments in case of DGF (4.7 ± 2.4 in NHBD, 3.7 ± 3.6 in HBD, $p = 0.14$). Graft survival Kaplan-Meier analysis showed a negative effect of DGF in HBD transplantations ($p = 0.03$), however there was no negative impact on graft survival analysis in the NHBD group ($p = 0.67$). Graft survival was identical when comparing NHBD grafts and standard-criteria HBD grafts, however NHBD graft survival was significantly better than extended-criteria HBD graft survival

Conclusion: Our results indicate that NHBD grafts can be utilised with comparable results to those of HBD-SC grafts, and better results than HBD-EC grafts. Whereas DGF is a known negative factor in HBD transplantation, its impact in NHBD transplantation is negligible.

P368

THE TRANSITION OF YOUNG ADULT RENAL TRANSPLANT RECIPIENTS INTO ADULT CARE: A WEST OF SCOTLAND PERSPECTIVE

Sonul Gajree¹, Marc Clancy²

¹University of Glasgow; ²Renal Transplant Unit, Western Infirmary Glasgow

Background: The transition between paediatric and adult care is a crucial time in the management of young adults with ESRD. As many as 35% of adolescent transplant recipients suffer graft loss within 3 years of transfer to adult care, which increases the strain on an already resource limited transplantation service as well as causing significant morbidity. In this retrospective study we investigated the outcomes of transition patients in the west of Scotland, and explored the reasons behind the high rates of graft failure.

Methods: Data was retrospectively analysed from patients aged under 25 who underwent renal transplantation at either a dedicated paediatric unit or at an adult unit in the west of Scotland between 2001 and 2010. Graft failure rates at one year and five years were compared with the corresponding adult population, between patients who transitioned to adult care before and after transplantation, and between previously reported rates.

Results: An overall graft failure rate of 8% after one year and of 21% after 5 years ($n = 90$) was seen in patients transplanted aged under 25, which is lower than that reported in the current literature for this age range. No significant difference in failure rates was seen between those who transitioned to adult care before or after transplantation, however, the failure rate in young adults (16-25) was double that of children aged 15 and under, at 22% compared with 11% ($p < 0.05$)

Conclusion: Transition to adult care generally takes place during the 16-25 years age group and the higher rate of failure seen in this group is likely a result of patient non-adherence during this challenging period. It has been shown elsewhere that a fully integrated transition service can significantly improve compliance rates and reduce these high rates of graft loss in young adults. Improving this transition period nationwide is key to increasing the rates of long-term graft survival and lowering morbidity in young adult transplant recipients.

P369

INCIDENCE OF URINARY TRACT INFECTION, HYDRONEPHROSIS IN THE FIRST YEAR POST-KIDNEY TRANSPLANTATION AND THEIR EFFECT ON GLOMERULAR FILTRATION RATE AT ONE YEAR POST-KIDNEY TRANSPLANTATION IN CHILDREN

Hamad Al Mojalli, Ashraf Al Muzain, Abbas Al Abbad

King Faisal Specialist Hospital & Research Centre

Renal transplantation is widely recognized as the treatment of choice for children with ESRD. The life expectancy benefit of renal transplant over chronic dialysis for these children may be as much as 25-30 years. Renal transplant has its own complications that can affect graft function and survival. Infections are of the most common of these complications, as these patients have multiple risk factors including immunosuppressive medications and structural anatomical urological abnormalities in some patients. UTI is the most common bacterial infection in kidney transplant recipients both in adults and children $>$ 5 years. The aim of this study to determine the incidence of Urinary Tract Infection, hydronephrosis and their effect on Glomerular Filtration Rate at one year post-kidney transplantation in children. To check the incidence of hydronephrosis detected by ultrasound done during the first year post kidney transplant and its effect on GFR.

Method: This is a retrospective study, included charts review of all pediatric kidney transplant patients transplanted at KFSH&RC in the period from September 2009 to September 2011 and followed up for at least one year post transplant. Statistical Analysis: the data collected from this study will be

electronically entered into a database. The departments from Research Centre the Biostatistics, Epidemiology and Scientific Computing or the National Biotechnology Center upon availability of the Statistician will carry out statistical analysis of the data utilizing the appropriate techniques. We hope to achieve all these activities in a period of 12 months.

Reference: 1. Fine RN. Renal transplantation for children-the only realistic choice. *Kidnet Int Suppl* 1985; 17(7):S15.

2. Davis ID, Bunchman TE, Grimm PC et al. pediatric renal transplantation: indications and special considerations. Aposition paper from the Pediatric Committee of the American Society of Transplant Physicians. *Pediatr Transplant* 1998;2(2):117.

P370

OPERATIVE MANAGEMENT FOR URETERAL STRICTURE INDUCED BY BK VIRUS ATER RENAL TRANSPLANTATION

Ho Chul Park, Hyung Joon Ahn, Sun Hyung Joo
Kyung Hee University

In recent years, incidence of BK virus infection in the kidney transplant population is on rise. BK virus is a human polyomavirus which is a member of the Papovaviridae family. Polyomaviruses are ubiquitous in nature and were first isolated 1971 from the urine of a renal transplant patient who developed ureteral stenosis post-operatively. BK virus is known to cause severe renal dysfunction, ureteral stenosis, and hemorrhagic cystitis in renal transplant patients. The incidence of ureteral stenosis due to BK virus infection among allograft recipients is approximately three percent, although stenosis has been traditionally attributed to causes other than BK virus infection. In this report, we describe a case of the patient presenting with hydronephrosis due to BK virus-induced ureteral stricture after renal transplantation who successfully treated by partial ureterectomy and re- ureteroneocystostomy. A 44-year-old man who had undergone a second renal transplantation. Graft nephrectomy for the first renal transplantation was performed due to renal artery thrombosis and the patient underwent a kidney re-transplantation 1 year later graft nephrectomy. The 17 months postoperatively, he was diagnosed to have hydronephroureterosis attributable to BK virus-induced ureteral stricture. The diagnosis was made virologically by BK virus PCR detection. He successfully underwent partial ureterectomy and re- ureteroneocystostomy. He was discharged with normal kidney functions. The patient is maintaining satisfactory graft function 31 months after surgery without clinical and serological evidence of recurrent BK virus infection.

P371

THE IMPACT OF PRE-RECOVERY MANAGEMENT OF DECEASED DONORS

Rose Marie Liquete, MA Zsarin Tuazon
Quirino Memorial Medical Center, Philippines

Background: Brain dead patients are referred for organ donation at variable periods of time. The best physiologic management should be instituted for optimum organ viability. This paper aim to identify critical points in pre-recovery management that has impact on the outcome of organs transplanted.

Method/Materials: Critical timelines and physiologic events prior to recovery were reviewed. The outcome on 41 kidney recipients from 21 donors from Quirino Memorial Medical Center, Philippines were followed up for 6 months to 3 years.

Results: Donor age range from 18 to 49 years (mean – 33 years). Recipient age range from 24 to 78 years (mean – 50 years). The interval between head injury to brain death (10–93 h, mean – 34 h) and from declaration to actual retrieval (6–17 h, mean – 15 h) vary, but the physiological state of these 21 patients were maintained. Donor creatinine ranged from 37.9 to 187.38 mmol/l (mean – 97.52) Three had transient cardiac arrest. Organs were transplanted at mean time of 12 h from brain death. Cold storage time ranged from 2 ½ hours to 25 h 50 min (mean – 9 h). Twenty eight patients had at least 1DR (68%); one had a fullmatch and the rest had either 0DR or no ABDR match at all. They received induction therapy (ATG – 32, Basiliximab – 9), Calcineurin Inhibitor (FK506 – 40, CyA – 1), mycophenolate and steroids. Forty recipients had good graft function at 1 month. Five of them (12%) initially required 2–4 hemodialysis sessions (4- ATN, 1- AR). One patient never recovered (CIT–16 h) and died of pulmonary embolism in one month. One month, 6 months, 1-year, and 2-years patient and graft survival are 97.6%, 92.68%, 90%, 89.4%, respectively. All three recipients transplanted 3 years ago still have excellent function.

Conclusion: The recovery of viable organs for transplantation is dependent upon aggressive and vigilant neurointensive care to achieve excellent recipient outcome .

P372

SINGLE CENTER EXPERIENCE OF FLOWCYTOMETRY CROSSMATCH POSITIVE KIDNEY TRANSPLANTATION

Young Hoon Kim, Han kyung Cho, Joo Hee Jung, Byung Hyun Choi, Sung Shin, Heung-Bum Oh, Seog -Woon Kwon, Su Kil Park, Duck Jong Han
Asan Medical Center

Background: Antibody against donor is a barrier to successful kidney transplantation. Flowcytometry crossmatch (FCXM) is a useful method for

detection and monitoring of anti-donor antibody; preoperatively, after desensitization, and after transplantation.

Methods: From Dec 2008 to Feb 2013 we had performed 99 cases of FCXM positive KT. Rituximab (500 mg), plasmapheresis (PP), and early use immunosuppressant based preconditioning was used. Among them five patients were CDC crossmatch positive patients. Target MFI ratio after desensitization was less than 2.0 (less than 77 as MCS: mean channel shift).

Results: FCXM positive KT accounts for approximately 15% of all living donor kidney transplantation in this center. In this cohort, Female was 65% (n = 64). Forty patients were high PRA (>50% by Luminex) including 10 re-transplantation. Mean recipient age was 45.4 year old (±11.9). Mean baseline MFI ratio was 5.6 ± 5.6 [Median 3.55 (2.0–32.7)]. After desensitization pre operative MFI ratio was 1.50 ± 0.51, and postoperative MFI ratio was 1.86 ± 0.99. Nine patients dose not reached target MFI ratio after desensitization. Out of 36 patients in whom MFI ratio was elevated (2.0) after transplantation, only four patients showed clinical renal dysfunction. During 635 days (± 420) of follow up period, six cases of early AMR, one case of mixed AMR/ACR, and three cases of ACR developed. All the rejection were responsive to anti rejection treatment especially PP & IVIG in AMR.

Conclusions: FCXM positive KT after desensitization is feasible and can expand donor pool. However careful recipient selection and postoperative management are required for successful outcome.

P373

MGUS IN RENAL TRANSPLANT: STILL A MATTER OF CONCERN?

Roberta Fenoglio, Elisa Lazzarich, Claudio Musetti, Daniele Cagna, Andrea Airoidi, Elisabetta Radin, Piero Stratta
Department of Translational Medicine, University

Background: The incidence of MGUS in patients (pts) undergoing evaluation for kidney transplantation (KT) have not been described. There is a paucity of information on the long-term outcomes of MGUS pts who received a solid organ transplant.

Methods: We evaluated all kidney transplant recipients between November 1998 – February 2012 in a single center. Pts with MGUS who received a KT were compared with pts on dialysis with MGUS. All patients with an MGUS underwent standard immunosuppression as per center protocol.

Results: Out of 851 enrolled patients, 16 pts were found to have a MGUS before transplant. Median follow-up was 7.8 years; 1 pt developed a myeloma. Moreover 16 pts with MGUS who received transplant were compared to pts with MGUS on dialysis, where none developed a myeloma. Lastly 26 pts developed a MGUS after kidney transplant, median follow up was 4.84 years, of which one developed a myeloma.

Conclusion: Our study represents one of the largest series of pts with MGUS pre or post-KT. The finding that only two out of 42 MGUS patients progressed to myeloma on a long term follow-up (comparable to the progression rate of the Italian general population) suggests that renal transplant milieu does not entail an increased risk for this evolution.

P374

DETERMINATION OF NEOPTERIN, KYNURENINE AND TRYPTOPHAN AS IMMUNE SYSTEM ACTIVATION MARKERS IN KIDNEY TRANSPLANT RECIPIENTS

Michaela Kubišová¹, Jakub Višek¹, Pavel Navrátil², Lenka Krémová¹, Miroslav Merta¹, Luboš Sobotka¹

¹III. Internal Gerontometabolic Clinic, University Hospital and Medical Faculty, Charles University; ²Urology Clinic, University Hospital and Medical Faculty, Charles University, Hradec Králové, CZ

Background: Early detection of acute rejection in renal transplant recipients is crucial for the graft function. No non-invasive tests are available to accurately and consistently predict the risk of allograft rejection. The development of less invasive diagnostic methods that additionally would provide insights into the pathophysiology of rejection, would be considerable evaluated.

Methods: Since the beginning of the year 2013 all patients after kidney transplantation are included in the study. Tryptophan metabolites and neopterin are daily determined in plasma during first fourteen days after kidney transplantation. Analysis is performed at high-performance liquid chromatography (L. Krcmova et al. *Talanta* 85 (2011) 1466–1471). The kidney biopsy will be performed in all patients in the third month after transplantation.

Results: The first data show that kynurenine, kyn/trp, and neopterin are significantly lower in transplant recipients having an uncomplicated postoperative course than in serum of patients at the time of an acute rejection episode.

Conclusion: Determination of Neopterin, Kynurenine and Tryptophan in the serum from patients after kidney transplantation can provide deeper knowledge about rejection after kidney transplantation and effectiveness of their treatment. Supported by the programme PRVOUK P37/12.

P375

EARLY POST TRANSPLANT MAJOR ADVERSE CARDIAC-VASCULAR EVENT (MACE) DOES NOT AFFECT RENAL ALLOGRAFT FUNCTION IN SURVIVING PATIENTS

Amal Rosli, Hemant Sharma, Chang Wong, Adham El-bakry, Khalid Abdulnabi, Matthew Howse, Daniel Ridgway, Ajay Sharma, Sanjay Mehra, Abdul Hammad
Royal Liverpool Hospital

Effective prevention and management of cardiovascular disease in kidney transplant recipients are integral to increasing patient longevity and improving graft survival. Approximately 50% of patients die with a functioning transplant, with approximately 50% of these deaths from cardiovascular disease or stroke. At Liverpool Transplant Unit, recipients undergo screening in multi-disciplinary setup prior to activation on transplant waiting list. AIM: To determine the incidence of post transplant major adverse cardiac-vascular event (MACE; myocardial infarction, new-onset angina, stroke and congestive heart failure) after renal transplant. To assess if MACE have an effect on renal graft function.

Methods: Retrospective study of all transplant patient between February 2010 to February 2013. The variables included were: donor and recipient age and gender, BMI. Serum creatinine were recorded at week 1, week 2, 1 month and 3 month post renal transplant.

Results: $N = 290$ patients were transplanted between February 2010–13. All recipients had either Basiliximab or Alemtuzemab induction. ($N = 13/290$, 04%) patients had documented MACE episodes within first 120 days of renal transplant. The median age of recipients was 56 (44–84) years. The median age of donors was 63 (44–74) years. Patients with documented MACE had a background history of diabetes mellitus in 69% (9/13), hypertension in 85% (11/13) patients. The median HDL was 1.3 $\mu\text{mol/l}$. Median BMI was 28 but 40% (5/13) patients had a BMI >30 . The overall mortality rate secondary to MACE event was 1% but the mortality in the MACE cohort was 30%. The median creatinine in the death censored MACE cohort was 322 (week 1), 180 (week 2), 169 (month 1), 145 (month 3) $\mu\text{mol/l}$.

Conclusion: The incidence of MACE and overall mortality was comparable to published literature despite advance age of donors and recipients in our series. MACE events had no significant effect on renal graft function on surviving patients.

P376

CARDIOLOGICAL STATUS OF PERSONS QUALIFIED FOR LIVING KIDNEY DONATION

Krzysztof Jankowski¹, Jolanta Gozdowska², Artur Kwiatkowski³, Andrzej Chmura³, Magdalena Durlik²

¹Department Internal Medicine and Cardiology, Medical University of Warsaw; ²Department of Transplant Medicine and Nephrology, Medical University of Warsaw; ³Department General and Transplantation Surgery, Medical University of Warsaw

Living kidney donation may increase the risk of cardiovascular diseases. It seems justified to identify cardiovascular risk factors and cardiological disorders (CD) prior to the kidney donation.

Aim: To determine the cardiological status of persons qualified as a living kidney donor.

Material and methods: We analyzed data of 109 potential living kidney donor, aged 25–70 years. They underwent clinical examination and lipid profile. The presence of risk factors of CD as hypercholesterolemia, diabetes mellitus, hypertension, obesity and smoking and any cardiological problems were registered.

Results: Among 109 persons, 48 (44%) were qualified for living kidney donation. As many as 40 of them has have ≥ 1 risk factors of CD (mild dyslipidaemia, overweight, smoking, hypertension). In 1 pt we diagnosed pre-excitation syndrome. The patient was treated successfully (ablation) and became a donor. In another person renal artery stenosis as the reason of hypertension was diagnosed. After nephrectomy renal artery angioplasty was performed and kidney was transplanted for his son. A normal function of the graft in the recipient and normalization of the donor's blood pressure was observed. 63 (56%) person were disqualified. In 15 (23.8%) person the reasons were cardiological. In 1 pt it was the abdominal aneurysm (AA) treated earlier with stentgraft, another person remain under observation due to AA. Both men smoked and have severe dyslipidaemias. In 3rd patient we observed atrial fibrillation and two risk factors of CD. The next 2 men have had the peripheral occlusive arterial disease. In 9 pts we have found ≥ 2 risk factors and in the last one morbid obesity was present. Nobody has diabetes mellitus.

Conclusion: In Poland candidates for living kidney donation have very often risk factors of CD and require appropriate management. Among the persons qualified for kidney donation cardiovascular problems are an important cause of disqualification.

P377

MONOCLONAL GLOMERULOPATHY RECURRING IN KIDNEY TRANSPLANTED FROM LIVING RELATED DONOR TO A RECIPIENT WITH MONOCLONAL GAMMOPATHY OF UNDETERMINED SIGNIFICANCE (MGUS) – A CASE REPORT

Jolanta Gozdowska¹, Agnieszka Perkowski-Ptasińska², Arkadiusz Urbanowicz², Magdalena Durlik²

¹Institute of Transplantology; ²Institute of Transplantology, Medical University of Warsaw

Monoclonal gammopathies are rare cause of end-stage renal disease (ESRD). MGUS is asymptomatic premalignant single-clone plasma cell proliferation, resulting in secretion of excessive homogeneous monoclonal light/heavy or light chains only. Abnormal protein is deposited in all renal structures resulting in their damage. Male aged 57, with ESRD due to MGUS, underwent a pre-emptive living related donor kidney transplantation. Maintenance immunosuppression consisted of tacrolimus, mycophenolate mofetil, and steroids. The first post-transplant 18 months were free of proteinuria, with good kidney function, thereafter the patient started to have proteinuria. Graft biopsy revealed no signs of cellular rejection, a suspicion of transplant glomerulopathy, recurrence of MGUS related glomerulopathy, and IF/TA grade I. On FREELITE test kappa/lambda serum and urine ratio were 3.6 (reference ranges: 0.4–3.1) and 147 (reference ranges: 2–10.4), respectively. Bone marrow biopsy was negative and diagnosis of recurrent monoclonal glomerulopathy was established. In order to treat MGUS and halt progression of glomerulopathy the administration of bortezomib/dexamethasone is now considered.

Conclusions: Definitive treatment of MGUS recurring in kidney graft has not been determined. To account for possible rapid recurrence of gammopathy in transplanted kidney transplantation from deceased donor should be preferred over living donation in ESRD patient due to MGUS.

References: Soltero, L. et al: Initial survival data of kidney transplant patients with pre-transplant monoclonal gammopathy. Clin Transplant 2012; 26:300–304. Horike K. et al: A case of recurrent light chain deposition disease after living-related renal transplantation – detailed process of the recurrence. Clin Transplant 2012; 26:64–69.

P378

GDF-15, HEPICIDIN IN RELATION TO ANAEMIA AND HEPICIDIN IN PREVALENT RENAL ALLOGRAFT RECIPIENTS

Ewa Koc-Zorawska, Irena Glowinska, Jacek Malyszko, Michal Mysliwiec, Jolanta Malyszko

Department of Nephrology and Transplantology

Anemia is more prevalent in renal transplant recipients than in GFR-matched CKD patients. Heparin is a small defensin-like peptide whose production by hepatocytes is modulated in response to anemia, hypoxia or inflammation. Growth differentiation factor 15 (GDF-15) was recently identified as a hepcidin-suppression factor that is expressed at high levels in patients with ineffective erythropoiesis. The aim of the study was to assess GDF-15 levels with relation to iron parameters in 62 stable kidney allograft recipients maintained on triple immunosuppressive therapy.

Methods: Complete blood count, urea, creatinine, and iron status were assessed by standard methods. We measured GDF-15, hepcidin, hemojuvelin, IL-6 and NGAL with commercially available assays.

Results: Mean levels of GDF-15, NGAL, hepcidin and hemojuvelin were significantly higher in kidney allograft recipients when compared to the control group ($p < 0.001$ for all). GDF 15 was significantly higher in patients with anemia according to WHO definition when compared to non-anemic counterparts ($p < 0.05$). GDF 15 levels were not dependent on the type of immunosuppressive therapy. In univariate analysis GDF-15 was related to kidney function (creatinine $r = 0.39$, $p < 0.01$, eGFR by MDRD $r = -0.37$, $p < 0.01$), urea ($r = 0.39$, $p < 0.01$), uric acid ($r = 0.42$, $p < 0.01$), hepcidin ($r = -0.32$, $p < 0.01$), IL-6 ($r = 0.28$, $p < 0.05$), hemoglobin ($r = -0.32$, $p < 0.05$), and NGAL ($r = -0.35$, $p < 0.01$). GDF-15 was not related to serum iron, or ferritin. In multivariate analysis, hepcidin was found to be a predictor of GDF-15 (beta value 0.32, $p = 0.03$) explaining 38% of the variation in GDF15 levels. In conclusion, our preliminary data may suggest possible mutual relations between GDF 15 and hepcidin in patients with kidney disease and that GDF15 might be involved in the pathogenesis of anemia in kidney allograft recipients. However, the role of inflammation should be also elucidated.

P379

A CASE CONTROL STUDY OF FACTORS ASSOCIATED WITH DELAYED GRAFT FUNCTION IN FILIPINO KIDNEY TRANSPLANT PATIENTS

Harvy Joy Liwanag¹, Jasmin Jiji Miranda¹, Christina Cabrera¹, Cilina Faith Cabreross¹, Ma. Victoria Carmela Dela Paz¹, Angeli Nicole Reinoso¹, Pamela Ann Uy¹, Harvey Yap¹, Rose Marie Liguete²

¹Ateneo de Manila University; ²St. Luke's Medical Center

Background: Patients with end stage renal disease (ESRD) have renal transplantation as an option for long-term kidney function replacement. This

study focused on delayed graft function (DGF) as a determinant of long-term kidney graft function. We assessed if duration of pre-transplant dialysis, sex match between donor and recipient, and total ischemia time were risk factors for DGF among Filipino patients after renal transplantation.

Methods: Hospital charts of 77 Filipino patients who underwent kidney transplantation from living donors between 2007 and 2009 were reviewed. Fifty two (52/77) were selected as subjects based on data availability on recipient age, gender, and the transplant variables of interest. DGF was defined as serum creatinine of ≥ 2 mg/dl on the third day post-transplantation. Twenty six cases were age-matched (± 5 years) with 26 controls.

Results: Mean age for both cases and controls were 46 ± 10 years. There were more males than females among cases (80.8%) than among controls (50%). No significant difference was noted between cases and controls for duration of pre-transplant dialysis and total ischemia time, while significant difference was noted for sex matching between graft donor and recipient ($p = 0.0309$). An inverse association was noted for the category "male donor to female recipient" (OR=0.13; 95% CI 0.02–0.84; using same-sex match as reference), suggesting that the factor was favorable.

Conclusion: Duration of pre-transplant dialysis of up to 2500 days and total ischemia time of up to 130 min may not increase the risk for DGF. Being a female recipient of a graft from a male donor may be a favorable factor, although further studies are recommended. The results support previous studies on the gender disparities among transplant patients and the role of donor-recipient gender considerations in preventing DGF. Furthermore, an analysis on the long-term outcomes of these cases is warranted.

P380

IRON STATUS IN RENAL REPLACEMENT THERAPY

Jolanta Malyszko¹, Jacek Malyszko¹, Ewa Koc-Zorawska¹, Nomy Levin-Iaina², Irena Glowinska¹, Michal Mysliwiec¹

¹Department of Nephrology and Transplantology; ²Department of Nephrology Tel Aviv

Introduction: All living organisms have evolved sophisticated mechanisms to maintain appropriate iron levels in their cells and within their body. Recently our understanding of iron metabolism has dramatically increased. Overt LPI (Labile Plasma Iron) represents a component of non-transferrin bound iron-NTBI that is both redox active and chelatable, capable of permeating into organs and inducing tissue iron overload. LPI measures the iron-specific capacity of a given sample to produce reactive oxygen species. We studied for the first time NTBI correlations with markers of iron status, and inflammation in prevalent hemodialyzed patients and kidney transplant recipient.

Methods: Complete blood count, urea, serum lipids, fasting glucose, creatinine, ferritin, serum iron, TIBC were studied by standard laboratory method in the hospital central laboratory. NTBI was assessed by FeROS ϵ eLPI kit (fluorescence-based assay intended for the *in vitro* semi-quantitative detection of both over and cryptic redox active forms of NTBI) by Aferix Ltd in Tel Aviv, Israel. A test result of 0.6 units of LPI or more indicates a potential for iron-mediated production of reactive oxygen species in the sample.

Results: Patients with LPI units ≥ 0.6 had higher serum iron, ESA dose, ferritin, hsCRP. In hemodialyzed NTBI correlated with hsCRP, ferritin. In kidney transplant recipients NTBI was correlated with TIBC, ferritin, and tended to correlate with CRP. Patients with LPI units ≥ 0.6 had higher serum iron ($p < 0.05$), TIBC ($p < 0.05$), ferritin ($p < 0.001$) and MCV. Very high ferritin together with high NTBI were found in patients undergoing multiple transfusion before and/or after transplantation. HD patients had higher NTBI when

Conclusions: Elevated NTBI as well as ferritin levels, in kidney transplant patients and dialyzed patients may be due to disturbed iron metabolism, since human body have no possibility to remove iron excess. NTBI could be responsible for excessive synthesis of reactive oxygen species, therefore it may be linked to complications due this phenomenon, such as atherosclerosis, frequently encountered in this population.

P381

POLYOMA BK VIRUS INFECTION AFTER KIDNEY TRANSPLANTATION – SCREENING AND CLINICAL OUTCOME

Svetlana Jovicic Pavlovic¹, Maja Cupic², Marija Milinkovic¹, Mirjana Lausevic³, Radomir Naumovic³

¹Clinic for nephrology, Clinical Centre of Serbia, Belgrade; ²Institute for Microbiology, University of Belgrade; ³Faculty of Medicine, University Belgrade

Background: Polyoma BK virus nephropathy was recognized as an important cause of allograft dysfunction and loss in kidney transplant recipients during last decade. Purpose of this study was to evaluate the prevalence of BK viremia, viruria and nephropathy in renal transplant recipients and to determine clinical outcome.

Materials and Methods: Between January 2011 and December 2012. Sixty kidney transplantations were performed in Clinical Centre of Serbia. Urine cytology for presence of decoy cells, plasma and urine BKV PCR examinations were done. The diagnosis of BK virus allograft nephropathy (BKVAN) was confirmed with histological analysis.

Results: The prevalence of decoy cells was 5% (3/60), viruria 15% (9/60), viremia 5% (3/60). BKVAN prevalence rate was 1.6% (1/60). In patients with BK viremia, after reduction of immunosuppression (mycophenolate mofetil < 1 g/day,

tacrolimus level < 6 ng/ml) and fluoroquinolone therapy, graft function was stabilized and urine cytology for decoy cells became negative. In the patient with BKVAN, graft function progressively deteriorate and graft loss occur in 16th month after transplantation.

Conclusion: Screening for BKV viremia and preemptive therapy prevented development of BKVN and allograft dysfunction.

P382

IS THERE A POSSIBLE LINK ELEVATED URINARY ANGIOTENSINOGEN AS A NOVEL BIOMARKER OF THE INTRARENAL RENIN-ANGIOTENSIN SYSTEM STATUS WITH LEFT VENTRICULAR MASS INDEX AND CAROTID INTIMA-MEDIA THICKNESS IN HYPERTENSIVE RENAL TRANSPLANT PATIENTS?

Ozlem Tiryaki¹, Celalettin Usalan¹, Sacit Coban², Fahrettin Yildiz²

¹Department of Nephrology, Gaziantep University School of Medicine;

²Department of General Surgery, Gaziantep University School of Medicine

Objectives and Aims: Cardiovascular diseases (CVD) is the main cause of morbidity and mortality in renal transplant recipients (RTR). The renin-angiotensin-system (RAS) is considered that regulates blood-pressure (BP) and also independent risk factor for left ventricular mass-index (LVMI) and carotid-intima-media-thickness (CIMT). The RAS blockage have provided evidence for the presence of BP independent renoprotective and cardioprotective effects. Recently, it has been reported that urinary-angiotensinogen levels provide a specific index of the intrarenal RAS status (index of the locally RAS) was significantly correlated with blood-pressure and proteinuria. The aim of this study was to evaluate the relationship of local intrarenal RAS with LVH and CIMT in hypertensive RTR.

Results: Ninety-six nondiabetic RTR (52 male 52.4 ± 18.6 years, 44 female 49.6 ± 16.6 years) were included in this study. All patients were in stable condition with GFR greater than 30 ml/min/ 1.73 m². Spot urine samples were obtained to measure urinary angiotensinogen (UAGT) and urinary creatinine (UCre). And also LVMI and CIMT were measured. UAGT/UCre was significantly higher in hypertensive patients compared with normotensives (12.64 ± 9.36 μ g/g vs. 6.64 ± 4.24 μ g/g, $p < 0.01$). LVMI and CIMT were significantly higher in hypertensive patients compared with normotensives (LVMI; 132.12 ± 32.08 g/m² vs. 96.64 ± 9.12 g/m²; $p < 0.001$ and CIMT; 0.92 ± 0.22 mm vs. 0.72 ± 0.16 mm; $p < 0.01$). Importantly, significant positive correlation was found between UAGT/UCre levels and LVMI ($r = 0.724$, $p = 0.012$) and also CIMT ($r = 0.452$, $p = 0.02$) in hypertensive RTR.

Conclusions: These data indicate that UAGT is increased in hypertensive renal RTR and local RAS probably plays a important role in the development of cardiovascular abnormalities in hypertensive RTR.

P383

EXTERNAL ILIAC ARTERY PTFE GRAFT INTERPOSITION AN EFFECTIVE RESCUE PROCEDURE FOR KIDNEY TRANSPLANT IN PROGRESSIVE INTIMAL DISSECTION

Vipin Tyagi, Sudhir Chadha, Harsha Jauhari

Sir Gang Ram Hospital

Background: Intimal dissection of external iliac artery is a known complication of renal transplant recipient surgery. We report our experience in five cases of living donor renal allograft recipients with the use of PTFE interposition graft of the external iliac artery with simultaneous anastomosis of renal vessels to the graft.

Methods: During our 25 year experience of over 3000 renal transplants we encountered five cases of progressive intimal dissection of external iliac artery which was jeopardising the lower limb perfusion. In all the five cases we found badly damaged intima not amenable to repair. Hence PTFE interposition graft was used and renal artery anastomosed to the graft end to side.

Results: All the patients had stabilized normal graft function after the surgery with no surgical complication.

Conclusion: It is a safe salvage procedure to save the lower limb and the graft kidney by using PTFE interposition graft following an intimal dissection.

P384

EARLY RENAL ARTERY STENOSIS ON DUPLEX SCAN OF RENAL ALLOGRAFT IS NOT A MARKER OF POOR GRAFT OUTCOME

Adham El-bakry, Hemant Sharma, Chang Wong, A Khalil, Khalid Abdulnabi,

Steve Powell, Daniel Ridgway, Ajay Sharma, Abdul Hammad, Sanjay Mehra

Royal Liverpool Hospital

Background: Last year the radiological reporting of early renal artery stenosis (RAS) at Liverpool transplant centre was perceived to be high as compared to previous years. We intend to assess if reported radiological findings had any correlation to graft function, graft survival and recipient related co-factors.

Methods: Eighty eight renal transplants carried out between March 2011 and February 2012 underwent routine post-transplant duplex scanning. The duplex scan velocities of renal artery were graded into Grade 0 (velocities-1-200 cm/s), Grade 1(201-400 cm/s), Grade 2(401-600 cm/s) and Grade 3 (>600 cm/s) with grade 0 as normal. All the other grades were marked as renal artery stenosis (RAS). The serial duplex scans were followed till graft dysfunction or intervention. Medcalc 18.1 was used for statistical analysis. Non Parametric Correlation was derived with Spearman Rho test. Parametric data was analysed using Mann-Whitney test. Univariate and multivariate analysis were done with significance levels set at <0.05.

Results: Retrospective analysis showed that sixty (68%) were males, 28 (32%) were females. $N = 220$ duplex scans were done, Grade 0-175, Grade 1-37, Grade 2-06, Grade 3-02. RAS reported were not associated with graft dysfunction during the first 6 months but RAS persistent for 24 weeks and beyond correlated to worsening graft function ($p = 0.2$). None of the grafts were lost due to reported RAS. Recipient diabetes ($p = 0.4$), hypertension (spearman rank correlation) and absence of aortic patch on the renal artery ($p = 0.3$) were not associated with development of RAS. Per-operative atherosclerosis was significantly related to RAS at 4 weeks ($p = .002$). The overall allograft success rate at Liverpool was comparable to previous years.

Conclusion: Probably because of the sensitive ultrasound technology and increasing experience of radiologist, there was reported increased incidence of RAS which was not significant in the first six months. Bigger sample size is required to prove the statistical significance and the study carries on prospectively.

P385

THE RELATIONSHIP BETWEEN THE FGF-23 LEVELS AND LEFT VENTRICULAR MASS INDEX AND CAROTID INTIMA-MEDIA THICKNESS IN RENAL TRANSPLANT PATIENTS

Ozlem Tiryaki¹, Celalettin Usalan¹, Fahrettin Yildiz², Sacit Coban²

¹Department of Nephrology, Gaziantep University School of Medicine;

²Department of General Surgery, Gaziantep University School of Medicine

Objectives: The elevation of serum fibroblast growth factor-23(FGF-23) is a common feature in chronic kidney disease (CKD). FGF-23 levels decrease dramatically after renal transplantation, but were still above normal. Cardiovascular diseases that is the main cause of morbidity and mortality in renal transplant recipients. Several near recent studies have demonstrated that elevated FGF-23 may be also involved in the left ventricular hypertrophy onset. In CKD patients, FGF-23 levels were significantly correlated with higher mean left ventricular mass index (LVMI). The aim of this study was to evaluate the relationship of FGF-23 with LVMI and CIMT in renal transplant recipients (RTR).

Results: Sixty-four RTR (38 male 48.4 b16.6 years 26 female 46.6 b12.4 years) were included in this study. All patients were in stable condition with GFR greater than 30 ml/min/1.73 m², mean GFR; 36 ml/min/1.73 m². Plasma FGF-23 levels were measured using a C-terminal human ELISA. And also LVMI and CIMT were measured. Plasma FGF-23 levels were significantly higher in renal transplant recipients compared with control group (72.36 b32.16 RU/ml vs. 36.18 b16.12 RU/ml). LVMI and CIMT were also significantly higher in RTR compared with the controls (LVMI; 112.12 b 28.08 g/m² vs. 92.64, b8.24 g/m²; $p < 0.001$ and CIMT; 0.86 b0.24 mm vs. 0.70 b0.18 mm; $p < 0.01$). Importantly, a significant positive correlation was found between FGF-23 levels and LVMI ($r = 0.642$, $p = 0.016$) and also CIMT ($r = 0.542$, $p = 0.024$) in renal transplant recipients.

Conclusions: These data indicate that FGF-23 is higher in renal transplant recipients and elevated FGF-23 levels probably plays a important role in the development of cardiovascular abnormalities in renal transplant recipients. Key Words: Renal transplant recipients, FGF-23, CVD.

P386

CARCINOID TUMOR ARISING MATURE CYSTIC TERATOMA IN THE LUNG AFTER KIDNEY TRANSPLANTATION

Pinar Seymen¹, Fatih Gokhan Akbay¹, Gokhan Ertugru², Gurkan Tellioglu², Alper Toker³

¹Istanbul Bilim University Medical Faculty; ²Florence Nightingale Hospital;

³Istanbul University Istanbul Medical Faculty

We report on a 45-year old man who developed teratoma and carcinoid tumor in the lung after kidney transplantation. He has end stage renal failure secondary to amyloidosis. He received kidney from his brother two years ago. Immunosuppression protocol was Tacrolimus, MMF and prednisolon. Post-transplant creatinine levels were between 1.3 and 1.5 mg/dl. He admitted with fever and graft disfunction in posttransplant 13th months. Banf1A cellular rejection, tacrolimus toxicity and BK virus nephropathy were determined in graft biopsy. Pulse steroid treatment was administered. Then immunosuppressive drug doses were decreased. Polypoid mass lesion at anterior segment of upper lobe of right lung was seen in Thorax CT. Then this lesion was removed via surgical operation. Pathologic findings was showing microscopic carcinoid tumor arising mature cystic teratoma. Beta HCG, AFP and LDH levels were normal. The patient was considered by oncologist who proposed PET CT imaging after 3 months. Teratoma is an tumor with tissue or organ components

resembling normal derivatives of all three germ layers. Carcinoid tumor is a slow-growing type of neuroendocrine tumor. Carcinoid tumors can found in the lungs. After kidney transplantation, teratoma and carcinoid tumor is not seen commonly. There is no any case together carcinoid tumor and teratoma after kidney transplantation.

P387

PEDIATRIC KIDNEY TRANSPLANTATION IN TURKEY? EXPERIENCE OF AN EVOLVING CENTER

Burak Kocak¹, Emre Arpalı¹, Cihan Karata¹, Turan Kanmaz¹, Ahmet Nayir², Munci Kalayoglu¹

¹Department of Solid Organ Transplantation, Istanbul Memorial Hospital;

²Faculty of Medicine, Department of Pediatric Nephrology, Istanbul University

Introduction: Reluctance to perform kidney transplants on children is an ongoing problem in Turkey. Moreover, urological pathologies still constitute the largest portion of the underlying etiologies in chronic renal failure patients. Here, we retrospectively analyzed the data acquired from our pediatric renal transplant patients and reviewed the registry of dialysis and transplantation data prepared by Turkish Society of Nephrology.

Material and Methods: Fifty live donor kidney transplantations were performed in children between 2008 and March 2013. Eighteen of the 50 (38%) transplants were preemptive. The mean age at operation time was 10.8 ± 5 years. The mean patient weight was 31.3 ± 15.8 kg (Range 9.4 kg to 66.4 kg). A detailed urologic evaluation was performed in every child with an underlying lower urinary tract disease. One enterocystoplasty and two ureterocystoplasties were performed for augmentation of the bladder, simultaneously.

Results: One-year death-censored graft survival and patient survival rates were 100% and 97.8%, respectively. Mean serum creatinine level was 0.8 ± 0.32 mg/dl (Range: 0.3-1.8 mg/dl). None of the patients had vascular complications or acute tubular necrosis. One patient suffered graft versus host disease at second month after renal transplantation and died with a functioning graft. In one patient with massive proteinuria detected after transplantation, recurrence of primary disease (Focal segmental glomerulosclerosis) was considered and the patient was treated successfully with plasmapheresis. One child had an acute cellular rejection and treated with pulse steroid treatment.

Conclusion: While challenging, all patients in all pediatric age groups can successfully be operated and managed with a careful surgical technique and close postoperative follow-up and efforts by the experienced and respectful surgical teams in this country could change the negative trends to perform kidney transplantation in Turkish pediatric population.

P388

FGF-23 IS RELATED TO HIGH SENSITIVE CRP (HS-CRP) AND PLASMINOGEN ACTIVATOR INHIBITOR TYPE 1 (PAI-1) LEVELS IN RENAL TRANSPLANT PATIENTS

Ozlem Tiryaki¹, Celalettin Usalan¹, Sacit Coban², Fahrettin Yildiz²

¹Department of Nephrology, Gaziantep University School of Medicine;

²Department of General Surgery, Gaziantep University School of Medicine

Background: The elevation of serum fibroblast growth factor-23 (FGF-23) is a common feature in chronic kidney disease (CKD). FGF-23 levels decrease dramatically after renal transplantation, but were still above normal. In CKD patients, FGF-23 levels were significantly correlated with inflammation, endothelial dysfunction and cardiovascular disease. Inflammation and endothelial dysfunction play a key role in the pathogenesis of atherosclerosis.

Materials and Methods: The aim of this study was to evaluate the relationship of FGF-23 with inflammation (hs-CRP) and endothelial dysfunction in renal transplant recipients. Sixty-four renal transplant recipients (38 male 48.4 b16.6 years, 26 female 46.6 b12.4 years) were included in this study. All patients were in stable condition with GFR greater than 30 ml/min/1.73 m², mean GFR; 36 ml/min/1.73 m². Plasma FGF-23 levels were measured using a C-terminal human ELISA. And also we have examined the plasma levels of the PAI-1 and hs-CRP.

Results: Plasma FGF-23 levels were significantly higher in renal transplant recipients compared with control group (72.36 b32.16 RU/ml vs. 36.18 b16.12 RU/ml). Plasma PAI-1 and hs-CRP levels were also significantly higher in renal transplant recipients compared with the controls (PAI-1; 32.4 b12.24 IU/ml vs. 12.2, b4.24 IU/ml; $p < 0.001$ and hs-CRP; 14.23, b9.6 mg/l vs. 3.80, b0.78 mg/l; $p < 0.01$). Importantly, a significant positive correlation was found between FGF-23 levels and plasma PAI-1 ($r = 0.720$, $p = 0.022$) and also hs-CRP ($r = 0.486$, $p = 0.024$) in renal transplant recipients.

Conclusion: These data indicate that FGF-23 is higher in renal transplant recipients and elevated FGF-23 levels probably plays a important role in the development of endothelial dysfunction and cardiovascular abnormalities in renal transplant recipients.

P389

ELEVATED URINARY ANGIOTENSINOGEN LEVELS IS RELATED TO HIGH SENSITIVE CRP (HS-CRP) AND PLASMINOGEN ACTIVATOR INHIBITOR TYPE 1 (PAI-1) LEVELS IN RENAL TRANSPLANT PATIENTS

Celalettin Usalan¹, Ozlem Tiryaki¹, Fahrettin Yildiz², Sacit Coban²

¹Department of Nephrology, Gaziantep University School of Medicine;

²Department of General Surgery, Gaziantep University School of Medicine

Background: The renin-angiotensin-system (RAS) is considered that regulates blood pressure and also play a key role inflammation and endothelial dysfunction. Locally produced RAS in most tissues have been recently. The RAS blockage have provided evidence for the presence of blood pressure independent renoprotective and cardioprotective effects of RAS blockers. Therefore, assessment of locally RAS activation is essential to investigate the pathophysiological mechanisms of hypertension and cardiovascular disease.

Materials and Methods: Recently, it has been reported that urinary angiotensinogen levels provide a specific index of the intrarenal RAS status was significantly correlated with blood pressure and proteinuria. The aim of this study was to evaluate the relationship of local intrarenal RAS with inflammation (hs-CRP) and endothelial dysfunction (PAI-1) in hypertensive renal transplant recipients (RTR).

Results: Ninety-six RTR (52 male 52.4 ± 18.6 years, 44 female 49.6 ± 16.6 years) were included in this study. All patients were in stable condition with GFR greater than 30 ml/min/1.73 m². Spot urine samples were obtained to measure urinary angiotensinogen (UAGT) and urinary creatinine (UCre). And also plasma PAI-1 and hs-CRP were measured. UAGT/UCre was significantly higher in hypertensive patients compared with the normotensives (12.64 ± 9.36 µg/g vs. 6.64 ± 4.24 µg/g, p < 0.01). Plasma PAI-1 and hs-CRP levels were also significantly higher in RTR compared with the controls (PAI-1; 28.3 ± 11.84 IU/ml vs. 12.2 ± 4.24 IU/ml; p < 0.001 and hs-CRP; 12.12 ± 8.4 mg/l vs. 3.80 ± 0.78 mg/l; p < 0.01). Importantly, a significant positive correlation was found between UAGT/UCre levels and PAI-1 (r = 0.642, p = 0.018) and also hs-CRP (r = 0.523, p = 0.032) in hypertensive RTR.

Conclusion: These data indicate that UAGT is increased in hypertensive RTR and local RAS probably plays a role in the pathogenesis of inflammation and endothelial dysfunction in hypertensive RTR.

P390

VARICELLA ZOSTER INFECTION IN RENAL TRANSPLANT RECIPIENTS: A SINGLE CENTER EXPERIENCE

Marija Milinkovic¹, Svetlana Jovicic Pavlovic¹, Radomir Naumovic²

¹Clinic of Nephrology, Clinical Center of Serbia; ²Clinic of Nephrology, Clinical Center of Serbia, School of Medicine, University of Belgrade

Introduction: Immunosuppression after transplantation renders the transplant recipient susceptible to a broad array of viral pathogens, including varicella zoster virus (VZV) reactivation. Case reports. Out of 31 patients transplanted during 2012. In our transplant center, six patients (19.3%) had VZV reactivation, and the median time from transplantation to reactivation was 6.2 months. At the time of transplantation, five patients were IgG positive for VZV, while all six were negative for IgM and without the previous history of herpes zoster infection. Induction therapy included antithymocyte globulin (ATG-Fresenius) in five and Basiliximab in one patient. Maintenance immunosuppression consisted of tacrolimus, mycophenolic acid and prednisolone. All patients received valganciclovir as a prophylaxis of CMV. In three patients disseminated vesicular skin rash was the sole manifestation of VZV reactivation. Two of them were successfully treated by aciclovir 10 mg/kg BD, while third patient was recovered after treatment with ganciclovir 5 mg/kg BD. In spite of adequate treatment complications of VZV reactivation occurred in three patients, initially hospitalized due to vesicular rash only. One patient had Ramsay Hunt syndrome, and two patient developed visceral VZV involvement: pneumonitis and encephalitis. Although patients were treated with full doses of acyclovir, 10 mg/kg/8 h, death occurred in both of them.

Conclusion: In 35 years old history of our transplant center, this was the first case of "epidemic" of VZV reactivation. VZV infection pre-transplantation does not necessarily indicate that the VZV-specific cellular immunity is sufficient enough to protect from HZ episodes post-transplantation. Given the potentially devastating consequences of VZV reactivation in renal transplant recipients, universally prophylaxis may be considered.

P391

MINIMIZING COLD ISCHEMIA TIME IN RENAL TRANSPLANTATION: IMPACT ON IN-HOSPITAL STAYING

Tainá Sandes-Freitas, Marina Cristelli, Tatiane Sanchez, Hélio Tedesco-Silva, José Osmar Medina-Pestana

UNIFESP, Hospital Do Rim E Hipertensão

Background: Cold ischemia time (CIT) is a modifiable factor associated to poorer renal allograft outcomes. The present analysis aimed to compare the

conventional approach of convoking the transplant candidates just after the final cross-match results (group 1) versus a new strategy of calling up them earlier, based on the absence of anti-HLA antibodies (group 2) and sought the effects on CIT, delayed graft function (DGF) and in-hospital staying.

Methods: Two hundred consecutive first single non zero-mismatch kidney transplants performed between 02/15/2012 and 07/10/2012 (group 1) was compared to other 200 similar consecutive ones, performed between 07/12/2012 and 11/08/2012 (group 2). In both groups, the transplant was performed only after the final cross-match result.

Results: Concerning donors, groups were similar according to age (44 vs. 42 years), brain death cause (cerebrovascular in 49% vs. 51%, trauma in 38% vs. 33%, other in 13% vs. 16%), initial serum creatinine (1.1 mg/dl in both groups) and final serum creatinine (1.9 mg/dl vs. 2.1 mg/dl). Concerning receptors, groups were similar according to male sex percentage (63% vs. 58%), age (44 vs. 45 years), time on dialysis (52 vs. 49 months) and sensitization (PRA < 20% in 81% vs. 80%). Calling up the candidates earlier (group 2) led to a significant 4.6 h reduction on CIT (24.4 vs. 19.8 h, p < 0.001). Additionally, group 2 had a significant 3-day shorter length of in-hospital staying (16.3 vs. 12.9 days, p = 0.012). Although there was no difference on the occurrence of DGF (64% vs. 61%), there was a trend on reduction on its length (11.9 vs. 9.1 days, p = 0.07).

Conclusion: Strategies of calling up the receptors earlier are safe and effective on reducing CIT, and may have benefits on reducing DGF length and in-hospital staying.

P392

RENAL TRANSPLANT IN OBSTRUCTIVE UROPATHY AND VOIDING DYSFUNCTION PATIENTS

Ismail Saad, Aziz Kohaif, Enmar Habib, Sahier Elkhashab, Sherif

Abdelrahman, Ahmed Morsy

Cairo University

Background: Kidney transplantation (KT) improves survival of ESRD patients compared to dialysis. ESRD patients with obstructive uropathy (OU) or voiding dysfunction (VD) are a challenge in preparing for KT. Urologic pathology can adversely affect outcomes. Ancillary procedures may be needed to optimize urinary tract (UT) prior to and/or after KT. We aimed to evaluate outcomes of KT in OU or VD ESRD patients.

Methods: A retrospective review of KT database of Kidney Transplant Unit of Cairo University, Cairo, Egypt. It included patients who underwent living donor KT for ESRD due to OU and VD from January 2007 through December 2011 with an assessment of procedures needed in optimizing UT. Patient and disease parameters were examined.

Results: The study included 25 KT recipients. 24/25 were males. Mean age was 19.3; A7.12 years at time of KT. ESRD was due to neurogenic bladder in 6, posterior urethral valves (PUV) in 5, urethral strictures in 5, urolithiasis in 5, vesicoureteral reflux in 3, and prune-belly syndrome in 1. There were 25 ancillary procedure performed with 5 patients undergoing γ 2 procedures, either prior to or after KT. Pretransplantation nephrectomy, augmentation ileocystoplasty, fulguration of PUV, VIU and urethroplasty were done in 16, 4, 5, 4 and 1, respectively. Mean follow-up was 24.96; A11.95 months. All patients were alive with functioning grafts at end of last followup. Mean creatinine (mg/dL) at 3, 6 months, and 1, 2, 3 and 4 years was 0.99, 1.16, 1.14, 1.27, 1.08 and 1.11, respectively. UTI occurred in 4 (16%). Age and UTI significantly affected creatinine at 1 year (p < 0.04 and p < 0.01, respectively). No correlation was found between creatinine at 2 years and any of examined parameters.

Conclusions: KT can be safely performed in ESRD patients due to OU and VD with acceptable outcomes. Ancillary procedures may be needed to optimize UT for KT. Only age and UTI significantly impacted creatinine at 1 but not 2 years following KT.

P393

POSSIBILITIES OF INFLUENCING THE OUTCOME OF KIDNEY TRANSPLANTATION BY NUTRITIONAL SUPPORT – A PILOT STUDY

Jakub Višek¹, Michaela Kubisova¹, Lenka Krcmova¹, Pavel Navrátil², Miroslav Merta¹, Vladimír Blaha¹, Luboš Sobotka¹

¹III. Internal Gerontometabolic Clinic, University Hospital and Medical Faculty, Charles University; ²Urology Clinic, University Hospital and Medical Faculty, Charles University, Hradec Kralove, Czech R

Background: Chronic diseases, especially chronic kidney disease are often associated with malnutrition. Malnutrition is a negative prognostic factor influencing the course of every disease and surgery. Aim of this project is to assess the possible relationship between initial nutritional status of patients with end stage renal disease and subsequent renal function of the transplanted graft.

Methods: The trial recruited patients after inclusion on the waiting list for a kidney transplant. The nutritional status using biochemical markers, bioimpedance measurements, anthropometry and measurement of muscle strength is assessed initially and periodically. The same observation is followed by one year after renal transplantation.

Results: Currently were enrolled eight patients and two of them underwent successfully a kidney transplant. Due to the small number of patients was not carried out statistical comparisons.

Conclusion: The aim of this work is to verify the hypothesis that nutritional status correlates with the function of the transplanted graft. Based on this work we would like to further develop the methodology of nutritional support in patients enrolled on the waiting list before a kidney transplant. Supported by PVOUK P37/12, IGA MH CR NT/12287-5.

P394

THE IMPORTANCE OF INTERFERON – GENE POLYMORPHISMS ON KIDNEY GRAFT FUNCTION

Milica Kravljaca¹, Vera Pravica², Voin Brkovic¹, Emina Savic², Radomir Naumovic³

¹Clinic of Nephrology, Clinical Center of Serbia; ²Institute of Microbiology and Immunology, School of Medicine, University of Belgrade; ³Clinic of Nephrology, Clinical Center of Serbia, School of Medicine, University of Belgrade

Background: Interferon- γ (IFN- γ), a cytokine produced by Th1 T-cells, plays an important role in the pathogenesis of acute kidney rejection. IFN- γ gene polymorphisms may cause increased or decreased cytokine production. The aim of this study was to examine the association between IFN- γ gene polymorphisms and kidney graft function.

Methods: The study included 92 kidney transplant recipients, treated by the same immunosuppressive protocol. DNA was isolated from whole blood samples. IFN- γ gene polymorphisms 874T/A were detected and analysed using SSP-PCR method. During the first year after transplantation frequency of acute rejection (AR) and delayed graft function (DGF) were recorded. We also followed the allograft function, measured by serum creatinine concentration, creatinine clearance and proteinuria. AR was diagnosed by allograft biopsy, or on the basis of deterioration of allograft function which improved after high-dose of corticosteroid treatment. DGF is defined as a need for hemodialysis during the first 2 weeks after transplantation.

Results: According to the results obtained for IFN- γ gene polymorphism, patients were divided into three groups. The first group included 25 TT genotype patients, the second 42 TA, and the third 25 AA genotype patients. The groups didn't differ regarding age and gender. Thirty-five acute kidney rejection episodes were evidenced, but there was no significant difference of AR between three groups (40% vs 33.3% vs 44%, $p = 0.64$). Allograft function also didn't differ between groups ($p > 0.05$). DGF was present in 25 patients, and the number of DGF was very evenly distributed among the groups (28% vs. 28.3% vs. 24%, $p = 0.95$).

Conclusion: According to our results, IFN- γ gene polymorphism hasn't impact on allograft function, however, we examined small number of patients and it is difficult to conclude whether or not IFN- γ gene polymorphisms have a significant impact on early kidney allograft function.

P395

BLOOD COUNT DURING THE FIRST MONTH AFTER KIDNEY TRANSPLANTATION: A SINGLE-CENTRE EXPERIENCE

Svetlana Jovicic Pavlovic, Natasa Jovanovic, Radomir Naumovic, Mirjana Lausevic, Voin Brkovic, Tamara Jemcov

Clinic of Nephrology, Clinical center, Belgrade, Serbia

Introduction: Anemia, leukopenia and thrombocytopenia are common complications during the first months after renal transplantation (RT). The aim of this study was to examine the influence of two different immunosuppressive protocols (IP) on blood count and need for blood transfusions during the first month after RT.

Methods: The prospective, observational one-centre study included 183 renal recipients since January 2008 to December 2012. According to the applied IP, the patients (pts) were divided in two groups. Group 1 (101 pts, mean age 44 ± 10.8 years, 69 males) received antithymocyte globulin (ATG) 9 mg/kg, tacrolimus (TAC) 0.15 mg/kg, mycophenolic acid (MPA) 2000 or 1440 mg/day depending on the drug preparations and low doses of corticosteroids. Group 2 (82 pts, mean age 39 ± 10.8 years, 49 males) received ATG 9 mg/kg, then 3 mg/kg for the next four days, TAC 0.3 mg/kg, mycophenolic acid 1000 or 720 mg/day and high doses of corticosteroids. Pts in Group 1 also received valganciclovir prophylaxis for cytomegalovirus infection. Blood count was assessed by standard laboratory methods. We recorded frequency of post transplant complications and their impact on anemia.

Results: Different IP and valganciclovir prophylaxis didn't influence significantly the incidence of anemia, leukopenia and thrombocytopenia in examined groups. Pts in group 1 needed a higher amount of blood transfusion ($p = 0.03$), they were older ($p = 0.002$), they had lower degree of MHC matching ($p = 0.04$) and longer cold-ischemia time ($p = 0.002$). The incidence of deceased donor transplantation was higher in Group 1 ($p = 0.001$). Multivariate regression model showed that older renal recipients need higher amount of blood transfusions ($p = 0.003$). Duration of cold ischemia time ($p = 0.015$) and incidence of surgical complications ($p = 0.023$) were predictive for DGF.

Conclusion: Reduction of ATG, TAC and corticosteroids dose with increase of MMF dose and valganciclovir prophylaxis didn't lead to a significant

decrease of blood count during the first month after RT. Older age and surgical complications influenced the degree of anemia after RT.

P396

COMPARING DIFFERENT METHODS TO EXAMINE DELAYED GRAFT FUNCTION IN KIDNEY TRANSPLANT RECIPIENTS

Jozef Matych¹, Ewa Majewska², Piotr Edyko¹

¹County Hospital M. Pirogow; ²Medical University of Lodz

Background: Delayed graft function (DGF) is common complication after kidney transplantation. The need for dialysis within the first week of transplantation is a common definition of DGF. In our study we try to find out if DGF can be diagnosed early and reliably by simple and objective criteria.

Materials and Methods: We performed this study on 40 kidney recipients whom obtain kidney from cadaveric donor. In prospective study we measured creatinine and cystatin C concentration before and 12 h after transplantation. We evaluated GFR (glomerular filtration rate) using different formulas based on cystatin C, creatinine or both concentration in two patient groups- with DGF and IGF (immediate graft function).

Results: We find out that the fastest change in eGFR can be found when we were using formulas based on cystatin C concentration or on cystatin C and creatinine concentration. Diagnosing DGF with creatinine concentration and formulas based on creatinine concentration was useless.

Conclusion: We suggest that comparing eGFR before and after transplantation can be useful in DGF diagnosing.

P397

PRE-OPERATIVE STRESS AND RECOVERY IN LIVING KIDNEY DONORS

Hannah Maple¹, Shanique Simmonds², Mary Tran², Joseph Chilcot³, John Weinman³, Nizam Mamode¹

¹Guy's Hospital; ²King's College London School of Medicine; ³Institute of Psychiatry (Health Psychology Section), King's College London

Background: Pre-operative psychosocial factors have been implicated in post-operative wound healing and recovery. The aim of this study was to evaluate the effect of stress on wound healing and recovery in living kidney donors undergoing hand-assisted laparoscopic donor nephrectomy.

Methods: Stress was measured pre-operatively using previously validated questionnaires. Wound healing was assessed on days 1-3 and at 2 weeks using 20 MHz high-resolution ultrasound. Median intensity (MI) was derived from image analysis to assess residual tissue oedema (lower MI = increased oedema). Comparative scores (normal skin MI minus follow-up wound MI) for each patient were computed. Higher scores suggest inferior wound healing.

Results: Thirty one donors participated. Age and gender were not correlated with anxiety or mood. Women demonstrated increased stress (6.5 vs. 4.1; $p < 0.05$). Pre-operative stress correlated significantly with length of stay ($r = 0.38$, $p < 0.05$). On multiple regression analysis, after controlling for gender and age, stress predicted ultrasound-derived measures of wound healing ($\beta = 0.80$, $p < 0.05$). This was demonstrated across two separate wounds.

Conclusion: Pre-operative stress has a negative impact on post-operative recovery in terms of length of stay and wound healing in living donors. Physical recovery may be improved by interventions to reduce pre-operative stress.

P398

BIOMARKERS IN THE DETECTION OF REJECTION IN ABO INCOMPATIBLE (ABOI) RECIPIENTS

Melanie Field¹, Andrew Bentall¹, Andrew Ready¹, Mark Cobbold², Simon T. Ball¹, Nicholas Inston¹

¹Queen Elizabeth Hospitals; ²MRC centre for Immune Regulation

Background: ABOi transplantation has become increasingly common and comprises 7% of live donors in the UK. In view of the immunological complexity of these patients any mechanism of detecting rejection earlier than current methods would be useful. We aimed to evaluate previously suggested biomarkers of rejection in this cohort.

Methods: Serum from 99 patients undergoing ABOi transplantation at 9 UK centres was analysed by Luminex for a panel of biomarkers (NGAL, KIM-1, VEGF, Cathepsin L, IP-10 and Cystatin C) at pre-transplant and post-transplant time points. Comparison was made between rejectors and non rejectors to see if differences in levels could be predictive of rejection.

Results: In patients who did not develop acute rejection a fall in biomarker levels was seen between pre-operative levels and levels at day 3 (not statistically significant for IP-10). Levels of those who developed rejection did not show a comparable decrease.

Conclusions: The failure of biomarker levels to decrease in patients who later go on to develop acute rejection may help identify those patients at higher risk of developing rejection and perhaps guide surveillance or immunosuppression, but certainly merits further examination in a larger groups of these immunologically complex patients.

P399

RENAL TRANSPLANT IN PATIENT WITH AUGMENTATION CYSTOPLAST: A NOVEL TECHNIQUE

Vipin Tyagi, Harsha Jauhari, Sudhir Chadha
Sir Ganga Ram Hospital

Background: A congenital or acquired genitourinary anomaly is identified as the etiology in a fifth of children with end stage renal disease and many have significant lower urinary tract dysfunction. There is some controversy about the safety of renal transplantation in a patient with an augmentation cystoplasty because of the increased possibility of urinary tract infections in immunosuppressed patients that can lead to pyelonephritis and graft loss.

Aims and Objectives: To evaluate the feasibility and success of anastomosing graft ureter with native ureter in cases where augmentation has been done previously.

Materials and Methods: We describe a case of renal transplant in a 16 year old patient who had cloacal anomaly at birth. She had undergone right nephroureterectomy in childhood followed by augmentation cystoplasty with mitrofanof continent diversion 3 years prior to transplant. Graft kidney was taken from a live related donor and patient maintained on tacrolimus based immunosuppression therapy. End to side Ureteroureterostomy was done at the time of transplant. Patient was instructed to continue with CISC at discharge.

Results: Patient has been doing well 1 year after transplant with stable graft function and no hydronephrosis of transplanted kidney. The patient didn't experience any morbidity due to technical complications. Patient has been continent and managing herself well with CISC.

Conclusions: Renal transplant can be performed in patient with reconstructed or augmented bladder. Graft ureter can be anastomosed to native ureter if there is no distal obstruction, no VUR and if low compliance normal volume reservoir is present.

P400

A STUDY TO EVALUATE THE EFFECT OF RATIO OF DONOR KIDNEY WEIGHT TO RECIPIENT BODY WEIGHT ON RENAL GRAFT FUNCTION

Vipin Tyagi, Sudhir Chadha, Harsha Jauhari
Sir Ganga Ram Hospital

Aim: To study the effect of ratio of donor kidney weight to recipient weight on short and long term graft function in live donor kidney transplant patients.

Methods: It was a prospective study of 81 live donor kidney transplant recipients from May 2008 to June 2011, conducted at Institute of Renal Sciences, Sir Ganga Ram Hospital, New Delhi. Patients were divided in three groups depending on the ratio of donor kidney weight in grams to recipient body weight in kilograms (dkw/rbw- <2, 2 to 3, and more than three in group 1, 2, and 3 respectively). Serum creatinine in milligrams percent on the day of surgery, 7th day, 1, 6 months, 1, and 3 years after the surgery, was recorded and their means compared. Patients with acute tubular necrosis, sepsis, drug toxicity and graft rejection were excluded. A Kruskal-Wallis test was conducted after which pairwise comparison was done using the Mann-Whitney U test.

Results: The mean creatinine value at 7 days, 1, 6 months, 1 and 3 years respectively was compared among the three groups. The comparison showed that the decrease in mean creatinine level was statistically significant in group three patients at 7 and 30 days (p value 0.023 and 0.029 respectively) and did not show a significant difference at 6 months, 1 year and 3 years.

Conclusion: The ratio of donor kidney weight to recipient body weight does not have a significant effect on long term graft function inspite of an early improvement in the function with increased donor kidney weight to recipient body weight ratio.

P401

CHANGES IN PROTEINURIA IN EARLY STAGES OF RENAL TRANSPLANTATION AND PROGNOSTIC SIGNIFICANCE IN THE LONG TERM FOLLOW-UP

Asunción Sancho Calabuig, Eva Gavela Martínez, Julia Kanter Berga, Sandra Beltrán Catalán, Belen Vizcaino, Luis Manuel Pallardó Mateu
Hospital Universitario Dr Peset

There is no information about the relation between the absolute or relative changes in proteinuria in early stages of transplantation and long term prognosis.

Aims: To analyze the effect of the magnitude of proteinuria and its relative changes from 3rd to 12th month after transplantation on long term graft and patient survival.

Methods: Retrospective analysis. Of 701 kidney transplants from deceased donors. Minimum follow-up: 1 year. Baseline proteinuria (3rd) and 12th month post-transplantation in 24 h urine were analyzed. It was categorized depending on its magnitude: 0-149, 150-299, 300-999 mg/day and >1 g/day, and the relative changes of proteinuria from 3rd to 12th month: reduction >50%, variation (Δ) <50%, and increase >50% from baseline.

Results: Of 593 patients, mean follow-up: 84.5 \pm 48.6 months. Proteinuria was present in 49.9% at 3rd and 47.0% at 12th months. Presence of increasing degrees of proteinuria at 3rd and 12th months were associated with long term

graft failure (p = 0.000) and mortality at 12th months (p = 0.000). The relative risk of graft failure and mortality increases from 300 mg/day at 3rd month (HR 2.083, p = 0.001) and in the 12th month (HR 2.271, p = 0.016). Progression of proteinuria >50% was an independent risk factor of graft failure (HR 5.385, p = 0.000) and mortality (HR 3.191, p = 0.035) and was associated with graft failure (p = 0.000) in every category of proteinuria analyzed (p = 0.000), and with mortality (p = 0.023). Anti-HLA antibodies post-transplantation were the only independent risk factor related to the progression of proteinuria >50% (HR 2.723, p = 0.038) in multivariate analysis.

Conclusion: The long term risk of graft failure and mortality increases with increasing amounts of proteinuria and with time from transplantation, since early stages of kidney transplant. Proteinuria progression >50% in early stages of renal transplantation could be considered as a marker of graft failure and mortality, regardless of baseline proteinuria, and expression of immunological damage.

P402

INCREMENTAL ROLE OF LIVING DONOR MINIMALLY INVASIVE NEPHRECTOMY IN AN AREA WITH LOW RATE OF DECEASED DONATION

Duilio Pagano¹, Davide Cintorino¹, Sergio Li Petri¹, Calogero Ricotta¹, Marina Romano¹, Pasquale Bonsignore¹, Marco Paci¹, Salvatore Gruttadauria¹, Tullio Bertan², Paola Salis², Bruno Gridelli¹, Marco Spada¹

¹Division of Abdominal and Transplantation Surgery, Istituto Mediterraneo per i Trapianti e Terapie a; ²Division of Nephrology, Istituto Mediterraneo per i Trapianti e Terapie ad Alta Specializzazione (IS)

Background: Laparoscopy nephrectomy (LN) for living donor kidney transplantation (LDKT) is a safe and appealing procedure to potential live donors and has increased the living donor pool at our center. This study aims to examine the role of LN for LDKT, which is a reliable alternative to cadaveric kidney transplantation (CKT).

Methods/materials: We performed 257 kidney recipients, including 126LDKT and 131CKT performed between 1999 and 2012. We report a single institution retrospective analysis from an ongoing clinical study on examining demographics, operative factors, and post-operative complications of donors for LN occurring over a 5-year period, focusing on the results of patients who underwent LN from 2007 to 2011 (n = 56).

Results: Mean donor age was 48 \pm 9 years; median operative time was 231 \pm 44' with an average estimated blood loss of 8 \pm 19 cc. The overall complication rate was 7%, with pleural effusion and prolonged post-operative pain (>4 days) being the most common. There were no cases of post-operative acute renal failure and no patients died during the post-operative course of 90 days. Donors from 2010 to 2011 (n = 32) enjoyed a shorter average length of stay (4 vs. 6 days) than patients from 2007 to 2009 (n = 24), (p = 0.04). Additionally, there was a trend towards decreased complications in the latter 2 years that did not reach significance.

Conclusion: The minimally invasive approach for living kidney donation is considered the "gold standard" compared to other surgical techniques due to its association with shorter organ harvesting procedures and shorter post-surgical hospitalization. In ISMETT, LDKT represents 49% of all kidney transplants performed since 1999: living donors not only benefited their recipients but also made cadaveric kidney graft available to other recipients. LN confirms LDKT as the newest and, both technically and ethically, most challenging development in kidney transplantation helping to combat organ shortage in an area with a low rate of deceased organ donation.

P403

ABO ANTIBODY REMOVAL OF PLASMAPHERESIS (PP) WITH INTRAVENOUS IMMUNOGLOBULIN (IVIG) BEFORE ABO-INCOMPATIBLE (ABOI) KIDNEY TRANSPLANTATION: SINGLE CENTER EXPERIENCE

Dong Ryeol Lee, Byung Chang Kim, Jong Pho Kim
Maryknoll General Hospital

Background: ABOI kidney transplantation is an inevitable option to overcome serious organ shortage. Outcome of ABOI grafts improved and became equivalent to compatible grafts. Variable protocols are adapted in different centers, however, there are few data on success rates of ABO antibody removal or relating to patients in who antibody removal fails. The purpose of this study was to evaluate the likelihood of achieving transplantation depending on ABO antibody titers.

Methods: Of 55 patients were enrolled between 2007 and 2012. We perform ABOI kidney transplantation using anti-CD20 antibody, tacrolimus and PP with IVIG. The median ABO titer was 1:64 (Range 8-4096). Transplantation was preceded when the ABO titer reached \leq 1:8. To determine the likelihood of achieving transplantation, the number of PP required to proceed transplantation and baseline ABO titer were analyzed.

Results: All 55 patients (100%) successfully completed transplantation after 5.75 \pm 4.3 PP with IVIG. Three patients did not reach target ABO titer and their achieved ABO titers at the time of transplantation were 1:16. The median follow-up duration was 18.1 month (Range 0.9-71.8). The mean age was 45.8 \pm 9.9 year and 65.6% were female. The median ABO titer was 2 (Range

1–16) at the time of transplantation, 4 (range 1–64) at 1 month posttransplantation and 4 (range 4–128) at the last follow-up, respectively. The number of PP to reach an ABO titer of $\geq 1:8$ was significantly correlated with baseline ABO IgG titers ($r^2 = 0.829$, $p < 0.001$) (Figure 1).

Conclusions: All 55 patients successfully performed ABOI kidney transplantation without failure to achieve transplantation. Three patients even failed to reach target titer at the time of transplantation, however, all of them were successfully transplanted. Though optimal ABO titer at the time of transplantation remains debatable, we carefully need to tailor protocol with target ABO titer of greater than or equal to 1:16 to expand kidney donor pool.

P404

THE IMPACT OF NATIVE KIDNEY DISEASE ON LONG-TERM ALLOGRAFT OUTCOME. A REPORT OF THE LAST DECADE

Elias David-Neto, Angelica Dias Lemos, Fabiana Agena, Nelson Zocoler Galante, Daisa Ribeiro David, William Carlos Nahas
Hospital das Clinicas – FMUSP

Studies usually address the impact of recurrent immune kidney diseases (KD) on renal allograft outcome. However, in the last decade, only a few have analyzed the outcome according to the clinical diagnosis of native KD, made at the time of renal transplantation. To address this issue we reviewed all non-sensitized (PRA $\leq 10\%$) first renal (only) transplants performed in adults/adolescents (≥ 14 years) between January 2000 to October 2011 as follows: Adult Polycystic Kidney Disease (ADPKD), $n = 83$ (7.0%); Immune KD, $n = 362$ (30.6%); Unspecified Chronic KD, $n = 276$ (23.4%); Chronic Tubulointerstitial Nephritis (CTIN), $n = 106$ (9.0%); Hypertensive Nephrosclerosis, $n = 194$ (16.4%); and Type II Diabetic Nephropathy, $n = 160$ (13.5%). During the decade, there was a progressive increase of type II DM as native KD but the other diagnosis remained stable. At transplantation, groups differed statistically regarding age, race, gender, pre-emptive Tx, donors and type of induction therapy. There were 46 recurrences of Immune KD during this study period. The 10-year death-censored graft survival (GS) analysis revealed ADPKD with the highest survival and Immune KD and nephrosclerosis with the lowest ($p < 0.01$), mainly due to higher incidence of recurrence (11%) in Immune KD and chronic allograft dysfunction (20%) in both groups. With ADPKD as a reference, univariate Cox analysis for death-censored GS showed a HR of 4.4 (95% C.I.: 1.07–33.38, $p = 0.039$) for Immune KD and 8.0 (95% C.I.: 1.92–33.1, $p = 0.004$) for Hypertensive Nephrosclerosis. By multivariate analysis that included all statistically significant variables at baseline, Nephrosclerosis as the diagnosis of native KD (HR: 6.2; 95% C.I. 1.48–25.99, $p = 0.03$) and recurrence (HR: 4.42; 95% C.I. 2.70–7.23, $p < 0.001$) were the risk variables for death-censored GS. These data indicate that not all native KD have similar outcomes and emphasize the importance of a more intense and detailed diagnosis at the time of renal transplantation.

P405

COMPARISON OF HIGH-PERFORMANCE-LIQUID CHROMATOGRAPHY-TANDEM MASS SPECTROMETRY VERSUS FLUORESCENT POLARIZATION IMMUNOASSAY FOR THERAPEUTIC DRUG MONITORING OF TACROLIMUS IN SOLID ORGAN TRANSPLANT RECIPIENTS

Yan Ting Yeo, Petrina Fan, Li Fang Goh, Puay Hoon Lee, Wai Yoong Ng, Terence Kee, Deepika Malya
Singapore General Hospital

Tacrolimus (FK) is an immunosuppressant used for prophylaxis of solid organ allograft rejection. It has a narrow therapeutic window and considerable intrapatient pharmacokinetic variability, making therapeutic drug monitoring (TDM) crucial. High performance liquid chromatography-tandem mass spectrometry (HPLC-TMS) is preferred to fluorescent polarization immunoassay (FPIA) as it measures the active parent FK drug and not its metabolites. Our hospital has replaced FPIA with a newer HPLC-TMS analytical method for TDM of FK. The primary aim of this study was to compare the performance of FPIA against HPLC-TMS for measurement of FK trough concentrations in solid organ transplant recipients (SOTRs). A secondary objective was to identify patient-specific factors that may influence the assay measurements of FK. A total of 528 pre-dose whole blood samples were drawn from 169 SOTRs receiving FK therapy. Samples were prospectively collected between June and September 2011. Analysis of FK concentrations was performed using HPLC-TMS and FPIA simultaneously. Relevant hematologic and biochemical data that could influence the assay results were collected. Median FK levels measured by HPLC-TMS was 0.6 $\mu\text{g/l}$ (-4 to 4.0 $\mu\text{g/l}$) lower compared to FPIA, corresponding to a percentage difference of 10.9% (-41 to 36.3%). The Spearman correlation coefficient was $r = 0.95$ and the resultant Deming regression equation was $\text{HPLC-TMS} = 0.87 \times (\text{FPIA}) + 0.13$. Multiple linear regression analysis suggests that the biochemical and hematological results have no significant influence on the difference in the assay results. Despite lower FK concentrations reported with HPLC-TMS as compared to FPIA, the difference was not clinically significant. High correlation was demonstrated between the methods. Thus our study suggests the transition of assay method from FPIA to HPLC-TMS for TDM of FK can be performed without adjustment to the current target therapeutic range.

P406

MELANOCYTE STIMULATING HORMONE TREATMENT DETERIORATES EARLY GRAFT FUNCTION IN EXPERIMENTAL BRAIN DEATH KIDNEY TRANSPLANTATION

Willem G. van Rijjt¹, Niels Secher², Rutger J. Ploeg³, Ulla Møldrup⁴, Anna K. Keller⁴, Yahor Chynau⁴, Harry van Goor¹, Rikke Nørregaard⁴, Henrik Birn⁴, Jørgen Frøkiær⁴, Søren Nielsen⁵, Henri G.D. Leuvenink¹, Bente Jespersen⁴
¹University Medical Center Groningen, the Netherlands; ²Aarhus University Hospital NBG, Denmark; ³University of Oxford, United Kingdom; ⁴Aarhus University Hospital Skejby, Denmark; ⁵Aarhus University, Denmark

Background: Delayed graft function (DGF) and primary non function (PNF) are serious complications following transplantation of kidneys donated after brain death (DBD). A renoprotective effect of α -MSH has been observed in various models of acute kidney injury. We hypothesized that α -MSH treatment of the recipient improves early renal graft function and reduces inflammation following DBD kidney transplantation.

Methods/materials: Twenty-four Danish landrace pigs were used. Brain death was induced in the donors ($n = 8$) by inflating a 22 Fr Foley urine catheter in the epidural space to increase intracranial pressure. After 4 h both kidneys were retrieved and stored for 18 h at 4°C in Custodioli₂ UW preservation solution. The recipients ($n = 16$) were randomized in a paired design into two groups transplanted simultaneously and treated with either α -MSH (200 $\mu\text{g/kg}$) or placebo at start of surgery, during reperfusion and 2 h post-reperfusion. The follow-up of the recipients was 10 h.

Results: α -MSH treatment reduced diuresis (Controls vs. $\hat{+}$ α -MSH: 2.1 vs. 1 ml/min at 10 h post-reperfusion; $p < 0.05$) and glomerular filtration rate (GFR, controls vs. $\hat{+}$ α -MSH: 14.4 vs. 9.6 ml/min at 10 h post-reperfusion; $p < 0.01$). Each gift of α -MSH resulted in decrease in mean arterial pressure (MAP) by 10 mmHg without any effect on heart rate. Also, at 10 h post-reperfusion LDH levels were increased in the α -MSH group (460 vs. 335 U/l; $p < 0.05$) while no differences in urea, ASAT or ALAT were observed. Cortical IL-6, IL-1 β or ICAM-1 mRNA expression was not reduced by α -MSH.

Conclusion: α -MSH reduced diuresis and GFR, which may be explained by decreased MAP. Markers of renal inflammation were not affected by α -MSH treatment. Thus, α -MSH showed no potential to improve early graft function following DBD kidney transplantation.

P407

POSTTRANSPLANT LYMPHOPROLIFERATIVE DISORDER PRESENTING AS A FACIAL PARESTHESIA WITH LOW CYCLOSPORINE LEVEL

Hyun Hee Lee, Yeon Ho Park, Woo Kyung Chung, Ji Yong Jung, Jae Hyun Chang, Han Ro
Gachon University

We need better understand the risk factors, clinical features, and the role of prolonged immunosuppression of late onset (>1 year) Posttransplant lymphoproliferative disorder (PTLD). Herein is reported an unusual presentation of very late onset PTLD. A 51 year old male received kidney transplantation in May 1995 and his immunosuppressive regimen was only cyclosporine with low trough level (70–90 ng/ml). He visited to the hospital with headache, tingling sensation of hand, and paresthesia on right cheek and right lower mandible area for 7 days. Neurologic examination including Brain MRI did not show abnormality. Ten days after, he admitted with aggravating paresthesia symptoms of right cheek and mandible area and newly developed pain on the left cervical lesion and parotid gland. The neck computed tomography showed infiltrative soft tissue involving left retropharyngeal, carotid space, and swelling of muscle within left masticate area. In addition, there were prevertebral soft tissue swelling and parotid gland enlargement. A biopsy of the soft tissue showed Burkitt lymphoma and Epstein Barr Virus (EBV)-encoded small RNA in situ hybridization for EBV was positive. At the time of PTLD, EBV infection in blood was negative. He was scheduled for chemotherapy but PTLD progressed rapidly. He died 2 weeks after admission. Late onset PTLD are associated with poor prognosis. It is necessary to have a high level of clinical suspicion and patient monitoring for prompt diagnosis of very late onset PTLD.

P408

A CASE OF THE SQUAMOUS CELL CARCINOMA IN NASAL CAVITY TREATED WITH SIROLIMUS IN A PATIENT WITH KIDNEY TRANSPLANTATION

Joon Seok Oh, Joong Kyung Kim, Yong Hun Sin, Kill Huh, Seong Min Kim, Jin Ho Lee
Bong Seng Memorial Hospital

There has been increased the interest on long-term complication of transplantation because of the increase the number of patients who maintain their graft for a long time. The use of target-of-rapamycin (m-TOR) inhibitors in immunosuppression-related malignancies has improved the quality of life and increased the survival in patients with solid organ transplantation. A 72-year-old male recipient of a living donor renal allograft (1998), who was immunosup-

pressed with cyclosporine, azathioprine, did initially well with acceptable renal function. Steroid was stopped at post-transplant 1 month due to new onset diabetes mellitus after transplantation. In 2011, the patient visit OPD for the onset of multiple inflammatory nasal polyps and it did not improved with local treatment for 3 months. Nasal polyp biopsy was performed at otolaryngology and the biopsy showed squamous cell carcinoma. Surgeons and dermatologists recommended the wide excision but patient refused surgery due to old age and cosmetic reasons. So cyclosporine was replaced by sirolimus. The size of local lesion was reduced after immunosuppressant conversion. Of 12 months after conversion, the lesion was disappeared in naked eye and recurrence has not been observed. In summary, a case of squamous cell carcinoma on nasal cavity in a renal transplant was treated by conversion cyclosporine to sirolimus without surgical removal. After 1 year of immunosuppression conversion, the local lesion showed good response.

P409

DEFINING PP65ENEMIA AND QPCR CUT-OFFS FOR PRE-EMPTIVE THERAPY OF CMV DISEASE IN LOW-RISK RENAL TRANSPLANTED RECIPIENTS

Elías David-Neto, Angelica Dias Lemos, Lucy Santos Vilas Boas, Acram Zahredine Abdul Latif, Fabiana Agena, Flavio Jota de Paula, Ligia Pierroti, Francine Lemos, William Carlos Nahas, Helio Caiaffa Filho, Claudio Sérgio Pannuti
Hospital das Clinicas, FMUSP

CMV disease mostly invasive gastro-intestinal with low viremia occurs in approximately 16% of CMV seropositive renal transplant recipients not receiving Thymoglobuline (ATG). Pre-emptive therapy (PETh) to avoid disease in this group should cover the majority of patients at risk (high Negative Predictive Value – NPV). To define cut-offs for whole blood real-time quantitative PCR (qPCR) and antigenemia (pp65) assays and use PETh for CMV disease we collected blood samples weekly from day 7 to 120 after TX in pts CMV IgG+ (IgG+ donors) who did not receive ATG. A suspicion of CMV disease required new qPCR/pp65 or biopsy. The highest value of pp65 and qPCR in pts without CMV disease one week before disease were used in ROC curves. 92 pts had completed the collections or developed disease. They were males (54%), caucasians (69%), mean age 45 ± 14 years, 61% deceased donors, all under TAC/MPA/Prednisone. Overall 12 pts had CMV disease (11 invasive gastro-intestinal/1 syndrome), at 64 ± 21 days, and 80 did not. Of these 80 pts, 56% presented at least one episode of asymptomatic viremia and cleared it spontaneously (18% had PCR+/pp65+; 56% Pp65+/qPCR– and 24% qPCR+/Pp65–). Among pts with viremia or disease there was a trend for a higher pp65+ cells for disease than for viremia (152 ± 352 vs. $31 \pm 131/106$ cells, $p = 0.073$), detected earlier for disease than viremia (64 ± 21 vs. 80 ± 25 days, $p = 0.049$). ROC curves (area 0.902 ± 0.036 , $p = 0.001$) revealed that pp65 of four cells had 83% sensitivity and 83% specificity to predict CMV disease. Using this cut-off, the NPV was 97%. The CMV copies detected by qPCR was higher for disease than for viremia (46657 ± 50671 vs. 5438 ± 16681 copies, $p = 0.001$) but time for detection was similar for both (74 ± 25 vs. 59 ± 18 days, $p = NS$). ROC curve (area 0.903 ± 0.056 , $p = 0.001$) revealed that qPCR–844 copies had 83% sensitivity and 86% specificity to predict disease with NPV of 97%. Both methods are adequate to detect CMV disease prior to its development in this low-risk population.

P410

QUESTION65 – A LONGITUDINAL STUDY DESCRIBING HRQOL IN ESRD PATIENTS OVER 65 YEARS LISTED FOR KIDNEY TRANSPLANTATION

Kristian Helda¹, Kjersti Lønning², Karsten Midtvedt²
¹Telemark Hospital; ²Oslo University Hospital, Rikshospitalet

Background: The incidence and age of patients who develop end stage renal disease (ESRD) are increasing. Consequently, an increasing number of elderly patients are becoming candidates for renal replacement therapy. Kidney transplantation is, in selected elderly patients, shown to provide superior survival compared to continued dialysis therapy. There is an ongoing debate whether elderly patients with ESRD should remain on dialysis or be wait-listed for transplantation. The documentation of how transplantation/immunosuppression interferes with health related quality of life (HRQOL) in elderly recipients is sparse.

Methods/materials: Patients >65 years will be asked to fill out the KDQOL-SF form at time of acceptance and every 6 months until transplanted or permanently removed from the transplant list. Post transplant, patients will receive a new form after 10 weeks, 6 months, 1, 3 and 5 years. We perform 300 renal transplantation/year and 25–35% of the recipients are >65 years. Mean waiting time for 1st renal transplantation has always been <12 months. Estimated inclusion-time is 2 years. Primary aim is change in scores between time of acceptance and 1 year after transplantation. Power calculation have concluded that 65 patients have to complete the study to reveal a difference of 10% in SF-36 GH score with a significance level (α) of 5% and a power (β) of 80%. The study is approved by the regional committee of medical ethics.

Results: From January 1st 2013 a total of 45 patients have been included and 4 of them are transplanted. No data analyses have been performed.

Conclusion: We believe that the study will provide important information about the effect of kidney transplantation on HRQOL in elderly recipients and thereby help clinicians in the choice between continued dialysis and transplantation for elderly patients with ESRD.

P411

POST-TRANSPLANT DIABETES MELLITUS AS RISK FACTOR

Alma Idrizi, Myftar Barbullushi, Nestor Thereska
UHC Mother Teresa

Background: Post-transplant diabetes mellitus (PTDM) has a reported incidence of 4–41%. It has been identified as one of the most important, being associated with reduced graft function and patient survival, and increased risk of graft loss. We have studied the prevalence of PTDM in patients followed in our renal transplantation unit.

Methods/materials: We undertook a retrospective analysis of the glycaemic status of 105 patients undergoing renal transplantation in the 5-year period.

Results: Thirteen patients developed PTDM (12.3%), 10 were males (9.5%) and three were females (2.8%). There was a variable onset and a wide range of symptoms. Six of males patients had body mass index (BMI) more than 30 kg/m². Insulin therapy was required for six patients with variable durations and with resolution of PTDM in all of them. High serum cholesterol and triglycerides levels were evidenced in all patients and hypertension was present in seven patients. PTDM did not adversely affect the renal graft function. Two of them were HVC positive.

Conclusions: The prevalence of PTDM in our patients is similar to that found in the literature. PTDM requires increased awareness among nephrologists and endocrinologists for early recognition and prompt effective intervention.

P412

CARDIOVASCULAR DISEASE AS RISK FACTORS AFTER RENAL TRANSPLANTATION

Alma Idrizi, Myftar Barbullushi, Nestor Thereska
UHC Mother Teresa

Background: The frequency of cardiovascular disease (CVD) is high after renal transplantation. Risk factors include pretransplant cardiovascular disease, diabetes, male sex, serum cholesterol, hypertension, cigarette smoking, and allograft dysfunction. The aim of this study is to find the frequency of CVD after renal transplantation.

Methods/materials: 105 transplanted renal patients, 26 females and 79 males, (mean age 34.8 ± 11.3 years, range 16–58 years) were studied during a period of 6 years.

Results: Patients with CVD were older than patients without CVD (age: 42.9 ± 12.08 vs. 36.7 ± 6.9 , $p < 0.01$), predominantly male (70% vs. 30%, $p < 0.05$). Prevalence of medical conditions was as follows: hypertension 72% (mean age 36.2 ± 8.3 years), ischemic heart disease 4%, dyslipidemia 47% and 20% were treated with statins, diabetes mellitus 12.3%, peripheral vascular disease 5%, cerebrovascular disease 2%.

Conclusions: CVD is the leading cause of mortality and morbidity. Arterial hypertension is highly prevalent after renal transplantation and may contribute to the risk of cardiovascular disease and graft failure. The prevalence and severity of CVD in our renal transplant recipients are frequent. They are related to numerous factors, including effects of kidney dysfunction and immunosuppressive drugs.

P413

EX VIVO FLEXIBLE URETERORENOSCOPY IN KIDNEY TRANSPLANTATION BULENT OKTAY, BERK KARATAS, MURAT SAMLI, HUSEYIN CELIK, SALIH GULTEN DEPARTMENT OF UROLOGY AND KIDNEY TRANSPLANT, ACIBADEM BURSA HOSPITAL

Berk Karatas, Bulent Oktay, Murat Samli, Huseyin Celik, Salih Gulden
Acibadem Bursa Hospital

Background: Routine CT angiography for screening of potential donors for kidney transplantation has been associated with an increase in the number of the patients with kidney stones. The optimal management of stone bearing kidneys at transplant is still unknown. We consider patient with small, unilateral, nonobstructing, incidental renal calculi for eventual renal donation. We performed *ex vivo* flexible ureterorenoscopic lithotripsy to make the kidney stone free at the time of kidney transplantation. We inspect the efficiency of *ex vivo* flexible ureterorenoscopic lithotripsy.

Methods/materials: After inspecting the metabolic evaluation, three patients with small nonobstructing unilateral urolithiasis diagnosed on preoperative CT angiography underwent donor nephrectomy. After cold arterial perfusion, flexible ureterorenoscopy was performed with cold saline irrigation. Stones was disintegrated with laser.

Results: Ureterorenoscopy was performed in three patients. A total of three calculi, largest diameter 4 mm, were visualized. Holmium laser lithotripsy was applied. After laser application all kidney was stone free. The mean treatment time was 20 min. There were no intraoperative complications.

Conclusion: *Ex vivo* flexible ureterorenoscopy safely made the kidneys stone free without complications. Performing this method with care in selected patients could increase the number of potential kidney donors.

P414

KIDNEY TRANSPLANTS – AN APPROACH FROM THE AGENCY THEORY APPLIED TO BRAZIL

Giácomo Balbinoto¹, Cassia Favoretto², Cassia Favoretto²
¹IATS/UFRGS; ²PPGE/UFRGS

Background: Brazil has the most public of transplants and occupies the second place (behind only the United States) in number (absolute) of surgeries of this size, with emphasis on the kidney transplant. **OBJECTIVES:** this paper aims to check and analyse the institutional mechanisms and incentives offered to hospitals that perform the abstraction of organs (especially kidneys) for transplants in Brazil using the theory of principal-agent.

Methods: The theoretical approach to be used is the principal-agent model under asymmetric information context (that is, when one side of the contract knows more on the other side). This theory is well suited to analyze this type of problem, because the main welfare (SUS) depends on the efforts of hospitals (agent) to capture the organs for transplants. SUS (principal) is responsible to prepare and propose a contract (developed from Brazilian legislation of transplants) hospitals (agent) to perform actions related to funding of organs for transplant.

Results and discussion: It is noteworthy that the level of effort made by the hospital depends on some measures which this does to improve uptake in organs and tissues, which are: training of transplant coordinators, acquiring knowledge of the clinical phases, bureaucratic and logistical donation process; regional meetings with intensivists; courses on organ donation and transplantation to all professionals who work in hospitals; regular meetings with journalists, communication experts and opinion formers; lectures and debates about organ donation.

Implications: It was found that the SUS has adopted various measures incentives for hospitals that perform the abstraction of organs, such as: creating a specific fund for financing of transplants; uniform payment to hospitals and universities; expansion of the types of hospital procedures to be paid by SUS.

P415

THE DIAGNOSTIC ACCURACY OF EARLY ULTRASONOGRAPHY AND DOPPLER PARAMETERS FOR KIDNEY GRAFT OUTCOME

Jadranka Buturović-Ponikvar, Senka Cerne, Andreja Ales-Rigler, Aljoša Kandus, Miha Arnot
 University Medical Center Ljubljana

Background: This study aimed to assess diagnostic accuracy of ultrasonography (US) and Doppler parameters of kidney graft measured at 1 month post-transplant to predict graft outcome.

Methods: The study cohort included 266 adult recipients of a deceased donor kidney transplant between Jan 2006 and Dec 2011. All patients had US-Doppler examination performed at 1 month post-transplant. Data collected were: graft length, parenchyma thickness, and Doppler indices measured at mid-segmental artery level. Parenchyma size index (PSI) was calculated by dividing parenchyma thickness with graft length. The primary outcome of interest was combined graft loss or doubling of the serum creatinine.

Results: After a median follow-up of 43 months, 37 patients reached the combined end-point. The receiver operator characteristic analyses demonstrated that PSI at 1 month post-transplant had good discriminatory ability to predict primary outcome with area under the curve (AUC) 0.71 (95% CI 0.63–0.78) and performed better when compared with graft size and parenchyma thickness (AUC 0.65 and 0.61, respectively). Among Doppler parameters, RI performed best with AUC 0.70 (95% CI 0.62–0.78). The PSI cutoff 1.35 mm/cm and RI cutoff 0.70 were associated with the best performance of the analyses (PSI: sensitivity 82%, specificity 72%; RI: sensitivity 85%, specificity 63%). At 1 month post-transplant, 116 patients (44%) had PSI <1.35 mm/cm and 27 (23%) patients reached the end-point versus 10/150 patients (7%) with PSI ≥1.35 mm/cm; 156 patients (59%) had RI ≥0.70 and 32 (21%) patients reached the end-point versus 6/110 patients (5%) with RI <0.70. In a multivariate Cox model, PSI <1.35 mm/cm (HR 2.90, 95% CI 1.40–6.03; p = 0.004) and RI ≥0.70 (HR 4.74, 95% CI 1.84–12.22; p = 0.001) were independent predictors of the combined end-point.

Conclusion: At one month after kidney transplantation, lower PSI and greater RI had good discriminatory ability to predict graft loss or a decrease in graft function.

P416

RESOLUTION OF TACROLIMUS-INDUCED CARDIOMYOPATHY AFTER CONVERSION TO BELATACEPT

Siddiq Anwar, Shane LaRue, Lyndsey Bowman, Timothy Horwedel, Daniel Brennan, Christina Klein
 Washington University School of Medicine in St. Louis

Background: Despite intensive cardiac screening for waitlisted patients, cardiac complications remain a leading cause of death in renal transplant

recipients (RTR). We present our experience of tacrolimus(tac)-induced cardiomyopathy(TICM) in an adult recipient which resolved after switching to belatacept.

Methods: A 62-year-old white female presented with new-onset congestive heart failure (CHF) and acute kidney injury six months after transplantation. She had received anti-thymocyte globulin induction and was maintained on tac (5–10 ng/ml), mycophenolate and prednisone. Left ventricular ejection fraction (LVEF), which was normal on stress echocardiography one month pre-transplant, was 30–35% at presentation.

Nuclear stress test was negative for ischemia. Her troponin levels, creatinine kinase, thyroid function, transplant doppler studies, B12 and folate levels, and viral screening were unremarkable. A transplant biopsy showed no evidence of rejection and donor specific antibodies were negative.

She had two further hospitalizations for CHF exacerbation and creatinine remained elevated at 3 mg/dl despite maximal medical therapy for CHF. Due to the concern of TICM, tac was changed to belatacept at 7 months post-transplant. LVEF normalized (55–60%) four months after belatacept conversion, and her renal function returned to 1.4 mg/dl.

Discussion: TICM has been reported in children and may involve its vasoconstrictive effects causing decreased blood supply to myocardium; however it is rare in adults. We describe a RTR with normal pre-transplant cardiac function developing non-ischemic cardiomyopathy within 6 months. LVEF normalized within months after tac withdrawal, and in the absence of other identifiable etiology and intervention strongly supports a TICM. Reinstitution of tac and recrudescence of CHF would have fulfilled Koch's postulates but was deemed unethical.

P417

COULD WEB-BASED DELAYED GRAFT FUNCTION CALCULATOR BASED ON WESTERN POPULATION APPLY ON OTHER ETHNIC GROUP?

Mee-Hyung Kim¹, Sang Il Kim¹, Young Kyun Kim¹, Jeong Kye Hwang², In Soo Park¹, In Sung Moon¹

¹Seoul St.Mary's Hospital, College of Medicine, The Catholic University of Korea; ²Daejeon St.Mary's Hospital, College of Medicine, The Catholic University of Korea

Background: Delayed graft function (DGF) occurs in approximately 5–50% of deceased donor renal transplantation (DDRT). It is associated with increased risk of acute rejection and poorer long-term graft survival. If we can predict the DGF before DDRT, we may assist in the allocation of marginal organs or direct interventions to prevent or ameliorate DGF. A novel web-based DGF risk calculator (www.transplantcalculator.com) was developed by Irish et al. It is an easily accessible tool for predicting DGF, but the predictive performance of this model has not been tested in Asians. The aim of study is to assess the usefulness of this prediction model in Korean DDRT.

Methods: A total of 195 subjects, who underwent DDRT in our hospital from January 2000 through December 2011, were reviewed. The recipient, donor, and transplant variables were recorded, and individual DGF risk was assessed using the web-based. Continuous variables were analyzed using Student's t-test and categorical data by chi square test. Logistic regression analysis was used to determine the odds ratio for DGF according to the calculated DGF risk value. DGF discrimination ability was measured by sensitivity, specificity, positive predictive value and ROC curve c statistic. All data analyses were performed using statistical software PASW Statistics 18 (SPSS, Chicago, IL, USA).

Results: The overall rate of DGF in our study was 15.9% and the average individual web calculated risk of DGF was 16.1% (15.2%). The mean calculated DGF risk was significantly different between patients with DGF (30.2% (21.2%) and those without (13.3% (12.0%), p < 0.00). The area under the ROC curve to predict DGF was 0.820 (95% CI 0.733–0.907, p < 0.000). The sensitivity, specificity and positive predictive value of a calculated DGF risk >14.5% were 76.9%, 75.9% and 38.5%.

Conclusions: This web-based DGF calculator can be usefully applied to predict DGF in Korean DDRT.

P418

THE NATURAL HISTORY OF THE ARTERIOVENOUS ACCESS AFTER SUCCESSFUL KIDNEY TRANSPLANTATION: FACTORS ASSOCIATED WITH SPONTANEOUS CLOSURE

Ji IL KIM¹, In Soo Kim¹, Mee-Hyung Kim¹, Jeong Kye Hwang², Sang Il Kim¹, In Sung Moon¹

¹Seoul St.Mary's Hospital, College of Medicine, The Catholic University of Korea; ²Daejeon St.Mary's Hospital, College of Medicine, The Catholic University of Korea

Purpose: After successful kidney transplantation (KT), arteriovenous (AV) access is neither used nor useful. There are many debates whether to preserve an AV access or to perform a systematic fistula closure. But there is no data concerning the fate of AV access after successful KT. The purpose of this study is to determine the natural history of AV access after successful KT, and to identify the risk factor of spontaneous access closure in KT recipients.

Methods: We performed a retrospective review of patients undergoing KT from June 2010 to July 2012. Among them, only 115 patients with functioning AV access on operation day were included. VA access patency was checked and recorded daily in hospital stay and every visit of outpatient clinic.

Results: Mean patients age was 46.8 (±9.3) years. There were 71 male. Mean duration from AV access construction to KT was 1937 (±1864) days and mean follow-up after KT was 385 (±25) day. The majority of patients (85.2%) had a native AV access and eighty patients (69.6%) had an AV access at wrist. At the end of follow-up, eighteen (15.7%) AV accesses were spontaneously closed. Mean time to closure was 119 (±163) days, and 12 out of 18 were closed within 90 days after KT. AV access was spontaneously closed in 8.5% of male patients and 27.3% of female patients ($p = 0.007$), 12.2% of native AV access and 35.3% of artificial AV access ($p = 0.016$), and 11.3% of wrist AV access and 25.7% of elbow AV access ($p = 0.049$). Spontaneously closed AV access had lower mean access flow when compared functioning access ($p = 0.019$). On multivariate analysis, only female gender, and AV access flow volume affected spontaneous AV access closure.

Conclusions: This study suggests the surgical closure of a functioning AV access in male patients or high output AV access could reduce unnecessary waiting times requiring spontaneous closure in patients with a high risk of AV access complications.

P419

REDUCTION OF BMD (BONE MINERAL DENSITY) AND LEVELS OF PTH IN KIDNEY TRANSPLANT PATIENTS

Valentina Nastasi, Domenica Taruscia, Brigante Fabiana, Mario D'Arezzo, Emilio Balestra, Maria Stefania Pugliese, Giovanni Maria Frasca
Nephrology, Dialysis and Transplantation Unit – Ospedali Riuniti, Ancona

Background: after kidney transplantation occurs reduction in BMD at the vertebral column and at the femoral neck, that is highest during the first months but can persist in the long term. The etiology is multifactorial: persistent hyperparathyroidism, pre-existing renal osteodystrophy, immunosuppressive therapy, VitaminaD deficiency. The aim of the study is to analyze the role of PTH in BMD reduction.

Patients and methods: Of 153 patients, 89 males and 64 females. Age 52.3 ± 0.8 years, follow-up 31.4 ± 1.4 months (mean ± standard error). Exclusion criteria: creatinine >2 mg/dl. Immunosuppressive therapy: basiliximab + steroids (1.6–2 mg/kg/die progressively reduced to 5 mg within 45 days) + calcineurin inhibitors + mycophenolate mofetil. The patients were studied by PTH and bone densitometry at the femur and at the vertebral column. Osteopenia was defined for T-score between –1 and –2.5, and Osteoporosis for T-score <–2.5. We considered two PTH levels to define hyperparathyroidism: 80 and 150 pg/ml. We analyze data by chi-square test. **Results:** 28.1% of patients had normal BMD at the femur and at the vertebral column. 46.4% and 16.3% of patients had respectively Osteopenia and Osteoporosis at the femur. 39.2% and 18.3% of patients had respectively Osteopenia and Osteoporosis at the column. 55.2% of patients had PTH > 80 pg/ml and 18.1% had PTH >150. In the group with PTH >80, 55.7% of patients had Osteoporosis/Osteopenia at the femur and 50.9% of patients had normal BMD (Odd Ratio 1.21, $p > 0.05$). 56.4% of patients had osteopenia/osteoporosis at the column and 56.1% had normal BMD (Odd Ratio 1.1, $p > 0.05$). In the group with PTH >150, 16.9% of patients had Osteopenia/Osteoporosis at the femur and 20% had normal BMD (Odd Ratio 0.75, $p > 0.05$). 16.4% of patients had Osteopenia/Osteoporosis at the column and 20.9% of patients had normal BMD (OR 0.75, $p > 0.05$).

Conclusion: There were no significant differences in the levels of PTH between patients with Osteopenia/Osteoporosis and patients with normal BMD. Not only hyperparathyroidism but also low levels of PTH are associated with reduced BMD.

P420

PREVALENCE AND TREATMENT OF PROTEINURIA IN LONG-TERM KIDNEY TRANSPLANT PATIENTS

Martha Belete¹, Sharon Frame², Francis Dickinson², David Goldsmith², Antonia Cronin³

¹King's College London; ²Guy's and St. Thomas' Hospital; ³Guy's and St. Thomas' Hospital and Kings College, London

Background: Survival rates following kidney transplantation have improved significantly. However mortality in long-term kidney transplant patients (LKT) remains high compared to age-matched general populations. Cardiovascular disease (CVD) is a major cause of morbidity and death among this group. Proteinuria (P) is an important independent risk factor for CVD. The degree of P has prognostic and diagnostic implications. ACE/ARB therapy has been shown to reduce P in CKD patients, and some studies suggest their anti-P action is additive. Use of ACE/ARB in LKT is more complex and less well defined.

Methods: Urinary PCR, GFR, BP measurements and drug lists of 335 LKT (>8 years from transplant) seen between 2010 and 2012 were retrieved and analysed.

Results: Of 257 (77%) LKT had PCR <50, 40 (12%) PCR 50–100, and 38 (11%) PCR > 100. Mean GFR was 45 ml/min (range 15–122) and mean BP 136/77. PCR >100 was associated with raised BP (mean 140/80) and lower

GFR (mean 41 ml/min). 33(13%)/19 (7%) LKT with PCR <50, 6 (15%)/5 (13%) with PCR 50–100 and 12 (32%)/15 (40%) with PCR >100 were on ACE/ARB respectively. 14 LKT with PCR >100 were not taking ACE/ARB. Of these: three had CKD stage 5; two died; four commenced ACE/ARB; two had PCR incorrectly recorded; two had recurrent UTIs and one had PCR >100 when pregnant. Three LKT with PCR >100 were on ACE and ARB: of these one had recurrent IgA; 1 FSGS and one had PCR >400.

Conclusion: The majority of our LKT have stage 3 CKD. PCR >100 is uncommon but not rare and associated with raised BP and lower GFR. LKT with PCR >100 were more likely to be on ACE/ARB. A significant proportion not on ACE/ARB had graft failure or died. Targeted ACE/ARB use may improve long-term graft survival and reduce mortality. Prospective follow-up of this cohort is warranted.

P422

KIDNEY TRANSPLANT (KTX) 13 YEARS AFTER LUNG TRANSPLANTATION (LTX) FOR BRONCHIECTASIAE

Mario D'Arezzo, Valentina Nastasi, Domenica Taruscia, Maria Stefania Pugliese, Emilio Balestra, Emilio Balestra, Fabiana Brigante, Giovanni Gaffi, Giovanni Maria Frasca

Nephrology, Dialysis and Transplantation Unit – Ospedali Riuniti, Ancona

Introduction: Patients with solid organ transplants (excluding kidney transplant) might develop renal failure in a percentage between 10% and 80% and 20% of these patients have an end stage renal disease (ESRD) 0.6% of patients with LTX have renal failure and the 12% of these have ESRD. A possible cause is the employment of calcineurin inhibitors. This study reports the case of a 70 years old woman with lung transplant who was underwent to dialysis and who received KTX.

Case report: Woman, 70 years old. When she was 4 years old, measles pneumonia and bronchiectasies were diagnosed. During the following years the patient had several respiratory infections and she developed respiratory insufficiency. When she was 56 years old, she underwent LTX. Immunosuppressive therapy: steroids + MMF + cyclosporine. After one year she developed renal failure and after 5 years she underwent dialysis. The Cyclosporine was stopped. For serious vascular access problems, she was placed on the waiting list for KTX. At that time the comorbidities were: HCV related hepatitis, CMV infection, recurrent pulmonary infectious episodes, respiratory insufficiency, pathological fractures. The patient underwent KTX 8 years after the start of dialysis. Immunosuppressive therapy: steroids + MMF. The postoperative course was characterized by the prompt recovery of renal function, but it was complicated by the onset of thrombosis at the femoral vein and severe respiratory failure secondary to aspergillus. At the hospital discharge the creatininemia was 1.2 mg% and the immunosuppressive therapy was prednisone 10 mg/day, tacrolimus 1 mg/day, MMF 180 mg/b.day.

Conclusion: Renal failure is a common complication of solid organ transplants and sometimes requires replacement therapy. Despite comorbidity, the patients with solid organ transplant in dialysis have longer survival if they received a KTX. The data of literature show that the survival is 60–70% better than patient on dialysis.

P423

THROMBOPHILIA AND PRIORITIZATION DUE TO DIALYSIS ACCESS FAILURE IMPACT EARLY ON PATIENT SURVIVAL AFTER KIDNEY TRANSPLANTATION

Jose O. Reusing Jr, Patricia S. Souza, Nelson Z. Galante, Fabiana Agena, Flávio J. Paula, William Carlos Nahas, Elias David-Neto
Hospital das Clinicas, FMUSP

Dialysis vascular access failure, recipient of a non-renal solid organ transplantation and previous kidney donation are current indications of priority allocation (PA) for kidney transplant (KT) at our centre. We analyzed a cohort of patients that received KT from Jan/2007 to Dec/2011. Long-term patient survival was compared between PA and non PA recipients transplanted in this period of time and clinical relevant data were analyzed.

Results: Of 948 KT were performed at our institution and 93 (9.8%) were included in our PA program. Most PA patients ($n = 86$) had access failure. Mean follow up time was 32 (0–69) months. 5-year patient survival was lower in PA patients (76 vs. 86%, $p = 0.001$). Twenty (21.5%) PA patients died, being 70% of them in the first 3 months. Final causes of death: infection (10 patients), bleeding ($n = 6$), uremia ($n = 1$), mesenteric ischemia ($n = 1$) and unspecified shock ($n = 2$). Because of this high mortality rate we compared patients who died in the first 3 months (group A) vs. those who survived (group B). Age, gender, previous kidney transplants, sensitization, pre-transplant DSA, pre-transplant diabetes, induction therapy, DGF, rejection, use of heparin and time from inscription in the PA program to transplantation were not statistically different between groups. Among 47 patients who were screened for thrombophilia, 83.3% from group A were positive vs. 31.7% from group B ($p = 0.01$). Infection after transplantation and hemorrhagic complications were more frequent in group A. Groups were not different regarding causes of death. Multivariate Cox proportional hazard models for patient survival showed a HR of 5.2 (95% CI, 1.02–26.74, $p = 0.047$) for thrombophilia.

Conclusion: PA patients have a lower survival and this excessive death rate occurs in the first 3 months after transplantation. Thrombophilia is very frequent in PA patients with HR 5.2 for death.

P424

DOES ATG REALLY BURDEN SURVIVAL DECEASED DONOR KIDNEY WITH DELAYED GRAFT FUNCTION TRANSPLANTS?

Hakan Sozen¹, Utku Yılmaz², Sükrü Sındel³, Galip Gür³, Aydın Dalgıç⁴
¹Gazi University Transplantation; ²Gazi University Transplantation Center; ³Gazi University Nephrology; ⁴Gazi University General Surgery

Delayed graft function(DGF) increases morbidity after transplantation, prolongs hospitalization and may lead to premature graft failure.
Aim: To assess outcome of ATG implementation in DGF developed deceased donor kidney transplants(DDKT).
Material and methods: Totally 62 DDKTs were performed at Gazi University Transplantation Center, Ankara/Turkey. Eight patients disqualified from study because of receiving only IL2r blocker. Fifty four patients received ATG and 42 out of 54 patients were suitable for DGF criteria. Data retrospectively collected from charts and hospital files who received ATG for DGF. ATG was given in case of DGF onset at D1 after transplantation from dose of 2-3 mg/kg/IV infusion until the serum creatinine(Cr) decreases spontaneously 50% or Cr <3 mg/dl.
Results: DGF was detected in 42(68%) out of 62 DDKT. There were 24 female and 18 male recipients. In patients with DGF, mean cold ischemic time was found as 21 ± 6.1 h. Mean mismatch was 3 ± 1.7. Mean donor age was 41 ± 19 years. The duration of ATG administration was 9.4 ± 4 days (median 10, 8-15 days). The median length of follow-up was of 42.5 months (range, 1-77 months). Six (14%) acute rejection (ARx) episodes were seen during follow-up. ARx treated successfully with pulse steroids. Totally five viral infections (3 BK, 1 CMV, 1 parvo) were detected. Totally six grafts were lost during median 42.5 months of follow-up; 2 BK, 2 HUS, 1 dual kidney, 1 unknown reason. No PDL or other malignancies in this study. Patient and death-censored graft survivals for 1, 3 and 5 years are 100%, 97%, 93% and 89%, 86%, 86% respectively.
Conclusion: Renal transplantation population continues to be negatively impacted by DGF. Patients with DGF seem similar patient and death censored graft survival compared with literature. However they experienced increased viral infections during the first year after transplantation and a substantially higher frequency of acute rejection rates.

P425

IVIG IN HEART VERSUS KIDNEY TRANSPLANTATION: A FRENCH NATIONAL SURVEY

Jacques Dantal¹, Romain Guillemin², Yvon Lebranchu³, Christophe Legendre⁴, Emmanuel Morelon⁵, Lionel Rostaing⁶, Shaïda Varnous⁷, Sophie Puget⁸
¹Hotel-Dieu Hospital, Nantes, France; ²Européen Georges Pompidou Hospital, Paris, France; ³University Hospital, Tours, France; ⁴Necker Hospital, Paris, France; ⁵Edouard Herriot Hospital, Lyon, France; ⁶University Hospital, Toulouse, France; ⁷Pitié-Salpêtrière Hospital, Paris, France; ⁸LFB Biomedicaments, Les Ulis, France

Intravenous Immunoglobulin (IVIG) preparations are increasingly used for controlling patients' immune response in kidney or heart transplantation to achieve desensitization or for prophylaxis/treatment of humoral acute rejection (HAR). In France, little is known about the management of renal and heart transplant patients. This French national survey aimed to identify indications requiring treatment with IVIG in transplant recipients and to evaluate management of these patients in each indication. Of 28 kidney and 16 heart transplant centers (76% of French centers) participated to face-to-face interviews between November 2011 and April 2012. The number of highly sensitized patients increased between 2009 and 2011: 38 to 64 patients in 16 heart centers and 600 to 973 in 28 kidney centers. In both pathologies, HAR prophylaxis increased between 2009 and 2011 (16 to 43 patients in heart centers and 137 to 251 patients in kidney centers). HAR treatment remained stable between 2009 and 2011 (19 to 22 in heart centers and 108 to 132 in kidney centers). Desensitization is seldom used in cardiology (11 patients in heart centers and 40 patients in kidney centers in 2011). In prophylaxis, patient's profile differs between kidney and heart transplant: MFI (Median Fluorescence Intensity) levels are taken into account by 88% cardiologists, whereas presence of DSA (Donor Specific Antibodies) or hyper-immunization are more relevant for kidney centers. In 2011, the HAR prophylaxis protocols are notified by seven heart versus 19 kidney centers: Plasmapheresis alone (14% vs. 26%); Plasmapheresis + IVIG (29% vs. 11%); Plasmapheresis + IVIG + rituximab (14% vs. 16%); IVIG alone (57% vs. 68%); IVIG + rituximab (14% vs. 21%). Heterogeneity of therapeutic care underlines the need for joint recommendations and for further clinical studies.

P426

PURE LAPAROSCOPIC TRANSPERITONEAL DONOR NEPHRECTOMY FOR LIVING DONOR KIDNEY TRANSPLANTS

Aydın Dalgıç¹, Utku Yılmaz², Metin Onaran³, Hakan Sozen⁴
¹Gazi University General Surgery; ²Gazi University; ³Gazi University Urology; ⁴Gazi University Transplantation Center

Laparoscopic donor nephrectomy has gained community acceptance by physicians and patients over the past decade. Aim of this study to report a single-institution results of pure laparoscopic donor nephrectomy (pLDN) by using transperitoneal approach.
Patients and methods: Totally 44 donors were enrolled for this study. Twenty five female and ten male subjects of mean age of 41.5 ± 9 (between 22 and 65 years) years were operated since Jan 2008 at Gazi University Transplantation Center, Ankara. Data retrieved from patient charts, hospital files.
Results: The mean operative time for laparoscopic donor nephrectomy was 214 ± 38.92 min (range 125-350 min), with a mean warm ischemia time of 3.2 ± 1.2 min (range = 2-5 min). Thirty nine of the donor kidneys were left kidney, five kidneys were right kidney. The donors' mean hospital stay was 8.3 ± 1.8 days (range = 5-12 days). Only one donor (2.2%) operation was converted to open nephrectomy because of abnormal anatomy. Only one donor needed to blood transfusions (one Unit erythrocyte suspension) after surgery. One patient was taken to the operating theatre after surgery due to bleeding from trocar entrance. Only one minor late surgical complication was registered (left inguinal hernia) among 44 donors. The mean creatinine level of the recipients' was 1.12 ± 0.38 mg/dl at the discharge. ATN was seen in one recipient at the first case. It was resolved by 5 days of ATG (2 mg/kg-day) administration. There were two urine leaks after transplantation in one pediatric and adult recipient as urologic complications. These leaks have been treated by conventional radiology by using retrograde nephrouretostostomy and DJ catheter insertion.
Conclusion: Today, pLDN has become the golden and standard approach for living kidney harvesting in many centers as well as in our institution. In this study we have demonstrated that transperitoneal pLDN is feasible and safe for donor and recipient.

P427

COMPARISON OF EARLY VERSUS LATE URETERIC STENT REMOVAL AFTER KIDNEY TRANSPLANTATION

Gwyn Lee¹, James Herzog², Charlotte Crotty², Keyur Shah¹, Michael L. Nicholson¹, Sarah A. Hosgood³
¹University of Leicester; ²University Hospitals of Leicester; ³Department of Infection Immunity and Inflammation, Leicester General Hospi, University of Leicester

Background: There is evidence that urological complications after renal transplantation are less frequent if the ureteric anastomosis fashioned over a JJ stent. The increase in rate urinary tract infection (UTI) associated with stenting may be prevented by septrin. Intra-operative suturing of the stent to the urethral catheter and subsequent co-removal (ESR) obviates the need for a second procedure to remove the stent (LSR).
Methods/materials: A retrospective review was carried out on the notes of 52 patients who underwent kidney transplantation at Leicester General Hospital between January and August 2011. Of 26 patients had ESR at 5 days post op. 26 patients in the LSR group had their stent removed cystoscopically at 5-6 weeks. Of 26 ESR and 23 LSR patients had septrin as PCP prophylaxis. The outcomes in this study were eGFR at 12 months, incidence of treated or microbiologically proven UTI, and incidence of stenosis, nephrostomy, leak (urological complications). Demographic information (age, gender, mode of donation rejection) were recorded for matching purposes.
Results: Average eGFR at 12 months: ESR: 45 SD 23 ml/min vs. LSR: 56 SD 15 ml/min (p = 0.127). Incidence of UTI in the ESR group was 14/26 (53%) vs. 8/26 (30%) for LSR (p = 0.16). Relative risk (RR) = 0.67. 95% confidence interval (CI) 0.41-1.1. Incidence of urological complications after ESR was 6/26 (23%) vs. 3/26 (12%) for LSR (p = 0.46). RR = 0.87 CI 0.096-1.97. Graft loss was equivalent at 1/26 (4%). p = 1, RR = 1, CI 0.06-17.
Conclusions: In this small study, ESR was associated with an excess of UTI, and urological complications. EGFR at 12 months was higher with LSR. None of the differences reached statistical significance. Graft loss was equivalent in both groups. Even though there are potential risks to the patient and extra costs associated with readmission of patients for stent removal, this small study suggests that LSR is associated with a lower rate of UTI and urological complications.

P428

A RARE CAUSE OF ULCERATIVE LESION OF THE PALATE AND FEVER IN A RENAL-TRANSPLANT RECIPIENT

*Paola Donato*¹, *Rosario Marchese-Ragona*², *Lorenzo Vallese*¹, *Francesco Marchini*³, *Paola Striton*², *Cristina Silvestre*¹, *Lucrezia Furian*¹, *Paolo Rigotti*¹
¹Kidney and Pancreas Transplantation Unit, University of Padova, Padova, Italy; ²Department of Neurosciences, Institute of Otolaryngology, Padova University, Padova, Italy; ³Nephrology Unit, Padua

A 60-year-old woman with a long history of renal transplantation was admitted to the hospital because of a long-lasting ulcerative lesion on the palate with halitosis, dysgeusia and fever. She underwent cadaveric renal transplantation 15 years ago. Immunosuppression was based on Cyclosporine, Azathioprine (switched to Mycophenolate Mofetil for the last four years) and Steroids. Nine months before admission, she experienced mild fever, associated with the occurrence of a deep ulcer on the left side of the posterior hard palate for which she underwent elsewhere, wide excisional biopsy on September 2010. The histological exam revealed inflammatory tissue without evidence of neoplastic changes. In absence of spontaneous resolution, another incisional biopsy of the ulcer was performed, on February 2011, which confirmed the same result. Blood samples revealed positive CMV-DNAemia and BKV-DNAemia. Aspergillus antigen, QuantiFERON-TB test and VDRL-TPHA testing were negative. Chest and neck CT scan were negative. A facial bones CT scan excluded bony erosions or presence of abscess of the palate. A clinical assessment on arrival at our Hospital suggested the clinical diagnosis of necrotizing sialometaplasia (NS). We carried out a further biopsy of the ulcer and histological examination showed oral mucosa with necrotizing ulcerative, inflammatory granulation tissue and pseudoepitheliomatous hyperplasia, suggestive of necrotizing sialometaplasia (NS). Treatment was based on 75% reduction of Cyclosporine dose, ceftriaxone and meropenem, switched subsequently to tetracycline and azithromycin, associated with nystatin and benzydamine hydrochloride mouth-washes obtaining prompt resolution of symptoms. One year later the patient is still in fair condition, the palatal ulcer completely healed and dysgeusia and halitosis disappeared. Immunosuppressive therapy reduction has led to a complete healing of NS. NS is a rare benign inflammatory reactive necrotizing process, manifesting itself as an ulcerative lesion on the palate, that can involve minor and major salivary glands. Recognition of necrotizing sialometaplasia is important because this lesion may mimic malignancy, and misdiagnosis may result in unnecessary surgical therapy. Complete healing of NS usually occurs without treatment within 3–12 weeks. The clinical course of the ulcer in our patient, longer than usual, can be explained by the effect of immunosuppressive therapy. The exact pathophysiology of NS is unknown but gland tissue ischaemia has been proposed as the aetiology. Its correlation with immunosuppression is unknown.

P429

HORSESHOE KIDNEY TRANSPLANTATION (HKT)

Francesco Nacchia, *Umberto Tedeschi*, *Francesca Fior*, *Rostand E. Momo*, *Luigino Boschiero*
 AOUI, Dipartimento di Chirurgia, Centro Trapianti Renali

Introduction: Transplant experience with HKT is limited, though transplanted after split or en bloc. Literature reports 23 en bloc and 57 split HKT.

Materials and methods: We report four HKT, one splitted and three en bloc; donors and recipients age was 33–72, 37–65 year-old respectively. The en bloc HKT consisted aorta end-to-side anastomosis to the common iliac artery (two cases) or external iliac artery (one case); inferior vena cava end-to-side to the common or external iliac vena. Cranial vessels ends closed immediately above the most cranial renal vessel to avoid a cul de sac. Separate stenting ureteroneocystostomies were performed. The split HKT had a single artery and complete double collecting system for each moiety; isthmus drained into left and right system separately by properly collecting system.

Results: Three patients had immediate function and one delayed graft function (DGF); no technical complication. Mean discharge creatinine 96 μM , three patients have good functions (mean creatinine 107 μM) after 3 years f-up, one died after 2 years (ischemic heart disease) with functioning kidney.

Conclusions: Many concerns exists about HKT. However, HKT may have acceptable results if performed by expert center, minimizing surgical complication.

P430

USE OF ECULIZUMAB IN A HIGHLY HLA-SENSITIZED RENAL TRANSPLANTATION PATIENT

*Federico Cicora*¹, *Javier Robert*², *Fernando Mos*¹, *Marta Paz*¹
¹Hospital Aleman, Buenos Aires, Argentina; ²FINAER, Buenos Aires, Argentina

Introduction: First reported case of eculizumab use in Latin America, administered to prevent antibody mediated rejection (AMR) in a highly HLA-sensitized renal transplant recipient.

Method and patient: A 51-year-old man referred poor life quality after 10 years of haemodialysis, and underwent second renal transplant, living related. PRA was >70%. He received 4 sessions of plasmapheresis with

intravenous immunoglobulin (IVIg) 100 mg/kg days -11, -9, -7, -5. On day -7, tacrolimus 0.1 mg/kg daily and MMF 1440 mg daily until day 0 were started. Induction: antithymocyte globulin 1.25 mg/kg before declamping, five doses of IVIg 400 mg/kg. Methylprednisolone 500 mg day 0, 250 mg day 1, 125 mg day 2. Prednisone 1 mg/kg daily to reach 20 mg daily on day 30. Tacrolimus continued with goal trough 8–12 ng/ml and MMF 1440 mg daily. Eculizumab protocol was 1200 mg 2 h before transplant, 600 mg on day 1, 600 mg weekly thereafter for 4 weeks, and, at day 30, 1200 mg (Stegall et al Am J Transplant 2011; 11:2405–13). Anti HLA reactivities were studied by Luminex, shown as mean fluorescence intensity (MFI). Endpoints: incidence of biopsy-proven AMR and creatinine level (Cr).

Results: Three months before transplant, crossmatch was negative for lymphocytes T and B, Luminex showed anti-HLA Class I and II antibodies, and MFI were 2976 for anti-A2, 5555 for anti-A66, and 11921 for anti-DQ6. One month before transplant, patient was immunized against pneumococcus and meningococcus. On day 0, Cr 10.4 mg/dl. Tacrolimus dose was reduced on day 2. On day 6, Cr 7.7 mg/dl, biopsy confirmed calcineurine inhibitors toxicity lesions, negative C4D, no capillaritis or glomerulitis. On day 14, patient was discharged, Cr 2.28 mg. On day 30, Cr 1.56 mg/dl, biopsy confirmed no cellular rejection or AMR, C4D negative.

Conclusion: Using eculizumab to prevent AMR, a highly sensitized renal transplant patient, with preformed donor specific anti-HLA antibodies showed good graft function in the short ter.

P431

PROSPECTIVE CONTROLLED PROTOCOL FOR 3 MONTHS STEROID WITHDRAWAL WITH TACROLIMUS, BASILIXIMAB, AND MYCOPHENOLATE MOFETIL IN RENAL TRANSPLANT RECIPIENTS

Chang-Kwon Oh, *Jong Hoon Lee*, *Ji Hye Kim*
 School of Medicine, Ajou University

Introduction: During the past few years, the new immunosuppressants such as tacrolimus, mycophenolate mofeti (MMF), and basiliximab, have led to important declines in the incidence of acute rejection and could provide a more potent substrate to attempt safe steroid withdrawal.

Methods: We analyzed the clinical outcome of 3 months steroid withdrawal protocol using tacrolimus, MMF, and basiliximab. This 12-month study was an open-label, prospective, controlled clinical trial in a single center. For the patients who entered the protocol, prednisolone was slowly withdrawn by 2.5 mg in every two weeks until 8 weeks after entering the protocol (5 months post-transplantation).

Results: Thirty de-novo renal transplant recipients were enrolled. During the steroid withdrawal, seven patients (26.0%) discontinued the protocol and maintained on steroid treatment. Among 20 patients with the steroid free immunosuppressions with tacrolimus and mycophenolate mofetil, eight patients (40.0%) re-started the steroid. At 12 months after transplantation, patient and graft survival were 100%. Estimated GFR at 3 months, 6 months, and 12 months post-transplantation were 58.9 \pm 16.4 ml/min, 53.2 \pm 17.9 ml/min, and 49.7 \pm 16.0 ml/min, respectively.

Conclusions: This study confirms that 3 months steroid withdrawal with tacrolimus, basiliximab, mycophenolate mofetil in kidney transplantation is not associated with increasing mortality or graft loss. Steroid withdrawal after 3 months is a strategy that could be well advised.

P432

KIDNEY TRANSPLANTATION USING GRAFT WITH SMALL NEOPLASTIC LESIONS

Francesca Fior, *Francesco Nacchia*, *Rostand E. Momo*, *Umberto Tedeschi*, *Luigino Boschiero*
 AOUI Verona, Dipartimento di Chirurgia, Centro trapianti renali

Introduction: The widening gap between kidney transplant demand and supply prompted the expansion of selection criteria for donation to increase the available donor pool. Among donors with expanded criteria are even those with small renal cancers. We report our experience on transplantation of kidneys with small renal neoplasm.

Materials and methods: We accidentally found, at bench surgery time pre-transplantation, six suspected neoplastic lesions on donor kidney. All lesions were excised and histological analyzed by frozen sections. Results was confirmed in permanent sections and staged with Fuhrman nuclear grade. Following cancer diagnosis surgical excision was enlarged with achievement of free resection margins. After informed consent all grafts except one were used for transplantation.

Results: Histological lesions type were: one clear cell renal cell carcinoma (RCC), three cystic RCC, one papillary RCC and one oncocytoma. We not utilized the graft with papillary RCC for the described risk of multifocality. We transplanted the other five kidneys and contralateral kidney of clear cell RCC. Table 1 shows donors, recipients and neoplastic characteristics. All recipients has been treated with CNI based immunosuppressive regimen and at mean follow-up of 56 months (min 16, max 136) have functioning grafts and no signs of neoplastic disease. One patient died two years after transplant for cardiovascular event.

Discussion: In our experience, kidneys with small tumors (T1a) can be used for transplantation. It is mandatory, in order to ensure to recipients an acceptable level of risk, careful evaluation of histological type and grading of neoplastic disease, free resection margins and strict follow up.

P433

MANAGEMENT OF UROLITHIASIS IN LIVING KIDNEY DONORS

Lilia Ben Fatma, Nadia Amri, Lamia Rais, Ghada Boulahya, Rania Khedher, Wided Smaoui, Madiha Krid, Soumaya Beji, Karim Zouaghi, Fatma Ben Moussa
La Rabta Hospital

Introduction: Calcium lithiasis is the most frequently diagnosed renal lithiasis and is associated with a high percentage of patients with metabolic disorders, such as hypercalciuria, hypocitraturia, and hyperoxaluria. Is the presence of Oxalate-calcium stone in living kidney donor before transplantation should make them unselected for kidney donation in all cases?

Patient and method: We conducted this study to analyze our experience in management of urolithiasis or hyperoxaluria in three renal potential donors.

Results: This report is about three females aged 49, 43 and 38 years old. All are proposed for kidney donation to their sister. All are not obese, without any medical history and without any pathological symptom such as nephretic colic. We noted no urinary lithiasis on radiographs. We performed a 24-h urine test, and examined PH, calcium and oxalate. For the first patient, we note a family history of urinary lithiasis and initial nephropathy for the recipient was undetermined. In the two other cases, we noted on tomodensitometry renal arterial subcentimeter calculi in two cases. In case 3, we noted vitamin D deficiency related hyperparathyroidism. The urine analysis showed in case 1: PH at 5.7, hypercalciuria with Ca/creatinuria at 0.818 mm and weddellite. In patient 2 we noted PH at 5.5, hyperoxaluria at 0.48 mm and oxalate/creatinuria at 0.057. In patient 3 with calculi, we noted PH at 6.6, mild hyperoxaluria with oxalate/creatinuria at 0.035 (normal rate <0.03). This patient underwent pre transplant extracorporeal shock, hyperdiuresis regimen with stone clearance. She donated a kidney for her sister. After a follow up of 16 months, there was no stone recurrence in donor or recipient. The other two patients were refused for kidney donation.

Conclusions: There is a controversial if the kidney stone formers can donate a kidney or not. Proper donor selection and follow up is crucial to success. This report shows the efficacy of pre transplant extracorporeal shock in living donors with subcentimeter calculi permitting kidney donation after stone clearance. When there is a family history of stone, metabolic disease or donor lumbar pain, screening for hypercalciuria and hyperoxaluria should be performed. American guidelines that a kidney stone former may donate a kidney if only one stone has ever formed or if stones have been multiple, but none have formed for >10 years and none are seen on radiograph and if the donor is screened for metabolic abnormalities and is offered life-long follow-up that includes periodic risk reassessment, medical treatment, and hydration.

P434

DECEASED KIDNEY DONORS WITH SEVERE ACUTE KIDNEY INJURY: OUTCOMES OF RECIPIENTS

Tariq Ali, Wael Dimassi, Mai Altalhi, Hazem Algamal, Amira Alabbassi, Mohamed Shoukri, Khalid Almehari
King Faisal Hospital Research Centre

Introduction: A significant number of kidneys from potential deceased donors are discarded due to raised terminal creatinine. Outcome data of utilizing kidneys with severe acute kidney injury (AKI) are limited. We determined the outcomes of recipients who received kidneys from deceased donors with severe AKI.

Methods: We included deceased kidney donors between 1/1/2000–30/7/12 with a terminal creatinine >300 µm. Primary outcomes were serum creatinine, patient and graft survival.

Results (Table): To date data were available for 35 patients. Ten donors (29%) fulfilled the criteria of expanded criteria donor. Mean creatinine on admission was 102 and 492 µm on retrieval. 43% of the donors had mean creatinine >500 µm. The cause of death was road traffic accident and cerebrovascular accident in 26% and 23% of patients respectively. The mean age of the recipients was 44 years. Mean cold ischemia time was 14 h and none of these kidneys were perfused by pulsatile perfusion machine. Most of the patients, 66%, had delayed graft function. The common causes of end stage renal disease were diabetes 31%, undetermined 26%, and glomerulonephritis 23%. Eighty-two percent of the recipients completed a follow up of at least 2 years, 65% at least 3 years and 30% patients completed follow up of 5 years. At one year follow up one patient had lost the graft and no patient had died. To date there is no further graft loss and one patient had died after 4 years of follow up. At 12 months the mean serum creatinine was 104 µm. Mean creatinine was <150 µm in 74% and 80% of those patients who had completed 3 years and 5 years follow up respectively.

Conclusion: The preliminary results of this study show excellent short- and long-term outcomes of recipients who received kidneys with severe AKI. This study should encourage the healthcare providers to accept such kidneys.

P435

PREEMPTIVE TREATMENT OF HEPATITIS B INFECTION WITH ENTECAVIR IN KIDNEY TRANSPLANT RECIPIENT

Lilia Ben Fatma, Nadia Amri, Lamia Rais, Ghada Boulahya, Rania Khedher, Madiha Krid, Wided Smaoui, Soumaya Beji, Karim Zouaghi, Fatma Ben Moussa
La Rabta Hospital

Introduction: Hepatitis B infection in kidney transplantation has a reactivation risk under immunosuppression such as fulminant hepatitis. In kidney recipients, Lamivudine is a safe and effective antiviral HBV treatment both before and after renal transplantation; many studies confirmed that preemptive Lamivudine therapy improves survival of renal transplant recipients with HBV infection but Entecavir has demonstrated greater suppression of viral replication compared with Lamivudine and also a lower potential of resistance.

Patients and method: Here we report 2 kidney recipient positive hepatitis B virus (HBV) young woman treated before transplantation by Lamivudine.

Results: It's about a 28 and 34 years-old females presenting an chronic renal disease, with a pre-transplantation hepatitis B infection. At diagnosis a significant viral load 10 900 UI/ml was detected in the serum in patient 1 and 9900 UI/ml in patient 2. Fibrosis, before treatment, according to Metavir score was A0 F1 in the two patients. Treatment with Lamivudine was administrated during 6 months in patient 1 and Entecavir in patient 2 and HBV DNA levels became undetectable and kidney living donor transplantation was performed. In patient 2, the kidney transplantation was pre-emptive with MDRD creatinine clearance at 18 ml/min. Post-transplantation immunosuppressive drugs include steroids and calcineurin inhibitor-based regimen. After the transplantation, the HBV DNA remained low (451 UI/ml in patient 1 and 300 in patient 2). Two months after transplantation, Lamivudine was switched by Entecavir in patient 1 to avoid emergence of resistance. After a follow up period of 12 months, HBV DNA is undetectable.

Conclusions: Antiviral nucleoside analogues are effective in the prevention and treatment of hepatitis B exacerbation in kidney transplant recipients, thereby improving patient survival rates.

P436

PANCREAS ALLOGRAFT REJECTION IS ASSOCIATED WITH INCREASED RISK OF PANCREAS AND KIDNEY REJECTION IN SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANTATION

Carola Arcal, Ana Sánchez-Escuredo, Nestor Rodríguez-Chivita, Joana Ferrer, María José Ricart
Hospital Clínic de Barcelona

Background: Simultaneous kidney-pancreas transplant (SPKT) is the best therapeutic option for diabetic patients with end-stage kidney disease. However it presents high risk of surgical complications and pancreas graft failure. The aim of the study is to evaluate early pancreas graft failure in SPK transplantation and the risk for subsequent kidney failure.

Methods: Retrospective observational study of 139 SPKT (enteric drainage) performed from year 2005 to 2011 with minimum follow up of 6 months and maximum of 24. All received induction immunosuppression and prednisone, FK and mycophenolic acid. We analyzed age, gender, time on dialysis and PRA.

Results: Recipient age was 40 ± 6 years, 62.5% man, 92.8% had 0% PRA. Donor age 31 ± 10 years, 61% man. We documented rejection in 35% of patients, 25% occurring within first 6 months. 7.2% of patients had a kidney rejection, 14.4% pancreas rejection and 14.4% rejected both organs during the follow up. After a pancreas rejection 46% of patients had a following rejection episode (23% kidney, 27% pancreas, 4% both), 25% after kidney rejection (17% kidney, 0% pancreas, 17% both) and 50% after simultaneous rejection (25% kidney, 33% pancreas, 0% both). We did not find differences in donor characteristics, PRA, HLA mismatches or time on dialysis in rejection group. At 2 years followup rejection group showed creatinine 1.46 ± 1.15, Glucose 92 ± 18, peptide C 3.31 ± 2.5 vs. 1.15 ± 0.3, 92 ± 19, 2.44 ± 1.2 in non rejection group. We detected eight pancreas lost at 6 months of SPKT in non-rejection group due to surgical complications and thrombosis and 0 in rejection group. At 2 years followup, six patients with rejection lost pancreas and three lost kidney, none did it in non-rejection group.

Conclusion: Suffering pancreas rejection after SPKT seems to be a risk factor for further rejection of pancreas, but also kidney. Most important causes of graft lost during the first 2 years after transplant are surgical complications for pancreas rejections for kidney.

P437

KIDNEY TRANSPLANTATION IN HIV POSITIVE PATIENTS TREATED WITH A STEROID FREE IMMUNOSUPPRESSIVE REGIMEN. A SINGLE CENTER EXPERIENCE

Nicola Bossini, Salvatore Casari, Gisella Setti, Francesca Valerio, Mauro Pezzotta, Valentina Mazzucotelli, Silvio Sandrini
Spedali Civili di Brescia

Introduction: HIV infection is no longer a contraindication to kidney transplantation (tx) and the results have been reported as good as in the

general transplanted population. However, there are no data on the use of steroid-free regimens in this subset of patients.

Purpose: To evaluate the effectiveness and the safety of kidney transplantation in HIV+ subjects treated with an immunosuppressive protocol without steroids.

Patients and methods: Between June 2007 and April 2012, 14 HIV+ patients, at low immunological risk (1° tx, PRA < 30%), underwent kidney transplantation from deceased donor, at our Centre. At tx, the length of dialysis was 5.0 ± 3.1 years but the time on the waiting list was 10 ± 8 months. The primary inclusion criteria were: CD4 count >200/mm³ and HIV replication suppressed by antiretroviral therapy. In all cases, induction therapy consisted of Basiliximab plus Steroids, followed by the maintenance therapy with Calcineurin Inhibitors and Mycophenolate Mofetil. Steroids were withdrawn (SW) on day 5 post-tx in 13 out of 14 patients, but it was definitively resumed in the event of acute rejection.

Results: The main study results have been reported in the table below. Donor age was 38 ± 12.5 years. After Tx, 7 out of 13 steroid-free patients (54%) suffered from acute rejection, biopsy proven in six cases (cellular AR = 2 cases, humoral AR = 1 case, Mixed AR = 3 cases). All the episodes recovered after the treatment with Steroids, plus Thymoglobuline in two cases and plasmapheresis plus Immune globulins IV in one case. One patient lost the graft 43 months later for chronic rejection associated with severe infectious disease. CMV pneumonia (1); malaria from donor (1); Kaposi's sarcoma of the skin (1).

Conclusions: Kidney transplantation in HIV+ subjects is safe and effective. However, in this subset of patients, early steroid withdrawal cannot be recommended because of the high incidence of ARs, that show humoral morphological aspects in 66% of cases.

P438

SINGLE CENTRE INITIAL EXPERIENCE OF HYPOTHERMIC ORGAN PERFUSION USING RM3 PERFUSION MACHINE

Anna Rizzello, Karim Hamaoui, Sotiris Mastoridis, Jeremy Crane, Nadey Hakim, David Taube, Vassilios Papalois
Imperial College, London, UK

Background: Delayed graft function (DGF) complicates renal transplantation in 30% of deceased kidney allograft (Nephrol Ther. 2005 Dec;1(6):325-34. Epub 2005 Nov 16). Hypothermic machine perfusion (HMP) may reduce DGF incidence and length. We present our initial experience with Waters Medical RM3 HMP.

Methods: Ten kidneys from deceased donor were pumped on HMP. Donors, recipients details, HMP parameters were recorded. Primary endpoint was DGF incidence. Secondary endpoints were patients and graft survival.

Results: Immunosuppression induction was Alemtuzumab in eight patients, Daclizumab in two. Mean follow-up was 5 months. Mean static storage before HMP was 488.7 min (330-570 min), HMP time was 597.4 min (330-960 min). Mean cold ischemia time was 18.9 h (8.6-27.58 h). One patient had antibody mediated rejection 1 week post-transplant. After rejection case exclusion, two patients had 4 days DGF (20%). Immediate graft function group mean flow and mean RI were not statistically different to DGF group. Of 100% patient and graft survival.

Discussion: Our early experience in small group of patients showed that HMP effectively reduces DGF incidence. Good results in terms of graft and patient survival. As cohort of patients increases, we will define and expand organ viability criteria.

P439

EARLY LEUKOPENIA, YET STABLE KIDNEY FUNCTION DURING STEROID FREE MAINTENANCE THERAPY WITH CYCLOSPORINE AND MYCOPHENOLATE MOFETIL

Inge Derad, Juergen Steinhoff, Martin Nitschke
UKSH Campus LÄ/beck, Nephrology

Steroids are potent immunosuppressive drugs but may induce deleterious metabolic side effects without adequate efficiency on the long-term outcome after kidney transplantation. In the present case steroids were stopped at day 7 after successful transplantation of a female, full-house kidney transplant in a 47 year old male. The patient was discharged with a creatinine of 138 ÅµM, clearance 60 ml/min. Kidney function remained sufficient at 78 ml/min with cyclosporine and mycophenolate (MMF 2 g/day), when leukopenia (1500 leucocytes/Åµl) occurred 6 weeks after transplantation. Leukopenia occurred after a treatment with azithromycin because of bronchitis and seemed to be drug induced together with cotrimoxazol and valganciclovir as concomitant prophylaxis for pneumocystis jirovecii and cytomegaly (D+/R- constellation), respectively. Leucocytes normalized within 2 weeks after stopping cotrimoxazol and reduction of MMF (1 g/day). After 2 weeks MMF was augmented to 1.5 g/day, cyclosporine levels 3 months after transplantation were 100-150 ng/ml. Kidney function remained stable and without albuminuria (II CKD, G2 A1, KDIGO 2009). It is discussed that similar to tacrolimus -in steroid free maintenance- high dosed cyclosporine (150-200 ng/ml) may induce leukopenia as well especially in combination with MMF, cotrimoxazol and valganciclovir. In the absence of steroids leukopenia might occur sooner than the well-known dip after 3 months.

P440

THROMBOTIC MICROANGIOPATHIA (TMA) IN A KIDNEY TRANSPLANT-RECOVERING ITS FUNCTION AFTER A SWITCH TO CALCINEURIN-INHIBITOR -FREE IMMUNOSUPPRESSION

Inge Derad¹, Juergen Steinhoff¹, Thorsten Wiech², M. Noriega², Martin Nitschke¹
¹UKSH Campus LÄ/beck, Nephrology; ²UKE Hamburg

Three years after successful kidney transplantation on a triple therapy a 46 year old man developed creeping creatinine (crea). Kidney biopsy of the full-house organ revealed acute tubular injury and calcineurin inhibitor (CNI) toxicity but no recurrence of IgA nephropathy. During the previous 3 months cyclosporine levels had been fluctuating (52-101 ng/ml). The patient had confirmed to take his drugs regularly, but once he had been given another preparation of cyclosporine by his pharmacy. Although drug levels were kept stable, kidney function further deteriorated, diarrhea and edema occurred. A second kidney biopsy in March diagnosed TMA with fragmentocytes in the glomerular capillaries. However, blood levels for thrombocytes, lactate dehydrogenase, complement remained normal and further differential diagnostics for hemolytic uremic syndrome were done. During therapy with plasma exchange (6x) and steroids, belatacept and low-dose tacrolimus (1-2 ng/ml) instead of cyclosporine, kidney function remained bad. A third biopsy in July showed still fresh signs of TMA, without other pathological signs. Only after cessation of the CNI and another six courses of plasma exchange, kidney function has stabilized until now. This case demonstrates drug-induced TMA in a kidney transplant, which stabilized during CNI free immunosuppression after ruling out D+/- HUS, rejection and recurrence of IgA-Nephropathy.

P441

SIROLIMUS ON BK NEPHROPATHY AFTER KIDNEY TRANSPLANTATION

Hyung Hwan Moon, Jae Berm Park, Shin-Seok Yang, Jinyong Choi, Wontae Cho, Sung-Joo Kim, Jong Man Kim
Samsung Medical Center

Background: BK virus-associated allograft nephropathy (BKVAN) is one of the important complications of kidney transplantation (KT) that leads to graft dysfunction and loss. There is no established anti-viral drug for BKVAN, and the reduction of immunosuppression has been used currently as a therapy to control BKVAN. Recent studies have reported that sirolimus, mammalian target of rapamycin (mTOR) inhibitor may control BK virus replication. We report the outcome of sirolimus-based treatment on BKVAN in a single center.

Patients and methods: Between September 2007 and December 2011, 534 patients received KT at our center. BK viral replication was monitored with urine and blood BK virus PCR per our BK virus monitoring protocol. We reviewed medical records including biopsy and BK virus PCR in the patients, who were treated with sirolimus-based immunosuppression (IS) change. BKVAN were proven by needle biopsy.

Results: In 15 among 534 patients BKVAN were proven by needle biopsy at a median of 5 months post transplantation. In nine recipients, their calcineurin inhibitor-based IS was changed into sirolimus-based therapy. Follow-up duration sirolimus-based therapy was a median of 18.8 months. In all nine patients BK viral load in blood decreased as with sirolimus-based IS. Six patients showed viral clearance in BK viral load PCR in blood at post-treatment 12 month. During the follow-up post-sirolimus treatment, one patient had biopsy-proven acute cellular rejection and received steroid pulse therapy. Another one patient showed sustained hypercholesterolemia, tacrolimus-based IS resumed maintaining in low trough level. There was no graft failure due to BKVAN after the treatment of sirolimus-based IS.

Conclusion: In recipients with BKVAN, sirolimus-based IS led to decrease in BK viral load in blood PCR and maintaining their graft functions. Long-term follow-up and controlled studies should be required for elucidating the effect of sirolimus on BKVAN.

P444

CLINICAL IMPLICATION OF THE RATIO OF GRAFT KIDNEY VOLUME TO RECIPIENT BODY SURFACE AREA ON GRAFT FUNCTION AFTER LIVE DONOR KIDNEY TRANSPLANTATION

Chang-Kwon Oh, Jong Hoon Lee
Ajou University School of Medicine

Functioning nephron mass is a determinant of the graft function of kidney transplant recipients. The graft kidney volume and its weight have been reported to be surrogates of the nephron mass. To investigate the impact of the ratios of the surrogates to recipient body surface area (BSA) and body weight on the graft function within 6 months post-transplantation, we measured the graft kidney volume, using computed tomography with 3-dimensional reconstruction before transplantation, and measured the graft kidney weight during surgery. Ninety-four cases of live donor kidney transplants were included in this study. The graft kidney volume/recipient BSA ratio was correlated with the glomerular filtration rate (GFR) of recipients at 1 month and 6 months post-transplantation ($r = 0.416$, $p < 0.001$ and $r = 0.381$, $p < 0.001$, respectively).

We found a difference in the graft function between recipients with a graft kidney volume/recipient BSA ratio of ≥ 90.9 ml/m² and those with a ratio of < 90.9 ml/m² ($p < 0.001$). Multivariate analysis demonstrated that the graft kidney volume/recipient BSA ratio and donor age are independent predictors of recipient GFR at 1 and 6 months post-transplantation ($p < 0.05$). During living donor and recipient matching, both the potential volume of the donated kidney and the body size of recipient should be considered.

P446

COMPARISON OF EXPANDED CRITERIA KIDNEYS WITH 2-TIER STANDARD CRITERIA KIDNEYS: ROLE OF DELAYED GRAFT FUNCTION IN SHORT-TERM GRAFT OUTCOME

Faissal Shaheen¹, Beshar Al Attar¹, Fayeze Hejail², Saleh Bin Salih², Abdullah Al Sayyar²

¹Saudi Center for Organ Transplantation; ²King Abdul Aziz Medical City and National Guard Hospital, Riyadh

Objectives: To compare transplant outcomes between expanded criteria donor kidney and standard criteria donor kidneys.

Methods: All adult renal transplants from deceased donors performed in Saudi Arabia over a 24-month period were included. Donor and recipient factors were recorded, and their effects on outcomes with expanded criteria donors and standard criteria donor kidneys were compared. Standard criteria donor kidneys were further subgrouped into optimal and suboptimal groups, and outcomes were compared.

Results: A total of 280 deceased-donor kidney transplants were performed during the study period. Of these, 61 (21.8%) involved expanded criteria donor kidneys. Cold ischemia time and prevalence of delayed graft function were similar between expanded criteria and standard criteria kidneys ($p = 0.7$ and $p = 0.8$). Graft survival rates at 2 years were also similar (93.3% vs. 94.6%; $p = 0.8$). Delayed graft function exerted a negative effect on 2-year graft survival in both the expanded group (hazard ratio, 4.9; 95% CI 3.2–7.5; $p = 0.001$) and the standard group (hazard ratio, 4.6; 95% CI 3.24–7.5; $p = 0.001$). No difference was found between the 2 standard criteria subgroups with respect to serum creatinine value at the end of follow-up ($p = 0.8$), delayed graft function prevalence ($p = 0.5$), or 2-year graft survival ($p = 0.8$). The only independent factor affecting graft survival was delayed graft function ($p = 0.001$). No independent effect was seen for expanded criteria donor versus standard criteria donor, donor serum creatinine level, or recipient age.

Conclusion: Similar short-term outcomes were found for the expanded criteria and standard criteria kidney recipients. Delayed graft function was associated with significant risk of graft loss in both groups, with decreases in 2-year graft survival of 33.3% and 18.3%. No difference was seen between the two subtypes of standard criteria donor kidneys.

P447

DE NOVO THROMBOTIC MICROANGIOPATHY (TMA) LOCALIZED ONLY TO THE GRAFT IN TWO APKD WITH THROMBOPHILIA

Davide Rolla¹, Iris Fontana², Jean Louis Ravetti³, Luigina Marsano¹, Diego Bellino¹, Ernesto Paoletti¹, Giovanni Di Maio¹

¹Divisione di Nefrologia Dialisi Trapianto, Ospedale San Martino, Genova;

²Unità Operativa Trapianto di Rene, Ospedale San Martino, Genova; ³Servizio di Anatomia Patologica, Ospedale San Martino, Genova

TMA is a serious complication of renal transplantation (Tx) and is mostly related to the prothrombotic effect of CNI. A subset of TMA (29–38%) is localized only of the graft. A young woman suffering from APKD underwent Tx. After 2 months she showed renal deterioration (Scr from 1.9 to 3.1 mg/dl), without hematological signs of SEU; LDH transient increase was detected. Renal biopsy showed TMA: temporary withdraw of TAC and plasmapheresis was performed. The renal function recovered and stabilized (Scr 1.9 mg/dl). By thrombophilia screening, we find a mutation of Factor V Leiden. An old man affected by APKD underwent Tx, with prolonged DGF; a first biopsy showed NTA, but a second biopsy in 35° day show TMA; no signs of SEU was detected. Again we observed only a light increase of LDH. The TAC was halved and LDH levels were observed: LDH levels normalized within 10 days and renal function improved (Scr 2.9 mg/dl). By thrombophilia screening, we find a mutation of Prothrombin gene. Renal biopsy only clarifies the diagnosis of TMA localized only to the graft, but pay attention to light increasing level of LDH. Mutation of genes encoding factor H or I, anticardiolipin antibodies, vascular rejection, cytomegalovirus or parvovirus B19 infection are proposed by some to trigger TMA, but we detected mutations of Factor II and Factor V Leiden, as facilitating conditions for TMA.

P448

COMPARATIVE ANALYSIS OF BODY MASS INDEX WITH THE INCIDENCE OF POSTOPERATIVE COMPLICATIONS IN RENAL TRANSPLANT RECIPIENTS

Tamer Ghatwary¹, Mohamed A. Hossain¹, Richard Akiboye¹, Ali Ghazanfar¹, Abbas Ghazanfar², Mohamed Morsy²

¹Department of Renal Transplantation, St Georges Hospital NHS Trust;

²Department of renal transplantation, St. Georges NHS Trust

Background: Patients with high Body Mass Index (BMI) are at higher risk of postoperative complications. We report the postoperative complications rate in different BMI groups immediately post renal transplantation.

Methods: A total of 118 renal transplant recipients (mean age 50 ± 13 years old, 69 males) (between October 2011 and September 2012) were included. Patients were grouped according to their BMI into three groups (Group 1: < 25 , Group 2: 25–30 and Group 3: > 30). Complications were defined as a single occurrence of an unexpected postoperative finding such as infection, haematoma, lymphocele and urinary leak. Chi-square and Fisher Exact tests were used to compare groups.

Results: Postoperative complication rate in all recipients was 30%. Complication rate was 33%, 24% and 40% for group 1, 2 and 3 respectively. Perinephric collection including lymphocele and haematoma was the commonest in groups 1, 2 and 3 (17%, 8% and 25% respectively). No significant differences in the post-transplant complications incidence between group 1 and 2 ($p = 0.31$), group 2 & 3 ($p = 0.19$) and group 1 and 3 ($p = 0.59$).

Conclusions: While the high BMI group had the highest rate of complications, the difference was not statistically significant. Further analysis of a larger population is needed.

P449

ULTRALOW DOSE CALCINEURIN INHIBITOR COMBINED WITH EVEROLIMUS IS AN EFFECTIVE REGIMEN FOR KIDNEY TRANSPLANT RECIPIENT

Ping Chin Lai, Ling Yin Chiu, Wen Hung Huang

Chang Gung Memorial Hospital, LinKou

Background: Calcineurin inhibitor is a mainstay of immunosuppressive therapy in kidney transplantation patients for decades. However, with recent advance in transplant pathology, physicians became more aware and cautious with calcineurin inhibitor related nephrotoxicity. Studies from other researchers showed that complete elimination of calcineurin inhibitor will incur more acute graft rejection. Therefore, in this preliminary study, we tested how low calcineurin inhibitor can be reduced to avoid nephrotoxicity without increase in acute rejection incidence, while enhance graft function.

Method: Renal transplant recipients within first 1 year with eGFR > 40 ml/min and urine total protein < 800 mg/day were included in the study. Between month 3 to month 12 post transplantation, patients were recruited and everolimus 1.5 mg/day were added. Their calcineurin inhibitor and mycophenolic acid were reduced by 50% overnight. Calcineurin inhibitors were further reduced to either cyclosporine 25 mg/day or tacrolimus 0.5 mg/day within 2–4 weeks. Their prednisolone was kept at 5–2.5 mg/day. Renal function, urine protein and biochemistry were monitored monthly. The trough levels of everolimus were kept between 3 and 8 ng/ml.

Result: Fifteen patients ($N = 15$) were included in this study. At the end of one year follow up, their eGFR increased by 7.1 ± 0.5 ml/min, while no acute rejection was noted. Urine daily total protein mildly increases by 118.6 ± 81.8 ml/min. There is no significant change in liver function, sugar, hematocrit, platelet and leukocyte count.

Conclusion: Ultralow dose of calcineurin inhibitor combined with everolimus is an effective regimen for renal transplant recipients. This approach could improve graft function safely without increase in acute rejection incidence.

P450

SUBCLINICAL BLADDER OUTLET OBSTRUCTION IN RENAL TRANSPLANT PATIENTS

Mesut Izzet Titiz¹, Ali Murat Gökçe², Bülent Yiğit³, Mustafa Canbakan², Murat Gücün², Sevinç Ibisoglu²

¹Haydarpaşa Teaching Hospital; ²Haydarpaşa Teaching Hospital Istanbul;

³Yalova University Yalova Turkey

Delay in the diagnosis and treatment of bladder outlet obstruction (BOO) in male patients due to urethral stenosis and benign prostatic hypertrophy affects the graft function. Between 2004 and 2012 359 male kidney transplantation were performed and patients are evaluated by urologist. The immunosuppressive regimen were triple immunosuppression, tacrolimus or cyclosporine, mycophenolate mofetil and corticosteroids and as a surgical technique extravesical ureteroneocystostomy using double j were performed in all cases and double j removed after 3 weeks. All patients underwent a complete urological assessment prior to surgery and posttransplant. Lower urinary tract symptoms (LUTS) were evaluated by urologist using international prostate symptoms score (IPSS), uroflowmeter for maximum urinary flow rate (Q max) and ultrasonography for postvoiding residual urine. If the Q max lower than 15 ml/s urethrography was performed. IPSS score was 9.6 ± 3.6 in patients without BOO and higher with 20 ± 4.2 in patients with BOO. The Q max also was lower

with 8.7 ± 2.4 in BOO patients. Mean residual urine was 98 ± 13 ml in BOO patients. Urethrocytostomy was performed in 22 patients. Urethral stenosis in 18 patients (mean age: 40.9 ± 12), bladder neck stenosis in one patient and obstruction due to benign prostate hyperplasia in three patients (mean age: 52) were observed. The time between the transplantation and cystostomy was 17.5 ± 24.3 months (1–85 months). Mean creatinine before and after urethrotomy was 1.88 and 1.43 mg/dl and before and after TUR-P was 1.93 and 1.57 mg/dl respectively. Urologic follow-up is necessary for diagnosis and treatment the subclinical BOU to prevent the proper function of the Tx kidney.

P451

HEMORHEOLOGY IN RENAL TRANSPLANTATION

Francesco Fontana, Marco Ballestri, Giacomo Mori, Francesca Testa, Riccardo Magistroni, Gianni Cappelli
Nephrology Dialysis and Renal Transplantation Az. Ospedaliero Universitaria Policlinico di Modena

Hemorheologic alterations (HA) are present in uremic patients (UP) undergoing dialysis (HD), but no definitive data are available on transplant patients (TP). We compared plasma viscosity (η_P), blood viscosity at low (η_{S1}) and high (η_{S200}) shear rate, erythrocyte aggregation index (EAI), blood yield stress (τ_0), erythrocyte-stiffness as Taylor's factor (Tk) and elastic modulus (G') in 47 healthy volunteers (controls), 90 UP pre and post-HD and 108 RT. Results are presented in table 1 and figure 1: RT compared to HD promotes a normalization of most parameters while Tk and G' are worsened. Differences in anti-rejection drugs do not seem to affect most of hemorheologic parameters. RT improves uremia-induced HA while results on Tk and G' could support an endothelial injury with related chronic organ damage.

P452

PERSISTENT SEROUS LEAK: AN UNUSUAL COMPLICATION OF A SYNTHETIC GRAFT USED AS AN ARTERIO-VEIN SHUNT FOR DIALYSIS ACCESS

Vishnu Venkat¹, Abbas Ghazanfar², Gabriele Dibenedetto¹, Titus Augustine¹
¹Manchester Royal Infirmary; ²St. George's Hospital, London

Methods: A case report of perigraft seroma that occurred in a patient who had a PTFE graft in the arm, is described. Consent was obtained from the patient to use all the details pertaining to the case. A detailed histological & electron microscopic analysis of the explanted graft was performed by the manufacturing company Vascutek Ltd. A literature search was performed and similar case reports were reviewed.

Results: The leaking graft had to be ultimately replaced by a gelatine coated PTFE graft. The explanted PTFE graft showed no physical defects with electron microscopy. Histological examination revealed medium term implantation with no evidence of inflammation or infection. Literature search showed the incidence of seroma formation in PTFE grafts to be 1.7%.

Conclusion: Perigraft leak and seroma formation after a PTFE graft for dialysis is a rare complication. Important causative factors seem to be location – in the arm, intra operative technique, and development of a fibroblast inhibitor. It is therefore suggested that they are preferably placed in the forearm with meticulous operative technique. Leaking grafts may be salvageable with a bypass of the affected segment. Replacement of the graft with a different material often gives the best cure rate.

P453

THE VIRTUAL EVALUATION OF THE RENAL GRAFT, AS A METHOD TO OPTIMIZE QUALITY IN RENAL TRANSPLANT: A NEW ARCHITECTURE BASED ON THE TELE-RADIOLOGY EVALUATION AND THE "VIRTUAL BENCHING" OF THE RENAL GRAFT, APPLIED ON TELEMEDICINE SYSTEMS

Constantinos S. Mamas¹, Spyros Geropoulos², Irene Grapsa³, Chrysoula Lemonidou⁴, Andreas C. Lazaris⁵, Georgia Kostopanagiotou⁶, Nicolaos Kavantzaz⁵, Eustratios Patsouris⁵

¹Surgical laboratory Prof. C. Tountas; ²Aretaieion University Hospital of Athens; ³Aretaieion University Hospital; ⁴National and Kapodistrian University of Athen, Nurse School; ⁵National and Kapodistrian University of Athen, Athens Medical School; ⁶Attikon University Hospital

Background: Damaged renal grafts were estimated to 11% in UK. The study determine feasibility, reliability of the integrated application of tele-radiology and the tele-pathology (virtual benching) evaluation of the renal graft using Telemedicine Systems (TS).

Material and methods: The study was based on a sensitivity-specificity analysis after: a. the development of a experimental TS, b. a simulating comparison of tele-radiological evaluation of the graft on 15 MR abdominal images with the classic film evaluation by two examiners, c. the virtual benching of the renal graft by 26 specialists based assessing damages and lesions of the projected renal grafts.

Results: (i) There was no statistically significant difference in the diagnostic performance between the two examiners. Their sensitivity and specificity rates, referred to renal injuries and lesions, were 100%. (ii) The virtual benching defined damages and lesions of the renal graft with a sensitivity of 96.2%. (iii) The overall remote evaluation of the renal graft has a sensitivity of 96.7% and a specificity of 100% (95% confidence intervals).

Conclusion: The tele-radiological evaluation before retrieval in combination with the virtual benching of the renal graft is feasible and reliable shaping a new architecture for i. minimization of damaged grafts and ii. for transplant planning.

P454

RECIPIENT UDP-GLUCURONOSYLTRANSFERASE UGT1A9 98T>C VARIANT DETERMINES TRANSPLANTED KIDNEY FILTRATION RATE

Joanna Pazik¹, Monika Oldak², Zbigniew Lewandowski³, Marcin Dabrowski², Elzbieta Sitarek¹, Marta Podgórska², Ewa Wazna Jabłońska¹, Jacek Szmidt⁴, Andrzej Chmura⁵, Jacek Malejczyk², Rafal Ploski⁶, Magdalena Durlik¹

¹Department of Transplantation Medicine and Nephrology, Medical University of Warsaw, Warsaw, Poland; ²Department of Histology and Embryology, Medical University of Warsaw, Warsaw, Poland; ³Department of Epidemiology, Medical University of Warsaw, Warsaw, Poland; ⁴General, Vascular Surgery and Transplantation, Medical University, Warsaw, Poland; ⁵General Surgery and Transplantation, Medical University, Warsaw, Poland; ⁶Department of Medical Genetics, Medical University of Warsaw, Warsaw, Poland

We previously reported association of UDP-Glucuronosyltransferase UGT1A9 98T>C variant with early graft dysfunction (Ann Transplant.2011, Oct-Dec;16(4):69–73). Study aim: to further evaluate variant allele impact on transplantation outcome. In recipients engrafted 2000–2007 in Warsaw Medical University, DNA isolated from peripheral blood, SNP detected using PCR restriction fragment length polymorphism (RFLP), confirmed by DNA sequencing. Generalized estimated equations and mixed analysis of variance used for statistical analyses (SAS System). Prolonged observation on larger cohort ($n = 243$) confirmed association of UGT1A9 98C allele with kidney function. Inversely to UGT1A9 98T allele homozygotes ($n = 231$), in minor alleleC carriers ($n = 12$) lower filtration rate and proteinuria presented within 2 weeks after engraftment and remained throughout observation (1, 2, 3, 6, 12 months, 2, 3, 5 and 8 years after transplantation), differences statistically significant for eGFR&G ($p < 0.001$) and proteinuria ($p < 0.067$). Minor allele effect on filtration was independent from delayed graft function, temporary hemodialysis was necessary in 32.7% alleleC carriers and 30% of common allele homozygotes. No differences in biopsy-confirmed rejection and graft loss were found. Association of transplanted kidney dysfunction with presence of UGT1A9 98T>C polymorphism maybe of more complex nature than its role in mycophenolic acid metabolism and prevention of immunological injury. Thorough examination of its impact on early post-transplant course is tempting.

P455

RENAL AUTOTRANSPLANTATION PRESERVES RENAL FUNCTION IN CAREFULLY SELECTED CASES

Suresh Hanji, Y.Li Goh, Zia Moinuddin, David van Dellen, Neil Parrott, Titus Augustine
Manchester Royal Infirmary

Background: Renal autotransplantation is an established treatment for conditions including loin pain haematuria syndrome (LPHS), renovascular abnormalities, renal tumours and ureteric aberrations. We aimed to establish outcomes and preservation of renal function following autotransplantation.

Methods: Retrospective analysis was performed of autotransplantations at a single unit (04/2001–02/2012). Patients were assessed regarding outcomes, renal function preservation and complications.

Results: Of 18 patients were included (14 females, four males). Indications were LPHS (9), renovascular hypertension (6), tumours (2), and bilateral recurrent pyelonephritis (1- bilateral). Renal function was measured as pre-operative and 6 week follow up Creatinine (73 [41–129] and 78 μM [45–98] respectively; median [range]; $p = \text{NS}$; paired t -test). Mean cold ischaemic time was 159 min (range 96–185). One patient who underwent bilateral sequential autotransplantation for recurrent bilateral pyelonephritis required renal replacement therapy and subsequent nephrectomies. There were 3 urinary tract infections, one pulmonary embolus, and one renal bed haematoma.

Conclusion: Our series demonstrates minimal risk to both kidney and patient. Follow up is limited by the nature of the patients. However, autotransplantation appears to offer an effective treatment modality for this varied patient group. Careful case selection, with robust indications, provides excellent outcomes. Systematic comparison with other treatment modalities requires further examination.

P456

DONOR KIDNEY "0" PUNCTURE BIOPSY RESULTS AS A PREDICTING FACTOR FOR GRAFT FUNCTION

Aleksandrs Malcevs, Janis Jushinskis, Sergejs Trushkovs, Diana Amerika, Rafails Rozentals
Pauls Stradins Clinical University Hospital

Background: Donor organ quality is one of the most significant factors for kidney graft function. Donor kidney "0" biopsy is a "gold" standard for evaluation of kidney graft quality. The aim of this study was to evaluate the impact of the initial kidney graft condition on the post-transplant results.

Methods/materials: This retrospective study include all consecutive kidney transplantations ($n = 90$) performed in the single transplant center in the time period from January 1, 2004 till November 30, 2007, where donor kidney "0" biopsy results were available. Information about rates of delayed graft function (DGF), acute rejection (AR), recipient serum creatinine levels at the time of discharge from the hospital and 5 years after transplantation, graft losses and recipient deaths within 5 years were summarized.

Results: According to Banff classification 97% ($n = 87$) of all biopsies were informative. Interstitial sclerosis higher than 15% was observed in 21% ($n = 18$) and was associated with increased donor age ($p = 0.026$) as also with increased duration of recipient stay in the hospital after transplantation ($p = 0.036$). Presence of glomerular sclerosis was observed in 23% ($n = 20$) and was associated with increased donor age ($p = 0.014$), increased duration of recipient stay in the hospital after transplantation ($p = 0.017$) and with increased risk of development of DGF ($p \leq 0.001$). Presence of both interstitial and glomerular sclerosis was associated with increased recipient serum creatinine level at the time of discharge from hospital ($p = 0.019$), increased risk of development of AR ($p = 0.029$) and DGF ($p \leq 0.001$). Presence of interstitial or glomerular sclerosis did not affect graft or recipient five-year survival after transplantation.

Conclusion: Kidney "0" biopsy is an investigation method with high informativity that can provide information on graft chronic changes and for prediction of the development of DGF, AR and for kidney graft function in early posttransplant period.

P457

THE ECD KIDNEY – OUTCOMES FROM A SINGLE CENTRE

Alex Vesey¹, Kerrick Hesse², Emma Aitken¹, Marc Clancy¹
¹NHS Greater Glasgow & Clyde; ²Glasgow University

Introduction: Due to the rising disparity between demand and availability, organs from expanded criteria donors (ECD) are increasingly used. The purpose of this study was to report outcomes in recipients of ECD renal allografts from a single centre.

Methods: This was a retrospective analysis of prospectively gathered data from a single centre for all renal transplants performed between 2001 and 2010 inclusive. The primary outcomes were 4-year graft and patient survival. Kaplan–Meier survival analysis was undertaken with patients placed into four strata (SCD/DBD, ECD/DBD, SCD/DKD, ECD/DKD). Differences in recipient demographics, cold (CIT) and warm (WIT) ischaemic times and pre-transplant length of time on dialysis (surrogate of chronic illness) were also compared using appropriate statistical tests. $p < 0.05$ was defined as significant.

Results: Of 730 renal transplants were performed. There was a significant difference in graft survival between groups (logrank for trend, $p = 0.03$) with ECD organs doing worse than SCD organs (Fig. 1). For patient survival, there was a difference that did not achieve significance ($p = 0.12$). SCD/DKD organs had a better outcome than SCD/DBD organs. CIT was significantly shorter in SCD/DKD organs compared to SCD/DBD organs ($p = 0.0001$) but there were no differences in WIT ($p = 0.19$), time on dialysis ($p = 0.09$), recipient age ($p = 0.30$) or sex (0.74) between these two groups.

Conclusions: As is already known, we have shown that ECD organs have a poorer outcome than SCD organs. SCD/DKD organs had the best outcomes. This is likely to be accounted for by shorter CIT as these organs are allocated locally. DBD organs also do not benefit from continuous *ex-vivo* perfusion preservation. Our study's main limitation is the number at risk in the ECD/DKD group; the graft survival curve was heavily influenced by a single death at 423 days.

Abbreviations: SCD, Standard Criteria Donor
 DBD, Donation after Brain Death
 DKD, Donation after Circulatory Death

P458

EIGHT-YEAR OUTCOMES OF "THE CKC SEQUENTIAL PROTOCOL"

Tarek Fayad¹, Emad A. William¹, Nasr T. Atalla¹, Boulos A. Habashy¹, Sameh Shokry Amin¹, Soha S. Khalil¹, Rashad S. Barsoum¹, Hazem Abo Youssef²
¹Cairo Kidney Center, Cairo University; ²School of Medicine Cairo University

We had previously developed a Rapamycin-based sequential immunosuppression protocol for kidney transplantation comprising two phases: de novo

Rapamycin (R) + cyclosporine A (CyA) + prednisolone (P) for three months, followed by switching to R + S+ mycophenolate mofetil (MMF). The two-year outcomes of patients on this protocol (Group A) showed a better graft survival compared to those on a conventional protocol comprising CyA + MMF + P (Group B) (Barsoum RS, et al. *Exp Clin Transplant*. 2007;2:649–57). In the present study we report the eight-year graft outcomes in the same cohort (76 patients in Group A and 37 in Group B). The intent to treat 8-year death-censored graft survivals were 93% for Group A and 95% for Group B. The patient survivals at 5- and 8-years were 82% and 79% for Group A and 78% and 73% for Group B. Throughout the study, 42.1% switched from group A to protocol B (for probable sirolimus adverse reactions) versus 43.2% of the other way round (usually for CNi toxicity or chronic allograft dysfunction). Secondary end-points including graft function, blood-pressure control, new onset diabetes and other drug-related adverse events are being analyzed.

Conclusion: The "CKC sequential protocol" was non-inferior to the conventional CNi/MMF-based protocol as regards patient and graft survival. The proportion of patients converted from one protocol to the other was similar. Data on secondary end-points will be presented. **Key words:** Kidney transplantation, Sirolimus, Sequential immunosuppression, CNi toxicity.

P459

CYTOMETRY OF BLOOD NEUTROPHILIC GRANULOCYTES IN THE DIAGNOSIS OF RENAL ALLOGRAFT PATHOLOGY

Ruben O. Zograban, Irina V. Gomolyako, Viktor M. Torak, Vladislav P. Zakordonetz, Vladimir V. Shelest

Ukrainian National Institute of Surgery and Transplantology of A.A. Shalimov

Development of noninvasive tests to monitor renal transplant recipients (RTR) and allograft state is actual. To determine the diagnostic value of a neutrophilic granulocytes (NG) morphometry method (MM) 280 peripheral blood cytograms from 37 RTR were investigated at different time periods after transplantation and compared with 56 cytograms from healthy controls. Peripheral blood NG MM suggests distinguishing four types of cells by size (s) and brightness of cytoplasm (int). This division is based on ultrastructural, cytochemical and morphometric characteristics of cells and permits to evaluate their structural and functional characteristics, as well as classify cells into nonactivated neutrophils (I) – s I(A)/int I(A), weakly activated (II) – s I²(B)/int ²(B), moderately activated (III) – s I²²(C)/int ²²(C) and degenerative (IV) – s IV(D)/int ^{2V}(D). In healthy individuals the distribution of NG between four intervals was: I – (16 ± 3.4)%, II – (62 ± 8.4)%, III – (20 ± 3.6)% and IV – (2 ± 1.6)%, that is s I²(B) and int ²(B) type of cells predominated significantly and harmonious relationship between the size and brightness parameters of cells was characteristic. In acute rejection the structure of NG was characterized by increased proportion of s I(A)/int ²²(C) cells. Chronic rejection was accompanied by the decrease of NG size, signs of reduction in their functional activity, excessive accumulation of one of three types of cells – s I(A)/int ²(A), s I(A)/int ²²²(C), s I(A)/int ^{2V}(D), as well as signs of escalation of morphofunctional failure of the system. The tendency to normalization of morphofunctional characteristics of NG was typical for rejection-free early posttransplant course and stable late graft function. The above data suggest that NG MM might be used as additional for noninvasive monitoring of RTR and renal transplant status. Further studies are needed to determine its value in the diagnosis of causes of renal allograft dysfunction.

P460

A RANDOMIZED CLINICAL TRIAL OF EARLY CONVERSION FROM TACROLIMUS TO EVEROLIMUS IN DECEASED DONOR KIDNEY TRANSPLANTATION

Alvaro Pacheco e Silva¹, Eduardo Tonato¹, Marcelino Durão Jr¹, Lucio Requião-Moura², Erika Arruda², Rogerio Chinen², Thiago Filliponi², Luciana Melo², Ana Matos²
¹Unifesp/H. I. Albert Einstein; ²Hospital Israelita Albert Einstein

Background: All kidney transplant recipients (KT) of deceased donor (DD) receive induction with thymoglobulin in our institution. Despite an excellent graft survival, the incidence of cytomegalovirus (CMV) is approximately 80% with our preemptive strategy of treatment.

Objective: Compare renal function and the incidence of CMV in KT of DD undergoing induction with thymoglobulin and early conversion from tacrolimus (TAC) to everolimus (EVR).

Methods: A prospective and randomized study with low risk KT of DD. The initial immunosuppression consisted of thymoglobulin induction, prednisone and mycophenolate sodium and sequentially TAC. The patients were randomized to two groups: TAC or EVR. Between the 2nd and 5th week those randomized to EVR were converted during a 3-day overlap with TAC. The diagnosis of CMV was performed by a positive antigenemia of 10 or more cells/400 000 neutrophils. Renal function was assessed by serum creatinine (sCr).

Results: The analysis included 31 patients, 16 in Tac group and 15 in EVR. Conversion to EVR occurred at a median of 30 days after the Tx. The incidence of CMV was 87.5% and 73.3% and the median time to diagnosis was 36 and 32 days after the Tx, respectively for TAC and EVR (NS). The mean sCr for EVR and TAC groups were respectively 1.6 and 2.6 mg/dl ($p = 0.03$); 1.3 and 1.6 mg/dl (NS) and 1.3 and 1.4 mg/dl (NS) for 30, 180 days and 1 year. There were six episodes of acute rejection after discharge (EVR = 4 and TAC = 2).

Only two episodes were considered more severe: both in EVR group. The first was reconverted to TAC regimen, and the second lost the graft due to superimposed neoplasia and impossibility of treatment.

Conclusion: Both strategies of immunosuppression showed comparable safety and renal function, however EVR group did not show significant reduction in the incidence of CMV. We believe that this reduction should most likely be achieved through the conversion even earlier than the currently practiced.

P461

OUTCOME OF RENAL TRANSPLANT IN PATIENTS WITH ALPORT SYNDROME

*Tahir Aziz, Ejaz Ahmed, Fazal Akhtar, Rubina Naqvi, Anwar Naqvi, Adib Rizvi
Sindh Institute of Urology and Transplantation*

Introduction: The aim of this study was to evaluate the results of renal transplantation in patients with Alport Syndrome vis a vis patient and graft survival, incidence of anti GBM and causes of graft failure.

Material and method: Between 1985 and 2012 we performed 3700 live related renal transplants SIUT. Out of these a total of 15 patients with Alport Syndrome underwent renal transplant with male: female ratio of 14:1. The mean age of the recipients was 39 years. Rejection episodes, anti GBM nephritis and other causes of graft failure were assessed in these patients.

Results: Patients with Alport Syndrome were compared with control group of 100 renal transplant recipients. One (7%) patient with Alport Syndrome and 10 (10%) in control group experienced delayed graft function. Acute rejection was confirmed in 3(18%) patients by graft biopsy in Alport Syndrome while control group had 17 (17%) rejection episodes and classic treatment yielded relative response. However two grafts in Alport patients failed after 24 and 36 months after renal transplantation. On pathologic examination no specific finding of anti GBM nephritis was found. Incidence of Cyclosporine toxicity and urinary tract infection were similar in both groups. Two patients returned to dialysis in patients with Alport Syndrome. The 1, 3 and 5 years graft survival rate in patients with Alport Syndrome was not different from those with the control group.

Conclusion: In spite of risk of anti GBM nephritis in patients with Alport Syndrome, it seems renal transplant can yield favorable results and anti GBM nephritis is not a common entity.

P462

SINGLE CENTRE RETROSPECTIVE ANALYSIS OF RESULTS OF SKTX IN CHILDREN ≤5 YEARS OLD AT UKT BETWEEN 2004 AND 2012

*Paolo Girotti, Silvio Nadalin
University Hospital*

Background: Single kidney transplantation (sKTx) in children from small pediatric donors (age ≤5 years and weight ≤10 kg) was often performed with reluctance because of multiple factors influenced an high rate of early/long term post-operative complication and graft dysfunction (DGF, PNF): -insufficient nephron mass -increase of incidence of acute cellular rejection -increase vascular and urinal complications Therefore small kidneys from pediatric donors are usually transplanted en-block also in children.

Aim: Single centre retrospective analysis of results of sKTx in children ≤5 years old at UKT between 2004 and 2011.

Patients and methods: Retrospective analysis of 20 sNTx, in children from adult and pediatric donors at UKT, divided in two groups: -Group 1: included patients receiving small kidney from donors ≤5 years ($n = 7$), -Group 2: included patients receiving kidney from donors ≥5 years ($n = 13$). Parameters recorded: -Operations data: CIT, WIT, type of vascular and urethral anastomosis, intraoperative complications. -Post-operative course and complications: hospital stay, ICU stay, need of dialysis, need of vasopressor support, GFR and crea. value, medical and surgical complications (collected according to Dindo-Clavien Classification). -Graft and Patient survival (mean follow up of 34 months) Univariate analysis was performed according to t-Student test and graft/patient survival was estimated by the Kaplan-Mayer method.

Results: Twenty sKTx in children from adults and small donors were performed in UKT between 2004 and 2011. In Group 1: six children were ≤5 years and one patient was ≥5 years; all these seven children received small graft from pediatric donors (age ≤5 years). Post-operative course data in group 1 showed: - average ICU stay: 5 days ± 1.2 - average hospital stay: 19 days ± 4.5 - No patient received post-operative dialysis or vasopressor support - Six complication were developed (five complications I-II grad) and only one re-operat.

P463

CORRELATION BETWEEN SERUM NGAL OF POST-TRANSPLANT 2, 3 WEEKS AND GRAFT FUNCTION UP TO 3 MONTHS AFTER TRANSPLANTATION IN PATIENTS WITH SLOW KIDNEY GRAFT FUNCTION

*Joon Seok Oh, Joong Kyung Kim, Seong Min Kim, Yong Hun Sin, Jin Ho Lee,
Kill Huh
Bong Seng Memorial Hospital*

Background: Neutrophil gelatinase-associated lipocalin (NGAL) has emerged as a new, noninvasive diagnostic tool for acute kidney injury. It is

known that NGAL associates with delayed graft function; the association has been shown in urine and serum samples taken on the day of, and very soon after, transplantation. But little is known about the correlation NGAL with kidney function in patients with slow graft function. The aim of our study was to examine whether serum NGAL levels correlates with the level of kidney function in patients with slow graft function.

Methods: Nineteen subjects with slow graft function were included in this study. Serum NGAL levels were measured at 14th and 21th day after transplantation in patients with slow graft function. And serum creatinine and estimated glomerular filtration rate (eGFR; MDRD equation) were measured at 2 and 3 month after transplantation. Correlation analysis was performed with this data.

Results: The correlation coefficient between serum NGAL levels (post-transplant 14th day) and serum creatinine of post-transplant 1st, 2nd, 3rd month were 0.476, 0.547, 0.481. And those between NGAL (post-transplant 21th day) and serum creatinine of post-transplant 1st, 2nd, 3rd month were 0.310, 0.364, 0.311. The spearman correlation coefficient between serum NGAL levels (post-transplant 14th day) and eGFR of post-transplant 1st, 2nd, 3rd month were -0.204, -0.0412, -0.242. And those between NGAL (post-transplant 21th day) and eGFR of post-transplant 1st, 2nd, 3rd month were -0.076, -0.225, -0.114. The NGAL levels showed a positive correlation with serum creatinine and negative correlation with eGFR but it's statistically association is not strong.

Conclusion: The serum NGAL levels on 2nd, 3rd week after transplantation may correlate with graft function up to 3 month post-transplant in patients with slow graft function. But the association is not strong, large-scale study will be needed.

P464

CALCINEURIN INHIBITOR-FREE IMMUNOSUPPRESSION IN DUAL KIDNEY TRANSPLANTATION FROM MARGINAL DONORS - SINGLE CENTRE EXPERIENCE

*Laura Taricotti¹, Daniele Sforza¹, Laura Fazzolari², Alessandro Anselmo¹,
Giuseppe Iaria¹, Giuseppe Tisone¹
¹University of Rome "Tor Vergata"; ²University of Rome*

Background: Kidneys from expanded-criteria donors may be susceptible to calcineurin inhibitor (CI)-mediated vasoconstriction and nephrotoxicity. In the early post-transplant phase, using CI may prolong ischemic injury; in the long term, chronic CI nephrotoxicity is of greater concern. To avoid these consequences of CI in kidneys from marginal donors, CI-free protocols have been introduced for maintenance immunosuppressive therapy. A CI-free protocol of basiliximab induction, sirolimus, mycophenolate sodium (MPA) and steroids has been adopted at our centre in recipients of dual kidney transplantation (DKT) from marginal donors.

Methods: Ten DKT performed since February 2009 on CI-free immunosuppression, retrospectively analysing patient/graft survival, surgical and medical complications, rejection episodes and renal function.

Results: No deaths or graft losses occurred after median follow-up of 30 months. Incidence of acute rejection was 20% ($n = 2$). Delayed graft function (DGF) was recorded in 20% of patients ($n = 2$). Renal function: patients presented a median Serum-Creatinine of 106 μM at one month, of 97 μM at 6 months and of 93 μM at 1 year.

Conclusions: After DKT from EDs, CI-free immunosuppressive regimen including basiliximab induction, sirolimus, MPA and steroids provides excellent results, with low DGF rate and good renal function.

P465

TRANSPLANT RENAL ARTERY STENOSIS: PREVALENCE AND PREDICTIVE FACTORS

*Bynwant Sandhu, Michelle Willicombe, Alok Chauhan, Jeremy Crane, Nadey Hakim, Vassilios Papalois, David Taube
West London Renal and Transplant Centre*

Background: The reported incidence of Transplant Renal Artery Stenosis (TRAS) varies from 1 to 23%. The aim of this study was to determine the prevalence and predictive factors of TRAS in a large transplant series with an active screening programme.

Methods: Records of patients undergoing deceased or living donor renal transplantation from 2005 to 2012 were retrospectively reviewed. All patients screened for TRAS were included. ABO and HLA incompatible transplants were excluded, as were early technical losses. Parameters analysed included mode of radiological screening, donor and recipient characteristics, type of transplant, time to diagnosis and follow-up.

Results: Of 999 patients undergoing renal transplantation, 847 (84.8%) were screened. TRAS was confirmed on angiography in 137 patients (16.2%). Mean time to diagnosis post-transplant was 3.2 ± 3.1 months. Deceased donor ($p = 0.019$), donor age ($p = 0.003$), diabetic recipients ($p = 0.004$) and non-Caucasian recipients ($p = 0.004$) were found to be predictors of TRAS on multivariate analysis.

Conclusion: This study confirms that TRAS is not an uncommon entity and identifies significant factors predictive of TRAS.

P466

ARTERIAL FUNCTION NON INVASIVE MONITORING IN PATIENTS WITH KIDNEY TRANSPLANTATION DURING THE EARLY PERIOPERATIVE TERM

Dávid Kovács¹, Lajos Löcsey¹, Laszlo Szabo¹, Roland Fedor¹, Renata Laczik², László Asztalos²

¹Institute for Surgery Center of Transplanta, University of Debrecen Medical and Helath Science Center; ²Institute of Immunology, University of Debrecen Medical and Helath Science Center

Background: Development of atherosclerosis is accelerated in kidney transplant patients. Impaired metabolic pathways have complex effect on the arterial wall which can be measured by non-invasive techniques. Only few data are available on the change of stiffness parameters in the postoperative course, so in this study we analysed the stiffness parameters of kidney transplant recipients during the perioperative period.

Patients and methods: Seventeen successful primary kidney transplant patients with uneventful postoperative period (seven female, 10 male; 46.16 years \pm 12.19 years) were involved in our short-term prospective longitudinal study. We analysed the correlation between non-invasively assessed stiffness parameters (pulse wave velocity [PWV], augmentation index [Aix], pulse pressure [PP]), Systolic and Diastolic Area Index (SAI, DAI), Diastolic Refl ection Area (DRA) ankle-brachial index (ABI) and laboratory parameters (creatinine, glomerular filtration rate, urea, haemoglobin, C-reactive protein). Stiffness parameters were measured with a TensimedTM Arteriograph. These parameters were assessed before the transplantation, 24 h, 1 and 2 weeks after surgery under standard conditions.

Results: We found that creatinine ($p = 0.0008$), C-reactive protein (CRP) ($p = 0.006$) serum levels decreased, and glomerular filtration rate (GFR) increased significantly ($p = 0.0005$). We revealed that PWV ($p = 0.0075$) and Aix ($p = 0.013$) improved significantly. There was no significant change concerning SAI and DAI. DRA had significant correlation with SAI and DAI. There was no significant change in case of ABI, PP and the other monitored parameters.

Conclusions: Along with the available data in the literature, our findings suggest that kidney transplantation has a positive effect on the arterial function. Improvement can be detected non invasively with Arteriograph in the early postoperative period.

P467

ANTI-HLA ANTIBODY REDUCED GRAFT SURVIVAL OF LIVING-RELATED TRANSPLANTS IN LONG TERM FOLLOW-UP

Kazuo Mizutani¹, Ryohei Hattori¹, Tsuneo Kinukawa², Momokazu Gotoh¹

¹Nagoya University Graduate School of Medicine; ²Urology, Chukyo Hospital

Background: Recently, many studies showed effects of HAL antibody to kidney transplants. However, longer behavior and impact of HLA antibody were not clear. In this study, the role of HLA antibodies in allograft rejection was examined utilizing a unique resource of sera collected annually and stored over a 23-year period from patients with rejected or retained grafts.

Methods: We selected 50 transplant patients who received kidney from 1984 to 1999, and whose serum samples were available annually. During 23 years, 32 patients were rejected their grafts and 28 had functioning grafts. Their samples were tested for HLA Class I and Class II antibodies by flow cytometry, ELISA, or cytotoxicity. For analyzing specific HLA antibodies, we used Labscreen Single antigen (One Lambda).

Results: HLA antibodies were found in 81% of patients who rejected grafts, compared to 50% with functioning transplants ($p < 0.05$). In addition, even if living-related transplants had good kidney function for a longer time, some living-related patients gradually developed HLA antibodies with stable functioning grafts.

Conclusions: In conclusion, patients who rejected transplants had HLA antibodies more frequently than those with functioning grafts. These antibodies found in the peripheral circulation, and their association with failure is consistent in long period.

P468

OUTCOMES FOLLOWING INTERVENTION FOR TRANSPLANT RENAL ARTERY STENOSIS

Bynvan Sandhu, Michelle Willicombe, Jeremy Crane, Nadey Hakim, Vassilios Papalois, David Taube

West London Renal and Transplant Centre

Background: Transplant renal artery stenosis (TRAS) is associated with allograft dysfunction and inferior allograft survival. This study reports a single-centre experience on outcomes following intervention for TRAS.

Methods: All patients with TRAS confirmed on Intra-Arterial Digital Subtraction Angiography from 2005 to 2012 were retrospectively reviewed. The type of intervention, complications and allograft function and survival were recorded.

Results: Of 137 patients with confirmed TRAS, 113 (82.5%) were treated with angioplasty and stent, 6 (4.4%) angioplasty alone and 18 (13.1%) had no intervention. The overall complication rate in the intervention group was 15.1%, the most common being stent malposition (4.2%). Twelve (10.6%) stented

patients developed a subsequent in-stent stenosis. There was a significant improvement in graft function in the treated TRAS group from 2 months post procedure ($p = 0.02$) which was sustained at 1 year ($p = 0.007$) and 3 years ($p = 0.013$). The presence of TRAS was an adverse prognostic factor for allograft survival ($p = 0.014$). Furthermore, allograft survival was better in the treated TRAS group compared to the non-treated group ($p = 0.039$).

Conclusion: Successful treatment of TRAS confers a sustained improvement in allograft function and survival.

P469

ASSOCIATION OF POST-KIDNEY TRANSPLANT COMPLICATIONS AND BODY MASS INDEX (BMI)

Ana Rita Martins¹, Rui Silva², Patricia Matias¹, Cristina Jorge¹, Teresa Adragão¹, Rita Birne¹, André Weigert¹, Margarida Bruges¹, Domingos Machado¹

¹Hospital Santa Cruz Centro Hospitalar Lisboa Ocidental; ²Hospital Espirito Santo Evora

Objectives: Recent data suggest that mild to moderate obesity may be associated with increased survival in hemodialysis; on this other hand, it may be associated with more complications post-kidney transplant. The aim of the study was to evaluate the influence of the BMI on the rate of posttransplant complications and on graft survival.

Methods: We retrospectively analysed data on the 208 patients who underwent kidney transplantation at our hospital between January 2008 and December 2010. We evaluated the BMI at transplantation, length of the posttransplant hospitalization, number of acute rejection episodes, episodes of delayed graft function (DGF), finding of proteinuria 12 months posttransplant, development of new onset Diabetes mellitus after transplant (NODAT) and graft (and patient) failure. Obesity was defined as BMI ≥ 30 kg/m² at transplantation.

Results: Nineteen obese and 189 non-obese patients received a kidney allograft during the study period. The average follow up period was 36.6 \pm 13.5 months. Obese patients were older ($p < 0.001$) and had more frequently coronary artery stents ($p = 0.018$). Using univariate analysis, an elevated BMI was positively correlated with longer admission period post-transplant ($r = 0.16$, $p = 0.02$), more frequent finding of DGF ($r = 0.15$, $p = 0.03$), higher frequency of proteinuria ($r = 0.16$, $p = 0.03$) and the development of NODAT ($r = 0.20$, $p = 0.005$). The BMI had no correlation with the development of acute rejection, but had reduced graft survival (log rank = 5.02, $p = 0.02$). Using Cox regression, obesity was an independent predictor of graft failure (HR: 4.45, CI: 1.38–14.39, $p = 0.013$) adjusting for age, presence of a coronary stent and presence of acute rejection.

Conclusion: An elevated BMI was associated with a longer admission period posttransplant, higher chance of DGF, proteinuria and NODAT, but had no influence in the number of acute rejection episodes. Obesity was also associated with reduced graft survival.

P470

DELAYED AND IMMEDIATE RENAL GRAFT FUNCTION – 5-YEAR OUTCOMES

Janis Jushinskis, Aleksandr Maltsev, Vadim Suhorukov, Ieva Ziedina, Rafail Rozental

Transplant Laboratory, Riga Stradins University

Background: Delayed renal graft function has negative effect on both early and late posttransplant results, influencing also graft and patient survival. The aim of this study was to analyze factors associated with graft losses and patient deaths during the five years after kidney transplantation in patients with delayed and immediate graft function (DGF and IGF, respectively).

Methods/material: Study included 248 consecutive deceased donor renal transplantations from performed in a single centre between January 01, 2004 to November 30, 2007, available for 5-year follow-up. All cases were divided according to the presence of DGF, defined as the need for at least one dialysis during the first posttransplant week. Donor and recipient transplantation factors were analyzed for association with graft losses (death-censored) and patient deaths during the follow-up.

Results: DGF was observed in 53 cases (21.4%). Factors, associated with graft loss and patient death in kidney transplantation showed differences between DGF and IGF: graft losses in DGF group ($n = 6$) were significantly associated with donor age, donor female gender, recipient male gender, female donor kidney into male recipient, and in IGF group ($n = 26$) – with donor age, recipient age, nontraumatic donor brain death diagnosis ($p < 0.05$ for all), as also trends toward significance observed for increased donor serum creatinine in DGF ($p = 0.107$) and for increased donor body mass index in IGF ($p = 0.059$). Patient deaths in DGF ($n = 14$) were significantly associated only with recipient age, but in IGF ($n = 40$) – with recipient and donor ages, nontraumatic donor brain death diagnosis ($p < 0.05$ for all).

Conclusion: Factors associated with graft loss and patient death in kidney transplantation are different in DGF and IGF, showing the need to consider it in further posttransplant treatment.

P471

EARLY SURGICAL COMPLICATIONS COMPROMISE LONG TERM SURVIVAL AFTER LIVING-RELATED KIDNEY TRANSPLANTATION

Markus Rentsch, Andrej Khandoga, Axel Kleespies, Joachim Andrassy, Markus Guba, Manfred Stangl
Department of Surgery, University of Munich

Surgical complications following living-related kidney transplantation (LRKT) are known to compromise the immediate graft survival. In addition, evidence from earlier studies suggests that long term survival might be impaired by early surgical complications. Aim of the present study was therefore the investigation of the interrelation between complications requiring re-surgery and graft- as well as recipient survival. Prospectively registered data of 317 consecutive LRKTs between 07–1985 until 11–2011 were analyzed. Besides graft- and patient survival and the incidence of surgical complications, data of age, BMI, waiting time on dialysis, immunosuppression, immunological prerequisites (HLA-mismatch, panel-reactive antibodies, rejections, BANFF-classification) were determined. Early graft function was monitored according to creatinine serum level development within 12 months and by the incidence of early graft dysfunction. Data assessment included univariate and multivariate (Cox-Regression) statistical testing in terms of the study aim. Graft- and patient survival ranged between 93/92% (1 year), 89/91% (3 years) and 84/91% (5 years), respectively. The overall percentage of complications with the consequence of surgical revision was 17.5%, with a majority of revisions required due to lymphoceles (30%), ureter complications (20%) and hematoma formation (20%) while normal graft function. However, early graft dysfunction was significantly associated with the event of surgical revision. Log rank analysis identified surgical complications to diminish graft- ($p = 0.019$) as well as recipient survival ($p = 0.008$). The observation was reconfirmed by cox-regression for patient-, but not for graft survival. However, the effect of a high degree HLA (DR) mismatch on patient survival was stronger than the impact of surgical complications. Complications requiring redo surgery impact long term survival following LRKT. A complication-free post-surgical result after LRKT determines.

P472

ACQUIRED CYSTIC KIDNEY DISEASE IN PATIENTS REGISTERED ON THE KIDNEY TRANSPLANT WAITING LIST

Magdalena Jankowska, Alicja Dębska-Śliźień, Bolesław Rutkowski
Medical University of Gdansk, Poland

Background: Acquired cystic kidney disease (ACKD) is a complication of chronic kidney disease that may influence outcome after organ transplantation. We describe prevalence and we investigate risk factors for ACKD among patients registered on the kidney transplant waiting list. We hypothesized that high parathyroid hormone (PTH) levels influence the ACKD incidence, because PTH is involved in cyst development in other kidney cystic diseases.

Methods: We analyzed medical histories of 138 patients placed on kidney waiting list in our center. Of 100 patients met inclusion criteria and underwent further analysis. ACKD was diagnosed in patients having at least three cysts in each kidney in the ultrasound examination. We analyzed influence of age, gender, the time since diagnosis of the kidney failure, BMI (body mass index) and PTH levels on ACKD occurrence. We used t-Student and Pearson's chi-squared tests for statistical analyses.

Results: Thirteen percent out of 100 patients fulfilled criteria for ACKD. ACKD prevalence was influenced by the time since diagnosis of the kidney failure ($p = 0.01$) and by PTH values. ACKD did not occur in patients registered on the waiting list preemptively. We divided subjects into two groups according to PTH levels. Group 1 had iPTH below or equal 300 pg/ml ($n = 46$) and group 2 above 300 pg/ml ($n = 54$). Mean iPTH values in both groups were: 128 and 659 pg/ml, respectively (<0.001). Groups were comparable in respect of age, gender and the time since diagnosis of kidney failure. The incidence of ACKD was higher in a group with higher PTH values ($p = 0.002$). No case of ACKD was noted in patients with PTH below 300 pg/ml.

Conclusions: The prevalence of ACKD among patients registered on the kidney transplant waiting list was 13%. Patients placed late on the waiting list and those with increased PTH levels needs careful attention to prevent complications of ACKD after transplantation.

P473

UNUSUAL CORRELATION OF LATE IGA-NEPHROPATHY RECURRENCE AND RENAL PAPILLARY CARCINOMA DEVELOPED IN A KIDNEY TRANSPLANT RECIPIENT

Fabio Melandro, Giovanni Battista Levi Sandri, Nicola Guglielmo, Kostantinos Giannakakis, Renzo Pretagostini, Pasquale Bartolomeo Berloco
Sapienza Università Di Roma

Background: IgA nephropathy (IgAN) is one of the most common glomerulopathies, causing an end-stage renal disease requiring kidney transplantation in 3–6% of cases. Risk of IgAN post-transplant recurrence is up to 60%; however, immunosuppression could be related to the development of “de novo” tumors (DNT). In renal graft recipients, 4% of patients experience a DNT.

Among DNT, development of a renal cell carcinoma (RCC) involving the renal graft is anecdotic (0.5% of cases).

Case report: A case of a 50-year-old Caucasian man transplanted in 1987 for an end-stage renal disease caused by an IgAN is reported. The graft was from a living donor. Immunosuppression regimen was based on cyclosporine, azathioprine and steroids. After 25 years of uneventful follow-up, the patient developed a generalized edema and was hospitalized. At blood tests, serum creatinine was 4 mg/dl and a marked proteinuria was reported (18 g/24 h). No renal masses were observed at ultrasounds. A renal biopsy was performed, showing granular deposits of IgA (+++), IgM (++), C3 (+), kappa (+) and lambda (++) light chains in the mesangium: IgAN recurrence was diagnosed. Drug regimen was modified with the intent to treat both the IgAN recurrence and the proteinuria; however, the status of poor renal function persisted. Six months later, a new ultrasounds control was performed, showing three lesions at the level of the allograft. A CT scan confirmed the diagnosis. A renal biopsy showed of a papillary renal cell carcinoma type 1. The patient underwent the explantation of the allograft. The tumor was confirmed at pathology on the specimen. The post-operative course was uneventful, and the patient is still alive after a period of 6 months, having restarted the substitutive therapy with haemodialysis. IgAN recurrence after transplant is common, while development of a tumor on the allograft is anecdotic; however no data exist in Literature about a contemporaneous presentation of both these pathologies.

P474

IMPACT OF WAITING TIME ON DIALYSIS ON KIDNEY TRANSPLANT OUTCOMES

Alberto Rodríguez-Beno¹, Auxiliadora Mazuecos², Miguel Ángel Gentil³, Josefa Borrego⁴, Antonio Osuna⁵, Mercedes Cabello⁶, Pablo Castro de la Nuez⁷, Manuel Alonso⁷

¹University Hospital Reina Sofía, Cordoba, Spain; ²Hospital Puerta del Mar, Cadiz, Spain; ³Hospital Virgen del Rocío, Sevilla, Spain; ⁴Complejo Hospitalario de Jaen, Spain; ⁵Hospital Virgen de las Nieves, Granada, Spain; ⁶Hospital Carlos Haya, Malaga, Spain; ⁷Coordinación de Trasplantes de Andalucía, Spain

Background: Waiting time for cadaveric kidney transplantation remains excessively long; median time surpassed 48 months in 2011 (Eurotransplant Report). Along this lengthy period on dialysis, comorbidities arise and progress conditioning patient life expectancy. Nonetheless, waiting time is not commonly one of the primary determinants in most organ allocation scores. We aimed to explore its possible influence on graft and patient survival.

Methods: All first adults kidney transplants performed in Andalusia, Spain, were prospectively included in the Andalusian Kidney Transplant Registry from 2000 to 2010. Descriptive statistics and survival analysis (Cox regression, Kaplan-Meier curves) were performed. Waiting time was categorized in quartiles.

Results: Of 3194 first kidney transplants were performed in the decade; median waiting time was 1.9 year, although a continuous increase was observed ranging from 1.6 year in 2001 to 2.3 year in 2010 ($p < 0.01$). In 2001, 20% of the cohort had to wait more than 48 months for transplantation; in 2010 it increased up to 33%. After adjusting for age, sex, diabetes and HLA mismatch, time on dialysis was independently associated to higher mortality; relative risk was 1.6 for quartile 3 (1.9–3.6 year on waiting list; $p < 0.01$) and 2.1 for quartile 4 (>4 year; $p < 0.001$); reference, quartile 1. Furthermore, time on dialysis was also predictor for graft loss when not censored for death, but this association was lost when censoring for it. In conclusion, dialysis patients on waiting list over 2 years are at higher risk for graft loss and for increased mortality. Waiting time should have more relevant consideration in allocation schemes.

P476

LONG TERM FOLLOW UP OF M-TOR BASED, CNI FREE REGIMEN IN RECIPIENTS OF DE NOVO KIDNEY TRANSPLANTS – A CASE CONTROL STUDY

Ninoslav Ivanovski, Elka Masin-Spasovska, Irena Rambabova-Busljetic, Igor Nikolov, Aleksandar Sikole
University Clinic of Nephrology, Medical Faculty

Introduction: Chronic use of CNI in transplant medicine is responsible for nephrotoxicity and graft loss during long-term follow-up. The early and late switch from CNI to m-TOR inhibitors based regimen have beneficial effect on long term graft function, post transplant malignancies and cardiovascular morbidity. Here we presented the long term follow up of kidney transplant recipients treated with Sirolimus based immunosuppression with a full avoidance of CNI after the surgery.

Methods: In retrospective case control study, 20 first renal transplant recipients with sirolimus based immunosuppressive therapy with MMF and Pred and without any CNI were analysed during the follow up of 96 months. The mean age of the patients was 55.07 years. The prevalence of male recipients was 57%; the overall mean weight, 64 kg (range 51 to 95). Sirolimus dose was adjusted according to the blood level kept between 6 and 10 ng/ml. The actual creatinine, GFR-MDRD, proteinuria, HBA1C, TGL, cholesterol and

glycaemia were analysed after 96 months of follow-up. The results were compared with 20 CNL based patients with comparable age (58.2 years) and mean follow up of 92 months.

Results: After the follow up the m-TOR group has a better renal function compared with CNL group (GFR MDRD 57.61 vs. 49.51 ml/min, $p < 0.01$), better HbA1C (5.71 vs. 6.04%, $p < 0.05$). The cholesterol concentration was higher in m-TOR group (5.66 vs. 4.96, $p < 0.05$) as well as triglycerides (1.9 vs. 1.47). There was no difference in Glycaemia (5.3 vs. 5.7, $p = ns$) and actual creatinine 135.6 vs. 138.6, $p = ns$) and proteinuria (0.7 vs. 0.61 g/24 h, $p = n.s.$)

Conclusion: The authors confirm the superior long term graft function in recipients with m-TOR based regimen and worse control of Cholesterol and triglycerides. Surprisingly there was no difference in proteinuria, glycaemia and actual creatinine. The authors conclude that m-TOR based regimen could be useful also from the very beginning after the surgery with complete avoidance of CNL in immunosuppression.

P477

CLINICAL OUTCOMES AND SERVICE IMPACT OF SUPER-EXPANDED CRITERIA DECEASED DONOR KIDNEY TRANSPLANTATION

Kerem Atalar, Jonathon Olsburgh, Christopher J. Callaghan, Pankaj Chandak, Nizam Mamode, Martin Drage, Rachel Hilton, Francis Calder, John Taylor, Geoff Koffman, Nicos Kessarar, Guy's and St. Thomas' NHS Foundation Trust

Background: Expanded criteria deceased donor (ECD) renal transplantation has been established as a framework to increase the donor pool. ECD donors are those aged ≥ 60 or aged 50–59 with two of the following factors: hypertension, death from cerebrovascular cause or terminal serum creatinine > 1.5 mg/dl. Our use of organs from deceased donors aged ≥ 70 , which we term super-ECD (sECD), has recently expanded. Data are limited for outcomes from such donors, and the impact on service provision is unclear.

Method: We analysed results for all deceased donor (DD) kidney transplants performed at our centre in 2012. Variables included graft loss, 3 month eGFR (MDRD), biopsy rate and length of inpatient stay (LOS).

Results: Of 114 DD transplants, 51% were ECD and 17% of all donors were aged ≥ 70 (sECD). Primary non-function rates were: 1.8% for standard criteria donors (SCD), 5.1% for ECD aged < 70 years, and 10% for sECD, and all-cause graft loss rates at 3 months were 5.4%, 7.7% and 10% respectively. Donor age negatively correlated with eGFR ($r = -0.44$, $p < 0.001$, Spearman test). ECD recipients had a lower median eGFR than SCD recipients (34 vs. 48 ml/min/1.73 m², $p = 0.003$, Mann Whitney test), however there was no difference in median eGFR between sECD and ECD < 70 years (30 vs. 36, $p = 0.32$, Mann Whitney test). Delayed graft function (DGF) was 32% in the SCD, 50% in ECD < 70 years and 58% in sECD. There was no significant difference in LOS between SCD, ECD < 70 years or sECD. There was weak positive correlation between donor age and number of biopsies within first 3 months ($r = 0.21$, $p = 0.03$, Spearman test).

Conclusions: Although the sample was small, these data show that sECD renal transplantation gave early functional outcomes that are not significantly different from other ECD donors. Whilst length of stay was not significantly increased with older donors, there was a trend towards increased biopsy rate, possibly due to the higher DGF. These data support continued but careful use of sECD organs.

P478

MEETING THE KDIGO AND KDOQI HAEMOGLOBIN TARGET LEVELS; CAN THESE BE MET IN THIRD WORLD PATIENTS FOR KIDNEY TRANSPLANTATION?

Ihab A. M. Ahmed, Mohamed Hafiz Gareeb-Allah, Walaa Eljack, Muna Elamin, Tayeb A.R. Ali, Nazik Khalifa, East Nile Hospital

Introduction: Both the KDIGO and KDOQI guidelines for haemodialysis patients recommend a target haemoglobin (Hb) ≥ 11 g/dl. Patients with lower Hb should be considered for Erythropoietin and iron therapy. However, this treatment is quite expensive and unaffordable in certain parts of the world. In addition, most of our haemodialysis patients frequently receive only two dialysis sessions per week. Hence, it is not unusual to find that patients with ESKD frequently have Hb < 11 g/dl. Offering renal transplantation to these patients is the only way to improve their health and well being. The aim of this study was to review the Hb level in patients undergoing kidney transplantation and the need for blood transfusion during the perioperative period. The primary end point was anaemia-related cardiovascular events. Secondary end point was the episodes of acute rejection.

Methods: Data of patients who underwent kidney transplantation during 2012 and had Hb < 11 g/dl were reviewed. Preoperative Hb and Hb on discharge, adverse cardiovascular events and episodes of acute rejection were recorded.

Results: The cohort consisted of 23 patients. The mean age was 28.9 years (range: 19–55). The mean pre-operative Hb was 10.13 g/dl (6.1–10.9). Eight patients needed blood transfusion during the perioperative period. The mean number of blood units transfused was 2.88 (range: 2–6). The mean Hb at

discharge was 7.8 g/dl (range: 5.5–11.5). None of the patients developed adverse cardiovascular event during the perioperative period. Three patients who received blood transfusion developed acute rejection (35%).

Conclusion: Offering renal transplantation to ESKD patients with low Hb was not associated with adverse cardiovascular events. The frequency of acute rejection episodes in this group was not higher than expected.

P479

LIVING DONOR TRASPLANT PROGRAM IN SALAMANCA, SPAIN. A YOUNG BUT SUCSEFUL STARTING

Guadalupe Tabernero Fernández, Pilar Fraile Gómez, Pedro García Cosmes, Karen Rivero García, Hospital Clínico Universitario

Background: Living donor kidney transplantation is a good choice for renal substitutive therapy. In our Hospital, we have started at the end of 2011, the living donor kidney transplantation to add another alternative of treatment for the chronic renal failure.

Materials and methods: Since 21st of November of 2013 until today, we have studied 12 pairs of donors and recipients, and we have done eight living donors kidney transplants. The exclusions were Diabetes Mellitus in two of the donors, transplantation from a deceased donor in one of the recipients, and anatomical malformation in other donor. All the donors were relatives, and had compatible blood group. The HLA mismatches were variable. The immunosuppressive regimen has been: tacrolimus, MMF, basiliximab and steroids. Recipients started to have immunosuppressive therapy 3 days before the surgery. We have done three preemptive, and five of patients on dialysis.

Results: After 16 months, our survival is 100%. All the surgeries have been laparoscopic left renal remove. The mean of warm ischemia time has been 2.5 min and the cold ischemia time 1 h 30 min. No surgical complications until the moment. All the allografts are working. The average of the creatinine after this time is 1.5 mg/dl. We have had four episodes of acute rejection, three in the same patient. This one was a son-mother, and they only had one mismatch. All of the rejections were mediated by T cells, and had good response to the treatment. We also have had three infections by CMV all of them with good response to valganciclovir treatment.

Conclusions: Living donor transplantation is a very good choice for the people who are in the waiting list and/or waiting to start dialysis. Less time of cold ischemia time, less probability of HLA mismatches, the possibility of doing it preemptive, and the possibility of getting a younger donor, may help to improve our results. However, we cannot forget, the high probability of rejection and in the recipient and take care of them.

P480

OUTCOME OF 36 PREGNANCIES IN 32 RENAL TRANSPLANT RECIPIENTS

Mariana Wohlfahrtova, Ondřej Viklický, Josef Cindr, Barbora Repova, Marcela Burgelova, Institute of clinical and experimental medicine (IKEM)

Pregnancy itself is not contraindicated in renal transplant recipients under certain conditions. The opposite is associated with a risk for child and graft function deterioration. Aim of this study was to identify whether a pregnancy after renal transplantation affects long-term renal graft function. In this single-centre retrospective observational study we investigated the outcome of 36 pregnancies in 32 renal transplant recipients who subsequently conceived. The non-pregnant controls were matched to studied cases on age at transplantation, years after transplantation and initial renal function. Patients were followed for 5 years after the delivery. We focused on long term graft function, incidence of rejections and graft loss. Differences between studied groups were compared using Mann-Whitney U test for non-normally distributed continuous variables. Data are expressed as median and interquartile range. The graft survival analysis was performed using Kaplan-Meier analysis. Median S-Cr at time of delivery ($i_{i/2M}$) was 104 (94.8–137) in the study group compared to 110 (101.5–148) in the control group ($p = 0.592$). 5 years after delivery, graft function remained the same in both groups (S-Cr 131 [101–495] in the study group, S-Cr 134.5 [103.3–203.8] in the control group, $p = 0.723$). Pregnant patients with baseline S-Cr of above 150 $i_{i/2M}$ have an increased risk of progression of allograft dysfunction resulting from the pregnancy ($p < 0.0001$) (Figure 1). There was an insignificant increase in proteinuria in the study group at the time ($p = 0.015$) and 3 months after delivery ($p = 0.022$) in comparison to the control group. Graft survival and rejection rate was similar in both groups. We confirm that pregnancy itself does not appear to have any adverse effect on the long-term graft survival if initial graft function is ideal.

P481

SIMULATION TRAINING FOR TRANSPLANT SURGEONS – DEVELOPING A MULTI-FACTORIAL TRAINING PROGRAM*Jonathon Olsburgh¹, Kerem Atalar¹, Clarissa Carvalho², James Barron², Neal Banga³**¹Guy's Hospital; ²KHP Simulation and Interactive Learning Centres; ³Royal Free Hospital*

Background: Transplant surgical training is still often an apprenticeship orientated approach. Technical skills are learnt on patients and non-technical skills are learnt via trial and error. We developed a simulation training program for transplant surgical trainees that aims to address these deficiencies in a safe environment away from patients.

Methods: The following domains were covered – technical skills for transplant surgery, patient safety, situational awareness, in-theatre error management and transplant organ resource allocation. Technical skills consisted of workshops practising open surgical techniques on porcine tissues and laparoscopic simulation training using the LapMentor TM laparoscopic nephrectomy module. Non-technical skills utilised high fidelity simulation manikins and patient actors. Simulation scenarios using the Simulation and Interactive Learning Centre (SaIL) Debrief Diamond Model to elucidate and explore Human Factors issues, Non-Technical Skills and Crisis Resource Management.

Results: Results from feedback were gathered before, during and after the course (including debriefs, videos, feedback sheets). Technical skills improved with repetition of activities including reduction in path lengths and number of movements with increase time on the laparoscopic trainer. There was improved understanding of Human Factors issues and increased confidence in candidates' leadership and communication skills. Candidates felt combining technical and non-technical skills effective in training.

Conclusion: We have developed a multi-modality transplant surgical simulation training program that addresses technical and non technical skills. This programme is transferable and modifiable for surgical trainees in a wide variety of specialties and countries. We believe simulation training should form an integral part of transplant surgical training in order to deliver safer surgeons for the future and optimise patient care and safety.

P482

RENAL TRANSPLANT SIMULATOR (RTSIM) – A SIMPLE DEVICE FOR TRANSPLANT TRAINEES*Saied Froghi**John Radcliffe Hospital*

Background: Simulation has long been used in surgical and medical specialties to improve proficiencies of the trainee clinicians. They test technical or non-technical skills and are postulated to aid the steep learning curve of trainees in a safe environment.

Method: Material for the renal transplant surgery used to construct the RTSim is as follows: 500 g pot of yogurt, three way tap junctions for IV access, cannula connectors, and two bag of normal saline with red dye. To test the device a pig, or sheep's kidney with perinephric fat and part of vasculature is required. Set-up: Initially four small holes are made at the bottom of the yogurt pot. One next to each other and the other two are placed opposite the first two holes. The holes are to accommodate the three way taps. Once the three way tap inserted two small vessels/fine plastic tubing (length = diameter of the pot) can be set onto the 3-way taps. The purpose of the 3-way taps is so they can imitate vascular clamps by switching the flow on/off. Next is to connect the bag of normal saline to the taps to create a flow in the vessels. Simulator properties: The depth of the yogurt pot has somewhat similar dimensions to an open abdomen during renal transplantation. This allows the trainee to practice vascular anastomosis in the confined area and acquire depth perception. In addition, it aids with gaining experience in technical skills such as vascular anastomosis.

Conclusion: The RTSim is a simple wet lab simulator to aid transplant trainees to gain experience and improve their technical skills. The dimensions of the RTSim make it a suitable training device however its content validity remains to be proven.

P483

OUR EXPERIENCE WITH SURGICAL COMPLICATIONS OF KIDNEY RETRANSPLANTATIONS IN UNIVERSITY HOSPITAL OF L. PASTEUR IN KOSICE (SK), IN YEARS 1989–2010*Stefan Hulik, Erik Toth, Peter Zavacky, Tana Baltsova, Jaroslav Rosenberger, Luboslav Bena, Jozef Radonak*
University Hospital of L.Pasteur

Background: In retrospective analysis of our group of patients in years 1989–2010 we focused on occurrence of surgical complications of kidney retransplantations and comparison of our results to larger transplantcenters in purpose to estimate surgical risks of kidney retransplantations in our conditions.

Patients and methods: In years 1989–2010 we performed 642 kidney transplantations in the University Hospital of L.Pasteur in Kosice, Slovak

Republic, 604 primary (94.08%), from DCD and living donors. Retrospectively we analyzed occurrence of surgical complications of retransplantation group of 40 patients (6.23%) in average age 36, 37 years (9–57 years) Three of retransplanted patients were diabetic. Of 34 transplantations (5.2%) were secondary, five transplantations (0.7%) were tertiary and one graft (0.1%) was transplanted quaternary, which was the first successful 4th retransplantation in the Slovak Republic. We collected data from available medical documentation from the Archives of University Hospital of L.Pasteur and compared to results of larger transplantcenters published in the specialized literature.

Results: Total occurrence of surgical complication we have observed in 10 cases (25%). Wound complications in six cases, Vascular in two cases, Urological in two retransplanted patients. Lymphocele was not verified in our group of retransplanted patients.

Conclusion: The limitations of our study are small group of patients and short time follow-up, thus we are not able to phrase responsible conclusions. Despite it we found our results comparable to larger analyses in world literature and our experience lead us to conclusion that we consider this method safe also in our conditions and we recommend it to our patients after previous graft failure.

P484

IMPAIRED RENAL FUNCTION IN DONATION AFTER CIRCULATORY DEATH DONORS DOES NOT INFLUENCE GRAFT SURVIVAL OR FUNCTION*Dermot Mallon, Elizabeth Wlodek, Neil Russell, Gavin J. Pettigrew, Kouros Saeb-Parsy**Addenbrooke's Hospital*

Introduction: Marginal donors are increasingly being utilized to increase the number of organs available for transplantation. Impaired renal function is a common reason for a potential kidney donor to be declined. The effect of impaired renal function in Donation after Circulatory Death (DCD) has not been conclusively determined.

Methods: A retrospective review of 255 DCD kidneys transplanted between August 2008 and August 2012 in a single centre in the UK was performed to determine the effect of pre-mortem impaired renal function on the incidence of Primary Non-Function (PNF) and Delayed Graft Function (DGF), serum creatinine at three months and graft survival. Survival analysis was performed using Kaplan–Meier plots and a Cox proportional hazards model. Impaired renal function was defined as donor serum creatinine >115 mg/dl or eGFR <60 ml/min/1.73 m².

Results: The incidence of PNF and DGF was not increased by either raised donor serum creatinine or reduced donor eGFR ($p > 0.05$). Similarly, three month serum creatinine was not affected by raised donor serum creatinine or reduced donor eGFR ($p = 0.45$ and $p = 0.14$, respectively). Moreover, Kaplan–Meier survival analysis as depicted in Figure 1 shows neither terminal eGFR nor terminal creatinine to be significantly associated with graft survival. This is also demonstrated by a Cox proportional hazards model that shows only Donor age and Recipient age to be significantly associated with graft survival.

Conclusion: Whilst it is possible that the kidneys accepted for transplantation with impaired renal function were otherwise of exceptional quality, it is apparent that acute renal failure alone need not be reason to decline kidneys for transplantation.

P485

OUTCOME WITH CHRONIC IMMUNOGLOBULIN TREATMENT OF FOCAL SEGMENTAL GLOMERULOSCLEROSIS AFTER KIDNEY TRANSPLANTATION*Manuel Rengel, Lorena Tana, Borja Quiroga-Gilis, Javier Reque, Laura Bucalo, Ursula Verdalles, Soraya Abad, Almudena Vega, Eduardo Verde*
Hospital General Universitario "Gregorio Marañón"

Recurrence of Focal Segmental Glomerulosclerosis after Kidney Transplantation (FSGS) is variable, between 15% and 50%. Graft survival rates are decreased in recipients with FSGS, especially if remission of the nephrotic syndrome is not achieved. Optimal treatment in order to induce remission has not been delineated. It was used plasma exchange, immunoadsorption, monoclonal antibodies and Immunoglobulin. We report on a 40 years female with end stage renal disease secondary to FSGS who received a second kidney graft from a deceased donor on august 2005. Recurrence of FSGS occurred on posttransplant period, confirmed by percutaneous kidney biopsy. She received several immunosuppressant treatment protocols, associate to immunoadsorption, chronic plasma exchange and monoclonal antibodies. Four years after kidney graft developed nephrotic syndrome (proteinuria >10 g/day) and plasmatic creatinine 2.2 mg/dl, hypogammaglobulinemia (IgG lower than 350 mg/dl). In this situation, high dose of i.v. Immunoglobulin treatment at 1 g/kg monthly was initiated. Renal function improved, with plasma creatinine 1.5 mg/dl and proteinuria lower than 4 g/day, after 3 years followup. No adverse effects were observed.

Conclusion: High dose i.v. Immunoglobulin is an effective treatment option for FSGS recurrence after kidney transplantation.

P486

CORTICOSTEROIDS WITHDRAWAL IN STABLE MAINTENANCE RENAL TRANSPLANT PATIENTS

Lorena Tana, Manuel Rengel, Borja Quiroga-Gillis, Javier Reque, Laura Bucalo, Úrsula Verdalles, Soraya Abad, Almudena Vega, Eduardo Verde
Hospital General Universitario "Gregorio Marañón"

Corticosteroids are powerful antiinflammatory with immunosuppressant effects utilized in maintenance therapy following kidney transplantation and are associated with a higher rate of side events in comparison with protocols involving early corticosteroid withdrawal. The present paper reports the results of cessation of steroids in stable maintenance renal transplant patients.

Patients and methods: One hundred fifty seven deceased kidney grafted patients (51% men), aged 56.5 ± 12.4 years, with follow-up of 72 months (1–247) and steroids withdrawal period of 48 months (1–198) follow-up steroid free were studied. Etiology of end stage renal disease was secondary to Glomerulonephritis 31%, Diabetes 22%, Polycystic disease 14%, Tubulointerstitial nephropathy 13%, Vascular 5%, Unknown 17%. The patients were on Prednisone 5–10 mg daily combined with Cyclosporine 50–150 mg/Tacrolimus 0.5–6 mg, associate to Mycophenolate Mophetyl 250–2 mg, Sodium Micophenolate, 360–900 mg or Azatioprine 50–75 mg, and Everolimus 1–4 mg. Steroids were diminished gradually in three months period and some patients receive monotherapy only.

Results: Basal serum creatinine was 1.54 ± 0.6 mg/dl and after five years followup 1.4 ± 0.5 mg/dl. Basal blood glucose concentration was 130 ± 12 mg/dl and after five years 109 ± 0.8 mg/dl. Weight was maintained. At 5 years, graft and patient survival were 100%. There was no acute rejection after steroids withdrawal. After withdrawal blood pressure control was achieved with less antihypertensive drugs. Lipids diminished slightly with less cholesterol-lowering drugs.

Conclusion: Corticosteroids could be withdrawn safely in stable renal transplant patients and avoid morbidity and adverse events related to chronic utilization improving survival and quality of life.

P487

OUTCOME OF KIDNEY TRANSPLANTATION WITH DONORS AFTER CARDIAC DEATH WITH EXPANDED CRITERIA DONORS STATUS

Manuel Rengel, Lorena Tana, Nayara Panizo, Javier Reque, Borja Quiroga-Gillis, Laura Bucalo, Úrsula Verdalles, Soraya Abad, Almudena Vega, Eduardo Verde
Hospital General Universitario "Gregorio Marañón"

Introduction: Donation after circulatory determination of death has been introduced into clinical practice in many countries as a potential solution to organ shortage, but this kidney transplantation programs are not popular yet, mainly because of logistical concerns and uncertainty about the long-term warm ischaemia impact on transplanted kidneys. Outcomes of kidney transplants that simultaneously exhibit donation after cardiac death (DCD) and expanded criteria donor (ECD) characteristics have not been well studied. We present preliminary results with DCD with ECD.

Patients and methods: We have performed 2 kidney transplantations from uncontrolled Maastricht Category II donors, aged 75 and 76 years, with arterial hypertension, type II diabetes mellitus and proteinuria, with serum creatinine of 0.9 mg/dl. Kidneys were harvested in another hospital with 60 min of warm ischemia and 2.30 h of hypothermic extracorporeal circulation. Recipients were a 65 year woman and a 76 year male. Mean cold ischaemia time was 18 h (16–20). The immunosuppression was performed with polyclonal antibodies (ATG-Fresenius), steroids and sodium micophenolate as induction protocol. Tacrolimus was introduced one week after transplantation. Both cases had delayed graft function. There was no acute rejection. Serum creatinine was 1.5 mg/dl at 13 months follow-up. Patient and graft survival was 100% respectively.

Conclusions: The use of ECD/DCD donor kidneys may be an appropriate strategy to expand the donor pool. Our results show encouraging outcomes, which give rise to further interest in this donor pool.

P488

FOLLOWUP AND OUTCOME OF RENAL TRANSPLANT PATIENTS WITH DECEASED AFTER CARDIAC DEATH DONORS (DCD)

Manuel Rengel, Lorena Tana, Nayara Panizo, Javier Reque, Borja Quiroga-Gillis, Laura Bucalo, Úrsula Verdalles, Almudena Vega, Soraya Abad, Eduardo Verde
Hospital General Universitario "Gregorio Marañón"

Introduction: Prior to the introduction, in the mid 1970s of legislation defining the diagnosis of brain-stem death, transplant organs were removed from DCD. Despite renewed interest in DCD kidney transplantation, very few clinical programs have been developed this type of grafting. Renal transplantation is the best cost effective treatment for end-stage renal failure and improves quality of life, when compared with dialysis. We analyzed the function and outcome of kidney transplants performed from DCD in our hospital.

Patients and methods: From 1999 until January 2013, 38 patients were grafted with kidneys from DCD. This group was compared with recipients of standard criteria donors (SCD) matched for age, sex, number of transplants and HLA. Immunosuppression was performed with Basiliximab, Prednisone, Tacrolimus and Micophenolate (Sodium/Micophenolate). Acute rejection episodes were treated with Methylprednisolone boluses, and ATG-FRESENIUS® when necessary.

Results: The delayed graft function rate was higher on DCD transplants than in SCD graft. Serum creatinine levels was significantly better in the DCD, 1.5 vs. 1.75 mg/dl in SCD. Graft survival at 5 years was 84% in DCD and 85% in SCD. Patient survival in both groups was 100%. Patients grafted with DCD were hospitalized longer and needed more dialysis. Acute rejection episodes were more frequent in DCD.

Conclusion: This source of kidneys has evidence of equivalent graft function and survival, compared with SCD and may contribute to expand the donor pool.

P489

EVEROLIMUS (EVE) IN MAINTENANCE RENAL TRANSPLANT RECIPIENTS CONVERTED FROM CALCINEURIN INHIBITORS (CNI) IMMUNOSUPPRESSION TREATMENT

Manuel Rengel, Lorena Tana, Borja Quiroga-Gillis, Javier Reque, Nayara Panizo, Laura Bucalo, Úrsula Verdalles, Soraya Abad, Almudena Vega, Eduardo Verde
Hospital General Universitario "Gregorio Marañón"

Introduction: Everolimus is a proliferation signal inhibitor utilized as immunosuppressant in combination with CNI in renal transplantation. This approach resulted in excellent efficacy but affect renal function outcomes due to potentiation of CNI nephrotoxicity. However, when Everolimus is combined with reduced exposure to CNI have yielded good renal function whilst maintaining efficacy. The present paper reports our experience with renal grafted patients treated with CNI who were switched to EVE in order to avoid CNI nephrotoxicity. 160 pacientes con trasplante renal de donante cadáver (105 hombres y 55 mujeres).

Patients and methods: From February 2005, 160 cadaver kidney grafted patients (105 men and 55 women), were switched from CNI to EVE. The age of patients was 56 ± 15 years, with 9 ± 6 (1–25) years follow-up period. The immunosuppression treatment was based on Prednisone, Mycophenolate Mophetyl/Sodium Mycophenolic Acid and Tacrolimus/Cyclosporine. CNI was stopped according to an abrupt conversion protocol. EVE was started at 1 mg day divided in two doses and blood concentration was maintained between 3 and 5 ng/ml. EVE indication was for neoplasia in 40%, elective/preventive 42% and INC toxicity in 12%.

Results: After EVE renal function improved in 60% of patients, with serum creatinine of 1.9 mg/dl, 30% remained without changes and 10% worsened. 10% of patients developed proteinuria. EVE concentration was maintained at 3.8 ± 1 ng/ml. No significant changes were observed in lipid metabolism or the necessity of statins, nor erythropoietin, ACE inhibitors doses.

Conclusion: Immunosuppressive therapy as maintenance EVE, replacing CNI-based immunosuppressive regimen in renal transplantation is safe and affects lipid metabolism slightly, with no impact on graft function.

P490

THE RELIABILITY OF PRE-TRANSPLANT LIVE DONOR RENAL BIOPSIES (PTLDB) IN PREDICTING THE GRAFT OUTCOME. A PROSPECTIVE COHORT SINGLE-CENTRE STUDY ON 58 TRANSPLANTED KIDNEYS

Gholamhossein Naderi
Tehran Medical Science

Background: Some studies have shown taking biopsy from deceased donors are of great value in predicting the efficacy and midterm and long term results of kidney transplantation. Goal: Observing the prevalence of pathologic changes in live donors' kidneys and their affects on the graft outcome.

Method: This is a prospective cohort study among the patients who have been through renal transplantation & have been referred to Dr. Shari'ati hospital from April 2010 to April 2011. Time-zero biopsy was taken from each donor's kidney & during the follow-up period grafted kidneys were evaluated by measuring serum Cr. The patients were divided into successful & unsuccessful groups & were compared based on biopsy results. After operation patients were observed during 1st, third, 6th, 9th, 12th months thereafter to check if there is any allograft dysfunction. During each step all patient's information were registered in his records & were edited by SPSS program and finally were analysed.

Result: The number of examined kidneys from live donors was 58 in total among which there are 32 males and 26 females. The average age of live donors was 29.7 with (21–52) while the recipient's was 38 ± 14 (9–64). Average weight of recipients was 62 ± 17 kg (22–109) & the average of the first day after operation urine volume among recipients was 10052 ± 3286 ml. Absence of allograft dysfunction was seen in 55 cases (94.8%) during a month, in 51 cases (87.9%) in 6 months and in 53 cases (91.3%) in a year. The most common observed disorder of biopsies was Glumerulosclerosis which was seen in 20 cases (34.5%) while Fibrosis was seen in nine cases (15.5%) Tubular atrophy in 5(8.6%) and intimal fibrosis in three cases (5.2%). The average of serum Cr

during the 1st month after transplantation was reported 1.15 ± 0.19 mg/dl, during 6 months afterward was 1.21 ± 0.2 mg/dl and during a year was reported 1.14 ± 0.22 mg/dl. The correlation between absent allograft dysfunction and fibrosis or intimal fibrosis had significant p-value ($p < 0$).

P491

LATE RECURRENCE OF KAPOSI'S SARKOMA IN RENAL TRANSPLANT: CASE REPORT

Stefania Mastro Simone, Margherita Mangino, Anna Brunello, Bice Virgilio, Maria Cristina Maresca
Transplant Center

A 47 years-old Caucasian man underwent in 1990 single renal transplantation from cadaveric donor. The immunosuppressive therapy was based on steroids, azathioprine, AntiLymphocyte Globulin and Cyclosporine. The post-operative period was complicated by acute tubular necrosis. At the time of discharge the renal function was again satisfactory and stable with average GFR (Glomerular Filtration Rate) of 43 ml/min. Three months after, the patient developed diffused Kaposi's sarcoma (KS), cutaneous and visceral, more specifically: 11 lesions into the oral cavity and on the limbs and 3 lesions on the gastric mucosa. Cyclosporine and azathioprine were stopped maintaining only the immunosuppressive therapy with steroids. An adjuvant course of radiotherapy was also done. The Kaposi's disease was completely sorted 6 years after and the renal function remained within normal range. Unfortunately 16 years after there was a chronic humoral reject of the graft, treated with high dose of steroids, plasmapheresis and for the purpose, rapamicyn was introduced. After starting the m-Tor inhibitor, respectively 7 months after the reject and 11 years after the complete remission of the first episode of sarcomatous disease, there was a recurrence of KS sarcoma together with a worsening of the renal function that required renal replacement therapy.

P492

DECREASED NK CD56BRIGHT AND NKP46 EXPRESSING CELLS ARE ASSOCIATED WITH IMPAIRED IFN γ PRODUCTION AT DIAGNOSIS OF CANCER IN KIDNEY TRANSPLANT RECIPIENTS

Marie-noelle Peraldi¹, Jeannig Berrou², Antoine Durrbach³, Vincent Vieillard⁴, Caroline Suberbielle⁵, Denis glotz⁵, Nicolas Dulphy⁵, Antoine Toubert⁵
¹Hôpital Saint-Louis; ²INSERM U940; ³Hôpital Bicetre; ⁴Xxxxx; ⁵Hôpital saint-Louis

Background: The incidence of cancer is increased after solid organ transplantation (SOT). NK cells have the machinery to deal with tumors through their activating receptors. Despite their potential involvement, only limited data are available.

Patients and methods: We conducted a matched case control multicentric prospective study including 42 kidney transplant recipients (KTRs) at the diagnosis of cancer and 41 KTRs without cancer. T cell and NK cells subsets analysis and phenotype were performed. NK cells functional tests were realized in a subset of patients.

Results: KTRs with cancer had a significantly higher incidence of both acute rejection ($p = 0.028$) and CMV infection ($p = 0.038$). They also had a significant lymphopenia when compared to control KTR ($p = 0.0001$) with a significant CD4⁺ lymphopenia ($p = 0.04$). Early differentiated CD4⁺/CD27⁺/CD28⁺ and CD8⁺/CD27⁺/CD28⁺ cells were decreased in KTRs at cancer diagnosis ($p = 0.007$ and $p = 0.02$ respectively). There was no difference in Treg (CD4⁺/CD25⁺/CD127^{low}) between these 2 groups. Total CD3⁺/CD56⁺ cell counts were similar in both groups. However, KTRs with cancer had a lower frequency of CD56bright NK cells ($p = 0.001$), a subset involved in cytokine secretion. Percentage of NKP46 expressing NK cells was decreased in KTRs without cancer in total NK cells ($p = 0.001$) and both CD56dim and CD56bright subsets. Degranulation ability quantified by the CD107a assay was decreased in KTRs with cancer compared to control patients (11% vs. 22%, $p = 0.01$), as well as the percentage of IFN γ secreting cells (7.5% in KTRs with cancer vs. 28.8% in the control group, $p = 0.01$).

Conclusion: We show an imbalance of NK cell subsets associated with functional defects in KTRs developing cancer at the onset of malignancy. There was a decreased number of IFN γ -producing cells, a key player in antitumor immune response. This study highlights the role of NKP46, a major activating NK cell receptor in the initiation of cancer.

P493

URINARY TRACT INFECTION IN RENAL TRANSPLANT PATIENTS - WHAT TO DO?

Karolin Thiel¹, Doerte Wichmann², Silvio Nadalin², Ruth Ladurner², Alfred Königsrainer²
¹University of Tuebingen, Clinic of General, Visceral and Transplantation Surgery; ²University of Tuebingen

Background: Urinary tract infection (UTI) is the most common bacterial complication in patients following renal transplantation. UTI is a source of

morbidity, is able to cause graft failure or death in renal recipients. Ureteral stents are inserted at the time of transplantation to prevent leakage or stenosis of the ureteroneocystostomy (UCN), but are associated with an increased relative risk of UTI. Intraoperative placement of urethral catheter should be also a source of bacterial UTIs after renal transplantation. We would present a collection of measures to reduce UTI-rate in renal transplant recipients.

Methods/material: We included all renal transplant patients with follow-up at our institution in 2010 and 2011. Patient's data like demographics, immunosuppression, specific data for surgery and infections were considered. Follow-up averaged 300 days, accounted at the minimum 180 days. Patients were allocated into two groups, depending on time of ureteric stent removal: S = short time ≤ 30 days ($n = 31$) and L = long time ≥ 30 days ($n = 44$).

Results: 57 patients received transplants from deceased donor and 18 from living donor. Seven simultaneous pancreas kidney transplantations and six "2-for-1"-kidney-transplantation were done. Double-J-Catheter (DJC) for stenting UCN was used always. In 17 renal recipients overall occurred no UTI (S $n = 8$, L $n = 9$). Most frequent bacteria caused first UTI in renal transplant patients were gram-negative Enterobacteriaceae, followed by gram-positive Enterococci.

Conclusion: Measures package to reduce UTI in patients following kidney transplantation composed of (i) Early removal of urinary catheter, (ii) Early removal of ureteral stent, (iii) Early calculated antimicrobial treatment in cases of typical symptoms.

P494

ANEMIA AFTER KIDNEY TRANSPLANTATION: PREVALENCE, RISK FACTORS, AND INFLUENCE ON GRAFT AND PATIENT SURVIVAL

Osama Gheith, Torki Al-Otaibi, Narayanan M.R. Nampoory, Medhat Halim, Hasanein Aboateya, Hani Adel, Prasad Anir
OTC

Introduction: Post-transplant anemia and its influence on transplant outcomes have not yet been reported from the Middle East in the era of erythropoietin.

Methods: Out of 2206 renal transplant recipients who were transplanted at Hamed Al-Essa Organ transplant center of Kuwait, 183 of them (9.15%) were maintained on erythropoietin. Six months post-transplant, patients who did not achieve target hemoglobin (HB>12 g/dl) comprised group 1 ($n = 36$), while those who had HB <12 will comprise group 2 ($n = 147$). We evaluated these cases for possible causes of resistant anemia.

Results: Majority of patients in both groups were females ($p = 0.86$) with mean age of 42.7 ± 16.3 vs. 37.2 ± 15.6 years ($p = 0.11$). Most of patients in both groups received anti-proliferative induction ($p = 0.85$) and were maintained on steroid, MMF and CNi ($p = 0.98$). Only 4(2.7%) cases of group 2 achieved target HB with EPO therapy. The majority of patients in both groups were comparable regarding C reactive protein, folic acid and vitamin b12, ($p > 0.05$); and most of them revealed negative proteinuria and low vitamin D level ($p > 0.05$). Serum iron was significantly lower in anemia group ($p = 0.01$). Most of the anemic patients received grafts from cadaveric or unrelated donors especially with preemptive cases, while most of non-anemic group got their grafts from related donors. ($p = 0.04$). We observed that patient age correlated negatively with serum iron ($p = 0.048$); serum ferritin correlate negatively with HB 6 months post-transplantation but not that at time of transplantation ($p = 0.004$ & 0.5 respectively). There was no significant difference in patient or graft outcome among the two groups ($p > 0.05$).

Conclusion: Post-transplant anemia is common, with suboptimal use of iron especially among pretransplant CKD patients. Live related donors and exogenous EPO gave protection. Presence of post-transplant anemia at 6 months did not influence graft or patient outcome in this short study.

P495

DOES KIDNEY TRANSPLANTATION WITH DECEASED OR LIVING DONOR AFFECT GRAFT SURVIVAL?

Eghlim Nemati, Behzad Einollahi, Mahboob Lesan Pezeshki, Vahid Poufarziani

Nephrology Urology Research Center of Baghiatallah Iatallah

Background and aims: There are growing numbers of patients with ESRD globally at an unexpected rate. The biggest challenge in transplantation today is organ shortage; hence, using deceased donor is encouraging. The aim of study was to investigate differences of survival rates between kidney transplant recipients with deceased donor and living donor.

Patients and methods: In a retrospective Cohort study of 218 kidney transplant recipients carried out in our institute from April 2008 to September 2010. Demographics and post-transplant follow up including immunosuppression regimens, rejection episodes, and survival rates were evaluated. The patients were divided into two groups according to donor kidney transplantation sources: group I, living donor kidney transplants; and group II, deceased donor kidney transplants.

Results: Although, there were not significantly differences between 1 year patient and graft survival rates in both groups, three years of patient and graft survival rates were significantly higher in living donor kidney transplants as compared to recipients who received kidney from deceased donor ($p = 0.006$ and $p = 0.004$, respectively). In Cox-regression model after adjusting of other

confounding factors such as age, gender, diabetes mellitus and first or second times of transplantation, overall patient and graft survivals were also significantly lower in deceased kidney transplantation than those came a kidney from living donor (HR = 3.5; 95%CI: 1.2–10.4, $p = 0.02$ for patient survival and HR = 5.4; 95%CI: 1.5–19.5, $p = 0.009$ for graft survival).

Conclusion: We found acceptable short-term survivals in both groups, but living donor recipients continue to have better long-term patient and graft survival rates.

Key word: Living Donor, Deceased donor, survival, kidney transplantation.

P496

LONG-TERM CLINICAL OUTCOMES OF KIDNEY TRANSPLANTATION FROM 1982 TO 2013 AT SINGLE CENTER IN KOREA

Ui Jun Park, Won Hyun Cho, Hyoung Tae Kim, Eun Ah Hwang, Seung Yeup Han, Sung Bae Park

Keimyung Univ. Dongsan Medical Center

Background: The present study aims to determine the long-term clinical outcomes of kidney transplantation and evaluate risk factors that impact on graft survival.

Methods/materials: Between 1982 and 2013, One thousand kidney transplantations were performed at the Keimyung University Dongsan Medical Center of Korea. We analyzed the clinical characteristics and outcomes of kidney transplant recipients retrospectively. Transplant era was classified according to immunosuppressive regimens.

Results: There were 1000 recipients with a mean age of 39 years, and 63% were male. Chronic glomerulonephritis was the leading cause of primary diseases. First kidney transplantation was 905 cases (91%). Composition of donor type was living, 74% and deceased, 26%. Overall, 1, 5, and 10-year graft survival were 95%, 80%, and 62%, respectively. Ten-year graft survival according to the transplant era was 35% (1982–1990), 55% (1991–2000), and 94% (2001–2013). A multivariate analysis revealed significant risk factors for graft survival included transplant era and the immunosuppressive regimen.

Conclusions: This review of 30-year experiences in a single center showed the graft survival has improved over the last three decades. Use of triple immunosuppressants regimen includes tacrolimus and MMF was associated with a significantly reduced risk of graft loss.

P497

CORTICOSTEROID AVOIDANCE IN ADULT KIDNEY TRANSPLANT RECIPIENTS RECEIVING ATG-FRESENIUS INDUCTION: 5 YEARS RESULTS OF A PROSPECTIVE AND RANDOMIZED STUDY

Laetitia Albano¹, Diego Cantarovich², Lionel Rostaing³, Nassim Kamar³, Didier Ducloux⁴, Georges Mourad⁵, Philippe Wolf⁶, Elisabeth Cassuto¹

¹CHU Nice; ²ITUN, Nantes University Hospital; ³CHU Toulouse; ⁴CHU Besançon; ⁵CHU Montpellier; ⁶CHU Strasbourg

One hundred ninety-seven adult and immunological low-risk recipients of primary deceased donor kidney transplants were included in a 1- and 5-year efficacy analysis of a prospective, randomized, open-label, multicentre, investigator-driven study (The FRANCIA Study): 99 patients received at least 6-month corticosteroid (Cs+) and 98 patients no corticosteroid at all from the day after surgery (Cs-). All patients received 5 ATG-Fresenius infusions, CsA from postoperative day 5 and MMF from the day of surgery. This the actual results after 5 years of follow-up of all enrolled patients are described. Patient survival was 91.3% (9 deaths) in the Cs+ group and 93.9% (6 deaths) in the Cs- group ($p = 0.507$). Graft survival (including death) was 80.6% (19 losses) in the Cs+ group and 86.7% (13 losses) in the Cs- group ($p = 0.276$). Although Cs- patients experienced significantly more biopsy-proven acute rejection episodes during the first year (17 vs. 7, $p < 0.031$), none of them experienced an acute rejection thereafter as compared to four patients in the Cs+ group. The overall 5-year event-free of acute rejection rate did not differ significantly among both groups (Cs+ = 81.8 vs. Cs- = 74.5%, $p = 0.144$). However, 5-year graft survival was significantly lower in Cs+ patients with history of acute rejection than Cs- patients: 55.6 vs. 92% ($p = 0.005$). Total number of AE as well as SAE did not differ among groups, however a trend for less insulin-dependent diabetes, dyslipidemia and high blood pressure was observed in Cs- patients. Although total number of patients developing neoplasm did not differ among groups (35 in Cs+ and 26 in Cs-), no PTLD was reported in the Cs- group as compared to 4 in the Cs+ group ($p = 0.049$). Furthermore, less Cs- patients were diagnosed having skin cancers (Cs+ = 11 vs. Cs- = 3, $p = 0.034$). Median serum creatinine, creatinine clearance and 24-h proteinuria were similar and stable in both groups throughout follow-up. De novo appearance of DSA was 11% in 151 tested patients, with no difference in both groups. In conclusion, Cs avoidance as compared to at least 6-month Cs therapy, in the context of ATG-Fresenius induction and CsA/MMF maintenance immunosuppression, was associated with more early acute rejections but without consequences on long-term graft survival. Cs+ patients were at risk for late (>1 year) acute rejection and subsequent graft loss compared to no late episode of acute rejection in Cs- patients. Nevertheless, graft and patient survival 5 years after transplantation were excellent and comparable in both

groups. A better metabolic profile, no case of PTLD and less skin cancers were also observed in Cs- patients. These findings may hope for better long-term (>5 years) efficacy and safety findings in these patients.

P498

LAPAROSCOPIC PYELOURETEROSTOMY WITH RECIPIENTS URETER IN A TRANSPLANTED KIDNEY WITH URETERAL STRICTURE

Dmitry Perlin, Ilya Aleksandrov, Alexey Nikolaev, Olga Shevchenko
Volgograd Regional Hospital of Urology

Background: Ureteral obstruction secondary to ischemia is the most common urologic complication of kidney transplantation. Pyeloureteral anastomosis with recipient ureter has shown most satisfactory long-term results in its management. Existing urinary infection and immunosuppression determine the high risk of wound complications. Till last time this procedure has been performed through open surgery, however in 2006 Orviato M.A. et al. first reported minimally invasive approach using the Da Vinci robotic system.

Methods: We have experience more than 30 procedures of ureteral strictures repair after kidney transplantation by open surgery during 20 years. Since February 2012 we used pyeloureteral anastomosis with recipient ureter in two patients by laparoscopic approach. The operations lasted 215 and 275 min. respectively. In both cases the surgery was performed after percutaneous nephrostomy because of deterioration of transplanted kidney function. Internal stent was indwelled laparoscopically. No drain tube was left.

Results: The nephrostomy tubes were removed after 7 and 10 days respectively. The stents were removed after 20 and 27 days respectively. No complications were seen during the surgery and postoperative period. Now serum creatinine level is 0.12 and 0.15 mm after 15 and 12 months after surgery respectively.

Conclusions: In spite of some difficulties related with topographic landmarks and severe tissues fibrosis after transplantation laparoscopic pyeloureterostomy in transplanted kidney is safe and feasible procedure. The main advantage is absence of risk of most serious complications related with wound infection in immune compromised patients. Moreover, early recovery to usual activity and diet facilitates to prevent pulmonary infections and to normalize intestinal absorbability of the immunosuppressive drugs.

P499

ANALYSIS OF VARIABLES IN NON-INVASIVE CARDIAC OUTPUT MONITORING DURING ANESTHESIA FOR KIDNEY TRANSPLANT SURGERY

Joon Seok Oh¹, Joong kyung Kim², Yong Hun Sir², Seong Min Kim², Jin Ho Lee², Kill Huh²

¹Bong Seng Memorial Hospital; ²Bong Seng Hospital

Introduction: Patients with end-stage renal disease (ESRD) can be hemodynamically unstable because of frequent changes in peripheral resistance and blood volume during kidney transplant surgery. Cardiac output (CO) is a key variable when describing and treating the cardiovascular system. Thermodilution via a pulmonary artery catheter is the most frequently used method, but it lacks accuracy. Non-invasive cardiac output monitoring (NICOM) measures CO based on chest bio-reactance. Validated data of NICOM in patients with kidney transplant surgery are lacking. So we had non-invasive cardiac output monitoring during anesthesia for renal transplant surgery.

Methods: CO values using NICOM were recorded during anesthesia in patients with renal transplant surgery due to ESRD. Correlation analysis were performed with variables measured 59 times from 20 subject.

Results: Stroke volume (SV) had strong negative correlation with total peripheral resistance (TPR) ($R = -0.81$, $p = 0.00$, Figure 1). But SV had poor correlation with mean arterial pressure (MAP) ($R = -0.26$, $p = 0.05$). And TPR had fair correlation with MAP ($R = 0.36$, $p = 0.01$).

Conclusions: Stroke volume and total peripheral resistance measured by NICOM showed a strong correlation in patients with renal transplant surgery. Additional studies in larger patient populations may be warranted for further validation.

P500

LESS REJECTION IN ABO INCOMPATIBLE LIVING DONOR KIDNEY TRANSPLANTATION AT THE TRANSPLANT CENTER OF ERLANGEN-NUREMBERG. A SINGLE CENTER EXPERIENCE OVER 7 YEARS

Katharina M. Heller¹, Johannes Jacobi¹, Wolfgang Legal¹, Hendrik Apel², Bernd Wullich², Kai Uwe Eckardt¹

¹Nephrologie Medizin 4 FAU Erlangen, Nürnberg; ²Urologie FAU Erlangen, Nürnberg

Background: Blood group incompatible (iABO) living kidney donation is experiencing increasing importance due to the lack of post-mortem organ donation in Germany. At the centre of Erlangen-Nuremberg 23% of living

kidney transplantation are iABO donated also to recipient at risk with pre-immunization or repeatedly transplanted.

Method/material: Retrospective analysis of 152 LSP-NTX in 2006–2013 with 117 (77%) blood group compatible (cABO) donors and 35 (23%) iABO donors. iABO recipients receive in 71% a non-relative donation, showing in 27% performed antibodies against human leukocyte antigen (HLA) and have been repeatedly transplanted in 17% (2nd/3rd kidney transplant, after heart, liver or pancreas transplantation). The cABO standard therapy is tacrolimus, mycophenolate mofetil, steroids and basiliximab. The iABO recipient conditioning is preoperatively extended by rituximab 4 weeks before and (Glycoex-). Immunoabsorption accordingly to blood group antibody titer (target 1:4).

Results: Patient survival after 7 years is 100% in both groups. Graft survival is 97% in iABO vs. 92% in cABO. No significant difference in eGFR between iABO (56 ml/min) and cABO (53 ml/min) at 12 months. Significantly fewer rejection episodes in the first 2 years in iABO (18%) with borderline or BANFF Ia compared to cABO (49%) with more BANFF II and humoral rejections ($p = 0.028$). Less incidence of polyomavirus nephropathy in iABO compared to cABO ($p = n.s.$).

Conclusions: The iABO living kidney transplantation is a successful expansion of the living donor program with good function rates, significantly less rejections and less polyomavirus nephropathy. Even recipients at risk with pre-immunization or previous transplantations will have a benefit from iABO transplantation.

P501

EXPERIENCES WITH CONVERSION TO ONCE-DAILY ADVAGRAF AND SIROLIMUS COMBINATION FROM TAC-MMF IN STABLE KIDNEY RECIPIENTS

Kwan Tae Park, C.W. Jung, Y.J. Choi
Korea University Medical Center

Introduction: With improvement in both short-term outcome and acute rejection rate, the main concerns in care of kidney transplantation (KT) recipients has shifted toward factors that constitute the long-term outcome such as safety profile, compliance and the patient's quality of life (QOL). The purpose of this study is to report our experiences of conversion to once-daily regimen using very low dose of advagraf (ADV) and sirolimus (SRL) in stable kidney recipients in comparison to Tac-MMF regimen.

Methods/materials: Of 40 KT recipients with stable renal function (more than 6 months after KT, 24-h urine protein <400 mg, creatinine variance <30% within 3 months) underwent conversion from tacrolimus (TAC)-mycophenolate mofetil (MMF) based regimen to once-daily ADV-SRL regimen. Mean conversion day after KT was 25.7 months and mean follow-up day was 12.4 months. The target trough concentration (C₀) of ADV and SRL were 2–4 and 5–10 ng/ml, respectively. The renal functions, rejection rate as well as compliance profile and QOL questionnaire were compared with case-matched TAC-MMF group.

Results: The ADV and SRL conversion group showed slight improvement in renal function at 3 months after conversion, evidenced by eGFR (63.4 ± 16.2 vs. 76.1 ± 16.4 ml/min/1.73 m²). Meanwhile, lipid profiles deteriorated in most patients, requiring more advanced medicine for management (LDL levels 63.8 ± 12.0 vs. 84.6 ± 18.4 mg/dl). Mean ADV and SRL C₀ were 2.97 ± 0.5 and 6.71 ± 2.1 ng/ml, respectively. One patient suffering from severe oral ulcer and two patients due to recurrent urinary tract infection and significant edema respectively returned to the original regimen. No recipient experienced acute rejection. The compliance profile was significantly improved and QOL survey revealed significant improvements in QOL.

Conclusions: Once daily ADV-SRL regimen can be a novel standard regimen giving benefits of improving renal function, compliance and QOL in stable kidney recipients.

P502

EX VIVO TREATMENT OF KIDNEY TRANSPLANT WITH NON-MYCOTIC RENAL ARTERY ANEURYSM

Caren Randon, Frank Vermassen, Patrick Peeters, Steven Vanlaecke
Gent University Hospital

Background: A Non-mycotic renal artery aneurysm of an autologous kidney is a rare condition with a prevalence of 0.1%. In kidney transplants, contrary to pseudo-aneurysms at the anastomotic site, only five case reports have been published so far. One patient had polycystic kidney disease, in the other three cases the origin of the renal failure was not mentioned.

Methods/material and results: We present the case of a 25-year-old woman with renal failure due to a branchio-otorenal syndrome who received a living related donor kidney. At 7 years follow up, a saccular aneurysm of both her renal arteries was diagnosed. The reconstruction was performed *in vivo* with a homologous greater saphenous vein as interposition graft for both arteries separately. A re-operation was needed for acute thrombosis of both arteries. The postoperative follow up was complicated by an ATN.

Conclusion: Renal artery aneurysm formation could be triggered by technical complication and genetic factors. Poststenotic dilatation, the use of saphenous vein interposition, or – as in our case – a primary dissection of the intima of the donor artery results in medial degeneration and aneurysm formation. Also both, branchio-otorenal syndrome and polycystic kidney disease, have a higher risk for aneurysms formation.

P503

LONG TERM RESULTS OF PERCUTANEOUS RADIOFREQUENCY ABLATION OF A RENAL CANCER IN A TRANSPLANTED KIDNEY

Luisa Berardinelli, Giovanni Paone, Mauro Raiteri, Antenore Giussani, Alessandra De Scalzi, Donata Cresseri
Fondazione Ca' Grande Osp. Maggiore Policlinico

Development of cancer in the transplanted kidney is a rare phenomenon. Treatment options include radical nephrectomy or nephron-sparing surgery. Percutaneous Radiofrequency Ablation (PRFA) of a renal mass in a kidney graft has been rarely reported and short term follow up periods are registered. We describe the case of PRFA for a small renal mass in a transplanted kidney. A 23-year-old patient received a living donor kidney from his 51-year aging mother in October 1994. At 13 years after transplantation, a spherical hypoechoic nodule of 16 mm in the upper pole of the graft was detected on annual ultrasonographic control. CT-scan confirmed the diagnosis of renal carcinoma; as the mass was small in diameter and the renal function was satisfactory (serum creatinine 1.74 mg/dl), a nephron-sparing surgery was planned, that was refused by the patient. An ultrasound guided PRFA was performed under local anesthesia without any complication. The graft was removed 44 months later due to chronic allograft nephropathy. Histology showed a minimal non infiltrating local recurrence. PRFA has a satisfactory oncologic efficacy for a small renal mass in renal allografts.

P504

POLYCLONAL ANTILYMPHOCYTE GLOBULIN INDUCTION: 30 YEARS SINGLE CENTRE EXPERIENCE AFTER KIDNEY TRANSPLANTATION

Diego Cantarovich, Magali Giral-Classe, Jacques Dantal, Gilles Blanchon, Maryvonne Hourmant, Florent Leborgne, Jean-Paul Souillou
ITUN, Nantes University Hospital

Thymoglobulin and Lymphoglobulin were started in our centre to prevent acute rejection in 1977 and 1981, combined to azathioprine and corticosteroids. The aim of this retrospective analysis was to evaluate graft and patient's outcome throughout three decades in all patients who received these polyclonals for induction. Among 4809 patients who received a kidney transplant in our centre, 1978 (1183 men and 795 women; mean age 44.114 years) received Thymoglobulin and 235 Lymphoglobulin (137 men and 98 women; mean age 39 ± 13 years) for induction. Ninety-seven percent of transplants were from deceased donors. Although initial dose of Thymoglobulin was similar throughout time (3 vials, 75 mg/day), duration of induction decreased from 3 weeks to 1 current week. Consequently, total cumulative dose was significantly diminished to <10 mg/kg. Lymphoglobulin (6 vials, 600 mg/day) was given in case of Thymoglobulin clinical intolerance or during periods of Thymoglobulin unavailability (its use was stopped in 2006). Dose of both polyclonals was adjusted according to the rosette test. Adjunctive immunosuppressive regimens varied within time, with the introduction of CsA in 1982, MMF in 1996 and Tac in 1999. Since 1982 (CsA initiation), corticosteroids were designed to be stopped between 2 and 3 months after transplantation and since 2000 designed to be avoided the day after surgery. When Basiliximab was introduced in 1995 for induction in immunological low-risk patients, Thymoglobulin was restricted to the remaining "high-risk" categories (PRA >25%, retransplants, cold ischemia >36 h). When compared to Lymphoglobulin, Thymoglobulin was associated with a significant higher graft survival throughout the three decades with almost 20% difference (i.e. 70 vs. 50% at 10 years; 50 vs. 30% at 20 years, including death; $p < 0.0001$). Patient survival was similar with Thymoglobulin and Lymphoglobulin (50% at 30 years). When only Thymoglobulin patients were analyzed, there was no statistical difference in graft and patient survival in recipients of primary or retransplantation throughout f/u. No difference was neither observed when compared >8 and <8 days of induction duration. When arbitrarily graft survival not censored for death was evaluated in three consecutive periods: 1977–1990, $n = 487$; 1991–2001, $n = 755$; 2002–2013, $n = 696$, a significant improvement was seen with a 30% gain in the last decade ($p < 0.0006$). This amelioration, despite the use of Thymoglobulin in a higher-risk transplant population within time (recipient age: 41, 44 and 46 years, $p < 0.0001$; retransplants: 15.6, 27 and 42%, $p < 0.0001$; donor age: 31.3, 37.3 and 44.6 years, $p < 0.0001$), was not due to less death (similar patient survival) but probably due to a significantly lower number of patients with acute rejection episode: 40.8%, 18% and 15.8%, respectively, $p < 0.0001$). CMV infection/disease was particularly decreased in the last decade from 28.8% to 11%, certainly due to the universal use of valganciclovir followed by valganciclovir. PTLD incidence decreased from 4% to 1% in the last d.

P505

KIDNEYS WITH FIBROMUSCULAR DYSPLASIA: SAFER RECONSTRUCTION USING PRE-OPERATIVE RECONSTRUCTIONS AT BENCH

Luisa Berardinelli, Claudio Beretta, Antonio Pasciocco, Riccardo De Carlis
Fondazione Ca' Grande Osp. Maggiore Policlinico

Fibromuscular Dysplasia (FMD) is one of the abnormalities that generally precludes kidney transplantation. Early/long term outcomes of 14 kidney recipients

transplanted with grafts affected by initial FMD and reconstructed at bench before transplantation are examined. In the entire series of 3082 kidney transplants, 14 kidneys (eight right and six left) coming from 12 LDs and two from DDs showed typical signs of FMD. The mean donors' age (11 females and three male) was 55.2 years. Two renal arteries were present in three cases. Various original microsurgical bench techniques were adopted to safeguard the following transplantation. All the 14 grafts showed immediate recovery and there were no postoperative complications or disease recurrence, either in the 12 LDs or in the recipients. The mean duration of the grafts was of 7.1 years, for a mean follow-up period of 8.4 years. Ten patients have their kidney still functioning, one patient died at 7 years after TX from a cancer, three patients lost their graft at a mean 7.6 years after transplantation. Reconstruction at bench of FMD-grafts prevents complications after transplantation, so safely widening the donor pool.

P506

PREGNANCY IN SAUDI KIDNEY TRANSPLANT RECIPIENTS: A LOCAL EXPERIENCE

*Adnane Guella, Eltayeb Mohamed
Military Hospital*

Background: Although conception rate is high in the Middle East as a whole, rare reports are available in the transplant population. We therefore report here our experience from the Eastern Province of Saudi Arabia.

Methods/materials: A total of 33 pregnancies in 15 kidney recipients transplanted in our center from 1992 to 2008 were reviewed. All data related to maternal, fetal and renal outcomes were recorded.

Results: The mean age at the time of conception was 26.5 ± 7.5 years. Mean transplantation-to-pregnancy interval was 23.6 months (range: 5–60). Renal function was stable at the start of conception. Twelve pregnancies (36.4%) were unsuccessful (10 abortions and 2 stillbirths), and 21 were successful (63.6%) including one twin pregnancy. Ten patients had caesarian section and 11 had normal delivery. Birth weight was low (<2.5 kg) in six children and normal (>2.5 kg) in 15. Nine ladies (60%) had more than one pregnancy. We noticed hypertension in five patients and preeclampsia in 2. No patient had rejection or gestational diabetes. All recipients were on cyclosporine, azathioprine and prednisolone. Renal function remained stable during pregnancy.

Conclusion: Our study showed that pregnancy in Saudi kidney transplant recipients had no deleterious effect on maternal and kidney graft outcomes. Fetal outcome was satisfactory.

P507

LAPAROSCOPIC DONOR NEPHRECTOMY: OUR EARLY RESULTS

*Mehmet Erikoglu, Tefik Küçükartallar, Ahmet Tekin, Sakir Tavli
Meram Medical Faculty Organ Transplantation Center*

Background: The increase in the number of patients waiting for organ transplants all around the world and the insufficient number of cadavers, has led to increased interest in transplants from live donors. For volunteer donors, the traditional open donor nephrectomy causes a long scar after the flank incision on the thoraco-abdominal wall, severe pain, risk of pleural injury, incisional hernia, long-term hospital stay, wound problems and a relatively long period of recovery.

Methods/materials: In a study of Laparoscopic Donor Nephrectomy (LDN) comprising 15 patients (seven female, eight male) the surgical technique, intraoperative findings, postoperative follow-up and morbidity were evaluated.

Results: All patients underwent laparoscopic left nephrectomy with a transperitoneal approach. Due to artery and vein anomalies in one patient, the open procedure was performed. The mean operative time was 115 min (90–135), the mean follow-up was 8.2 months (1–19), the average length of hospitalization was 2.9 days (2–4), and the mean warm ischemia time was 190 s (100–240). No perioperative complications were observed and none of the patients showed signs postoperative wound infection.

Conclusion: With increased surgical experience, LDN is a method that might have a lower rate of mortality and morbidity compared to open nephrectomy. We carry the conviction that LDN is the gold standard for living donor nephrectomy.

P508

LCP-TACRO-ASSOCIATED IMPROVEMENT IN TAC-INDUCED TREMORS IS ALSO ASSOCIATED WITH IMPROVEMENT IN QUALITY OF LIFE: RESULTS OF A SWITCHING STUDY OF KIDNEY TRANSPLANT PATIENTS WITH TREMOR (STRATO)

*Roberto Gedaly¹, Steven M. Steinberg², Anthony Langone³, John C. Morgan⁴
¹University of Kentucky; ²California Institute of Renal Research; ³Vanderbilt University; ⁴Medical College of Georgia*

Background: Tremor, a manifestation of tacrolimus (TAC)-associated neurotoxicity, is common in kidney transplant recipients (KTR). Two hour (peak) serum concentrations are correlated with this toxicity. Reduction or cessation of TAC dosing may reduce tremor symptoms but increases the risk for rejection. LCP-Tacro™ (extended-release once-daily MeltDose® formulation, Veloxis

Pharmaceuticals) is a novel form of TAC that has a reduced peak concentration but comparable AUC exposure, at a reduced dose of ~30% versus standard TAC. Converting patients who have tremor with a standard TAC formulation to LCP-Tacro resulted in a measurable reduction in tremor rating score (improve 15.6%, $p < 0.05$; Langone A., et al. American Transplant Congress, 2013, abstract B1022). The present analyses examined if patient reported quality of life (QoL) improves after conversion, and if changes in QoL correlate with tremor rating scale.

Methods: In this open-label, multicenter, prospective Phase 3b exploratory clinical study, stable KTR on Prograf or generic TAC, experiencing tremor, were enrolled. Following seven days of their pre-enrollment twice-daily TAC, patients were switched to LCP-Tacro. Tremor pre- and 7 days post-conversion (Day 14) was evaluated using the Fahn-Tolosa-Marin (FTM) tremor rating scale; patients completed the QUEST (QoL in Essential Tremor).

Results: Thirty-eight of the 44 enrolled KTR had FTM and QUEST data available. There was a significant ($p < 0.001$) improvement in QUEST score at Day 14 (mean [SD] absolute and percent change from baseline: -7.04 [9.41]; -39.08% [39.43%]). Change in QUEST score was significantly ($p = 0.006$) correlated (Pearson Coefficient $R = 0.44$) with change in FTM score (Figure); in particular, change in physical ($R = 0.48$) and psychosocial ($R = 0.47$) QUEST subscales were significantly ($p < 0.004$) correlated with change in the functional disabilities component of the FTM. There were no safety concerns.

Conclusions: Results from this exploratory study suggest a significant improvement of QoL with tremor experienced by KTR who switch from Prograf or generic TAC to LCP-Tacro, and is consistent with improvement of tremor experience assessed by tremor rating scale.

P509

LIVER ALLOGRAFTS DO NOT ALWAYS PROTECT FROM KIDNEY ALLOGRAFT REJECTION IN SENSITIZED RECIPIENTS OF SIMULTANEOUS LIVER-KIDNEY TRANSPLANTS

Laura Lladó¹, Oriol Bestard¹, Taco Sánchez Omar Enrique², Josep Maria Grinyó³, Baliellas Carme³

¹Hospital Universitari de Bellvitge; ²Nephrology Department, Hospital Universitari de Bellvitge, IDIBELL, L'Hospitalet de Llobregat, Barce; ³Hospital Universitario de Bellvitge

The impact of pre-existing and de novo circulating anti-HLA antibodies (DSA or not, in simultaneous liver-kidney transplants (SLKT) still remains controversial. We evaluated the impact of pre-transplant humoral sensitization in a group of 39 adult recipients that underwent a SLKT between 1988 and 2011. 11/39 patients had different degree of humoral sensitization; all recipients received an immunosuppressive regimen based on a calcineurin inhibitor, an antimetabolite and induction therapy with either monoclonal (19/30) or polyclonal (20/39) antibodies. Acute kidney rejection (AKR) occurred in three patients (2 AHR, and 1 T-cell mediated); eight patients developed post-transplant acute cellular liver rejection; neither type of maintenance immunosuppression, delayed graft function, HCV nor CMV infection influenced the development of AKR. Conversely, acute liver rejection (ALR) was numerically higher among patients receiving CsA as compared to those receiving TAC ($p = 0.08$), but not related to induction therapy, HCV or CMV infection. A positive pre-transplant CDC crossmatch was obtained in 5/39 SLKT. Four of them did also show pre-transplant PRA>25%. Sensitized transplant recipients displayed a significantly higher incidence of AKR and those with a positive pre-transplant crossmatch developed Antibody-mediated AKR ($p = 0.038$). On the contrary; all eight patients developing T-cell mediated ALR had a negative cross-match. Kaplan-Meier analysis of kidney allograft survival regarding the degree of pre-transplant peak of PRA sensitization showed that those SLKT recipients with a previous PRA>25% were at increased risk of kidney graft loss as compared to those with low or undetectable anti-HLA antibodies. In summary, liver allografts may not be fully protective of the renal allograft in terms of rejection or function, especially among sensitized patients.

P510

GASTROINTESTINAL TRANSIT IN RENAL TRANSPLANT PATIENTS TREATED WITH MYCOPHENOLATE MOFETIL

Luciana Cora¹, Maria Carmo Borges Teixeira¹, Thayrone Miranda Barreto¹, Thainara Torres Oliveira¹, Ricardo Brandt Oliveira², Jose Ricardo Arruda Miranda³

¹Alagoas State University of Health Sciences; ²University of Sao Paulo; ³Sao Paulo State University

Background: Mycophenolate mofetil (MMF) is effective to prevent renal allograft rejection but gastrointestinal (GI) side effects such as diarrhea are common. Despite this, studies on GI disorders after renal transplantation are scanty. Biomagnetic methods such as AC Biosusceptometry (ACB) are non-invasive and radiation-free and are used for monitoring GI motility. The aim of this work was to employ ACB to evaluate gastrointestinal transit in renal transplant patients treated with MMF.

Methods: Protocol was approved by local ethics committee and was registered with clinicaltrials.gov (NCT01777204). Seven stable renal transplant patients treated with prednisone, tacrolimus and MMF, and 7 healthy volunteers were eligible for study entry. Participants were not diabetics or

had GI chronic diseases. After an overnight fast, they received standard breakfast and magnetic markers. ACB sensor was used to monitor gastric and colonic regions at regular time intervals for 36 h. Gastric emptying time (MGET), colonic transit time (MCTT) and inter-subject coefficients of variation (COV) were calculated. Results are expressed as mean \pm SD and were compared between groups using unpaired Student's *t*-test. *p*-values <0.05 were accepted as statistically significant.

Results: MGET for patients and volunteers was 84.55 ± 69.86 and 148.40 ± 45.36 , respectively. COV for patients was 82.62% and for controls was 30.56%. Despite expressive inter-subject variability, no differences were observed in gastric emptying ($p = 0.065$). MCTT for MMF and controls was $15h30 \text{ min} \pm 1 \text{ h}$ and $30 \text{ h} \pm 3 \text{ h}$, respectively. Colonic transit was significantly faster in patients compared to volunteers ($p < 0.001$).

Conclusion: Our preliminary data suggest that immunosuppressive drugs influence GI motility. Further studies to establish if differences on bioavailability could be the mechanism to explain the relationship between diarrhea and MMF treatment are needed.

P511

PRECISION DIAGNOSIS FOR PERSONALIZED MEDICINE FOLLOWING KIDNEY TRANSPLANTATION

David Perkins, Alan Ropski, Patricia Finn, David Perkins
University of Illinois

A major objective in clinical practice, including transplantation, is to develop more focused and personalized approaches for both diagnosis and treatment. There have been several recent successes in correlating specific polymorphisms with drug responses; however, the goal of personalized medicine is challenging for multiple reasons. (i) Humans are outbred with numerous genetic polymorphisms, (ii) each individual confronts different sets of environmental exposures, and (iii) as analysis focuses on smaller subsets or an individual patient the statistical power is increasingly diminished. In addition, the "gold standard" for diagnosis following kidney transplantation is pathological analysis of a graft biopsy; however, studies have shown approximately 20% variation among diagnoses between blinded pathologists. To address these challenges we focused on the largest available dataset of microarray data analyzing kidney biopsies (GEO accession GSE21374) and combined samples from multiple studies to increase statistical power. After filtering the data, we used multidimensional scaling (MDS) to eliminate 11 samples which were statistical outliers ($>2 \text{ SD}$). The 11 outliers did not correlate with any of the diagnoses and appear to include excessive technical noise. Next, we identified subsets of each diagnosis based on silhouette width, Dunn index and connectivity criteria using three types of clustering algorithms (hierarchical, *k*means and *pam*). These results indicate that the dataset represented 21 distinct molecular diagnoses (expanded from the 11 pathological diagnoses). The subsets of a pathological diagnosis were often extensively different. For example, we identified 849 genes that were significantly different ($\text{fdr} < 0.05$) between two subsets of T cell mediated rejection (TCMR) indicating substantial differences in gene expression despite the same pathological diagnosis between the two sub-clusters of TCMR. To identify the biological functions of each sub-diagnosis, we identified.

P512

INFLUENCE OF MDR1 GENE POLYMORPHISMS ON LIPID LEVELS IN RENAL TRANSPLANT PATIENTS

Hayriye Senturk Ciftci¹, Tzevat Tefik², Yasar Caliskan³, Ismet Nane², Aydin Turkmen³, Fatma Savran Oguz¹, Mehmet Gurtekin¹, Filiz Aydin¹

¹Department of Medical Biology, Istanbul Medical Faculty, Istanbul University;

²Department of Urology, Istanbul Medical Faculty, Istanbul University;

³Department of Nephrology, Istanbul Medical Faculty, Istanbul University

Background: Hypertension, hyperlipidemia are well-recognized risk factors for the development of cardiovascular events post-transplantation. Renal allograft dysfunction can effect the risk of cardiovascular complications. Causes of dyslipidemia after renal transplantation are usually multifactorial, the type of immunosuppression regimens and genetic predisposition. P-glycoprotein (p-gp) is an important ATP-dependent membrane transporter which is involved in the absorption, distribution and elimination of numerous drugs, including lipid-lowering drugs. The difference of p-g's function resulted from single nucleotide polymorphisms in MDR1 may be the cause of inter-individual difference. The aim of our study was to evaluate the effect of MDR1 polymorphism on serum levels of lipids before and after atorvastatin.

Materials and methods: The study included 100 renal transplant patients. Of 35 hypercholesterolemic patients were selected and treated with 10 mg/day atorvastatin. C3435T and G2677T polymorphisms were determined by polymerase chain reaction (PCR) followed by restriction fragment length polymorphism (RFLP).

Results: Genotype frequencies in C3435T polymorphism were 31.4%, 45.7%, 22.9% for CC, CT, TT respectively and genotype frequencies in G2677T polymorphism were 37.1%, 51.4%, 11.4% for GG, GT, TT respectively for 35 hypercholesterolemic patients. No significant difference was found between C3435T polymorphism and serum lipid levels. Similarly, there was no significant difference between baseline serum levels of lipids and G2677T polymorphism. However, we found a relationship of G2677T genotypes with

atorvastatin response. The high cholesterol levels for patients with mutant heterozygous 2677 TT genotype ($270.00 \pm 88.76 \text{ mg/dl}$) were found higher compared to patients with the other 2677 GG and GT genotypes (GG; 247 ± 89.54 and GT; 189.88 ± 52.59) ($p = 0.047$).

Conclusion: MDR1 polymorphism may have an important role in the treatment response of serum lipid levels.

P514

CORONARY HEART DISEASE RISK ESTIMATION AND ITS IMPROVEMENT WITH A GENETIC RISK SCORE IN PATIENTS WITH KIDNEY TRANSPLANT

Emilio Rodrigo¹, Isaac Subirana², Sara Pich³, Carles Ferrer³, Gema Fernández-Fresnedo¹, Ramón Brugada⁴, Roberto Elosúa², Manuel Arias¹, Eduardo Salas³

¹Servicio de Nefrología, Hospital Universitario Marqués de Valdecilla; ²IMIM;

³Gendiag.exe; ⁴Gencardio

Background: The spectrum of kidney disease (KD) is broad ranging from mild chronic KD to end-stage renal disease, which requires dialysis and kidney transplantation (KT). Coronary heart disease (CHD) is prevalent in KD patients, and contributes substantially to the morbidity and mortality of these patients. However, the classical CHD risk equations have shown limited clinical utility in KD patients. Aims of our study were to assess the predictive capacity of a CHD risk function based on clinical variables and to evaluate whether the inclusion of genetic variants improve CHD risk estimation.

Methods: Our cohort study included 632 KD patients (200 with KT) with a median follow-up of 9.13 years. Mean age was 53.4 (± 10.6) years and 32.4% of the patients were male. Seventy three coronary events (fatal- or non-fatal acute myocardial infarct or acute angina) were identified in the follow-up. The clinical CHD risk score included KD status, age, sex, HDL, diabetic condition, hypertension condition, dyslipemic condition, hemoglobin A1c. In a second model, we also included a weighted genetic risk score (GRS) (Cardio inCode Score) with variants previously identified to be associated with CHD and not related with classical cardiovascular risk factors (rs10455872, rs12526453, rs1333049, rs17465637, rs501120, rs6725887, rs9818870, rs9982601, rs10507391, rs17222842, and rs9315051).

Results: The discrimination of the CHD risk function improved with the GRS (*c*-statistic = 72.0 vs. 68, p -value = 0.015). The calibration assessed by the Hosmer-Lemeshow test was 9.6, $p = 0.088$ (i.e., calibration was good with no statistical differences between the events predicted and the observed). The reclassification of the patients also improved with the GRS (Net reclassification improvement = 22; 95%CI: 5.5; 38.6).

Conclusion: The inclusion of a GRS improves risk prediction of CHD in patients with KD, especially with KT. Genetic screening could help to prevent CHD events in this group of patients.

P515

KIDNEY EXCHANGE PROGRAM AT SINGLE CZECH INSTITUTION SINCE 2011: 19 TRANSPLANTS – PRACTICALITIES AND OUTCOMES

Jiri Froněk, Libor Janousek, Tomas Marada, Jiri Mendl, Hana Slavickova, Pavel Chromy, Ondřej Viklický, Pavel Trunecka
Institute for Clinical and Experimental Medicine

Background: Usually, about a third of donor/recipient pairs are incompatible, either ABO, HLA or both. Kidney Exchange program can increase the number of live donor transplants.

Methods: Kidney paired donation has been at first performed at our institution in 2003, until 2011 some three 2-way exchanges were performed. Since 2011 the kidney exchange started at our institution as proper program. All the incompatible pairs were collected prospectively in the database. The matching runs were performed every three months. Pairs get matched using specially designed software, matching is based on blood group as well as HLA match.

Results: Since 2011 we performed twice the 2-way kidney exchange, one 6-way domino chain and one 5-way domino chain, one 4-way kidney exchange, in total 19 live donor kidney transplants were performed. The participation of two altruistic Samaritan donors made the domino chains possible. Two surgeons preformed all the transplants, one did all the miniinvasive nephrectomies. Some 13 were first transplants, five were second and one third transplants. There was no delayed graft function observed, all kidneys started to work immediately. The program did help some 19 patients so far. Our scheme currently includes some 45 pairs awaiting matching run.

Conclusions: Kidney paired donation program can be run at single institution, this limits some of the highly sensitised pairs as well as blood group 0 recipients. Wider possibility e.g. European scheme would increase the chance for even more exchange kidney transplants.

P516

THE IMMUNE MONITORING IN KIDNEY TRANSPLANT RECIPIENTS COULD PREDICT ACUTE REJECTION BY COMBINATION OF FRACTALKINE AND IL-17

Pu-Xun Tian

Department of Kidney Transplantation, First Affiliated Hospital of Medical College of Xi_j⁻a

Background: The aims of our study were to examine (i) whether Fractalkine, IP-10, IFN- γ and IL-17 predict the acute kidney allograft rejection; (ii) whether the sensitivity and specificity for prediction of allograft rejection are improved by combination of two markers.

Methods: The expression of serum Fractalkine, IP-10, IFN- γ and IL-17 in 77 kidney transplant recipients (including 32 recipients with AR and 45 recipients with STA) and 20 HC were researched, by high-throughput liquid protein microarray technology. The serum samples from patients were detected on pre-transplantation, days 1, 4, 7, 14, 21, and 28 after kidney transplantation. The values of those biomarkers for prediction of acute allograft rejection were evaluated.

Results: The pre-transplantation mean levels of Fractalkine and IFN- γ in AR were significantly higher than STA, however, the mean levels of IP-10 and IL-17 between AR and STA were no significant differences. The results of ROC analyses highlight the superiority of Fractalkine on day 0, IFN- γ on the 1st, and IL-17 on the 4th post-KTx days over those on other post-transplantation days in prediction of acute rejection episodes. The AUC in combination of Fractalkine on day 0 and the IL-17 level on the 4th day were the most for predicting acute rejection, and its sensitivity and specificity for the prediction of acute allograft rejection was 79.3% and 91.1%.

Conclusion: This study was demonstrating the promising and elegant markers of serum Fractalkine and IL-17 for prediction of early acute rejection. The complex predictive model exhibits a better ROC score and provides a much more powerful prediction than any single-marker prediction model.

P518

IFN-ELISPOT AS A BIOMARKER COULD PREDICT ACUTE REJECTION

Pu-Xun Tian

Department of Kidney Transplantation, First Affiliated Hospital of Medical College of Xi_j⁻a

Background: The aims of our study were to examine (i) how IFN- γ ELISPOT concentrations change over time in the early KTx; (ii) whether IFN- γ ELISPOT predict the acute kidney allograft rejection.

Methods: There were 24 cases of acute rejection (AR, further pathological diagnosis, including nine cases of grade I, seven cases of grade IIA, four cases of grade IIB and four cases of grade III), 168 subjects with stable allograft function (STA) after surgery, randomly selected 64 cases of STA, 50 healthy donors served as healthy controls (HC). IFN- γ ELISPOT detect memory T cell frequency in different groups of patients before and after renal transplantation. ROC curves were evaluated the uniting value of IFN- γ ELISPOT in the diagnosis of acute rejection.

Results: IFN- γ ELISPOT values of AR group in AR occur significantly higher than that of STA group ($p < 0.05$). Compared with HC group, STA group significantly increased ($p < 0.05$). Before and the 1th, 2th, 4th, 7th, 14th, 21th days after renal transplantation in AR group, IFN- γ ELISPOT was higher than that in STA group ($p < 0.05$). Second day after operation in STA group reached maximum value. AR group at second and fourteenth days after operation appeared two peaks, and between second to fourteenth days continuously maintained at a high level, after fourteenth days decline to normal rapidly. There are no significant differences between before and after donor nephrectomy surgery, always remain at low levels (< 5 spots/5 iA 105 PBLs). IFN- γ ELISPOT gradually increased before 1 week AR occurring, increased significantly in the first 5 days, decreased significantly at third day after treatment. IFN- γ ELISPOT is a clinical diagnosis of AR 5 days in advance. IFN- γ ELISPOT diagnosis of AR the best threshold was 15 spots/5iA105 PBLs, sensitivity 92%, specificity 87.5%, AUC 0.92.

Conclusion: This study was demonstrating the promising and elegant markers of serum IFN- γ ELISPOT for prediction of early acute rejection.

P519

PRIMARY EFFUSION LYMPHOMA IN A RENAL TRANSPLANT RECIPIENT – A CHALLENGE DIAGNOSIS

Joana Santos¹, Isabel Tavares², Ana Nunes², Susana Sampaio², Manuel Bustorff², Carla Santos², Manuel Pestana²

¹Fellow; ²Hospital São João

A caucasian, 78 year old male diagnosed with end stage renal disease of unknown cause, was started on hemodialysis therapy in January 2003 and received a first deceased donor kidney transplant in March 2007. Maintenance immunosuppressive regimen consisted of mycophenolate mofetil, cyclosporine and prednisone. At 7 months post-transplant a herpesvirus 8 (HHV-8) positive Kaposi's sarcoma was diagnosed in a leg lesion. Immunosuppression was altered to everolimus and treated with radiotherapy and chemotherapy

(doxorubicin). In January 2011 pulmonary infiltrate and left pleural effusion was detected. The etiologic study was consistently negative for infectious cause. Flow cytometry study of the bronchoalveolar lavage performed revealed a predominance of CD8⁺ lymphocytes. Pleural biopsy was negative for malignant cells. Everolimus pneumonitis with pleural effusion was suspected and everolimus suspended. Despite this, patient presented recurrent pleural effusion. Afterwards, results of immunophenotyping and pleural fluid cytology were consistent with lymphoma of serous/cavities - "primary effusion lymphoma" (PEL). A multidisciplinary team (Nephrology, Pneumology, Hematology, Palliative Care) set a conservative strategy. The following year patient presented frequent hospitalizations by hypervolemia with pleural effusion and progressive deterioration of renal function. In February 2012 recurrence of pleural effusion occurred, large pericardial effusion was detected and patient started hemodialysis. The patient died one year later by cardiovascular cause. **Conclusion:** PEL is a rare condition associated to HHV-8, that should be part of the differential diagnosis of a lymphocytic pleural effusion in a renal transplant recipient. Flow cytometry may be an essential clue to this difficult diagnosis, associated with a high morbidity and mortality. This case highlights the important interaction between virus, immunosuppression and neoplasm in renal transplant recipients.

P520

VITAMIN D FOR IMPROVING THE OUTCOME AFTER KIDNEY TRANSPLANTATION: RATIONALE, DESIGN, AND BASELINE CHARACTERISTICS OF THE PARTICIPANTS OF THE VITA-D RANDOMIZED CONTROLLED TRIAL

Ursula Thiem¹, Georg Heinze¹, Ute Gössler², Thomas Perkmann¹, Stefan Winkler¹, Rodrig Marculescu¹, Franz Kainberger¹, Alois Gessl¹, Thomas Wekerle¹, Enikő Kallay¹, Walter H. Hörl¹, Ferdinand Mühlbacher¹, Kyra Borchardt³

¹Medical University of Vienna; ²Vienna General Hospital; ³Dialysis Institute Klagenfurt/Wörthersee, Medical University of Vienna

Background: The active metabolite of vitamin D is considered to exert renoprotective effects by different mechanisms of action such as modulation of the immune system and inhibition of the renin-angiotensin-aldosterone system. In kidney transplant recipients (KTRs), vitamin D deficiency is common and might impair these potential beneficial effects. So far, it is unknown whether correction of vitamin D deficiency would affect the outcome after kidney transplantation.

Methods: The VITA-D study is a randomized double-blind placebo-controlled study (NCT00752401). It was designed to test the hypothesis that treatment of vitamin D deficient KTRs with vitamin D3 during the first year after transplantation improves the clinical outcome. As primary endpoints graft function as well as the occurrence of allograft rejections and infections one year after transplantation are assessed. Adult KTRs with vitamin D deficiency (calcidiol < 50 nm) were stratified by calcidiol levels (< 25 or $25-50$ nm) and randomized in a 1:1 ratio to vitamin D3 at 6800 International Units/day or placebo. We excluded patients who underwent retransplantation more than twice or were highly immunized as well as those who had a history of gastrointestinal diseases that lead to impaired intestinal vitamin D absorption.

Results: Of 577 kidney transplant recipients screened between May 2009 and July 2013, 202 were randomized. Approximately 75% of the screened patients had calcidiol levels < 50 nm. Baseline characteristics of the study population will be presented. The study will be completed in one year and the final results are expected for autumn 2014.

Conclusion: The VITA-D study should help to determine the potential beneficial effects of vitamin D3 on the post-transplant outcome as well as its safety in vitamin D deficient KTRs.

P521

SEQUENTIAL ANALYSIS OF GLOMERULAR ALBUMIN PERMEABILITY, SOLUBLE UROKINASE RECEPTOR, AND ANGIOTENSIN 1 RECEPTOR ANTIBODY IN A RENAL TRANSPLANT RECIPIENT WITH RECURRENT FOCAL SEGMENTAL SCLEROSIS

Siddiq Anwar, Nima Naimi, Muhammad Ashraf, George Jarad, Helen Liapis, Daniel Brennan

Washington University School of Medicine

Recurrent focal segmental sclerosis (rFSGS) in kidney transplant (KT) is difficult to predict and causes graft loss. Early rFSGS is hypothesized to be secondary to one or more circulating factors: glomerular albumin permeability factor (Palb), soluble urokinase receptor (suPAR), and angiotensin-1 receptor antibody (AT1Rab).

Methods: We analyzed stored samples 1 year pre-transplant, at transplant and on recurrence for Palb, suPAR, and AT1Rab in a 23 years. white male. He presented 8 months after one haplotype match KT with rFSGS and acute renal injury (AKI) requiring dialysis (HD).

Results: All three biomarkers were elevated 1 year pre-transplant when he was not on HD. At transplant, Palb and AT1Rab were elevated, but suPAR level was not. Four months later he developed CMV viremia and antimetabolite was stopped with resolution of viremia. Subsequently maintained on prednisone

and tacrolimus. Eight months after KT, develops AKI and biopsy showed rFSGS with no rejection. C4d and anti-HLA antibodies were negative. At recurrence, all three biomarkers were elevated. Seven days after therapy with aborted plasma exchange (secondary to side effects) plus high dose steroids, Palb and suPAR remained significantly positive but AT1Rab was borderline positive. Twelve weeks into treatment with high-dose steroids, rituximab and galactose, patient remains on HD.

Conclusion: Previous reports suggest elevated suPAR and high Palb at transplant confers risk of rFSGS. Although an $N = 1$ study, this highlights uncertainties and difficulties in monitoring and interpretation of Palb, suPAR and AT1Rab pre and post transplantation. Further studies are needed to validate published reports and establish better surveillance protocols.

P522

MDR1 GENE POLYMORPHISM IN NORMO AND HYPERURICEMIC RENAL TRANSPLANT PATIENTS RECEIVING CYCLOSPORINE

Tzevat Tefik¹, Hayriye Senturk Ciftci², Taner Kocak¹, Orhan Ziyil¹, Meltem Savran Karadeniz³, Aydin Turkmen⁴, Fatma Savran Oguz², Filiz Aydin², Ismet Nane¹

¹Department of Urology, Istanbul Faculty of Medicine, Istanbul University;

²Department of Medical, Istanbul Faculty of Medicine, Biology Istanbul

University; ³Department of Anesthesia, Istanbul Faculty of Medicine, Istanbul

University; ⁴Department of Nephrology, Istanbul Faculty of Medicine, Istanbul University

Background: Hyperuricemia frequently develops during early post-renal transplantation. Patients with hyperuricemia experience poorer graft survival rates. We aimed to investigate the relationship between hyperuricemia in MDR1 polymorphism and graft survival among Turkish post-renal transplant patients receiving cyclosporine.

Methods/materials: One hundred living-donor transplant patients receiving cyclosporine underwent C3435T (exon 26) and G2677T (exon 21) single nucleotide polymorphisms (SNP) genotyping using polymerase chain reaction-restriction fragment polymorphism. The normouricemic and hyperuricemic patients were evaluated regarding acute rejection.

Results: There was no statistical significance in normo and hyperuricemic recipients regarding C3435T polymorphism frequencies. GG genotype was significantly ($p = 0.046$) more frequent compared to T allele in normo-uricemic, whereas TT genotype was significantly ($p = 0.043$) more frequent compared to G allele in hyperuricemic patients regarding G2677T polymorphism. No significant difference was found in normo and hyperuricemic patients regarding acute rejection among C3435T polymorphism. Whereas individuals with GG genotype (G2677T polymorphism) had significantly more frequent acute rejection episodes in hyperuricemic patients ($p = 0.024$).

Conclusion: GG genotype may be risk factor of acute rejection in hyperuricemic renal allograft Turkish recipients using cyclosporine immunosuppression regarding MDR1 G2677T polymorphism.

P524

THE ARG753GLN TOLL-LIKE RECEPTOR 2 POLYMORPHISM AND RENAL ALLOGRAFT REJECTION IN TUNISIAN PATIENTS

Henda Krichen¹, Imen Star¹, Rafika Bardi¹, Mohamed Mongi Bacha², Ezzedine Abderrahim², Taieb Ben Abdallah¹, Youss Gorgi¹

¹Laboratory of Research in Renal Transplantation and Immunopathology

(LR03SP01), Charles Nicolle Hospital; ²Nephrology Department, Charles

Nicolle Hospital, Tunis, Tunisia

Introduction: Acute graft rejection is a complex process which involves several cells of the host immune system and might lead to chronic allograft dysfunction and organ destruction. The role of innate immunity has been revisited with a special interest in Toll-like receptors (TLRs). Clinical and laboratory studies have shown that TLRs may participate in organ graft rejection and transplant immune tolerance.

Aim: In this study, we investigated, in Tunisian renal recipients, the distribution of genotypes and alleles frequencies of the Arg753Gln polymorphism (arginine [G] to glutamine [A] substitution) of TLR2 with the aim to explore a potential correlation with the occurrence of acute rejection (AR) or chronic allograft nephropathy (CAN).

Patients and methods: The Arg753Gln polymorphism was genotyped using DNA samples from 125 renal recipients using Restriction Fragment Length Polymorphism (RFLP) assay. Patients were classified into two groups according to the HLA-haplotype similarity between donor and recipient: Group I included 29 HLA-identical haplotype allograft recipients and Group II included 96 recipients showing one or more mismatches in the HLA haplotype. Forty-seven patients (37.6%) developed at least one AR episode, and twenty-nine of them (23.2%) were identified as CAN cases by biopsy scored according to the Banff criteria.

Results: Occurrence of AR and CAN was statistically associated with the pre-existing anti-HLA antibodies in patients ($p = 0.03$; CI 95% OR = 3.85 [1.58–9.39] and $p = 0.017$; CI 95% OR = 3.05 [1.21–7.68] respectively). Incidence of CAN was also significantly more important in the Group II than Group I ($p = 0.047$; CI 95% OR = 3.21 [0.898–11.54]). The frequency of G/G genotype was higher in AR patients comparing with non-AR ones ($p = 0.039$; CI 95% OR = 2.87 [1.05–4.37]). However, no differences were found in genotypes or alleles distribution according to CAN. No association either was noted with the incidence of infection in post-transplantation.

Conclusion: In conclusion, this study showed that, set apart the immunological factors, the Arg753Gln polymorphism of TLR2 may increase the risk of acute renal allograft rejection in Tunisian patients.

PS12-LIVER

P525

INTRAHEPATIC BILE DUCTS: ANATOMIC VARIATIONS, CLASSIFICATION AND CLINICAL APPLICATION FOR LIVING DONOR LIVER TRANSPLANTATION

Eleazar Chaib, Alexandre F. Kanas
FMUSP

Background: Accurate knowledge of the anatomy of intrahepatic bile ducts (IHD) is critical for successfully hepato-biliary surgery and the implications of its variations are essential for living donor liver transplantation (LDLT).

Methods: From 1996 to 2011 we have collected data of the main IHD classification and its anatomic variations. 2032 and 1014 anatomical variations of right and left IHD were reviewed and classified according to the branching pattern of the right anterior and posterior hepatic duct and also segment IV insertion.

Results: The frequencies of each type of right IHD variations were: Type A1 – 1247(61.4%); Type A2 – 296(14.6%); Type A3 – 272(13.4%); Type A4 – 124 (6.1%); Type A5 – 21(1%) and others – 72 (3.5%) and of left IHD variations were: Type B1 – 773(76.2%); Type B2 – 153(15.1%); Type B3 – 38(3.7%); Type B4 – 9(0.9%); Type B5 – 29(2.9%) and others – 12 (1.2%).

Conclusion: A preoperative understanding of bile duct variation, the knowledge of IHD, familiarity with the variations of hepatic confluence is useful for hepatic surgery and also will help to exclude donors with anatomical contraindications and avoid possible surgical misadventure in LDLT.

P526

PREDICTIVE CRITERIA IN FULMINANT HEPATITIS AFTER MARS

Vincenzo Morabito¹, Massimo Rossi¹, Quirino La², Francesco Pugliese³, Pasquale Bartolomeo Berloco¹, Gilnardo Novelli¹

¹Sapienza University of Rome, General Surgery and Organs Transplant;

²Azienda Ospedaliero Universitaria Pisana; ³Anaesthesia and Intensive Care, Sapienza University of Rome

Background: The aim of this study was to confirm the improvement of prognostic parameters after treatment with the Molecular Adsorbent Recirculating System (MARS) in patients (pts) with fulminant hepatitis (FH).

Materials: Of 71 pts with FH, treated with MARS were enrolled.

Results: The score showed a high AUC (91.4%). Arbitrary cut-off values of 2 and 4 showed high sensitivity (81.4 and 48.8%) and specificity (92.9 and 96.4), respectively. Pts corresponding to the low risk group (scoring points: 0-2; n = 36) did not experience deaths, and only 8 (23.5%) of them underwent a Liver Transplant (LT). Pts with intermediate risk (3-4 points; n = 22) were mainly transplanted (20 pts; 90.9%). In this group, only two patients survived without LT. In the high risk group (5-6 points; n = 13), no patient survived. Only 2 (15.4%) pts were transplanted, while the remaining cases died before LT.

Conclusions: The following criteria: GCS \geq 11 with ICP $<$ 15 mmHg, lactate level $<$ 3 mm, TNF- α $<$ 20 pg/ml, IL-6 $<$ 30 pg/ml, and a change in hemodynamic instability from hyperkinetic to normal kinetic conditions, enabled us to divide patients into three groups and determine their outcomes.

P528

TRANS-ARTERIAL CHEMOEMBOLIZATION AND HEPATIC ARTERY COMPLICATIONS IN LIVER TRANSPLANTATION

Fabrizio Panaro, Francis Navarro
Montpellier University Hospital

Background: Hepatic artery (HA) complication in patients who underwent liver transplantation (LT) is an important risk factor for worse outcomes and graft loss. Transarterial chemoembolization (TACE) is widely used in patients before and during the waiting list for cancer control or downstaging. Conventional TACE is directly applied into the HA and may therefore damage it. Herein, we describe the relationship between the pre-operative TACE and the apparition of histological and radiological HA complications.

Patients and methods: All patients with hepatocellular carcinoma who underwent LT in our center between January 2009 and October 2012 were included in this study and divided in two groups: TACE (group 1) and no-TACE (group 2). HA complications are reviewed and compared between groups. Recipient HA close to the anastomotic site underwent histological analysis to detect HA wall injury.

Results: Sixty-seven patients were reviewed, 31 for group 1 and 36 for group 2. Both groups were similar for gender, age, cirrhosis origin, and ASA score. There were more patients classified WHO 2 and CHILD score C in group 1 compared to group 2 (p = 0.005 and p = 0.008, respectively). Fourteen patients were within Milan criteria in group 1 and 25 in group 2 (p = 0.03). In group 1 TACE was selective with drug-eluting beads in 24 patients. At 1 year of follow-up, eight radiological HA complications occurred; five in group 1 (1 HAT, three stenoses, one pseudoaneurysm) and three in group 2 (one HAT, two

stenoses) (p = 0.29). One-year overall graft and patient survival were 93%. Histological screening showed 10 histologic HA injuries in group 1 and 3 in group 2 (p = 0.05).

Conclusion: Even if our study didn't show statistical difference between groups, we found a major trend towards HA complications in TACE group.

P530

THE SAFE USE OF RIGHT LOBE GRAFTS WITH PORTAL VEIN VARIATION IN LIVING DONOR LIVER TRANSPLANTATION

Necdet Guler, Murat Dayangac, Onur Yaprak, Yusuf Gunay, Fatih Taskesen, Gulum Altaca, Yildiray Yuzer, Yaman Tokat
Florence Nightingale Hospital

In living donor liver transplantation (LDLT), portal vein (PV) variations are of immense clinical significance. Herein, we describe our PV reconstruction techniques in 52/386 (13%) right lobe (RL) grafts with variant PV anatomy and evaluate the impact of accompanying biliary variations. The PV reconstruction techniques included back-wall plasty (n = 21), saphenous vein (SV) graft interposition (n = 5), back-wall plasty with SV graft interposition (n = 6), iliac vein Y-graft interposition (n = 6), and quiltplasty (n = 3). There was no donor mortality. In a median follow-up of 29 months, none of the recipients had vascular complications. Anomalous PV anatomy was associated with a high (54%) incidence of biliary variations. Vascular and biliary variations render LDLT technically more challenging. By employing appropriate reconstruction techniques, it is possible to successfully use RL grafts with PV variations without endangering recipient and donor safety.

P531

SUSTAINED VIROLOGIC RESPONSE IN THE ANTIVIRAL TREATMENT OF HCV-INFECTION AFTER LIVER TRANSPLANTATION

Ekaterina Yaroshenko, Maxim Kornilov, Yan Moysyuk
Federal Research Centre of Transplantation and Artificial Organs Academician V.I. Shumakov

OLT to 31 HCV-positive recipient were performed in our center in period from december 2004 to december 2012. Of the 14 patients who carried AVT with PEG IFN + ribavirin, 9 (64.3%) achieved a SVR. AVT in patients who achieved SVR, began a period of 2, 7, 12, 15 months after OLT on monotherapy with tacrolimus or cyclosporine A. 1 case of fibrosing cholestatic hepatitis C. In four patients with rapid progression of fibrosis F0-F 2 for 6 months. 3 patients had genotype 3a, 6-1b. In 1 case, the AVT lasted 72 weeks in the form of a slow virologic response, in the other treatment was discontinued at week 6 in mind persistent increase in serum bilirubin despite negative HCV RNA at second week of treatment. Remaining patients treated by consistent protocol regarding genotype of hepatitis C virus (24-48 weeks). In 1 case, the AVT was stopped after EVR at 15 weeks, because of an abscess of the liver. After 3 months, in this case the level of viremia was 2.8×10^7 IU/ml. Retry after 8 months had led to a EVR and SVR. In conclusion: achieving high frequency SVR possible recipients after liver transplantation, regardless of the start time of antiviral therapy.

P532

MELD ORIENTED ORGAN ALLOCATION POLICY AND WAITING LIST FOR LIVER TRANSPLANTATION IN ROMANIA

Liana Gheorghie¹, Speranta Iacob¹, Gabriela Smira¹, Corina Pietreanu¹, Doina Hrehore², Vladislav Brasoveanu², Razvan Iacob¹, Cristian Gheorghie¹, Irinel Popescu²

¹Gastroenterology and Hepatology Center, Fundeni Clinical Institute; ²General Surgery and Liver Transplantation Center, Fundeni Clinical Institute

Background: The aim of the present study was to characterize the dynamics of the Romanian waiting list (WL) for liver transplantation (LT) evaluating mortality on the WL during 2 time periods 2004-2007 vs. 2008-2011.

Methods: Of 1085 patients listed for LT have been included in our analysis. **Results:** One, 3 and 5 years mortality on WL were 25%, 46.3% and 57.3% respectively. Death on the WL was significantly higher before 2008 (37% vs. 26.4%, p = 0.0001) and risk of dying while on WL was 60% higher. Waiting time on the WL was with 75% longer and time until LT was with 102% longer before 2008 compared to the second time period (p = 0.0001). After 2008, 62.3% of patients were listed for LT with Child Pugh class C compared to 22.1% (p < 0.0001). MELD score at inclusion was a good predictor of mortality on the WL during 2008-2011 (AUROC 0.72).

Conclusion: A significant reduction of mortality has been registered on the Romanian WL for LT after 2008, despite the increased severity of liver disease.

P533

THE EFFECT OF MTOR OR CNI BASED MAINTAINANCE IMMUNOSUPPRESSION ON MEASURED RENAL FUNCTION AFTER LIVER TRANSPLANTATION

Silvia Schaffellner¹, Jürgen Gutschl¹, Sabine Zitta², Andreas Meintzer³, Daniela Kniepeiss⁴, Gilbert Reibnegger⁴, Alexander R. Rosenkranz⁵, Doris Wagner¹

¹Division for Transplantation, Department of Surgery, Medical University of Graz; ²Division for Nephrology, Department of Internal Medicine, Medical University of Graz; ³Department of Laboratory Medicine, Medical University of Graz; ⁴Department of Physiological Chemistry, Medical University of Graz; ⁵Division for Nephrology and Hemodialysis, Department of Internal Medicine, Medical University of Graz

Background: Mammalian target of rapamycin inhibitors have been proposed to preserve renal function by estimated renal clearance rates. The presented study investigated their effect compared to calcineurin inhibitors (CNI) on renal function defined by a measured GFR.

Methods: GFR was measured in patients on mTOR ($n = 28$) or on CNI ($n = 51$) treatment following liver transplantation using the inulin clearance (IC). Estimated GFR was determined using the MDRD 4 formula at baseline, 6, 12, 18 and 24 months. Changes in renal function were compared in patients on CNI or mTOR based immunosuppression.

Results: The eGFR declined in patients on CNI (81 vs. 61 ml/min 1.73 m², $p = 0.01$) and on mTORs (82 vs. 60 ml/min 1.73 m², $p = 0.01$). The IC did not change throughout the study period in CNI (62 vs. 61 ml/min 1.73 m², $p = n.s.$) or mTOR (58 vs. 60 ml/min 1.73 m², $p = n.s.$) patients. The proportion of patients with proteinuria increased significantly in the mTOR group (50% vs. 62%, $p \leq 0.03$) and not in the CNI group.

P534

A RETROSPECTIVE STUDY OF STEROID-FREE VERSUS STEROID-BASED IMMUNOSUPPRESSION AFTER LIVER TRANSPLANTATION

Carl Axelsson, Maria Castedal, Styrbjörn Friman, William Bennet

Transplantation Center, Sahlgrenska university Hospital, Gothenburg, Sweden

Background: The aim of this study was to evaluate the incidence of new-onset diabetes mellitus (NODM), rejection rates and patient- and graft survival following liver transplantation (Ltx) using steroid-free immunosuppression (IS).

Methods: Adult Ltx performed 2008–2011 were analysed retrospectively with regards to treatment and outcome. Group 1 ($n = 155$) received steroid-based IS (TAC, CS ± MMF) and group 2 ($n = 83$) steroid-free IS (TAC, MMF). The median follow-up times were 976 days and 412 days, respectively.

Results: The incidence of NODM in the steroid-group was 31% compared to only 6% in the steroid free group ($p < 0.0001$). The incidence of biopsy proven acute rejection was 28% in both groups. The incidence of NODM in hepatitis C (HCV+) patients receiving steroid-based IS was 34% compared to 9% in HCV+ patients receiving steroid-free IS ($p = 0.05$).

Conclusion: Steroid-free immunosuppression after Ltx is safe and reduces the incidence of NODM in both non-HCV+ and HCV+ recipients.

P535

REVERSED SAPHENOUS BY-PASS FOR HEPATIC ARTERY PSEUDOANEURYSMS

Hassan Bouyabrane, Jean Pierre Carabalona, Francis Navarro, Fabrizio Panaro, Al Warith Al Hashmi
Montpellier University Hospital

Background: The incidence of hepatic artery pseudoaneurysm (HAP) is found in 1–2% of liver transplantation (LT) patients. This article discusses the presentation, etiology, types, treatment indications and vascular procedures used to manage this complication.

Methods: From 2004 to 2011, 464 LTs were performed at our institution. Of these, nine consecutive patients underwent surgical treatment of HAP. In all cases, revascularization with a reversed autologous saphenous vein by-pass was performed.

Results: The median delay between the LT and the HAP diagnosis was 39.6 days. The median diameter was 15.3 mm. In six cases, a biliary leakage was associated with the LT and, in the remaining 3, a mycosis was recorded. At the 5-year follow-up, five patients had normal arterial anatomy and the other three patients had stenosis that was successfully treated by stents. Our conclusions support surgical revascularization with reversed saphenous grafts as a feasible and efficient treatment in cases of HAP.

P536

EFFECTS OF THE TRANS-ARTERIAL CHEMOEMBOLIZATION ON HEPATIC ARTERY COMPLICATIONS IN PATIENTS UNDERWENT LIVER TRANSPLANTATION

Fabrizio Panaro, Hassan Bouyabrane, Jeanne Ramos, Francis Navarro
Montpellier University Hospital

Background: Transarterial chemoembolization (TACE) in patients with hepatocellular carcinoma (HCC) is directly applied in hepatic artery (HA) and may injure it. We describe relationship between pre operative TACE and the apparition of radiologic and histologic HA complications.

Methods: All cirrhotic patients with HCC underwent liver transplantation in between 2009 and 2012 are included and divided in two groups: TACE (1) and No-TACE (2). HA complications are reviewed and compared. The recipient HAs were histologically analysed.

Results: Sixty-seven patients were reviewed, 32 for group 1 and 35 for group 2. At a mean follow up of 17 months, 10 radiologic HA complications occurred; six in group 1 and four in group 2 ($p = 0.2953$). Histological screening showed 12 HA injuries in group 1 and 3 in group 2 ($p = 0.0124$).

Conclusion: We found a significant higher rates of histological HA injury in patients underwent to TACE.

P537

LIVING DONOR LIVER TRANSPLANTATION IN SEPTUAGENARIANS

Arzu Ozcelik, Murat Dayangac, Necdet Guler, Levent Oklu, Onur Yaprak, Murat Akyildiz, Yildirim Yuzer, Yaman Tokat
Florence Nightingale Hospital

The demand for liver transplantation (LT) in older patients is increasing. In living donor LT (LDLT), older recipient age was reported to be a significant independent risk factor of graft failure. Thus, many centers now accept 70 years as the cut off limit for LDLT. This retrospective study was undertaken to review the outcome of LDLT in patients aged ≥ 70 years. Out of 256 patients who underwent LDLT between October 2005 and June 2011, there were eight patients (3.1%) who were 70 years or older at the time of LT. The major complications were limited to bile leak in one case, and vertebral fracture in another patient. There was no perioperative mortality and all patients are alive in a median follow-up of 34 (14–64) months. Our study emphasizes that age by itself should not be used to limit LT. With proper evaluation and careful consideration of donor and recipient factors, septuagenarians can undergo LDLT with acceptable outcome.

P538

RELATIONSHIP BETWEEN NT-PROBNP PLASMATIC LEVELS AND CIRRHOSIS ETIOLOGY IN CANDIDATES TO A LIVER TRANSPLANTATION

Maria Dolores Espinosa¹, Flor Noguera¹, Carmen Olmedo¹, Karim Muffak-Granero¹, Ana Maria Comino¹, Trinidad Villegas¹, Daniel Garrote Lara², Javier De Teresa¹, Pablo Bueno¹, Jose Antonio Ferron Orijuela¹
¹University Hospital Virgen de las Nieves; ²Virgen de las Nieves University Hospital

Objectives: To study relationship between cirrhotic miocardiopathy determined by NT-proBNP plasmatic levels and cirrhosis etiology.

Patients and methods: Of 81 candidates to a liver transplantation were studied, 40 enolic cirrhotic patients (group 1). 35 viral cirrhotic patients (group 2) and six primary biliary cirrhosis patients (group 3). Severity of cirrhosis was estimated using Child-Pugh and MELD scores. Clinical ascites was estimated, and Body Mass Index (BMI). A group of healthy volunteers was included as reference group. NT-pro-BNP values were determined in plasma blood samples.

Results: There was no significant differences among groups in sex, age, BMI, ascites, and Child-Pugh or MELD scores. NT-proBNP values in male of groups 1 and 2 were significantly enhanced compared to reference group ($p < 0.005$). Male NT-proBNP values in group 1 were significantly higher than in male of group 2 ($p < 0.005$). There was no significant differences in female NT-proBNP values.

Discussion: NT-proBNP plasma values are enhanced in cirrhotic patients, this is indicative of cirrhotic miocardiopathy. NT-proBNP plasma values were significantly enhanced in enolic patients suggesting an important miocardiopathy.

Conclusion: An enhancement of NT-proBNP plasma values in cirrhotic patients is an indication of miocardiopathy, which is more severe in enolic cirrhotic patients.

P539

ABSOLUTE MONOCYTE COUNT PREDICTS TUMOR RECURRENCE AFTER LIVER TRANSPLANTATION*Young-Kyu Kim, Seong Hoon Kim, Seung Duk Lee, Sung-Sik Han, Sang-Jae Park*

National Cancer Center

The aim of this study is to investigate whether pretransplant absolute monocyte count in peripheral blood (AMCPB) predicts posttransplant outcomes in patients undergoing liver transplantation (LT) for hepatocellular carcinoma (HCC). We retrospectively analyzed 256 patients who underwent LT for HCC between 2005 and 2012. By using ROC curve analysis, AMCPB $>200/\text{mm}^3$ was considered. On multivariate analysis, pretransplant high AMCPB, positivity of pretransplant 18F-FDG PET and pathologic maximal tumor size >5 cm and presence of microvascular invasion were independent risk factors for recurrence-free survival. When subgroup analysis was done according to the Milan criteria, AMCPB ($>200/\text{mm}^3$) was an independent factor to predict tumor recurrence in patients with HCC over the Milan criteria ($p = 0.012$). Pretransplant AMCPB would be considered as a useful and cost-effective biomarker to predict tumor recurrence after LT for HCC, particularly in patients over the Milan criteria.

P540

EVEROLIMUS AND SORAFENIB FOR RECURRENCE OF HEPATOCELLULAR CARCINOMA AFTER LIVER TRANSPLANTATION*Paolo De Simone, Daniele Pezzati, Quirino Lai, Davide Ghinolfi, Laura Coletti, Arianna Precisi, Giulia Leonardi, Paola Carrai, Franco Filippini*
University of Pisa Medical School Hospital

Background: Combination therapy with everolimus (EVR) and (SORA) is being investigated for recurrence of hepatocellular carcinoma after liver transplantation (LT).

Methods: This was a single-center, retrospective analysis on LT recipients with unresectable recurrence of HCC undergoing combination therapy with EVR and SORA.

Results: Seven patients (males 100%; median age [IQR] 53 [9] years) were included. HCC recurrence was diagnosed at a median (IQR) of 9 (126) months after LT, and patients received EVR+SORA at a median of 11 (126) months after LT. At a median (IQR) follow-up of 6.5 (14) months, 5 (71.4%) patients are alive and 4 (57.1%) with tumor progression as per mRECIST. Median (IQR) time to progression was 3.5 (12) months. Adverse events led to temporary SORA discontinuation in 2 (28.6%) patients, and to SORA dose reduction in 3 (42.8%).

Conclusions: Treatment of HCC recurrence after LT with a combination regimen challenging in terms of SORA-related complications.

P542

EVEROLIMUS MONOTHERAPY AFTER LIVER TRANSPLANTATION*Paolo De Simone, Paola Carrai, Giulia Leonardi, Arianna Precisi, Quirino Lai, Daniele Pezzati, Davide Ghinolfi, Franco Filippini*
University of Pisa Medical School Hospital

Background: Scanty information is available on feasibility of long-term everolimus (EVR) monotherapy after liver transplantation (LT).

Materials: This was a retrospective analysis of EVR-based immunosuppression at a single institution. The endpoint was evaluation of feasibility of EVR monotherapy.

Results: Of 212 patients who received EVR at any time point during their post-LT follow-up, 211 (99.5%) were included. 176 patients (83%) attempted EVR withdrawal, while 35 (16.5%) were on combination with EVR + reduced-calceineurin inhibitors (CNI) exposure (r-CNI). A total of 141 (66.5%) patients are alive and on EVR at the latest follow-up (range 1–84 months). Among these latter, 113 (53.3%) are on EVR monotherapy, while 28 (13.2%) are on combination with EVR and r-CNI. Feasibility of EVR monotherapy was 76.7% (135/176) and associated with a 13.9 ± 5.6 ml/min increase in eGFR.

Conclusion: EVR monotherapy was feasible in 76.7% of patients and beneficial for renal function.

P543

TUMOR RECURRENCE PREDICTS HBV RECURRENCE AFTER LIVER TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA*Seong Hoon Kim, Young-Kyu Kim, Seung Duk Lee, Sung-Sik Han, Sang-Jae Park*

National Cancer Center

This study assessed outcomes and identified risk factors of posttransplant hepatitis B virus (HBV) recurrence in patients who received prophylaxis with both entecavir (ETV) and hepatitis B immunoglobulin (HBIG) after liver

transplantation (LT). We retrospectively analyzed the outcomes and risk factors of posttransplant HBV recurrence in the 155 patients who received prophylaxis with a combination of ETV and HBIG. Posttransplant HBV recurrence occurred in six patients (3.9%) without any ETV-resistant mutants. The overall rates of HBV recurrence at 1, 3 and 5 years were 1.3%, 4.7% and 6.8%, respectively. We found that recurrent HCC was an independent risk factor of HBV recurrence ($p = 0.003$). Prophylaxis with a combination of ETV and HBIG resulted in a low HBV recurrence rate following LT without any emergence of ETV-resistant mutants. Recurrent HCC was an independent risk factor of HBV recurrence in patients who received prophylaxis with both ETV and HBIG for prophylaxis following LT.

P544

SUCCESSFUL FULL-SIZE LIVER TRANSPLANTATION FOR AMANITA POISONING IN A 20 MONTH CHILD*Aliaksei Shcherba, Alexander Dzydzadko, Evgeni Santotski, Andrew Minou, Denis Efimov, Maryanna Hurava, Oleg Rumo*
RSPC for Tissue and Organ Transplantation

The youngest child reported who underwent LT for amanita-induced liver failure was a 2 year old girl. To date no criteria for LT were evaluated in children under 5 year old. A girl weighing 13 kg (BMI = 17.8) was referred to our center 5 days after poisoning, presented with vomiting and diarrhea 12 h after mushroom consumption. Her grandmother died because of the same poisoning 1 day before and grandfather developed liver and renal failure but survived. At admission the girl had a Glasgow coma score of 10, AST 2050 U/L, ALT 4019 U/L, INR 6, bilirubin 64 μM , creatinine 11 μM , factor V – 23% and factor VII – 4%. Her mother started prompt evaluation for possible emergent LDLT. Encephalopathy deteriorated rapidly and she developed seizures and coma on the same night. Next morning (6th day after ingestion) the patient developed hypoglycaemia (2.2 mmol/L), urea level dropped to 0.6 mmol/L and clac level raised up to 9.2 mmol/L. That day a pediatric donor became available and she underwent full-size LT from 8-month-old deceased brain donor (BMI = 13, GW = 270 g) using piggy-back technique. HTK solution was used for preservation. Arterial anastomosis was performed between common hepatic arteries of both donor and recipient using the operative microscope and magnification $\times 6-8$. Biliary reconstruction was performed in duct-to-duct manner with interrupted 7-0 PDS stitches using the operative microscope and magnification $\times 6-8$. Both above mentioned anastomoses were performed with the help of microsurgeon. Explant pathology showed $>60\%$ necrosis. She became conscious and breathed spontaneously on POD 2. The girl was discharged 15 days later without complications. Of 18 months later the child is thriving with good graft function and no signs of arterial and biliary strictures.

P546

LIVING-DONOR LIVER TRANSPLANTATION FOR PRIMARY BILIARY CIRRHOSIS IN A SINGLE CENTER EXPERIENCE: IMPACT OF HLA MISMATCH AND ANTI-M2 LEVEL BEFORE TRANSPLANTATION*Chikashi Nakanishi¹, Naoki Kawagishi¹, Kazushige Sato¹, Shigehito Miyagi¹, Ikuo Takeda¹, Satoshi Sekiguchi¹, Akira Sato¹, Noriaki Ouchi²*¹Department of Transplantation, Reconstruction and Endoscopic Surgery, Tohoku University Hospital; ²Department of Surgery, Tohoku University Hospital

Background: In living-donor liver transplantation (LDLT) for primary biliary cirrhosis (PBC), the recurrence rates have been reported to range 1–40%. In this study, we review our experience in LDLT for PBC.

Methods: From June 1997 to December 2012, 153 LDLT were performed, of which 18 (11.8%) patients were indicated for PBC at Tohoku University Hospital. Among them, 14 patients survived for more than 6 months, and were the subjects of the present study. The follow-up period for these patients ranged from 199 to 3524 days after transplantation (median 1758 days). Calcineurin inhibitor at 6 months was tacrolimus in nine patients and cyclosporine in five patients. Mycophenolate mofetil was administered in 10 patients. One patient who underwent ABO-incompatible LDLT received Rituximab. Basiliximab were administered in 11 patients. All patients were maintained by ursodeoxycholic acid. Steroid therapy was discontinued in all except four patients.

Result: Male/female ratio was 1:13 and mean age was 52 years old. Two patients died from tongue cancer and drug-induced graft failure, respectively. Rate of biopsy proven rejection was 50%. Although biopsy proven PBC recurrence has not yet seen, increased ALP and rGTP or total bilirubin level probably due to recurrence was seen in five patients. All of them are asymptomatic. In multivariate analysis, the number of HLA mismatch <3 was related to recurrence. Non- or blood related donor factor, and type of immunosuppressant did not correlate with recurrence, prognosis and rate of biopsy proven rejection. Furthermore, sustained elevation of ALP level was seen in seven patients except the patient with metastatic bone cancer. Low serum anti-M2 level before LDLT was related to these abnormality in ALP after transplantation.

Conclusion: Although there are some patients with a sign of recurrence, LDLT in PBC showed favorable long-term outcome. Low number of HLA

mismatch seems to be a risk factor for recurrence of PBC after LDLT. Furthermore, low anti-M2 level may predict the sustained elevation of serum ALP after LDLT.

P547

OUTCOME OF LIVER TRANSPLANTATION IN FULMINANT HEPATITIS A (HA) WITH ACUTE KIDNEY INJURY (AKI)

Chun Soo Lim¹, Jung Pyo Lee¹, In Mok Jung¹, Yon Su Kim²

¹Seoul National University Boramae Medical Center; ²Seoul National University Hospital

Liver transplantation (LT) is the treatment of choice for hepatorenal syndrome (HRS). We investigated the outcomes of LT in patients with AKI by acute HA comparing to those of patients with HRS by other causes. A total of 20 acute HA with AKI patients (HA group) were compared with 76 patients with HRS by other causes (HRS group). Preoperative prothrombin time and serum creatinine level were higher in HA group. Total bilirubin level was lower in HA group. There was no difference in model for end-stage liver disease score. Patients' and grafts' survival rate were not different. More patients in HA group needed posttransplant hemodialysis. However, posttransplant eGFR until two months was similar, thereafter, it was better in HAV group than in HRS group. No patients needed long term renal replacement therapy. Pre- and peri-transplant kidney function of HAV group was poorer than that of HRS group. However, posttransplant long term renal outcome could be better in HAV group.

P548

EARLY EXPERIENCE OF DONOR MORBIDITY FOLLOWING LIVING DONOR LIVER TRANSPLANTATION: INITIAL 15 CASES

Kwan Woo Kim¹, Jeong-Ik Park¹, Sung-Gyu Lee²

¹Department of Surgery, Haeundae Paik Hospital, College of Medicine, University of Inje, Busan, Korea; ²Department of Surgery, Asan Medical Center, College of Medicine, University of Ulsan, Seoul, Korea

Background: Living donor liver transplantation has been increasingly performed to alleviate the shortage of cadaveric liver graft. The main disadvantage of this procedure is the risk of complications or even death in a healthy donor who does not derive any medical benefits from the operative procedure. We present the initial experience of donor morbidity following LDLT at Haeundae Paik hospital during 2 years after opening the hospital.

Materials and methods: From August 2010 to July 2012, 13 LDLTs and 1 deceased donor LT were performed at our hospital. Donor demographics, graft type, complications, length of stay and overall survival were evaluated. Donor morbidity was assessed objectively using the modified Clavien-Dindo classification.

Results: There were 11 cases of modified right lobe graft (MRL) and two cases of dual grafts (left lobe plus left lateral segment and two left lobe). Median follow-up was 18.5 months. Mean donor age, donor BMI and hospital stay was 25.6 years, 21.5 kg/m² and 12.4 days. There was no donor mortality. Wound problem was three cases and fever of unknown origin was developed in one case. All donor morbidities were Grade II (Clavien-Dindo classification) and donor morbidity was 4/15 (26.6%).

Conclusion: Although small cases, our experience shows that donor hepatectomy for living donor liver transplantation is a safe procedure in a small volume center. Our donor morbidity of 26.6% is comparable to most high volume centers across the world. Meticulous preoperative evaluation, careful operation and proper remnant volume are guarantee for the safety of donors in LDLT.

References: 1. L. Kousoulas, N. Emmanouilidis et al. Transplantation Proceedings, 43, 3584-3587 (2011).

2. V. A. Wakade & S. K. Mathur. Indian J Surg (January-February 2012) 74 (1):118-126.

P549

DONOR COMPLICATIONS IN LIVING DONOR LIVER TRANSPLANTATION: A SINGLE CENTER EXPERIENCE

Ahmed Nabil, Ahmed Hussein, Mostafa Elshazli, Adel Hosny
Cairo University

Background: Living donor liver transplantation is widely used for patients with end-stage liver diseases. However, this procedure exposes the donor, a healthy individual, to morbidity and mortality. The overall donor complication is 14.5% and mortality is 0.2%.

Patients and methods: This retrospective study analyzes the complications in 110 living donors. Male donors were 84 and females were 26. Right hepatectomy was done in 92 donors, left hepatectomy in four donors and left lateral segmentectomy in 14 donors.

Results: We had 30 complications in 30 donors (27.3%). Biliary leakage occurred in 11% of donors, wound infection in 5.5%, re-exploration for hemoperitoneum in 4.5% and chest complications in 3.6%. According to the modified Clavien classification system 12 complications out of 30 were grade I

(40%), nine complications were grade IIIa (30%) and nine complications were grade IIIb (30%). We had no donor mortality.

Conclusion: Meticulous technical and preoperative evaluation will reduce complications.

P550

LIPOCALIN-2 AS POSSIBLE PREDICTIVE MARKER FOR ACUTE ALLOGRAFT REJECTION AFTER LIVER TRANSPLANTATION

Natalie Vallant¹, Herbert Maier¹, Philipp Schumpp¹, Markus Kofler¹, Stefan Schneeberger¹, Robert Öllinger, Johann Pratschke, Felix Aigner

Department of General Surgery, Innsbruck

Background: Lipocalin-2 (Lcn-2) has been described as a marker and modulator of inflammation during ischemia/reperfusion injury (IRI) following solid organ transplantation. Aim of this study was to analyze Lcn-2 serum expression in the early phase after liver transplantation and to correlate its expression with acute rejection episodes, renal function and longterm graft survival.

Methods: Sera of 68 patients undergoing orthotopic liver transplantation were collected perioperatively from days 0 to 15. Lcn-2 expression was analyzed by ELISA and correlated with clinical parameters of allograft rejection, dialysis and graft survival.

Results: Lcn-2 serum levels were significantly higher in patients with poor renal function and a significant increase of Lcn-2 was seen in patients before diagnosis of acute rejection. Furthermore, an increase of Lcn-2 expression of more than the median of 115 ng/ml during the observed period was associated with a worse 5-year graft survival compared to patients with an increase below (not statistically significant).

Conclusion: Lcn-2 is a marker which is upregulated prior to and during acute graft rejection that can be used for the early diagnosis of acute rejection in liver transplantation and its increase during the early posttransplant phase may predict the outcome in the long term.

P551

WHAT SHOULD BE A "LOW DOSE OF TACROLIMUS" AFTER LIVER TRANSPLANT (LT)?

Faisal Hanif¹, R.S. Theth², Abdul Hakeem¹, Magdy Attia¹, Ernest Hidalgo¹

¹St James University Hospital; ²University of Leeds

Aims: To determine the renal function (Glomerular Filtration Rate) at 12 weeks in adults receiving a LT with a Tacrolimus based immunosuppression regimen and to identify potential predictive factors.

Methods: Retrospective single centre analysis of 115 adult LT recipients from deceased donors in 2011/12. Immunosuppression consisted of Prograf (trough level 5-10 ng/l initial 3 months), Mycophenolate mofetil (1 gram twice daily) and Prednisolone (20 mg to be stopped in 6 weeks). We recorded GFR and tacrolimus trough levels pre and post-operative at week 1, 2, 3, 4, 6, 8 and 12. Variables were compared using student t test or Mann-Whitney when appropriate. Association between GFR week-12 and other variables was established by means of Correlation Coefficients and linear regression (SPSS 19.0).

Results: Following LT, a gradual decline in renal function was noted (despite an initial improvement) with a mean and median GFR week-12 of 76 and 72 ml/min/1.73 m² respectively (Table and Figure 1). That was significantly lower than pretransplantation (p = 0.001). Pretransplant renal function was significantly correlated with GFR week-12. Tacrolimus trough level plateaued at 7 µg/l at week-4. At that point, GFR week-4 had a strongly significant correlation with future GFR week-12 (R = 0.716, square-R of 0.512, p = 0.001) and predicted accurately its value by means of a linear regression: GFR week-12 = 25.6 + (0.595 x GFR week-4).

Conclusion: In our cohort of patients, tacrolimus level reached 7 µg/l at week-4 and remained largely unchanged until week-12. That was associated with a loss of a quarter of GFR at 3 months. Aiming for a Tacrolimus trough level of 3-5 µg/l at 4 weeks, may result in a better renal function after LT when using the triple immunosuppression regimen.

Table 1. Correlation of GFR week-12 with previous GFR (ml/min/1.73 m²) and Tacrolimus trough levels (µg/l) after LT. Data expressed in mean (standard deviation) and median. Not Significant (NS).

P552

INCIDENTAL HEPATOCELLULAR CARCINOMA: ANALYSIS OF TUMOUR CHARACTERISTICS AND LIVER TRANSPLANTATION OUTCOMES

Renata Bartakova, Sona Frankova, Martin Oliverius, Jan Sperl, Eva Honsova, Dana Kautznerova, Pavel Trunecka, Julius Spicak

Institute for Clinical and Experimental Medicine, Prague, Czech Republic

Introduction: Hepatocellular carcinoma (HCC) detected incidentally in the liver explant after liver transplantation (LT), denoted as incidental HCC (iHCC), is not infrequent. We aimed to determine the tumour characteristics and outcomes of LT in patients with iHCC compared to those with previously known HCC (pkHCC).

Methods: We retrospectively reviewed 806 adult patients who underwent LT in our centre. Evidence of HCC before LT was confirmed by two imaging methods and alpha-fetoprotein (AFP) level and/or biopsy. Incidental HCC was defined as HCC found postoperatively in the explant.

Results: Eighty-one patients were transplanted for pKHC and in 33 patients HCC was diagnosed incidentally in the explant. There were no differences in sex, aetiology of underlying liver disease, time on the waiting list (WL), and level of AFP between the group of pKHC and iHCC. Further patients' and tumours' characteristics are shown in Table. Neither 3- and 5-year overall survival nor 3- and 5-year recurrence-free survival differed in iHCC patients compared to those with pKHC. The 3- and 5-year survival of both groups, iHCC and pKHC, was significantly lower than in patients transplanted for other diagnoses ($p < 0.001$). Sixteen patients had recurrence of HCC (pKHC vs. iHCC, $p = NS$). Risk factors for recurrence of HCC in iHCC patients were younger age ($p = 0.038$) and the presence of vascular invasion ($p = 0.04$) compared to the presence of vascular invasion ($p = 0.003$), the size of the largest lesion ($p = 0.007$), and shorter time on the WL ($p = 0.006$) in pKHC patients. The only prognostic factor affecting significantly patients' survival was poor tumour differentiation-G3 ($p = 0.03$) in those with pKHC, no factor was identified in the group of iHCC.

Conclusion: Despite an incidental finding, patients with iHCC do not differ from pKHC in terms of recurrence-free survival and overall survival. The occurrence of iHCC significantly influences the post-transplant prognosis similarly to the patients with pKHC.

P553

POSTREPERFUSION HYPERFIBRINOLYSIS IS COMMON, BUT SPONTANEOUSLY RESOLVES DURING LIVING DONOR LIVER TRANSPLANTATION

Heejin Roe, Justin Sangwook Ko, Misook Gwak, Gaab Soo Kim, Suk-ko Lee Samsung Medical Center

Background: Incidence of hyperfibrinolysis and application of antifibrinolytics were widely studied during deceased donor liver transplantation. However, living donor liver transplantation (LDLT) may be different in many aspects including fibrinolysis. So we investigated the incidence of hyperfibrinolysis during LDLT.

Methods/materials: We reviewed the medical records of 200 liver transplantation recipients from May 2011 to Sep 2013. Antifibrinolytics were not routinely administered during LDLT in our hospital. Histidine-tryptophan-ketoglutarate solution was used as preservation solution. Hyperfibrinolysis was diagnosed by thromboelastograph (TEG) when LY60 was greater than 15.

Results: After excluding adult deceased donor liver transplantation ($n = 44$), pediatric recipients ($n = 27$), error TEG case ($n = 1$), and antifibrinolytics before reperfusion ($n = 5$), 123 adult LDLT recipients were included in the final analysis. Recipients included 94 men and 29 women, and age was 52.1 ± 8.5 years. MELD score of recipients was 15.0 ± 8.8 . Main indications of LDLT were hepatitis B virus-related liver cirrhosis (13%) or hepatocellular carcinoma (HCC) (55%). Other indications were hepatitis C virus-related liver cirrhosis (2%) or HCC (5%), alcoholic liver cirrhosis (10%), and etc. Hyperfibrinolysis were uncommon in prehepatic phase; 2% before incision and 7% at the start of anhepatic phase. Hyperfibrinolysis was increased during anhepatic phase and peaked immediately after reperfusion; 30% at 1 h after anhepatic phase and 80% at 5 min after reperfusion. However, hyperfibrinolysis nearly disappeared without antifibrinolytics and did not recur; 2% at 1 h after reperfusion and 0% at 3 h after reperfusion.

Conclusion: Hyperfibrinolysis frequently occurred after reperfusion of LDLT, and rapidly resolved without specific treatment. The significance of hyperfibrinolysis and the application of antifibrinolytics during LDLT should be investigated with further study.

P554

CURRENT STATUS OF LIVING DONOR LIVER TRANSPLANTATION IN ASAN MEDICAL CENTER

Sung-Gyu Lee, Chul-Soo Ahn, Ki-Hun Kim, Tae-yong Ha, HyungWoo Park, YongKyu Chung, EunKyung Jwa, Dong-Hwan Jung
Division of Liver Transplantation and Hepatobiliary Surgery, Department of Surgery, Asan Medical Cen

Backgrounds: First pediatric living donor liver transplantation (LDLT) was performed in 1994. In 1997, the first successful right-liver LDLT for adults was performed at the Asan Medical Center. The number of LDLTs has increased annually, with 317 transplantations performed in 2011.

Methods: From 1994 to Sep.2012, we performed more than 3000 LDLT. We reviewed the recent changes of LDLT during this period.

Results: Most common indication of pediatric LDLT was biliary atresia and acute liver failure. HBV associated liver cirrhosis (HBV LC) was most common indication of adult LDLT. Proportion of HBV LC has been decreasing from 80% to 67% and alcoholic LC and HCV LC have been increasing up to 11% and 6% recently. Recently urgent LDLT including UNOS I and 2A decreased due to national increase of DDLT. Proportion of hepatocellular carcinoma positive patient in adult LDLT has been increased up to 52.3%. The goal of donor evaluation is to determine whether the donor is medically and psychologically suitable for living donation. Anatomical limitation in living liver donor depends on availability of living donor and technical feasibility of individual centers and donor complication rate. Laparoscopic-assisted, hand-assisted, or minimal

Incision donor hepatectomy has been increasing. Major reasons of rejection as suitable live-donors have been ABO blood group incompatibility, unsafe donor liver anatomy concerning small remnant liver volume, small-for-size graft, and the associated donor comorbidities. Dual LDLT, donor exchange LDLT, ABO incompatible LT can expand donor pool in LDLT field. We performed more than 300 adult dual LDLT with various types of graft. There were 26 cases donor exchange for ABO incompatible adult LDLT at AMC from July 2003 to December 2011. 125 cases ABO incompatible LDLT from November 2008 to July 2012 have been performed. The proportion of ABO incompatible LT was increased to 23.1% of all adult LDLT in 2012.

Conclusions: LDLT has evolved to become an indispensable surgical strategy of end stage liver disease. Minimal morbidity and zero mortality of live donors is utmost requirement of LDLT.

P555

MUTATIONAL PATTERN OF PATIENTS WITH TRANSTHYRETIN ASSOCIATED FAMILIAL AMYLOID POLYNEUROPATHY IN GERMANY

Yesim Avsar¹, Theodor Todorov¹, Andree Ziber¹, Iyad Kabar¹, Vito R. Cicinnati¹, Susanne Beckebaum¹, Christoph Röcken², Ana Barreiros³, Hartmut Schmidt¹

¹University Hospital Münster; ²Christian-Albrechts-Universität Kiel;

³Universitätsmedizin Mainz

Background: Familial amyloid polyneuropathy (FAP) is most commonly associated with a mutation of the transthyretin-gene (TTR) with more than 80 amyloidogenic variants known so far. The phenotype is highly variable and linked to the underlying mutation, with significant effects on the outcome of liver transplantation, currently the only curative treatment option. To optimize patient selection for transplantation, emphasis should be placed on the specific mutation involved. High frequency mutations have been detected in endemic areas such as Sweden, Portugal and Japan. Common mutations in Germany have yet to be identified.

Aim: The distribution of amyloidogenic TTR variants in Germany was studied. **Methods:** Of 81 patients with histologically confirmed TTR-amyloidosis from 40 unrelated families were included. The mutation was identified by genomic DNA extraction from patient's blood and direct sequencing. Patients were examined for clinical signs and symptoms.

Results: The two most prevalent mutations Val30Met and Gly47Ala, were detected in 43/81 and 21/81 patients, respectively. Patients with the Val30Met variant presented mainly with polyneuropathy, whereas cardiac manifestations were prominent in patients affected by the Gly47Ala mutation. Further mutations identified in the remaining patients were Leu58His, Ile107Val, Gly53Ala, Asp39Val, Arg34Thr, Val20Ile, Thr59Lys, Thr60Ala and Glu89Gln. Of 16 patients received a liver transplant and 21 patients are currently being treated with Tafamidis. Outcomes are still being followed.

Conclusions: This is the first analysis reporting on the genetic pattern of TTR-amyloidosis in Germany. Similar to Portugal, Sweden and Japan, we found Val30Met to be the most prevalent mutation. The second largest group was found to have the Gly47Ala variant. Ongoing analysis of FAP-patients may help us to identify prognostic factors for patients treated with Tafamidis and/or liver transplant.

P556

COMPARATIVE PROSPECTIVE STUDY OF THREE SOLUTIONS FOR LIVER PRESERVATION: UNIVERSITY OF WISCONSIN (UW), CELSIOR (CEL) AND INSTITUT GUSTAVE LOPEZ (IGL-1).

Adam René, Karam Vincent, Sebahy Mylène, Saliba Faouzi, Samuel Didier, Castaing Denis

Centre Hépatobiliaire, AP-HP Hôpital Paul Brousse

Minimization of damage from cold ischemia and reperfusion is critical to the success of liver transplantation (LT). A variety of solutions are today used worldwide. IGL-1 solution is a new solution containing the polyethylene glycol component but is not as yet widely used in liver grafts. The aim of this study was to compare the liver function of transplanted grafts stored in IGL-1 to that of grafts stored in CEL or UW. We analyzed data of 400 first cadaveric full-size LTs (117 IGL-1, 160 CEL and 123 UW) performed between 2007 and 2012 in our center. Primary dysfunction (PDF) and non-function (PNF), kinetics of liver function, reperfusion biopsy, patient and graft survival, and cause of death or graft loss were compared for the three groups. The three groups were similar in terms of donor, recipient, and surgical techniques variables. In post-LT outcome data: (i) the peak of Alanine aminotransferase was lower with IGL-1 than with CEL or UW ($p < 0.04$), and INR at day-5 was lower in CEL than in IGL-1 or UW ($p < 0.03$); (ii) proportion of PDF-PNF were similar in the three groups; (iii) graft survival was not statistically different with UW, CEL or IGL-1 (91%, 92% and 98%, respectively at 3 months, and 85%, 85% and 89%, respectively at 1-year); (iv) Cause of graft loss was similar in the three groups. In conclusion, liver graft injury seems to be reduced and liver function recovery better with IGL-1. However incidence of PDF-PNF and graft outcome were comparable with the three solutions.

P557

RISK FACTORS FOR THROMBOCYTOPENIA IN LIVER TRANSPLANT RECIPIENTS

Gabriela Droc, Mihai Popescu, Dana Tomescu, Irinel Popescu
Fundeni Clinical Institute

Background: Postoperative thrombocytopenia by increasing bleeding risk can become a serious problem in liver transplant (LT) recipients. The aim of the study was to assess risk factors for early postoperative thrombocytopenia.

Material/method: After approval of the local ethics committee we retrospectively analyzed 50 consecutive patients who underwent LT between March and December 2012. Spleen size, coagulation status were recorded prior to surgery. Intraoperative blood loss and blood product transfusion (BPT) were measured. Platelet count (PLT) was assessed at 8 h interval for 48 h and then twice daily. A statistical analysis was performed using SPSS v.19.0.

Results: Preoperatively, 23.6% of the patients had severe thrombocytopenia (<50 000 elem/mm³); the mean PLT before LT being 70 000 elem/mm³. Eighty percent of patients (n = 40) had hypersplenism with a median spleen size of 159.5 mm. Median intraoperative blood loss was 4525 ml requiring a median BPT of 7 units packed red blood cells (PRBC). Twenty-one patients (43%) required platelet transfusion with a median value of 5 units. The mean value of PLT immediately postoperatively was 46 000 elem/mm³, on the 5th day of 39 000 elem/mm³ and then of 50 000 elem/mm³ on the 7th day. Risk factors for low PLT immediately after surgery were: pretransplant low PLT (p < 0.001), size of the spleen (p = 0.034), intraoperative blood loss (p = 0.043) and BPT (PRBC-p < 0.001). In the multivariate analyses only the size of the spleen and pretransplant PLT remained statistically significant.

Conclusion: Intraoperative blood loss and transfusion requirements as well as low values for PLT due to hypersplenism before LT procedure influence PLT in the postoperative period, and at least one of those causes is amendable, the intraoperative blood loss.

P558

PHYSICAL FITNESS BEFORE AND AFTER LIVER TRANSPLANTATION: A LONGITUDINAL STUDY

Leen Schepers¹, Rik Gosselink², Frederik Nevens¹, Jacques Pirenne¹, Diethard Monbaliu¹

¹University Hospitals Leuven; ²Katholic University Leuven

Background: Liver transplantation (LTx) has become the first line treatment for patients suffering from irreversible end-stage liver disease. Exercise capacity and muscle strength are often impaired in patients with end-stage liver disease and data of recovery after LTx are scarce. The aim of this study was to examine the effect of LTx on recovery of physical fitness.

Methods: Patients on the active waiting list were included for this observational study. Maximal ergospirometry (VO₂max) measuring exercise capacity, 6 min walking distance (6MWD) assessing functional exercise capacity and peripheral muscle strength (quadriceps and handgrip force) were measured the moment of activation on the waiting list (before LTx), shortly (~3 weeks) after LTx and 3 months after LTx.

Results: Of 21 patients (age 55 ± 11 years, 10 male) were included. Indications were cirrhosis (n = 6), HCC (n = 8), non-alcoholic steatohepatitis (n = 2), cholestatic liver disease (n = 3) and other (n = 2). Before LTx, 6MWD (69 ± 21%pred) and quadriceps force (61 ± 20%pred) were severely impaired. VO₂max (84 ± 30%pred) and handgrip force (87 ± 27%pred) were moderately impaired. Using repeated measures ANOVA, significant changes were observed for 6MWD (p < 0.0001) and quadriceps force (p < 0.01): at 3 months, 6MWD (79 ± 19%pred) had improved compared to shortly after LTx (62 ± 20%pred; p < 0.001) and before LTx (p < 0.05). At 3 months, quadriceps force (68 ± 18%pred) had increased significantly compared to shortly after LTx (54 ± 14%pred; p < 0.01) in contrast to before LTx (p = 0.11). There were no significant changes of VO₂max (p = 0.21) or handgrip force (p = 0.14), which at 3 months remained lower than predicted (75 ± 21%pred, and 86 ± 23%pred respectively).

Conclusions: Exercise capacity and muscle strength are impaired in LTx candidates. At 3 months after LTx, quadriceps force and 6MWD improve but all measurements remain impaired. Longer follow-up data are now collected.

P559

CIRROTHIC PATIENTS FAIL TO REGAIN MUSCLE MASS AFTER LIVER TRANSPLANTATION

Michela Giusto

Gastroenterology, Department of Clinical Medicine, Sapienza Università di Roma, Italy

Background aim: Muscle wasting is a common complication in patients undergoing liver transplantation (LT). Although malnutrition has been identified as a predictor of poor outcome after surgery, less information are available regarding the sequential changes of body composition after LT. This study aims to investigate changes in body composition after LT.

Methods: Adult patients eligible for elective LT were included. Nutritional assessment (anthropometry and Dual-energy X-ray absorptiometry [DEXA]) was performed in all patients before and 1, 3, 6 and 12 months after LT. Triceps-skin fold thickness (TSF) was measured and Mid-arm muscle circumference (MAMC) was calculated according to standard equation. Fat-Free Mass Index (FFMI, kg/m²) and Fat Mass Index (FMI, kg/m²) were calculated by whole body DEXA scan.

Results: Sixty-four adult patients awaiting for LT were initially studied. Results refer to 27 patients who were transplanted and completed 1 year of follow-up (Table 1). At LT 33% of patients presented a fat-free mass depletion while 4.8% showed a depletion in fat mass. During the first year after LT, while fat mass (TSF and FMI) increased progressively (from 15.4 to 19 mm, and from 6.7 to 7.7 kg/m², before and 12 months after LT, respectively, p < 0.05), fat free mass (MAMC and FFMI) failed to ameliorate. The percentage of patients with fat-free mass depletion (FFMI below 10th percentile) was even increased 1 year after LT (from 33% before LT to 63% 12 months after LT p < 0.05) (Figs 1 and 2).

Conclusion: During the first year after LT the fat mass is progressively regained while the recovery of the fat free mass is insignificant and may require a longer period.

P561

ASSOCIATION OF SERUM CYTOKINE PROFILES WITH TACROLIMUS-INDUCED CHRONIC NEPHROTOXICITY IN CHINESE LIVER TRANSPLANT RECIPIENTS

Jiangtao Tang¹, Yuning Sh², Junlong Zhang¹, Yi Li¹, Yunfei An¹, Lanlan Wang³

¹Department of Laboratory Medicine, West China Hospital of Sichuan University; ²Department of Nephrology, West China Hospital of Sichuan University; ³Department of Laboratory Medicine, West China Hospital

Background: Calcineurin inhibitors (CNI) associated chronic nephrotoxicity has become a serious problem which threatens the prognosis of liver transplant recipients. This study was aimed to find out the relationship between serum cytokines, chemokines and chronic tacrolimus (Tac) induced nephrotoxicity. We detected the posttransplant serum inflammatory cytokines and chemokines levels in liver transplant recipients to illuminate the correlations of inflammatory cytokines or chemokines with the chronic renal injury.

Methods: A total of 136 living donor liver transplant recipients (107 males and 29 females) and 150 healthy controls (120 males and 30 females) were enrolled in this study. All the recipients had normal Cystatin C (Cys-C) and normal urine microalbumin before transplantation and received Tac-based immunosuppressive regime (Tac+MMF+ prednisone) afterwards. A human 10-plex antibody bead kit (BioSource, Camarillo, CA) was used to measure the levels of 10 cytokines and chemokines in 50 ml of serum from each transplant patient and controls. After transplantation, serum Cys-C and urine microproteins including ¹A1 microalbumin (¹A1M), microalbumin (MA), transferrin (TRU) and IgG (IgU) were measured among 136 allo-liver recipients to evaluate whether they had early renal injury and the probable location of the renal lesion.

Results: The levels of IL-6, IL-10, IFN- γ , IP-10 and MCP-1 in the recipients' group were significantly higher than those in the control group (p < 0.05), while the levels of IL-8 was on the contrary (p < 0.05). In early renal damage group (Cys-C > 1 mg/l), the concentration of IP-10 was much higher compared to the group with normal renal function (Cys-C₁U1 mg/l), whereas the concentration of MCP-1 in early renal damage group was lower than the group with normal renal function. The concentration of IP-10 in the group with tubulointerstitial injury (¹A1M > 12.5 mg/l) was much higher compared with the group without such injury (¹A1M₁U12.5 mg/l).

Conclusions: IP10 may be the important cytokine leading to chronic CNI-induced nephrotoxicity, especially the tubulointe.

P562

DIABETES AND HYPERTENSION IN LIVER TRANSPLANT RECIPIENTS: PREVALENCE AND PREDICTORS

Nouman Algarem, Moustafa Elshazly, Amany Sholkamy,
Ahmed Daoud
Faculty of Medicine, Cairo University

Background: Chronic HCV infection is known as a national problem in Egypt. Egypt has a very high prevalence of HCV infection and a high morbidity and mortality from chronic liver disease, cirrhosis, and hepatocellular carcinoma. With the availability of liver transplantation as an effective therapy for chronic end stage liver disease and with the progressively improved outcome and survival; the occurrence and the prevalence of post transplantation complications are increasing. The occurrence of post liver transplantation diabetes mellitus, or hypertension are increasingly recognized as a contributor to cardiovascular complications and late morbidity and mortality in transplanted patients.

Aim: The aim of our research was to study post-liver transplantation diabetes and hypertension as regards evaluation of the overall prevalence of the

diabetes and hypertension and identification of the predictors for posttransplant diabetes and hypertension.

Methods: Our study involved 40 patients. We collected the data of the patients from the database of the patients in the liver transplant unit in Almanial Altakhasosy hospital. We collected data regarding age, sex, BMI, preoperative labs of the patients, their child class, cause of the liver transplant, the immunosuppressants received by the patients, whether they received pulse steroids or not, whether the patients were diabetic and hypertensive before the transplant and the treatment they used to receive if so, and whether they developed DM or hypertension after the transplant and if so the treatment they received.

Results: 10% of the patients involved in our study were diabetic before the transplant, 25% of them acquired diabetes after the transplant to give a total of 35% diabetic patients after the transplant. Predictors of PTDM were pretransplant FBS and Child class C. 25% of the patients developed posttransplantation hypertension. Predictors of posttransplantation hypertension were BMI and using Neoral.

PS12-LIVER

P563

IMMUNOSUPPRESSIVE EFFECTS ON CELLULAR IMMUNE IN ALLO-LIVER RECIPIENTS WITH TACROLIMUS-BASED REGIMEN

Bei Cai¹, Yi Li¹, Yangjuan Bai¹, Yuangao Zou¹, Lvnan Yan², Lanlan Wang¹
¹Department of Nephrology, West China Hospital, Sichuan University; ²Center of Liver Transplantation, West China Hospital of Sichuan University

Background: The dynamic immune effects of tacrolimus on peripheral CD4+ CD25+ Foxp3+ regulatory T cells (Treg), CD8+ CD28- suppressor T cells (Ts) and CD8+ CD28+ effector T cells (Teff) in allo-liver recipients were rarely discussed.

Methods: Of 81 allo-liver recipients, 54 patients with end-stage liver disease (ESLD) and 47 healthy volunteers (HC) were included. Peripheral Treg, Ts and Teff cells were detected by flow cytometry.

Results: %A Percentage of Ts cells and Teff cells in recipients increased and decreased, respectively. With time going Ts cells was increasing, and Teff cells was decreasing (all $p < 0.05$). %E In recipients percentage of Treg cells was significantly lower than that in HC and ESLD. With time going, proliferation of Treg cells was blocked. %C A good negative correlation between Tac concentration and percentage of Treg cells or Teff cells was shown ($r = -0.347$ ($p = 0.047$) and $r = -0.361$ ($p = 0.039$), respectively).

Conclusions: The immunosuppressive effect of tacrolimus was mainly on suppressing the proliferation of Treg cells and Teff cells, and the suppressive effect of Ts cells should be worthy of attention in recipients.

P564

ASSOCIATION OF CELLULAR IMMUNE MARKERS AND THE DEVELOPMENT OF HEPATITIS B RECURRENCE AFTER LIVER TRANSPLANTATION

Jie Chen, Lanlan Wang, Bei Cai, Yi Li, Yang Fu, Limei Luo, Yun Liao
 Department of Laboratory Medicine, West China Hospital of Sichuan University

Background: Success of liver transplantation is limited by recurrent graft infection. This study is to explore the relationship between soluble costimulatory molecules and hepatitis recurrence.

Method: Of 81 end-stage liver disease secondary to HBV who underwent liver transplantation were included. They received a calcineurin inhibitor (CNI) based regimen after transplantation. There were 11 patients had HBV recurrence. Soluble Cytotoxic T Lymphocyte-Associated Antigen-4 (sCTLA-4), sCD28, sCD80, sCD86 and IFN- γ concentrations in plasma were measured by enzyme-linked immunosorbent assay (ELISA) (eBioscience).

Results: There was no significant difference about plasma concentration of sCD28, sCTLA-4, sCD80 and sCD86 between the two groups: HBV recurrent and no recurrent after liver transplantation, however IFN- γ significantly decreased in HBV recurrent recipients.

Conclusions: In HBV recurrent transplantation recipients, the decrease levels of sCTLA-4 and sCD86 result in the increase of the interaction of mCTLA-4/CD86, down-regulating Th1 response and activation of CD8+ T, resulting in impairment of killing immunity. The decrease of IFN- γ may indicate the down-regulation of CD8+ T and results in impairment of antiviral immune response.

P565

LACK OF ASSOCIATION BETWEEN CYP2C8 POLYMORPHISM AND CYTOKINE/CHEMOKINE LEVELS WITH THE KIDNEY LESION IN CHINESE LIVER TRANSPLANT RECIPIENTS

Yun Liao, Jiangtao Tang, Yi Li, Lanlan Wang
 Department of Laboratory Medicine, West China Hospital, Sichuan University

Background: With increasing liver transplant recipients with chronic kidney lesion, we investigated the role of CYP2C8 and cytokines in the pathology of chronic kidney injury in the liver transplant recipients.

Methods/materials: High resolution melting curve was used to genotype CYP2C8 polymorphism. Cytokines/chemokines in our study including IL-6, IL-8, IL-10, IL-17, IFN- γ , IP-10 was assessed using Elisa kits.

Results: In total, 185 patients were recruited in this study including 141 males and 44 females. We successfully genotyped CYP2C8 and found only two genotypes (160 patients with CYP2C8*1*1, 25 patients with CYP2C8*3*1) in the patients. After logistic regression adjusting for age and sex, Neither the CYP2C8 polymorphism nor cytokine/chemokine results (CYP2C8, $p = 0.102$; IL-6, $p = 0.322$; IL-8, $p = 0.362$; IL-10, $p = 0.335$; IL-17, $p = 0.525$; IFN- γ , $p = 0.332$; IP-10, $p = 0.588$) associate with the chronic kidney injury.

Conclusion: Our study showed that none of the surmised factors including CYP2C8, cytokine or chemokines contribute to chronic kidney injury based on our current data.

P566

METABOLIC SYNDROME AS A COMPLICATION OF LIVER TRANSPLANTATION

Ahmed Daoud, Amany Shoulqamy
 Faculty of Medicine, Cairo University

With increasing survival after orthotopic liver transplantation (OLT), metabolic syndrome and its individual components, including diabetes mellitus, hypertension, dyslipidemia, and obesity, are increasingly being identified and contributing to cardiovascular complications and late morbidity and mortality. MS develops in 43% to 58% of patients after OLT; this is higher than the prevalence of MS reported in the normal adult population 24%. Metabolic Syndrome (MS) increases the risk for Coronary Artery Disease, stroke and diabetes. As a result of increased incidence of development of metabolic syndrome and its complications, outcome of liver transplantation becomes poor. Predisposing factors may include higher age at transplant, an increase in BMI post-OLT, pre-OLT diabetes, a history of smoking, the immunosuppressant regimen used, and the indication for OLT (hepatitis C, alcohol, or cryptogenic cirrhosis). There are some published studies that have specifically reported the development of individual components of MS following OLT especially Diabetes and Hypertension. The estimated prevalence of PTDM and posttransplant hypertension varied from a study to another and there is a debate between researchers about their predisposing factors. However, HCV ad Tacrolimus are considered by most authors to be predisposing to PTDM while Cyclosporine is believed to increase the incidence of posttransplant hypertension.

P567

SURGICAL OUTCOME OF LIVING DONOR HEPATECTOMY: SINGLE-CENTER EXPERIENCE

Hakan Sozen, Utku Tonyuk, Ayдын Dalgic
 Gazi University

Living donor hepatectomy (LDH) for living related liver transplantation (LRLT) has begun an accepted and widely used worldwide.

Aim: To assess surgical outcome of living donor hepatectomies as a single center experience.

Material and methods: Totally 22 living donor hepatectomies were performed at Gazi University Transplantation Center/Ankara/Turkey since 2006. All data retrospectively collected from hospital charts.

Results: There were 13 female, nine male as donor. Donors' origin was 12 parents, four siblings, two spouses, one aunt, 1 nephew and two others. Mean age of the donor was 32 ± 7.5 years (between 23–48 years). Mean BMI of the donor was 27.2 ± 1.9 (median 27). Eleven out of 22 right hepatectomies, 8 out of 22 left and 2 left-lateral hepatectomies were performed. The mean remnant liver left at the donor liver percentage for right hepatectomy was 33.8 ± 4 (median 35) and median graft-to-recipient body weight ratio of the right lobe was 1.7% (between 0.9% and 1.5%). The mean intraoperative blood transfusion was 1.3 ± 1.4 U (0–6 U ES). Donors' average hospital stay was 9 ± 3 days (6–17 days, median 9 days) found. We have not seen any late surgical complications. But as early surgical complication, postsurgical bleeding ($n = 1$; 4.5%) detected in this study group. Patient re-explored and was found that blood was coming from left gastric artery stump. Stump successfully repaired again without any problem. This patient discharged at D7 after surgery. We have not seen any vascular complication at the post-hepatectomy period.

Conclusion: Donor hepatectomy for living liver transplantation is a safe procedure. We believe that, donor safety should be the first priority of all living liver donor programs and it is efficient way of treatment method whom are at the waiting list.

P568

DO WE HAVE RELIABLE CRITERIA TO AVOID RECURRENCE OF HEPATOCELLULAR CARCINOMA AFTER LIVER TRANSPLANTATION?

Juliane Liese¹, Christian Moench², Teresa Schreckenbach¹, Andreas A. Schnitzbauer¹, Martin Welker³, Wolf Otto Bechstein¹, Frank Ulrich¹
¹General and Visceral Surgery, Goethe University, Frankfurt; ²General, Visceral and Transplantation Surgery, Westfalz Klinikum, Kaiserslautern; ³Gastroenterology and Hepatology, Goethe University, Frankfurt

Introduction: Liver transplantation (LT) is the most radical treatment of hepatocellular carcinoma (HCC) with high rates of long-term survival. Nevertheless, tumour recurrence after LT is still a relevant problem. The aim of our study was the evaluation of predictive markers of tumour recurrence.

Methods: In a retrospective single centre study we included all patients with LT for HCC in our institution (01/2007–08/2012). Beside demographic data, we analysed course, complication rates, bridging therapies as well as the correlation of imaging and histopathology of our recipients.

Results: During the study period we performed 91 LT (73 men, 18 women) with HCC. 15 (16.5%) patients developed a recurrent HCC after LT. In this subgroup, transarterial chemoembolization was performed in 12/15 cases as a bridging therapy before LT as well as chemoperfusion in one patient. Two other patients were bridged by liver resection. Our subgroup with tumour recurrence

after LT presented with a mean disease-free survival of 11.9 months and an overall survival of 22.7 months. 9 of 15 patients died after a mean period of 5.6 months after diagnosis of tumour recurrence. The other 6 patients demonstrated a mean survival of 34.9 months. Their tumour-specific therapy included chemotherapy with Sorafenib, resection of a single metastasis, RFA of a recurrent tumour in the liver and switching immunosuppressive therapy to everolimus. In our study group neither Milan criteria, waiting time, bridging therapies, AFP blood levels nor pathological grading had an influence on the tumour recurrence. Only microvascular invasion was a major risk factor for HCC recurrence.

Conclusion: Reliable prognostic markers related to tumour biology and adjuvant therapies are still missing. Novel molecular profiling techniques and novel therapies getting more and more important in times of severe organ shortage.

P569

HYPERTENSION IN LIVER TRANSPLANT RECIPIENTS: INCIDENCE, PREDISPOSING FACTORS, CARDIOVASCULAR COMPLICATIONS AND TREATMENT

Ahmed Daoud¹, Amany Shoulqamy²

¹Faculty of Medicine, Cairo University; ²Cairo University

One of the known complications of liver transplantation is posttransplant hypertension. According to most authors more than 50% of liver transplant recipients develop hypertension. Cyclosporine is believed to induce posttransplant hypertension. However, there are only few studies identifying other risk factors for development of posttransplant hypertension after liver transplant. BMI, diabetes and metabolic syndrome were identified by some authors as risk factors for posttransplant hypertension. Some studies were done on liver transplant recipients to identify suitable treatment options for posttransplant hypertension and especially Cyclosporine-induced hypertension and to understand their mechanism of action. Posttransplant hypertension is believed to be a risk factor for cardiovascular events. To determine the individual risk of cardiovascular events, several risk scores based on large cohort studies have been established. It should be noted that not all these risk scores are valid in liver transplant recipients.

P570

APPLICATION OF FULL COVERED METALLIC STENTS FOR TREATMENT BILIARY STRUCTURES AFTER LIVER TRANSPLANTATION

Maxim Kornilov, Yan Moysyuk

Federal Research Centre of Transplantation and Artificial Organs Academician V.I. Shumakov

The aim of the study is to present our experience in treatment of biliary structures after liver transplantation by placement of fully covered self-expandable metallic stents (FCSEMS). From 12/2004 to 11/2012 we performed 136 cadaveric liver transplantations to adult recipients. Biliary reconstructions were choledochocolicostomy without external drainage – 96 (70.1%). With T-tube 20 case (14.7%). Choledochocenterostomy – 20 recipients, accounting for 14.7%. Our data shows that the incidence of early and late biliary structures is 5.4%. Seven patients were treated by placement of FCSEMS. Four stents had been installed by retrograde cholangiopancreatography, 2 by ante-grade within 1–12 month after liver transplantation. Mean follow up time was 12 months. No severe complications were observed after, only two patients developed mild cholangitis. We can conclude that application of FCSEMS is safe and effective method of treatment biliary structures after liver transplantation. Long-term follow-up results should be evaluated.

P571

DESIGN OF THE H2307 STUDY: EVEROLIMUS WITH REDUCED TACROLIMUS IN LIVING DONOR LIVER TRANSPLANTATION

Guido Junge¹, Gi-won Song², J.W. Joh³, E. Pomfret⁴, Patricia M. Lopez¹, J.M. Hexham⁵, Shinji Uemoto⁶, K.S. Suh⁷, Gary Levy⁸

¹Novartis Pharma AG, Basel, Switzerland; ²Asan Medical Center, Seoul, Korea; ³Samsung Medical Center, Seoul, Korea; ⁴Lahey Clinic, Boston, MA, USA; ⁵Novartis Pharmaceuticals, East Hanover, NJ, USA; ⁶Kyoto University Medical Center, Japan; ⁷Seoul National University Hospital, Seoul, Korea; ⁸University of Toronto, Toronto, Canada

Background: The H2307 study is designed to evaluate the efficacy and safety of everolimus (EVR) with reduced tacrolimus (rTAC) versus standard TAC (TAC-C) in living donor liver transplant (LDLT) recipients.

Methods: This is a 24-month (mo), multicentre, randomized study in *de novo* LDLT recipients. Patients will be randomized (1:1) to receive EVR+rTAC or TAC-C (figure). The primary endpoint is the rate of composite efficacy failure events (treated biopsy proven acute rejection, graft loss or death) at 12 mo post-transplantation. Secondary endpoints: evolution of renal function, inci-

dence of adverse events, recurrence of hepatocellular carcinoma, load of hepatitis C virus and progression of graft fibrosis, and allograft regeneration. At least 470 *de novo* LDLT recipients will be enrolled from Europe, Asia and North America.

Results: Expected in early 2016.

Conclusion: This is the first study designed to evaluate the efficacy and safety of EVR+rTAC versus TAC-C in LDLT recipients.

P572

LIVER TRANSPLANTATION IN LYMPHOMA PATIENTS WITH HEPATITIS B VIRUS REACTIVATION

Nuri Lee, Jong Man Kim, Jin Youg Choi, Wontae Cho, Shin-Seok Yang, Seunghwan Lee, Hyung Hwan Moon, Milljae Shin, Jae Berm Park, Choon Hyuck David Kwon, Sung-Joo Kim, Jae-Won Joh, Suk-Koo Lee

Department of Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine

Background: Acute-on-chronic liver failure (AoCLF) occurs in lymphoma patients secondary to hepatitis B virus (HBV) reactivation due to chemotherapy. Liver transplantation (LT) is generally not performed in these patients. We aimed to identify characteristics of patients who underwent LT because of AoCLF that occurred due to HBV reactivation in the setting of lymphoma and to compare these patients with AoCLF patients who did not have lymphoma.

Methods: Twenty patients underwent LT due to AoCLF between February 2009 and June 2011. Among these patients, five patients were diagnosed with lymphoma prior to liver transplantation and assigned to Group 1. The remaining patients ($n = 15$) did not have lymphoma were assigned to Group 2.

Results: Hospitalization after transplantation in Group 2 was longer than in Group 1 ($p = 0.014$). However, there were no statistical differences in other variables between the two groups. The overall survival rate of Group 1 was lower than that of Group 2, but there was no statistically significant difference between the two groups ($p = 0.134$). With the exception of one patient, the median time from complete remission to liver transplantation in Group 1 was 4.5 months (range, 1–15) in Group 1. Lymphoma recurrence occurred in only one patient 8 months after transplantation.

Conclusion: Our study revealed that LT is a feasible and effective approach in AoCLF due to HBV reactivation in selected lymphoma patients.

P573

EVOLUTION OF DONOR COMPLICATIONS IN LIVING RELATED LIVER TRANSPLANTATION: ANALYSIS OF 600 CASES

Sezayi Yilmaz¹, Cuneyt Kayaalp¹, Dincer Ozgor¹, Abuzer Dirican¹, Mustafa Atesh¹, Fatih Gonultash¹, Mehmet Yilmaz¹, Nuru Bayramov², Ruslan Mammadov², Cengiz Ara¹

¹Inonu University Liver Transplantation Institute; ²Azerbaijan Medical University

Background: To evaluate the incidence and severity grade of postoperative complications in living liver donors by using Clavien classification was the aim of this study.

Materials and methods: We retrospectively analysed results of 600 living donor hepatectomies which were performed during 2007–2012 years in Ynönü University Liver Transplantation Institute. Mean age of donors was 31 (18–65) years, body mass index 27.4 (24–36) kg/m², follow-up duration 39 month (2–58). Right hemihepatectomies were performed in 538 (89.6%) donors, left hemihepatectomies in 19 (3.1%) and left lateral sectorectomies (two and three segments) were done in 43 (7.2%) donors. Mean remnant liver volume for donors was 37% (26–87%), duration of operation – 327 min (205–440 min), intraoperative blood loss – 310 ml (100–800 ml) and hospital stay was 7.2 days (5–13 days).

Results: There was no mortality. The 187 postoperative complications were observed in 116 of 600 (19.3%) donors. According to Clavien classification first degree complications were occurred in 91 (15%) cases, second degree in 20 (3.3%), IIIa degree in 32 (5.3%), IIIb degree in 43 (7.3%) and IVa degree complication in 1 (0.16%) donor. Most of complications were mild (59.3%) and managed conservatively. Biliary complications which included biliary leakage, bilioma and strictures were observed more frequently (10.6%). Reoperations were needed in 34 donors.

Conclusion: Most of the postoperative complications in living liver donors are mild degree and biliary complications are more frequent.

P574

LIVER ALLOCATION: THE BEST CHOICE FOR PATIENTS

Maurizio Valeri¹, Gianfranco Teti, Roberta Durante, Paola Piovano, Aurela Meçule, Teresa Altobelli, Nicola Torlone, Domenico Adorno
Centro Regionale Trapianti Lazio

Background: Regional Transplant Center of Lazio (CRTL) coordinates the activity for liver transplant of four centers for adult transplants and one for the

pediatric ones; until the end of 2012 every liver was allocated in order to a regional rotation system. But this model not always allowed the transplant for patients in clinically worst conditions, except for those case of well defined urgency.

Methods/materials: For this reason, at the beginning of 2013 CRTL started to use a new regional system that allocates the liver following an algorithm according to MELDNa value, time in waiting list, combined transplant, identity/compatibility AB0.

Results/conclusions: We observed that for the first two months of 2013 the medium MELD-Na value for transplanted patients was 22.3 (15 pts) vs. 19.8 of 2012 (98 pts) and it seems to confirm that we are going to a more ethical direction to give organs to clinically worst patients.

P575

COMPUTER ASSISTED SURGICAL PLANNING IN ADULT-TO-ADULT LIVE DONOR LIVER TRANSPLANTATION: HOW DOES IT HELP? A SINGLE CENTER EXPERIENCE

Christian Wilms¹, Susanne Beckebaum¹, Vito R. Cicinnati¹, Tobias Schroeder², Hartmut Schmidt¹, Heinz-Otto Peitgen³, Christoph E. Broelsch⁴, Massimo Malagó⁵, Arnold Radtke⁶

¹Department of Transplant Medicine, University Hospital Muenster;

²Department of Diagnostic and Interventional Radiology, University Hospital Essen;

³MeVis Center for Medical Diagnostic Systems and Visualization, University of Bremen;

⁴Department of General, Visceral, and Transplantation Surgery, University Hospital Essen;

⁵Department of Hepatobiliary Surgery, Royal Free University Hospital, London; ; ⁶Department of General and Visceral Surgery, University Hospital Muenster

Background: Pre-operative imaging and donor selection are cardinal components of adult live donor liver transplantation (ALDLT). Evaluation of 3D-CT image-derived computer assisted surgical planning (3D CASP) in ALDLT.

Methods: Of 83 consecutive ALDLTs (71 right, 12 left) were planned with 3D CASP. Graft, remnant, and total liver volume compliance were compared to actual intra-operative values. Computed risk analysis encompassing territorial liver mapping, functional volumes, outflow congestion volumes in grafts/remnants was utilized for the management of the middle hepatic vein (MHV).

Results: Graft volume compliance was $13.5 \pm 4.4\%$. Small-for-size (SFS) grafts with lethal SFS syndrome (SFSS) had poor volume compliance with maximal graft-volume-body-weight-ratios (GVBWR) <0.83 . SFS grafts with reversible/absent SFSS had maximal GVBWR of 0.9–1.16. Significant differences were identified for: (i) graft/remnant congestion volumes of risky vs. non-risky MHV-types ($49 \pm 6\%/34 \pm 7\%$ vs. $29 \pm 8\%/33 \pm 12\%$), (ii) functional-(f)- vs. surgical-(s)-volumes of grafts (527 ± 119 ml vs. 963 ± 176 ml) and remnants (419 ± 182 ml vs. 640 ± 213 ml).

Conclusions: CASP allowed for (i) prevention of SFS syndrome in extremely small grafts by predicting donor liver plasticity (ii) individualized MHV management for donors and recipients based on computed risk analysis.

P576

PREDICTION OF EMERGENCY READMISSION AFTER LIVER TRANSPLANTATION

Chutwichai Tovikkai¹, Susan C. Charman², Jan H.P. van der Meulen³, Alexander E. Gimson⁴, Raaj K. Praseedom⁴

¹University of Cambridge; ²Royal College of Surgeons of England; ³London School of Hygiene and Tropical Medicine; ⁴Cambridge University Hospital NHS Foundation Trust, Addenbrooke's Hospital

Background: Emergency or unplanned readmission after liver transplantation can be resource-consuming, and should be minimised. We explored risk factors associated with emergency readmission after liver transplantation.

Methods: A linked UK liver transplant – Hospital Episode Statistics database of adult first liver transplants between 2000 and 2009 was analysed. Emergency readmissions within 30 days after discharge were identified. Of 17 pretransplant recipient factors, six donor factors, four operative factors and transplant length of stay (LOS) were considered. Univariable logistic regression was used to identify factors associated with emergency readmission. Those factors with $p < 0.2$ in the univariable analysis were included in a multivariable model, which was further adjusted for age, sex, indication and centre.

Results: Of 3311 adult liver transplant patients were included, of whom 929 (28.1%) had emergency readmission within 30 days. Life style activity score ($p = 0.09$) and LOS ($p = 0.09$) were weakly associated with emergency readmission rate; the odds ratio for patients with life style activity score 4–5 compared to 1–2 was 1.3 [95%CI: 1.0–1.6], while the odds ratio for patients with LOS >60 days compared to 14–60 days was 1.4 [95%CI: 1–2].

Conclusion: Liver transplant patients with poor life style activity and longer transplant length of stay may have a higher risk of emergency readmission within 30 days after discharge.

P577

LOW-DOSE ANTIVIRAL TREATMENT FOR HEPATITIS C VIRUS FOLLOWING LIVING DONOR LIVER TRANSPLANTATION WITHOUT SPLENECTOMY

Atsushi Takebe, Takumi Fukumoto, Masahiro Kido, Kaoru Kuramitsu, Yonson Ku

Kobe University Hepato-Biliary-Pancreatic surgery

Background: Patients with hypersplenism after liver transplantation (LTx) have low tolerance to early initiation of combined antiviral treatment with full-dose interferon (IFN) and ribavirin (RBV) for the recurrent hepatitis C. Thus we perform LTx without splenectomy and initially treat recurrent hepatitis C with low-dose IFN/RBV and persist the treatment for the extended period.

Objective: To evaluate the long-term result of antiviral treatment for hepatitis C virus (HCV) following living donor liver transplantation (LDLT) without splenectomy.

Patients: We studied 23 adult recipients who underwent LDLT for HCV related liver cirrhosis. Antiviral treatment was initiated with low-dose pegylated IFN alpha2b ($1 \mu\text{g/kg/week}$) and RBV (300 mg/day) promptly after pathological diagnosis as hepatitis C. IFN/RBV was continued for at least 24 months after the serum HCV-RNA became negative with dosage adjusting. Even if recipient was null responder, antiviral treatment was not canceled.

Result: The median age of the patients was 60y (39–68). The median Model for End-Stage Liver Disease score was 11 (5–24). Eighteen patients received antiviral treatment. Median platelet count at the initiation of antiviral treatment was $10.3 \times 10^4/\mu\text{l}$ ($4.1\text{--}31.4 \times 10^4$). The treatment was initiated an average of 4.1 months (0.7–12.1) after LTx. Even though, dose reduction was temporarily needed in all patients, HCV-RNA was not detected in 11 patients (61.1%) an average of 12.4 months (0.9–34.9) after the initiation. These 11 patients achieved sustained virological response (SVR). During follow-up period (median 47.4 months: 14.3–107.2), there was no Relapser in the SVR group and mild fibrosis of liver parenchyma was detected only in 2 of 7 patients (28.8%) who did not achieve SVR. At one year after LTx, platelet count was preserved (median $8.4 \times 10^4: 2.2 \times 10^4\text{--}14.7 \times 10^4$).

Conclusion: Low dose and long-term persistence IFN/RBV therapy following LDLT without splenectomy is feasible with acceptable outcome.

P578

RIGHT-SIDED DIAPHRAGMATIC HERNIA AFTER LIVING DONOR RIGHT HEPATECTOMY: A RARE COMPLICATION AFTER LIVING DONOR

JunChul Jung, Choi Gyu-seong, HyungChul Kim

Soon Chun Hyang university hospital Bucheon

Background: Right-sided diaphragmatic hernia after living donor Right hepatectomy has been rare complication. we report a Right-sided diaphragmatic hernia in a living donor.

Methods: A 26-year-old man underwent donor right hepatectomy for living donor liver transplantation. Three months after liver donation, he presented with upper abdominal pain and vomiting. Computed Tomography revealed a diaphragmatic hernia of the right thorax with stragulation.

Results: He underwent laparotomy and a 3 cm defect in the right diaphragm was identified and repaired with interrupted polypropylene suture, after operation, the patient remains well.

Conclusions: Throughout the expansion of living donor liver transplantation, the safety of the donor is most important thing. Diaphragmatic hernia is a rare complication of right donor hepatectomy but may occur. And early diagnosis and prompt management is needed for donor safety.

P579

LIVING DONOR LIVER TRANSPLANTATION IN A JEHOVAH'S WITNESS – THE FIRST ADULT LIVING DONOR LIVER TRANSPLANTATION IN KOREA

Gyu-seong Choi, HyungChul Kim, JunChul Jung

Soon Chun Hyang university hospital Bucheon

Purpose: Orthotopic liver transplantation is typically associated with large volume blood loss. Technological and pharmacological advances permit liver transplantation in patients who formerly were not candidates for this surgery because of strict limitations on blood product administration. We describe a liver transplant in a Jehovah's Witness with liver cirrhosis related with HBV infection.

Clinical features: A 52-year-old Jehovah's Witness with liver cirrhosis related with HBV infection and end stage liver disease presenting with uncontrolled ascites underwent orthotopic liver transplantation. MELD score was 18. Recombinant human erythropoietin ($10\,000 \text{ IU sc every } 2 \text{ days for } 4 \text{ weeks}$, then $10\,000 \text{ IU sc every day for one week}$) established a normal hemoglobin concentration preoperatively ($>13.1 \text{ g/dl}$ compared with 7.3 g/dl baseline). Intraoperatively, strategies for reducing risk of blood product transfusion included avoidance of hypothermia (temperature $>35^\circ\text{C}$), minimal blood sampling (1 ml samples only four times), normovolemic hemodilution (3 units) and return of blood (300 ml) scavenged from the operative field. Estimated blood loss was 800 ml. The preoperative and postoperative hemoglobin

concentration was 13.4 g/dl (hematocrit 0.38) and 11.4 g/dl (hematocrit 0.32), respectively. No blood products were required and he was discharged 15 days postoperatively without complication.

Conclusion: Technological and pharmacological advances allow patients to undergo surgery traditionally associated with large volume blood loss with reduced risk of blood product administration.

P580

DO DONOR SPECIFIC ANTIBODIES AFFECT GRAFT LIVER OUTCOMES IN LDLT?

A-Lan Lee¹, Su Hyung Lee¹, Jung Jun Lee¹, Kyung Ok Jeon², Man Ki Ju¹, Kyu Ha Huh¹, Myoung Soo Kim¹, Dong Jin Joo¹, Jin Sub Choi¹, Gi Hong Choi¹, Soon Il Kim¹

¹Yonsei University College of Medicine; ²Research Institute for Transplantation

Background: Highly sensitized patients in organ transplant field have more chance to meet rejection, which result in decreased graft function. Circulating donor specific antibodies (DSAs) immunologically challenge to vascular endothelium and bile duct. However, liver is well known as an immune tolerant organ that can escape from immunologic challenges. This study was designed for analysis of adult living donor liver transplantation (LDLT) undergone in recipients with DSA.

Patients and methods: A total 219 recipients who underwent LDLT between June 2006 and August 2012 in our center were enrolled. We retrospectively analyzed the patients dividing into two groups according to presence of DSA. **Results:** Among 219 patients, 32 patients (14.6%) showed presence of DSA and 187 patients (85.4%) showed no DSA. Class 1 DSA presented in 19 patients, class 2 in six patients, and both in seven patients. Seven patients (3.2%) showed DSA in HLA-A, four patients (1.8%) showed in HLA-B, seven patients (3.2%) showed in HLA-DR, and 14 patients (6.4%) showed in two or more of them. Pre-transplant clinical features (donor sex, donor age, relation, recipient age, MELD score) of two groups were not different from each other. However, more female recipients showed DSA than male recipients in DSA+ group (59.4% vs. 16.0%, respectively). DSA+ group showed significantly higher both PRA class 1 and 2 than DSA- group (54.8%; 39.5% vs. 4.7%; 12.1% in class 1, and 42.1%; 39.3% vs. 0.9%; 1.6%, respectively). There were no significant differences in incidence of primary non-function, acute rejection, vascular complications, and biliary complications. Also, graft survival rate of two groups showed no significant difference (Fig. 1).

Conclusion: In LDLT, DSA cannot affect graft outcomes such as vascular and biliary complications, acute rejection, and graft survival rate.

P581

TEMPORARY PORTOCAVAL SHUNT BY PIGGYBACK CAVA IN LIVER RE-TRANSPLANTATION

Bulent Unal¹, Ruslan Mamedov¹, Cengiz Ara¹, Cemalettin Aydin¹, Nuru Bayramov², Cüneyt Kayaalp¹, Sezai Yilmaz¹

¹Inonu University, Medical Faculty, Liver Transplantation Institute, Malatya;

²Azerbaijan Medical University

Background: Retransplantations are difficult procedures and have higher morbidities and mortalities due to dense adhesions. Some facilitating maneuvers of retransplantations are challenging and here we described one of them.

Methods/materials: A 27-year old man with chronic artery thrombosis after three months ago deceased liver transplantation was admitted for retransplantation. A related living right lobe liver transplantation was planned. During recipient hepatectomy, hepatic hilum was transected first but retroperitoneal dissection and identification of the original vena cava were very difficult. Prolonged operative time and blood loss caused intestinal congestion and a temporary porto-caval shunt required. For porto-caval shunt, we used the recipient portal vein and the lower pole of the piggy-back vena cava. It was performed without clamping the original vena cava so caval blood from the first cava went on. The liver was removed by preserving bot vena cava (Figure 1). Living donor graft was implanted to the piggyback vena cava as well. The temporary shunt was divided and portal vein was anastomosed to the graft portal vein. Arterial anastomosis was performed with recipients gastroepiploic artery and the biliary reconstruction was fashioned by Roux-en-Y hepaticojejunostomy.

Conclusion: As a conclusion, when a temporary porto-caval shunt required during retransplantation, piggyback cava can be used safely.

P582

MULTICENTER STUDY OF ELECTIVE LIVER RETRANSPLANTATION IN SPAIN

Carmen Bernal Bellido¹, Martín Prieto Castillo², Jorge Ortiz de Urbina³, Trinidad Serrano⁴, Antonio Poyato⁵, Alejandra Otero⁶, Magdalena Salcedo⁷, Gloria Sánchez Antolin⁸, Manuel Rodríguez García⁹, Santiago Tomé¹⁰, Valentin Cuervas-Mons¹¹, Rafael Bárcena¹², Miguel Angel Gómez-Bravo¹³
¹Hospital Virgen del Rocío; ²Hepathologic Unit, Hospital Univ. i Politecnia La Fe; ³Hospital de Cruces; ⁴Hospital Clínico Lozano Blesa; ⁵Hospital Reina Sofía; ⁶Complejo Hospitalario A Coruña; ⁷Hospital Gregorio Marañón.; ⁸Hospital Río Hortega; ⁹Hospital Univ. Central de Asturias; ¹⁰Hospital Clínico de Santiago; ¹¹Hospital Puerta de Hierro; ¹²Hospital Ramón y Cajal; ¹³Hospital Virgen del Rocío

Background: The urgent retransplantation (reLT) (which take place in the first week after the first transplant, usually occurs by primary graft failure or vascular complications, retransplantation of the liver is the only option for survival when the transplanted graft fails. The causes for elective reLT are different from the urgent reLT. While ReLT remains controversial because of inferior survival outcomes compared with primary-LT, so elective retransplantation is controversial when donors want to optimize and prevent mortality on waiting lists.

Methods/materials: We performed a retrospective analysis of 224 adult patients who underwent elective reLT with deceased donor, in 12 centers in Spain between 1 January 2000 and 31 December 2010. We performed a database of donor and recipient variables, patients were analyzed according to the risk scores Rosen (formula of Risk = 10*0.0236*(age at second listing) + 0.125*(bilirubin) + 0.438 (creatinine) - 0.234 * (interval to reLT)) to separate patients into low (<16), intermediate (16.1-20.49), and high (>20.5) risk groups and MELD score >25 or MELD score <25 at the time of reLT. Patients were analyzed in two groups: 116 non-HCV and 100 HCV and has made a study of survival in these patients. Continuous data were reported as median ± standard error. Survival estimates were calculated using the Kaplan-Meier method. Comparisons of outcome among the groups were made using the log-rank test. A p value of <0.05 was considered statistically significant. SAS version 9.2 for Windows was used for data analysis.

Results: The mean age of patients was 50, 2 (DE:11.7) years. The causes of elective reLT were: recurrence of base disease 30%, ischemic cholangiopathy 27% and 19% rejection. The mean age of the donor was 49 years (DE: 18.5). Overall survival of elective retransplantation at 1, 3 and 5 years was 66.4%, 56.9% and 51.4%. We found no differences in survival of elective retransplantation in HCV vs. non-HCV, at 1, 3 and 5 years: 65.8, 55.7 and 53.2 vs. 67.3, 58.3 and 49.4 (p = 0.9652). No differences in survival of patients HCV and non-HCV in different age group of donors and recipients. We found differences in survival at 1.3 and 5 years of the 135 patients retransplanted with MELD score <25 and 52 patients with MELD score >25: 74, 62.8 and 55.1 vs. 51.9, 45.5 and 45.5 (p = 0.0093). We found differences according to Rosen index of 1, 3 and 5 years: Rosen low: 71.7, 60 and 53.9, Rosen moderate 71.1, 63.8 and 56.9 and higher Rosen: 44.4, 39.5 and 39.5 (p = 0.047).

Conclusion: The ethical implications in reLT are many and diverse, especially with limited organ availability. At present in Spain found no differences in the survival of patients electively retransplanted HCV versus non-HCV. Therefore, recipients HCV is not a contraindication for reLT; all variables should be used to evaluate a potential candidate. Patients with high MELD score (>25) and high rate Rosen (>20.5) have a mortality of 50% in the first year, so they must be questioned in elective retransplantation. Patients candidates for elective retransplantation should be prioritized on waiting lists to prevent deterioration.

P583

LAPAROSCOPIC VERSUS OPEN RENAL PROCUREMENT FOR ADULT RECIPIENTS OF LIVING DONOR RENAL TRANSPLANTATION: A RETROSPECTIVE STUDY

Taylan Özgür Sezer, Cüneyt Hocokun, Sait Sen, Özgür Fýrat, Hayrullah Yıldýrym, Ömer Vedat Ünalp, Hakan Haldun Yavaş, Hüseyin Töz, Murat Sözbilen

Ege University School of Medicine

Background: In this study, the course of posttransplant graft functions and histopathological findings at the time of transplantation (zero-hour) after open or laparoscopic nephrectomy were investigated.

Methods/materials: A total of 28 patients transplanted between February 2008 and July 2009 were evaluated retrospectively in this study.

Results: Fifteen open nephrectomies and 13 laparoscopic nephrectomies were performed. Cold ischemia time in the laparoscopic group (64 ± 17 min vs. 46 ± 10 min) was longer (p < 0.05). In the early period, there was no graft loss in both groups. Graft function was similar in both groups during the first month. There were no delayed graft function in both groups. Four acute rejection was detected in Open Donor Nephrectomy group, there was only 1 for Laparoscopic Donor Nephrectomy group. Acute rejection rate was higher for Open Donor Nephrectomy group but not significant, p = 0.19. According to the zero-hour biopsy results, there was no difference between the two groups in terms of tubular necrosis, tubular regenerative/degenerative changes, and interstitial infiltration, tubular atrophy and changes in blood vessels. While glomerular collapse was found in four patients in the

laparoscopic group, it was not observed in the open nephrectomy group ($p < 0.05$).

Discussion: Both open and laparoscopic nephrectomy procedures have equivalent safety in terms of early graft function. Longer cold-ischemia time and more glomerular collapse incidence in laparoscopic group showed no negative effect on clinical course.

P584

MANAGEMENT PROTOCOL FOR EXTERNAL BILIARY DRAINAGE IN ADULT PATIENT UNDERGONE LIVING DONOR LIVER TRANSPLANTATION USING DUCT-TO-DUCT ANASTOMOSIS

Bo-hyun Jung, Shin Hwang, Yo-han Park, Hyung-Woo Park, Sung-Hwa Kang, Wan-Joon Kim, Min-Ho Sin, Young-In Yoon, Yong-Kyu Chung, Eun-Kyoung Jwa, Gi-Won Song, Dong-Hwan Jung, Chul-Soo Ahn, Ki-Kun Kim, Deok-bog Moon, Tae-yong Ha, Sung-Gyu Lee
Asan Medical Center

Background: Biliary complication is the most common and intractable complication after adult living donor liver transplantation (LDLT). We have performed external biliary drainage (EBD) with expectation to decrease biliary complications. This study intended to optimize the management protocol for EBD tube clamping during early posttransplant period.

Methods: The study patients were selected from the adult LDLT pool during 4 months from January 2011 to April 2011. The selection conditions were right lobe graft implantation, single duct-to-duct anastomosis (DDA), DDA with EBD, and exclusion of salvage liver transplantation, by which 60 patients were selected. We prepared a protocol of rapid EBD tube clamping for 2-3 days. This study was prospectively performed with special concern on early successful clamping of EBD tube.

Results: There was no difference in the success rates of tube clamping in low-output (<300 ml/day, $n = 35$) and high-output (≥ 300 ml/day, $n = 25$) EBD groups (85.7% vs. 68%, $p = 0.100$). There was no statistical difference between the success and failure groups in graft duct size, serum aspartate transaminase, alanine transaminase, total bilirubin, alkaline phosphatase and posttransplant days at tube clamping. The transfixed external tube was released after 6 months and removed during 6 to 12 months after LDLT. Bile peritonitis from bile leak after spontaneous or incidental removal of the catheter occurred in 2 patients.

Conclusions: Our current protocol based on bile output drainage appears to be effective method leading to uneventful clamping of EBD tube, leading to minimization of patient discomfort.

P585

EARLY EXPERIENCE OF PERCUTANEOUS TRANSHEPATIC PORTAL VEIN ANGIOPLASTY AND STENT PLACEMENT AFTER LIVER TRANSPLANTATION

Nam Kyu Choi, Seong Pyo Mun, Seong Hwan Kim, Byung Gon Na
Department of Surgery, Division of Hepatobiliary Surgery and Transplantation, Chosun University Hosp

In living donor liver transplantation (LDLT), vascular complications are more frequently seen than in deceased donor transplantation. In five patients who underwent liver transplantation, portal vein stenosis was associated with esophageal varices and significant ascites and these complications that can lead to graft loss and patient death. In a third liver transplant patient, portal vein stenosis was suspected when evidence of hepatic ischemia was revealed at liver CT scan. This patient was treated with percutaneous transhepatic portal vein angioplasty. The interval between liver transplantation and stent placement was 13 days. However, these treatments are limited due to their technical difficulty and multiple complicating factors. This early experience of percutaneous transhepatic primary stent suggests that transhepatic portal vein interventions are feasible in patients who have received liver transplants and may prove useful at least in the early postprocedure period. In addition, long-term PV patency following stent placement was excellent.

P586

RISK FACTOR OF MORTALITY AFTER LIVER RETRANSPLANTATION

Hyung Hwan Moon, Jae-Won Joh, Suk-Koo Lee, Choon Hyuck Kwon, Jong Man Kim, Milljae Shin, Wontae Cho, Shin-Seok Yang, Seung Hwan Lee
Samsung Medical Center

Background: The survival rates of liver retransplantation (ReLT) are 20-50% lower than those of first transplantation. The objective of this report was to identify the risk factor of mortality after ReLT and suggest a proper decision process for ReLT.

Patients and methods: Between October 1996 and December 2011, 39 patients underwent ReLT. We performed a retrospective analysis of these patients using their medical records. Clinical characteristics, postoperative

complications, survival rate and causes of death were investigated. Multivariate analysis was performed to identify the risk factors.

Result: The rate of ReLT is 3.3% (39/1178). The overall survival rate for ReLT was 55.8%, 39.1% and 32.3% at 3 months, 1 and 3 years, respectively. Multivariate analysis revealed a serum total bilirubin of more than 22 mg/dl was the factors related to survival. ($p = 0.039$) Also, there were no differences between living donor ReLT and deceased donor ReLT in operation interval, operation time, post transplant ICU stay, total hospital stay and survival.

Conclusion: ReLT for the patient with a serum total bilirubin level of more than 22 mg/dl should be considered cautiously. And, LDLT for ReLT may be an alternative for well-selected patients.

P587

LIMITS OF CT SCAN IN THE EVALUATION OF SARCOPENIA IN CIRROTIC PATIENTS

Michela Giusto¹, Barbara Lattanzi¹, Alessio Farcomeni², Alessia Galtieri¹, Valerio Giannelli¹, Cristina Lucidi¹, Kameliya Koryukova¹, Michele Di Martino³, Carolina Albanese³, Carlo Catalano³, Stefano Ginanni-Corradini¹, Manuela Merli¹

¹Gastroenterology, Department of Clinical Medicine, Sapienza Università di Roma, Italy; ²Dipartimento di Sanità Pubblica e Malattie Infettive Sapienza Università di Roma; ³Dipartimento di Scienze Radiologiche, Sapienza Università di Roma

Background and aims: Sarcopenia evaluated by Computed Tomography scan (CT) was found to be associated with higher mortality in patients awaiting for liver transplantation (LT). No data are available on the correlation between CT and other methods for the detection of muscle mass in cirrhosis. In this study we aimed to evaluate the relationship between CT, dual-energy-X-ray absorptiometry-DEXA and anthropometry to assess sarcopenia in cirrhotic patients.

Methods: Adult patients eligible for elective LT for whom CT was available were considered. Skeletal muscle cross-sectional area was measured by CT and sarcopenia was defined using previously published gender-specific cutoffs. Mid-arm muscle circumference (MAMC, cm) was calculated according to standard methods. Fat-Free Mass Index (FFMI, kg/m²) and Appendicular Skeletal Muscle Index (ASMI, kg/m²) were calculated using DEXA. Agreement was assessed through Kendall's tau statistic. We used multi-state-models to model survival taking into account the possible intermediate transplant event.

Results: Fifty-nine patients (78% males, median age 59 years, 56% post-viral, 41% with HCC) were included. Median MELD was 16 in patients without HCC and 12 in patients with HCC. CT sarcopenia was diagnosed in 45 patients (76%) with similar prevalence in males and females. A reduction of FFMI (<10 th percentile of an age- and sex-matched population) and ASMI (≤ 7.26 kg/m² for women and ≤ 5.5 kg/m² for men) was observed in 42-52% of the patients while 52% showed a MAMC <10 th percentile. A significant but slight correlation between FFMI, ASMI and CT was observed, while MAMC significantly correlate with CT only in males (Table 1). Eight patients died before and 7 within 12 months after LT. CT sarcopenia did not correlate with mortality, while MAMC and FFMI (only in males) were associated with higher mortality ($p \leq 0.005$).

Conclusions: The slight correlation between CT and others techniques of muscle evaluation together with the contrasting results on its relationship with mortality suggest caution in considering this techniques as gold standard for sarcopenia in cirrhosis.

P588

TRANSPLANT OUTCOME IN LIVER TRANSPLANTATION IN PATIENTS WITH HIGH SCORE OF MODEL FOR END-STAGE LIVER DISEASE

Ben-Hur Ferraz-Neto¹, Maria Paula Villela Coelho¹, Renato Hidalgo¹, Romerito Fonseca Neiva², Kelly Harada², Ivana Schmidtbauer², Rogerio Carballo Afonso¹

¹Instituto do Fígado-Hospital Beneficência Portuguesa de São Paulo/Hospital Israelita Albert Einstein; ²Instituto do Fígado - Hospital Beneficência Portuguesa de São Paulo

Background: The Model for End-Stage Liver Disease (MELD) score is the system adopted for organ allocation and besides scores of 40 or higher are considered at very risk for transplantation, there are no guidelines describing limitations for transplantation. Since then, the number of transplants performed with scores over 40 has increased. The aim of this study is to analyze the outcome of patients with pretransplantation MELD score of 40 or higher.

Methods: This retrospective study includes 860 consecutive deceased donor liver transplantations performed between June 2005 and September 2012 in a single transplant center. The patients were grouped according to the pretransplantation MELD score (MELD \geq 40 and MELD $<$ 40), calculated using the United Network for Organ Sharing formula and compared regarding hospital and intensive care unit (UCI) length of stay, incidence of biliary, renal and vascular complications and 1 year patient survival.

Results: Median time of total hospitalization and length of stay UCI were longer for MELD \geq 40 (21 vs. 13 days – hospitalization; 8 vs. 2 days for UCI). Among incidence of posttransplant complications, renal was significantly higher on MELD \geq 40 group (64.3% vs. 45.1%, p -value = 0.003), whereas for other complications were similar: biliary (10% vs. 7%), vascular (7.1% vs. 6.7%) and graft (42.9% vs. 37.2%). Kaplan-Meier 1-year patient survivor rate was 66.2% for MELD \geq 40 group and 87.6% for MELD $<$ 40, p -value log rank $<$ 0.001.

Conclusions: The increased complexity of patients with MELD \geq 40 requires more post-transplant health care resources. Furthermore, this study suggests a relationship between patient survival and MELD score, and besides inferior survival rate for MELD \geq 40 group, transplant is preferable to these patients rather than the waiting list.

P589

“PASSING LOOP TECHNIQUE”: PORTAL INFLOW MODULATION IN PARTIAL PORTAL VEIN THROMBOSIS

*Firas Zahr Eldeen, Yasser ElSheikh, Mohammed Al Sebayel
King Faisal Specialist Hospital*

Background: Incidence of Portal vein thrombosis (PVT) in Liver transplant (LT) patients is 4.9–10.6% and re-thrombosis could reach 28% after the surgery. Unfortunately, patency of PV after thrombectomy can neither be adequately evaluated nor objectively assessed. Accurate knowledge of portal venous anatomy and hemodynamics is essential to strategize surgical options for graft inflow.

Aim: Herein, we describe a modification of inflow restoration in patients with partial PVT. Case report: Two patients with liver disease and PVT underwent LT; however, after thrombectomy, portal flow was still inadequate; this might be either due to inadequate thrombectomy or due to collaterals and possible porto-systemic shunts. Cryopreserved vein graft “Passing Loop” was tunneled through mesocolon; connecting dilated Superior Mesenteric Vein to a distal healthy part of PV. Intrahepatic portal flow improved by Intraoperative Ultrasound $>$ 35 cm/s.

Results: Passing loop is patent in one patient after one year follow up. In second patient, it was thrombosed few days after transplant, yet, had patent inflow through main portal route. Both have satisfactory liver functions on follow up outpatient visits.

Conclusion: Rerouting part of the portal flow through a “passing loop” might be a salvage “safeguard” procedure against deleterious complications of graft hypoperfusion due to portal vein pathological narrowing or re-thrombosis; however, augmenting or rerouting effects on portal pressures and hemodynamics are yet to be elucidated.

P590

THE COMPARISON OF THE MEAN PLATELET VOLUME IN PATIENTS WITH LIVER CIRRHOSIS OF DIFFERENT ETIOLOGIES

Krzysztof Jankowski¹, Zuzanna Rymarczyk¹, Beata Agiewska², Marek Pacholczyk², Ewelina Mikocka-Dybcio¹, Katarzyna Irzyk¹, Anna Karpinska¹, Piotr Pruszczyk¹

¹Department of Internal Medicine and Cardiology, Medical University of Warsaw; ²Department of General and Transplantation Surgery, Medical University of Warsaw

Introduction: It was demonstrated that mean platelet volume, an easy to test and repetitive biochemical parameter, can be regarded as an indicator of increased platelets activity and a predictor of cardiovascular episodes. Increased values of MPV have been recognized as an independent risk factor for myocardial infarction and stroke.

Aim: To compare the mean platelet volume in groups of patients with liver cirrhosis of different etiologies.

Material and methods: The group of 124 patients qualified to liver transplantation was analyzed. Nobody had the symptoms of spontaneous bacterial peritonitis or other bacterial infections. Studied patients were divided into 3 groups of comparable age. Group 1 consisted of 57 pts with hepatitis C virus-related liver cirrhosis, group 2 included 26 pts with alcohol-related cirrhosis, group 3 consisted of 41 pts with other etiologies of cirrhosis.

Results: Mean values of platelet volume (MPV) in all examined groups did not exceed the norm (norm: 7–12 fL). In group 1 MPV was significantly higher than in group 2 (11.63 \pm 1.23 fL vs. 10.81 \pm 1.11 fL, p < 0.01) although the mean MELD score in group 1 was significantly lower than in group 2 (13.69 \pm 4.47 vs. 16.24 \pm 5.01, p < 0.05). There were no statistical differences in MPV and the mean MELD score between group 1 and group 3 (respectively MPV: 11.63 \pm 1.23 fL vs. 11.34 \pm 1.19 fL, ns; MELD: 13.69 \pm 4.47 vs. 13.66 \pm 4.73, ns). In group 2 MPV was insignificantly lower than in group 3 (10.81 \pm 1.11 fL vs. 11.34 \pm 1.19 fL, ns), although the mean MELD score was higher in the group 2 (16.24 \pm 5.01 vs. 13.66 \pm 4.73, p < 0.05).

Conclusions: In studied group the patients with the alcohol-related liver cirrhosis had lower mean platelet volume than in patients with liver cirrhosis of another etiologies. Interestingly, in patients with alcohol-related liver cirrhosis mean platelet volume was significantly lower than in patients with hepatitis C virus-related liver cirrhosis although higher the mean MELD score.

P591

DE NOVO HLA DONOR SPECIFIC ANTIBODIES (DSA) AFTER ABO COMPATIBLE LIVER TRANSPLANTATION (LT)

*Arnaud Del Bello, Nicolas Congy, Nassim Kamar, Lionel Rostaing
Chu Toulouse Rangueil*

Background: The incidence and consequences of occurrence of *de novo* DSAs after LT is not well known. So, we investigate the incidence, kinetic of occurrence, and complications associated with *de novo* DSAs. Patients & Method Between February 2008 and February 2012, all liver transplant recipients were tested for anti-HLA antibodies, with the Luminex SA™ assay, at Day 0, M1, M3, M6, M9, 1 year and every year until the last follow-up.

Results: A total of 119 patients were included in this study. At last follow-up, realized at 757 DAYS (46–1570) post-transplantation, 15 patients (12.6%) without preformed anti-HLA DSAs had developed DSAs. 10/15 patients (67%) with *de novo* DSAs have presented at least one episode of rejection, vs. only 20/104 patients (19%) without *de novo* DSAs (p = 0.0003). 4/15 patients (27%) with *de novo* DSAs have developed an early acute rejection (i.e before M3), and 10/104 patients without DSAs (10%), (p = ns). 7/15 patients (47%) with DSAs have presented at least one episode of late acute rejection (i.e after M3), and 7/104 (7%) DSAs-free patients (p = 0.0002). 14/15 patients have developed DSAs before graft rejection. No difference was observed between the two groups concerning survival after LT.

Conclusion: Occurrence of DSAs after LT is a frequent complication and is associated with an increased risk of rejection.

P592

ABO-INCOMPATIBLE LIVER TRANSPLANTATION UNDER COLLABORATION BETWEEN FUKUSHIMA AND HIROSHIMA: TWO VICTIMS OF IRRADIATION IN JAPAN

*Takaaki Koshiba¹, Hiroshi Uenishi², Yusuke Kohno³, Kohei Ishiyama⁴,
Yasutoshi Saitou³, Hideki Ohdan⁴*

¹Department of Disaster and Comprehensive Medicine, Fukushima Medical University; ²Sendai Syakai Hoken Hospital; ³Souma Central Hospital; ⁴Division of Frontier Medical Science, Hiroshima University Hospital

Introduction: In 1945, the world first atomic bomb was dropped on the city of Hiroshima. The 2011 tsunami led to nuclear disaster in Fukushima. Unfortunately, concern about irradiation exposure from Fukushima people to others exists that may be too intense or needless. (Case) A 61 year old female patient with cirrhosis had lived within 20 km from the Fukushima nuclear station when the tsunami disaster occurred on the 11th of March in 2011. To avoid radio-nuclear irradiation exposure, she moved to a city more than 100 km from the station. During her 1 month stay in this city, she consulted a hospital due to symptoms associated with cirrhosis. They expressed intense concern about their own irradiation exposure from her. After she returned to Fukushima, she often experienced hepatic encephalopathy and complained of massive ascites. She needed ABO incompatible liver transplantation (Ltx). However, there is no Ltx center which is very willing to perform ABO incompatible Ltx near the station. She hypothesized that there was less concern about a Fukushima patient in Hiroshima and Nagasaki which were victims of the atomic bomb. She was sent to Hiroshima University and received ABO incompatible liver graft from her son past August in 2012. She returned to her home town in Fukushima this February and she is followed at a hospital 40 km from the station under collaboration with Hiroshima University. Of note, she noticed no concern about their irradiation from her during her 6 month stay in Hiroshima and she was satisfied with hospitality there.

Conclusion: To our knowledge, this is the first ABO-incompatible Ltx performed under collaboration between two victims of irradiation in Japan. If good hospitality experienced by our Fukushima patient in Hiroshima was associated with common catastrophic experience between the two, one may consider referring a Fukushima patient to Hiroshima for a psychosocial reason in addition to medical issue

P593

LESSONS LEARNED FROM LIVING DONOR LIVER TRANSPLANTATION AT CAIRO UNIVERSITY: SINGLE CENTER EXPERIENCE

Mostafa Elshazli¹, Adel Hosny¹, Ayman Salah², Shaimaa Elkholy², Ezz Korashi³

¹Faculty of Medicine Cairo University; ²Cairo University; ³Faculty of Medicine Cairo University

Background: Living donor liver transplantation (LDLT) is widely used for patients with end-stage liver diseases. However, this procedure exposes the donor, a healthy individual, to morbidity & mortality which makes it of low applicability.

Methods: We did a retrospective analysis regarding our experience in LDLT of 116 cases during the past 9 years.

Results: We transplanted 116 cases, 25 pediatric cases (due to congenital or hereditary disorders) and 91 are (mostly post hepatitis HCV cirrhosis) adult

cases. We have mortalities 22.4% infections and severe sepsis are the most common cause of mortality in our patients. The most common causes of morbidity among those patients are the biliary complications (31%), followed by rejection (20%), followed by infections (18%) mostly due to viral infections.

Conclusion: Starting to take the left lobe in order to minimize the biliary complications. Venous outflow optimization by using the Anterior venous patch to the right hepatic vein more than 5 mm for reconstruction of segment V&VIII. using intraoperative biliary stents with interrupted sutures may decrease biliary complications. Portal pressure measurement intraoperative may help us in prediction of small for size syndrome. Hepatic artery thrombosis can be detected early before shooting of liver enzymes. Patients with hepatocellular carcinoma are preferably transplanted if they are within the MILLAN criteria as it has better outcome on recurrence.

P594

LONG TERM RESULTS IN LIVER TRANSPLANTATION

Mariá García Nebreda, Carmelo Loinaz Segurola, Edume Alvaro, Alejandro Manrique Municio, Cristina Alegre Torrado, Jorge Calvo Pulido, Sandra García Aroz, Felix Cambra Molero, Carlos Jiménez Romero, Enrique Moreno
Hospital Universitario 12 de Octubre

Background: There are few studies reporting long-term outcomes for Liver Transplantation (LT) up to present date. The main goal of our study is looking into long-term complications and quality of life, in order to learn about possible complications and needs on our long survival patients.

Patients and methods: We performed an observational prospective study including 252 LT from April 1986 to December 1992, considering: – age, sex, diagnosis, date of transplantation, – acute/chronic rejection, re-do transplantation, latest histology, function tests, – re-admissions, – postoperative development of tumours, – immune suppressors.

Results: Out of 252 LTs, there are 56 alive patients and 48 with overall survival over 20 years. Abnormal liver function was found in 45.8%. Histology showed Hepatitis in 60%. 20.8% LT developed some kind of tumor. Median of readmissions per patient was 4. 60.4% needed further operations, most frequently incisional hernia. 14.6% of re-do transplantation. At the end of the study 35.4% patients were on CyA (76.4% monotherapy), 31.2% on FK (86.6% monotherapy), 25% on MMF, 6.2% on mTOR. Karnofsky's index for quality of life: 98.3 ± 5.2 (80–100)

Conclusion: Twenty-five percent of patients live over 20 years having good performance status and few transplant-related complications. References: Clinical features of 32 patients after 8 years of a liver transplantation. C.Loinaz et al. Transplantacion procc 31, 2475–2476(1999), Liver transplantation: The Spanish experience. R Matesanz, G de la Rosa. Digestive and Liver Disease 2009 (suppl 3) 75–81.

P595

RARE INDICATIONS FOR LIVER TRANSPLANTATION: SINGLE CENTER EXPERIENCE

Aydincan Akdur, Mahir Kirnap, Feza Yarbuc Karakayalı, Sedat Yildirim, Gokhan Moray, Mehmet Haberal
Faculty of Medicine, Baskent University

Background: Orthotopic liver transplantation (LT) is the only reliable treatment for end stage liver disease. All over the world the common indications for liver transplantation are hepatitis B, hepatitis C, alcoholic cirrhosis and hepatocellular carcinoma. But we know that some rare clinical issues can lead to end-stage liver disease. The aim of this study was to evaluate the efficacy of liver transplantation for rare liver diseases.

Methods/materials: The results were retrospectively analyzed from 340 patients, who underwent LT from 2001 to November 2012 at our liver transplant center in Turkey. 173 of them were adult patients and 167 of them were pediatric.

Results: The rare indications for LT which performed in our center were, Alagille syndrome ($n = 5$), Caroli's disease ($n = 1$), Crigler Najjar syndrome type 2 ($n = 4$), congenital hepatic fibrosis ($n = 2$), oxalosis ($n = 2$), neonatal hepatitis ($n = 3$), alpha 1 antitrypsin deficiency ($n = 2$), alveolar hydatid disease ($n = 2$), glycogen storage disease type 1 ($n = 2$). Four of them were cadaveric LT and 19 of them were living related LT. The 15 patients were male and eight patients were female. No protocol liver biopsy specimens were obtained, and biopsies were performed only for investigation of biochemical abnormalities (elevated serum transaminase or bilirubin levels). Acute cellular rejection occurred in 3 patients and all of them were treated with steroid therapy and there were no graft lost. Five patients passed away after the early period of transplantation (brain death; $n = 2$, sepsis; $n = 3$). There was not any donor mortality or major morbidity.

Conclusions: LT appears to be a feasible option and is associated with a better quality of life for patients with rare liver disease. Their outcomes were comparable with that of the common causes of end-stage liver disease.

P596

PREGNANCY AND THE PROCESS FOLLOWING LIVER TRANSPLANTATION: FOUR CASE REPORTS

Mahir Kirnap, Aydinca Akdur, Cihan Fidan, Polat Dursun, Gokhan Moray, Mehmet Haberal
Faculty of Medicine, Baskent University

Background: The first known pregnancy following liver transplantation was in 1978. There wasn't any statistically significant difference in the incidence of fetal malformations between general population and the pregnant women with liver transplantation. It was also found that pregnancy didn't affect graft functions and survival.

Case Report: In our center, the pregnancy, natal and postnatal periods of four women with liver transplantations, which were performed in 1988 due to Wilson disease and 2006 due to primary sclerosing cholangitis, in 2004 due to familial intrahepatic cholestasis and in 1999 owing to cryptogenic cirrhosis were examined and assessed. When these patients became pregnant, they were at the age of 21, 22, 24 and 29, respectively. All of the patients were using tacrolimus. Mycophenolate mofetil and steroid treatment of these patients were stopped before pregnancy. Two of these pregnant women gave birth through vaginal channel in the 39th week. The third patient is in her 20th week and the fourth patient is in her 16th week still pregnant.

Conclusion: When we examine these four cases in terms of pregnancy and graft functions following a liver transplantation, they provide the evidence that patients in their reproduction age can have a healthy pregnancy period without having serious difficulties, of course with a close and careful follow-up. Although conceiving a baby is possible after liver transplantation, it should be remembered that the rates of complications are relatively higher when compared to general population. Pregnancy care requires a multi-disciplinary approach as well as high motivation and compliance of the pregnant patient.

P597

POSTTRANSPLANT MALIGNANCIES IN LIVER TRANSPLANT RECIPIENTS

Gokhan Moray, Aydinca Akdur, Mahir Kirnap, Feza Yarbuc Karakayalı, Sedat Yildirim, Mehmet Haberal
Faculty of Medicine, Baskent University

Background: The overall incidence of malignancy in the transplant recipient has been estimated to be as high as 20% in the 10-year period after transplantation. In the present study, we present our experience with de novo malignancies encountered after both deceased and living donor liver transplantations.

Methods/materials: We retrospectively reviewed the medical records of 335 patients who underwent OLT at our institution from September 2001 to December 2012 to identify subjects with de novo malignancy in orthotopic liver transplantation recipients.

Results: Fourteen patients (4.1%) developed de novo post-LT malignancies. De novo malignancies included post-LT lymphoproliferative disorders (PTLD) in seven patients who were treated with chemotherapy; thyroid papillary carcinoma in one patient who was treated with total thyroidectomy and radioactive iodine therapy; squamous cell carcinoma in two patients who were treated with surgical resection; gastric stromal tumor in one patient who was treated with surgical resection; ovarian carcinomas in one patient who was treated with radical surgical resection and chemotherapy but passed away within 1 year of diagnosis; lung cancer in one patient who was treated with chemotherapy but he had bone metastasis and passed away within 1 year of diagnosis; and neuroblastoma one patient who was treated with chemotherapy. In all patients the immunosuppression therapy were changed.

Conclusion: Transplant recipients generally have advanced stage cancers at the time of diagnosis with a poor prognosis. Since some neoplasms are common early detection of cancer is important to decrease cancer related mortality and morbidity.

P598

LIVER TRANSPLANTATION DUE TO FULMINANT HEPATIC FAILURE

Sedat Yildirim, Aydinca Akdur, Mahir Kirnap, Figen Ozcay, Gokhan Moray, Mehmet Haberal
Faculty of Medicine, Baskent University

Background: Fulminant hepatic failure (FHF) is a clinical condition characterized by a severe, acute decline in liver function associated with encephalopathy. FHF, is defined as an international normalized ratio of at least 1.5 and any degree of mental alteration (encephalopathy) in a patient without preexisting cirrhosis and with an illness of more than 26 weeks' duration. FHF is a potentially fatal condition if emergency liver transplantation (LT) is not performed. In this study, we examined the epidemiology, causes, complications, and mortality of liver transplantation following fulminant hepatic failure at our hospital.

Methods/materials: Among the 335 liver transplantations (LT) performed from September 2001 to November 2012, 32 of them (9.5%) were performed

for FHF in 25 pediatric and seven adult cases. We retrospectively analyzed the data of these patients.

Results: 4(12.5%) of them were cadaveric LT and 28 (87.5%) of them were living related LT. The 18 (56.3%) patients were male and 14 (43.7%) patients were female. The patients mean age were 12.5 years old (range, 18 month to 42 years). The etiology of the FHF was; acute hepatitis B in four cases, hepatitis A in eight cases, hepatitis non A non E in 7, Wilson disease in eight cases, autoimmune hepatitis in two cases, CMV hepatitis in 1 and toxic hepatitis in 2. Seven patients passed away after the early period of transplantation (brain death; $n = 4$, sepsis; $n = 3$). Two patients developed chronic rejection during the long term follow up. There was not any donor mortality or major morbidity.

Conclusions: LT should be considered one of the first-line treatment options in patients with FHF. LT offers a safe and effective modality of treatment for FHF for both pediatric and adult patients. In this study, results appear comparable to other liver transplant recipients.

P599

POSTOPERATIVE INTRAABDOMINAL BLEEDING AFTER LIVER TRANSPLANTATION

Aydincan Akdur, Mahir Kirnap, Feza Yarbuc Karakayaly, Sedat Yildirim, Gokhan Moray, Mehmet Haberal
Faculty of Medicine, Baskent University

Background: In this study, we examined the incidence and management of postoperative abdominal bleeding after orthotopic liver transplantation (OLT) and to identify risk factors for abdominal bleeding.

Methods/materials: We retrospectively reviewed the medical records of 335 patients who underwent OLT at our institution from September 2001 to December 2012 to identify subjects with posttransplantation abdominal bleeding, defined as any hemorrhage requiring laparotomy within the first month.

Results: 42 (13.5%) patients showed abdominal bleeding, requiring laparotomy within the first month, occurring at a mean of 4.9 days (range, day 1 to 21 days). 11(23.8%) of them were cadaveric LT and 32(76.2%) of them were living related LT. The 26(62%) patients were male and 16(38%) patients were female. The bleeding sites requiring laparotomy were the hepatic artery ($n = 3$), diaphragm ($n = 2$), inferior vena cava ($n = 12$), abdominal drain insertion site ($n = 1$), portal vein anastomosis ($n = 2$), abdominal wall ($n = 5$), liver graft cut surface ($n = 9$), hilar plate ($n = 3$), and greater omentum ($n = 5$). In all patients, active bleeding was controlled with surgical ligation or vascular reconstruction. No patients passed away due to abdominal bleeding.

Conclusions: The risk of bleeding from coagulopathy, because of used anticoagulants and iatrogenic injury is high during the early posttransplantation period. This risk of bleeding can be minimized by meticulous surgical dissection and bleeding control.

P600

PERIOPERATIVE MECHANICAL VENTILATION IN LIVER TRANSPLANT PATIENTS

Tomescu Dana, Popescu Mihai, Droc Gabriela, Dima Simona, Popescu Irinel
Fundeni Clinical Institute

Introduction: The timing of extubation in patients undergoing liver transplantation (LT) is still in debate. The aim of this study was to determine risk factors for prolonged mechanical ventilation (MV) and reintubation in the early postoperative period.

Methods/materials: We retrospectively analyzed 44 consecutive patients who underwent LT between March – December 2012. Preoperative, intraoperative and postoperative data were collected from the patients charts including acid-base status, arterial oxygen pressure (PaO₂) and arterial carbon dioxide (PaCO₂) pressure, fraction of inspired oxygen (FIO₂), pulmonary complications, timing of extubation, need for non-invasive mechanical ventilation (NIV) and reintubation (RI).

Results: The median duration of postoperative MV was 12 h (range 0–128 h). Sixteen patients (26.3%) required NIV in the early postoperative period and 6.5% ($n = 4$) had to be reintubated. Pulmonary complications were observed in 57% of patients ranging from mild (22.7%) to severe (4.5%). Risk factors for prolonged mechanical ventilation were: age ($p = 0.014$), intraoperative blood loss ($p = 0.002$), blood products transfusion ($p = 0.001$), haemodynamic instability ($p = 0.026$), high vasopressor dose ($p = 0.036$) and PaO₂/FIO₂ under 300 at the end of surgery ($p = 0.011$). Pulmonary complications were associated with platelets transfusion ($p < 0.001$), intraoperative vasopressor dose ($p = 0.039$) and duration of postoperative mechanical ventilation ($p = 0.003$). Non-invasive ventilation was used in 36.4% ($n = 16$). In a multivariate analyses risk factors for RI were platelet transfusion ($p = 0.025$), reintervention ($p = 0.05$) and pulmonary complications ($p = 0.05$).

Conclusion: Mechanical ventilation is associated with a higher risk of pulmonary complications. Age, intraoperative haemodynamic profile, blood loss and platelets products transfusion represent risk factors for prolonged postanaesthesia mechanical ventilation.

P601

INITIAL LIVER GRAFT REPERFUSION BY HEPATIC ARTERY: MORE DELETERIOUS THAN BENEFICIAL FOR THE PATIENTS IN PEDIATRICS LIVER TRANSPLANTATION

Catherine Boucaud¹, Yves Bouffard², Berangere Cogniat¹, Sylvie Combet¹, Khalid Berrada¹, Thomas Gelas¹, Remi Dubois¹, Dominique Chassard¹
¹HFME-Lyon Bron; ²HEH, Lyon

Surgical procedure for liver transplantation are multiple and if there seems to be a consensus on a peegy back realisation with retrohepatic vena cava preservation, reperfusion of the graft could be un discussion subject. At reperfusion time, the blood flow is then generally restored via the portal vein but some surgeons have suggested that restoring the circulation through the hepatic artery initially may improve the outcomes.

Method: We studied 16 pediatrics patients undergoing liver transplantation, five girls and 12 boys. Nine of them underwent a portal vein reperfusion (group 1), but seven had a temporary portocaval anastomosis and an hepatic artery initial graft reperfusion (groupe 2). We compared the venous blood lactates levels at the end of anhepatic phase and 30 min after graft reperfusion. We looked at the incidence of reperfusion syndrome and the necessity to use norepinephrine to maintain the haemodynamic status of the patients.

Results: We did not found any difference between the both surgical techniques regarding to the onset of postreperfusion syndrome (PRS) or use of norepinephrine. Concerning the lactates levels, although lactate levels at the end of anhepatic phase were not different between the two groups, we found a significant difference in the level of lactate after reperfusion. Patients/lactates mm End anhepatic Reperfusion * Groupe 1: portal vein 3.25 (±1.6) 3.92 (±1.1) Groupe 2: hepatic artery 4.97 (±2.6) 7.92 (±3.2) **p = 0.0019 (Test F).

Conclusion: Lactic acidosis is responsible for myocardial failure, vascular hyporesponsiveness and a decrease in sensitivity to vasopressor agents. Restoring the blood flow in the liver graft through the hepatic artery seems to present more risks than benefits for paediatrics patients.

P602

A SINGLE CENTER EXPERIENCE OF EXTENDED HEPATECTOMY (EH); IS THE RIGHT POSTERIOR SECTOR (RPS) OF THE LIVER MORE IMPORTANT THAN THE LEFT LATERAL ONE?

Arianeb Mehrabi, Nassim Fard, Mohammadreza Hafezi, Zakarya Khalil, Hamidreza Fonouni, Mohammad Golriz, Nuh Nabi Rahbari, Koosha GhaziMoghadam, Markus Mieth, Michael Kremer, Beat Mueller, Peter Schemmer, Markus W. Buechler
Heidelberg University

Background: EH is the only curative procedure for large or multi nodular, particularly centrally located liver tumors.

Methods: We present the analytic results of our non-selected EH experiences during the last decade. Pre-, intra- and post-operative data of 171 EHs, were obtained from our center database, analyzed and compared in term of right or left EH (rEH or lEH). In our review of the literature, after searching the Medline database, all original articles about EH with more than 20 cases were selected, analyzed and lately compared with the result of our center.

Result: Data of 122 rEH and 49 lEH were evaluated in our case-series. Portal vein embolization was performed in 6.6% of the cases, all in rEH group. The mean operative time was 310 min and Pringle maneuver was applied in 17% of the cases with mean duration of 15 min. The average amount of blood loss during our EH was 1560 ml. Intraoperative RBC and FFP transfusions were recorded in 42% and 29% of our entire patients, respectively. Except from blood loss all the other evaluated variables were observed with higher rate in our rEH rather than lEH which is also supported by the result of the review of literature. The amount of postoperative substituted RBC and FFP as well as the mortality rate were significantly higher in rEH group compare to lEH group. The average overall morbidity and mortality rates were 56% and 9%, respectively. Despite occurring postoperative complications in about 1/3 of lEH group, there was no in-hospital mortality in this group; whereas, all of our deaths occurred after rEH with an average rate of 13%. All these findings were within the range of analyzed review of the literature.

Conclusion: lEH can be safely performed specially for centrally-located liver tumors, when the surgeon has the choice to decide the side of the EH; however, rEH is technically easier. Better surgical outcomes associated with lEH, showing the high value of preserving the RPS rather than left lateral one.

P603

MODEL OF LIVING DONOR EVALUATION PRIOR TO SPLIT LIVER TRANSPLANTATION

Thomas Karbe¹, Robert Kütemeier¹, Siegbert Scheibner¹, Martina Sterneck²
¹Department of Quality Management, University Medical Center Hamburg;
²Department of Hepatology, University Medical Center Hamburg

Background: Living donors prior to liver transplantation have been evaluated retrospectively from 2001 to 2010. The Emphasis of this program lies in a structured medical and psychological III- phase evaluation procedure.

Method: During the different phases routine tests are taken prior to the first phase. Furthermore, MRI diagnostic, biliary system, hepatic vasculature, celiac angiography, abdominal ultrasound, 3D reconstruction of CT scan for precise liver volume calculation and abdication as well as a detailed psychological interview take place.

Results: Of 648 documented potential living donors were assessed. Total 76.4% of the candidates have been rejected for donation due to various reasons. 30.1% of the potential donors were abandoned from living donation due to general medical contraindications, prior to the three-phases-evaluation. Within the first phase 28.3% of the potential donors have been excluded from donation because of medical contraindications due to specific blood test results. During the second phase, 31.9% of living donors failed due to CT scan findings. Within the third phase, 8.1% of the donors were declined due to different reasons. In 1.6% cases the donor operation was aborted.

Conclusion: Finally (22.4%) living donor liver transplantations took place. Among the documented donors, parents were the biggest group of likely donors (51%) followed by first degree related children (25%), siblings (4%) and spouses (3%). The rest of the donors (17%) consisted of relatives (12%) and emotionally related people (5%). Finally 22.4% transplantation took place.

P604

TELBIVUDIN AS PROPHYLAXIS FOR HBV RECURRENCE AFTER LIVER TRANSPLANT: EFFICACY AND SAFETY

*Alessandro Perrella, Donatella Pisaniello, Antonio Ceriello, Fulvio Calise, Oreste Cuomo, Alfonso Galeota Lanza
Liver Transplant Center AORN A. Cardarelli*

HBV recurrence after OLTx may represent a severe clinical comorbidity after liver transplantation represents a plausible and severe condition may represent a severe. The current standard for prophylaxis essentially comprises specific immunoglobulin and lamivudin. However at the present time, other effective antiviral drugs are available, particularly some of these (Telbivudin) seems to have a minor impact on renal function. In the present study we report our experience on 10 transplanted patients receiving Telbivudin 600 mg/day while on the waiting list followed by treatment after liver transplantation with 12 months follow-up compared to 10 transplanted patients under lamivudin prophylaxis.

Methods: Our series consisted of males with HBV related end stage liver disease. The viral load decreased rapidly while on the waiting list once the patient was started on antiviral treatment. All patients were evaluated for liver and renal function tests, immunosuppression trough levels, CPK before liver transplant at (T0), 1 month (T1), 3 months (T3), 6 months (T6) and 12 months (T12).

Results: All patients received a CNI immunosuppression based regimen. Creatinin Clearance (MDRD) did not show any different a T0 between two groups, however patients receiving Telbivudin showed and improvement of Creatinine Clearance during follow-up ($p < 0.05$ U Mann-Whitney Test). Neither CPK or transaminase serum levels increased throughout the studied period and once HBV-DNA was cleared while on waiting list, it remained negative throughout follow-up period in both groups.

Conclusion: Telbivudin prophylaxis for HBV is safe and effective and seem to be related to renal function improvement compared to Lamivudin. Further studies are required to better elucidate these results.

P606

CORTICOSTEROIDS ABROGATE THE ANTIVIRAL ACTIVITY OF PLASMACYTOID DENDRITIC CELLS: RELEVANCE FOR HEPATITIS C RECURRENCE AFTER LIVER TRANSPLANTATION

*Petra de Ruiter, Patrick Boor, Qiuwei Pan, Jeroen de Jonge, Herold J. Metselaar, Hugo W. Tilanus, Jaap Kwekkeboom, Luc J.W. van der Laan
ErasmusMC*

Background: Plasmacytoid dendritic cells (PDC) are cells of the innate immune system that play a major role in anti-viral immunity as the principal producers of interferon (IFN- α). PDC are abundantly found in hepatitis C virus (HCV) infected livers, and HCV-infected hepatocytes directly stimulate IFN- α secretion. Corticosteroid treatment of acute cellular rejection is associated with severe HCV recurrence after liver transplantation (LTX), but the mechanism is unknown. The aim of this study was to investigate the effect of corticosteroids on the antiviral activity of PDC and on IFN- α signalling.

Methods: HCV-replication and IFN-signalling were investigated in Huh7 hepatoma cells, stably expressing luciferase reporter genes coupled to an HCV replicon (Huh7-ET) or an interferon response element (Huh7-ISRE-luc). Human PDC were stimulated with a synthetic TLR7-agonist or co-cultured with Huh7-ET cells, in the absence or presence of corticosteroids. In addition, conditioned media of stimulated PDC (CM) were tested.

Results: Both co-culture of PDC and Huh7-ET, and addition of PDC-CM significantly inhibited HCV replication. These anti-viral effects of PDCs were completely abrogated by treatment with corticosteroids. No apoptosis of PDC was observed at these corticosteroid concentrations. The inhibitory effect could be recapitulated by addition of PDC-CM and was completely abrogated by addition of an IFN- α receptor blocking antibody to Huh7-ET cells, showing that the antiviral effect of PDC is mediated through secretion of IFN- α . Corticos-

teroids alone did not directly affect HCV replication, IFN- α mediated inhibition of HCV replication or IFN- α signalling.

Conclusion: Corticosteroids do not directly affect HCV replication or interfere with the antiviral action of IFN- α , but inhibit the antiviral capacity of PDC by suppressing IFN- α production. This mechanism may contribute to aggravated HCV recurrence associated with high-dose corticosteroid treatment after LTX.

P607

LONG TERM SURVIVAL OF LIVER TRANSPLANTATION (LT) FOR HCC AT SINGLE INSTITUTION

*Dario Lorenzin, Edoardo Scarpa, Mina Carducci, Silvia Lazzaro, Serena Concina, Umberto Baccarani, Andrea Risaliti
University Hospital Udine*

Liver transplantation (LT) is a treatment for HCC on cirrhosis within defined criteria. Aim of the study is to analyze a single center long-term experience in LT for HCC. From 1998 to 2012, 108 patients underwent LT for HCC. 98 male (90.7%) and 10 female (9.3%) mean age was 56 (range 37–68). All patients fulfilled the Milan criteria preoperatively. HCC diagnosis was based on preoperative imaging and alfa-fetoprotein, no tumor biopsy was performed. Number and diameter of HCC nodules were respectively 2 ± 1 , 3 ± 1 cm at CT and 2 ± 1 , 4.3 ± 3.2 cm at pathology, alfa-fetoprotein was 79 ± 244 . TACE or RF/PEI were done in all cases, 6 patients (5.5%) performed major hepatic resection prior to LT. Mean MELD was 11 (range 6–23). At histology 14.8% (16 cases) had microvascular invasion. Tumor grading was 1 in 8%, 2 in 61%, 3 in 31%. According to the modified pTNM 16% were T1, 27% T2 and 56% T3. Immunosuppression was tacrolimus in 71 patients (65.5%) and ciclosporin in 29 (26.8%), tacrolimus plus everolimus in 8 (7.4%). 14 patients (13%) developed HCC recurrence. Eight patients (7.4%) hepatic, 4 (3.7%) lung and 2 (1.8%) bone. All patients died, except two which are alive with recurrent disease. At histology 7 of 14 patients who experienced recurrence (50%) had microvascular invasion. Tumor grading was G2 in 6, G3 in 7, G4 in 1 patient. All patients were switched to mTOR inhibitors and received Sorafenib after HCC recurrence, those with localized hepatic recurrence had TACE, one performed pulmonary resection. At a mean follow-up of 52 months (range 1–164) the estimated 1, 3, 5 and 10 years survival rates were 87%, 76%, 68% and 61%. Our data confirm that LT represents the principal option for patients with HCC within well defined criteria achieving an optimal survival not only in the mid-term but also at 10 years after transplantation.

P608

WHEN THE LIVER KILLS THE PATIENTS – WHAT IS THE RIGHT TIME FOR HEPATECTOMY?

*Alfred Koenigsrainer, Ruth Ladurner, Silvio Nadalin,
Doerte Wichmann
University of Tuebingen, Department of General,
Visceral and Transplantation Surgery*

Background: Toxic liver syndrome and fulminant hepatic failure (FHF) are synonymous for acute, severe, and extensive liver necrosis associated with cardiovascular shock and acute renal failure with or without respiratory failure. The etiology of this multiorgan failure (MOF) in acute liver failure is multifactorial, caused by toxic metabolites released from the necrotic liver and vasoactive effects. By eliminating the source of toxins, other organs can recover. Hepatectomy ensued with the objective of temporary hemodynamic and metabolic stabilization. Pre-emptive hepatectomy (PEH) denote hepatectomy with temporary portocaval shunt as a bridging procedure before transplantation. Indications for emergency, PEH in the case of acute liver failure remain controversial. It is difficult to identify patients who benefit from this procedure.

Results: We cover five cases of acute liver failure with PEH following liver transplantation and three cases with PEH without an opportunely graft-offer.

Conclusion: In sufficient time a PEH in selected patients may have benefit to improve toxic liver syndrome. We introduce a new score to detect patients, who profit by pre-emptive hepatectomy.

P609

IATROGENIC GLUE EMBOLISATION OF HEPATIC ARTERY RESULTING IN ISCHAEMIC CHOLANGIOPATHY

*Satheesh Iype, Raaj K. Praseedom
Cambridge University Hospital*

Case report: A 61 year old lady with no co-morbidities presented with acute upper gastrointestinal bleeding to her local hospital. Oesophagogastroduodenoscopy (OGD) revealed a bleeding duodenal ulcer which was controlled with adrenaline injection. She developed recurrent bleeding within 24 h and repeat OGD showed an actively bleeding vessel in the ulcer. The bleeding ulcer was injected with cyanoacrylate glue (N-butyl-2-cyanoacrylate) and lipiodol, successfully controlling the haemorrhage. Shortly thereafter she developed severe abdominal pain. This appeared to settle initially with conservative management. However, she developed recurrent right upper quadrant abdominal pain and a computed tomography (CT) scan of the abdomen showed total occlusion of the entire hepatic artery and its distal intra hepatic branches. At this stage she was managed conservatively. However, she subsequently presented with recurrent abdominal pain, rigors and fever. A further CT scan and MRI showed

no flow through the intrahepatic part of hepatic artery, intrahepatic abscesses, and multiple strictures of the intrahepatic biliary tree suggesting ischaemic biliary necrosis. Liver biochemistry remained stable without decompensation. Blood cultures were negative. The patient continued to get biliary sepsis, in spite of broad spectrum antibiotics, and had several relapses. As she had progressive worsening of sepsis with multiple liver abscesses, she was assessed for liver transplantation and listed for it. She was transplanted 3 weeks after listing. As the hepatic artery was occluded, she needed an infrarenal conduit for arterial inflow. She also required a roux loop reconstruction of the bile duct. The histopathology of the explanted liver showed ischaemic cholangiopathy with candida albicans cholangitis. She made an uneventful recovery from the transplant and is currently doing well.

P610

LIVER TRANSPLANT RECIPIENTS WITH HIGH BODY MASS INDEX (BMI) – SHORT AND LONG TERM OUTCOMES

*Satheesh Iype, Paul Gibbs, Andrew Butler
Cambridge University Hospital*

Background: Incidence of obesity is increasing in the general population. There is a proportionate increase in BMI of the liver transplant recipients. Worse outcome is predicted in high BMI patients following major surgery. We analysed the short and long term outcomes of the liver transplant recipients with high BMI.

Methods: We analysed a retrospective cohort of 875 consecutive liver transplants from 2000 to 2012. The liver transplant recipients were classified into two BMI groups were; <30–697 (80%), >=30 to 178 (20%). The impact of BMI on various graft outcomes such as primary non-function (PNF), Acute rejection, early dysfunction, retransplantation, patient and graft survival were assessed.

Results: There was significantly higher incidence of diabetes in the high BMI recipients. (Table 1) Non alcoholic steatohepatitis (NASH) related cirrhosis was a significant etiology in the high BMI group. PNF, acute rejection and retransplantation were significantly high in the high BMI group. Early graft dysfunction, IT stay, Hospital stay and 30 day mortality were similar in both groups. The 5 year graft survival was 79% and 75% respectively in low and high BMI groups. The 5 year patient survival was 80% and 78% respectively in both groups.

Conclusion: High BMI recipients were at higher risk of Primary non-function and re-transplantation. However, high BMI recipients had similar long term graft outcomes as in low BMI recipients.

P611

LEFT LATERAL SPLIT LIVER TRANSPLANT: SINGLE CENTER EXPERIENCE IN SAUDI ARABIA

*Firas Zahr Eldeen, Hamad Al Bahili, Yasser Elsheikh, Talal Algoufi,
Mohammed Alshagrani, Martin Burdelski, Mohammed Al-Sebayel, Dieter Broering
King Faisal Specialist Hospital*

Background: Left lateral split liver transplant (SLT) creates two allografts from a single deceased donor (DBD), a left lateral (LLS) and a right extended liver graft (ERL) to be transplanted into a one child and one adult respectively. This brief report is the first to outline the experience in Left Lateral Split Liver Transplant in Saudi Arabia (KSA).

Methods: Since Nov 2010, fifty two whole livers out of 128 potential DBD (40.6%) were utilized, 26% of Donor pool (Living and deceased); three (5.7% of usable livers) were found 'splittable'; three adults received (ERL) and 2 pediatric recipients received 3 (LLS).

Results: LT in KSA is driven by LD; 27% received grafts from DBD of which 2.5% received split grafts. Mean survival for whole group was 294 days, median follow up of 8 months (range 6 days–20 months). One child received two SLT due to segmental hepatic artery thrombosis, and one adult patient died on day 18 from pulmonary embolism.

Conclusion: SLT has been already established as a feasible option. Previous results showed that safety and outcomes in ERL and LLS were comparable to other recipients. However, patient selection and use of good quality organs are paramount to ensure best outcomes.

P612

LIVER TRANSPLANTATION IN BUDD-CHIARI SYNDROME: A SINGLE CENTRE EXPERIENCE IN SAUDI ARABIA

*Yahia Saleh, Firas Zahr Eldeen, Yasser Kamel, Monther Kabani, Mohammed Al-Sebayel, Dieter Broering
King Faisal Specialist Hospital*

Background: Patients suffering from Budd Chiari Syndrome are considered as potential candidates for liver transplantation (LT) if not responding to other modalities. Early intervention in relatively stable can improve the outcome and survival.

Patient and methods: This is the first article from Saudi Arabia to describe our experience in LT in patients with BCS. Data for patients, who underwent LT between Mar 2001 and Oct 2012, were analyzed. Six patients with BCS underwent LT (1.4%). Diagnostic work up such as imaging modalities and hematological evaluation was part of work up.

Results: All patients received whole liver transplant from deceased donor. They were started on therapeutic heparin infusion and triple therapy immunosuppression, according to our protocol, then warfarin was introduced for long term control. Two patients (33%) died; one from bleeding caused by DIC; second succumbed after 5 months of pneumonia and multiorgan failure. One patient had recurrence after portal vein thrombosis nine months post LT. The predictors of mortality in our cases are renal failure, previous abdominal surgery and low BMI.

Conclusion: Treatment of BCS follows a therapeutic algorithm that should start by anticoagulation and might end by liver transplantation, which seems to be feasible in our experience.

P613

LONG-TERM SURVIVAL OUTCOME OF LIVING DONOR LIVER TRANSPLANT RECIPIENTS HAVING PATHOLOGICALLY NON-VIABLE HEPATOCELLULAR CARCINOMA

*Park Hyung Woo, Jung Yong Kyu, Jwa Eun Kyung
Asan Medical Center*

Background and purpose: Complete necrosis of hepatocellular carcinoma (HCC) lesions has been occasionally found in the explant pathology after neoadjuvant treatment such as transarterial chemoembolization and radiofrequency ablation. This study intended to investigate the long-term prognostic effect of loss of tumor viability after pretransplant HCC treatment in living donor liver transplantation (LDLT) recipients.

Methods: The study patients were 37 patients who demonstrated non-viable HCC on explant pathology and followed up for more than 5 years. Patient medical records were reviewed retrospectively. Patients who did not meet the Milan criteria at any time before LDLT operation, patients undergone salvage transplantation and perioperative mortality cases were excluded.

Results: Common primary disease was hepatitis B virus-associated liver cirrhosis ($n = 37$). Their explant tumor profiles were single tumor in 29 and maximal tumor size was 35 mm. There was no case showing microvascular invasion. Their median value of alpha-fetoprotein was 12 ng/ml (range: 1–1160). Only one patient showed recurrence at 20 months, but he is still alive for more than 6 years after adrenalectomy and repeated pulmonary metastasectomy. Five-year recurrence rate was 2.1%. There were only two late mortality cases, each one due to graft failure and gastric cancer recurrence. Overall patient survival rate was 97.3% at 5 years and 92.7% at 10 years.

Conclusions: The results of this study revealed that pretransplant treatment-induced loss of tumor viability definitely decreased the risk of posttransplant HCC recurrence. Therefore, the patients showing non-viable HCC can be regarded as belonging to the super-Milan or super-selection group having minimal risk of HCC recurrence, thus routine HCC screening is exempted.

P614

ACUTE LIVER FAILURE DUE TO VASCULAR COMPLICATIONS ASSOCIATED TO IATROGENIC BILE DUCT INJURIES AFTER LAPAROSCOPIC CHOLECYSTECTOMY

*Sandra García Aroz, Oscar Caso, Manuel Abradelo, Jorge Calvo, Alvaro García Sesma, Alejandro Manrique, Felix Cambra, Carmelo Loinaz, Carlos Jimenez
Hospital Universitario 12 De Octubre*

Introduction: Bile duct injuries (BDI) are infrequent but potentially devastating complications after biliary tract surgery and have become more common since the introduction of laparoscopic cholecystectomy (LC). We also have seen an increase in associated vascular injuries, which normally have a subclinical course. A right approach of these patients requires a multidisciplinary treatment. There are several reported cases, in which vascular injuries can produce liver necrosis with progression to acute liver failure (ALF), requiring liver transplantation (LT).

Case report: We report the case of a 55 years female with no past history who underwent LC developing iatrogenic BDI. The patient was reoperated performing biliary tract reconstruction with Roux-en-Y hepaticojejunostomy. Five days after this surgery, a CT-scan showed the presence of right hepatic artery (RHA) pseudoaneurysm with active bleeding. A selective arteriography with embolization of the RHA was performed. After 48 h, a new arteriography proved persistent bleeding, so a new embolization was tried. The clinical course worsens and the patient developed an ALF. She was transferred to our department and was accepted for emergency LT. LT was performed with a whole graft from brain death donor. The postoperative period was complicated but successful. One year after LT, the patient remained asymptomatic with normal graft function. There are 14 cases reported in the literature in which LT was required due to vascular injuries associated with iatrogenic BDI after LC. Only 4 of these cases describe a pure injury of the RHA. In two of them, LT was

performed due to secondary biliary cirrhosis and in the other two cases because of ALF.

Conclusions: Bile duct injuries with associated vascular complications after LC are potentially fatal lesions in which sometimes LT should be considered.

P615

LIVER TRANSPLANTATION WITH DONORS OVER 70 YEARS IN NON-HCV PATIENTS. RESULTS AFTER LONG-TERM FOLLOW UP

Oscar Caso Maestro, Carlos Jiménez Romero, Alejandro Manrique Municio, Felix Cambra Molero, Jorge Calvo Pulido, Rebeca Sanabria Mateos, Naim Fakh Gomez, Edurne Alvaro, Cristina Alegre Torrado, Alvaro García Sesma, Manuel Abradelo, María García Nebreda, Ricardo Ceron, Ursula Guerra Monasterio, Carmelo Loinaz Seguro, Enrique Moreno Gonzalez Hospital 12 De Octubre

Background: Donor age is one of the vital criteria used for donor selection in liver transplantation (LT). Conservative approaches toward age ensure quality of the donor organ; however, applying a too severe restriction could unwittingly exclude organs that would be suitable for transplantation.

Material and methods: Retrospective review of all LT performed in our department with grafts from donors over 70 years excluding HCV+ patients.

Results: From April 1986 to December 2008, we performed 46 LT using grafts from donors over 70 years in non-HCV patients. The recipients were 40 men and 6 women with a mean age of 53 + 10 (27–71) years. Donors were 20 men and 26 women with a mean age of 76 + 5 (70–89) years. Intensive care unit (ICU) stay of donors was 36 + 29 (9–144) h and only 10 donors needed vasoactive drugs perfusion. Etiology of the cirrhosis was: alcohol in 27 patients, hepatitis B virus in 12, and other causes in 7. LT was uneventful in all cases with a cold and warm ischemia mean time of 438 + 174 (210–795) min and 58 + 11 (45–90) min, respectively. Mean transfusion requirements were 8 + 7 red blood cells units, 18 + 23 fresh frozen plasma units, and 3 + 5 platelets units. There was 1 primary graft failure and 1 acute arterial thrombosis requiring retransplantation. After a mean follow-up of 96 + 62 (0–225) months, 17 (37%) patients died. Patient survival at 1, 3 and 5 years were 84.7%, 84.7% and 77.6%, respectively, and graft survival were 84.4%, 82.2% and 71.9%, respectively.

Conclusions: Aged donors over 70 years are an excellent alternative to improve the donor pool in non-HCV recipients.

P616

LIVER TRANSPLANTATION WITH SPLIT GRAFTS IN HCV+ PATIENTS

Oscar Caso Maestro, Alejandro Manrique Municio, Naim Fakh Gomez, Jorge Calvo Pulido, Rebeca Sanabria Mateos, Sandra García Aroz, Felix Cambra Molero, Alvaro García Sesma, Manuel Abradelo, Edurne Alvaro, Alberto Marcacuzco Quinto, María García Nebreda, Cristina Alegre Torrado, Ursula Guerra Monasterio, Carmelo Loinaz Seguro, Enrique Moreno Gonzalez, Carlos Jiménez Romero Hospital 12 De Octubre

Introduction: Hepatitis C (HCV) remains the most common indication for liver transplantation (LT). Early data suggests that patients with HCV who receive a partial liver graft have worse outcomes, but more recent data also underlines that there is no difference in recurrent HCV between recipients of partial grafts and a whole one.

Patients and methods: Retrospective review of all our HCV patients undergoing LT with grafts from liver bipartition (Split) and study of the results.

Results: From April 1986 to December 2012 we have performed 6 LT with Split grafts in HCV patients. All patients were male with positive CMV serology, without associated alcoholic disease, and only two patients had associated hepatocarcinoma (HCC). Two cases were HCV genotype 1 (33%) and only one patient received antiviral treatment before LT, but without virological response. All donors were male, with a mean age of 28 + 16 years. The transplantation was uneventful in all cases with a warm and cold ischemia mean times of 451 + 283 min, and 67 + 13 min, respectively. After a mean follow-up of 96 + 46 months, the histologic progression of HCV recurrence was normal/minimal changes in 2 cases (33%), moderate hepatitis (<= " td=">.

P617

RESECTION OR TRANSPLANTATION FOR EARLY HCC: SINGLE CENTER EXPERIENCE

Matej Kocik, Alexandros Valsamis, Martin Oliverius, Libor Janousek, Milos Adamec, Milos Kucera, Pavel Trunecka, Jiri Fronek IKEM

Background: The optimal management of patients with hepatocellular carcinoma (HCC) and early cirrhosis is still under debate. The aim of our

study is to compare outcomes of patient with HCC within UCSF criteria who underwent liver transplantation or resection at our institution.

Methods: From April 2004 to November 2010, 33 patients underwent liver transplantation and 16 patients underwent liver resection for HCC meeting UCSF criteria. Overall and recurrence-free survival rates were calculated using Kaplan–Meier method. Groups were compared by log-rank test.

Results: Overall and disease-free 1-, 3- and 5-year survival rates were 88%, 76%, 76% and 85%, 76% and 71% for transplanted patients and 81%, 75%, 63% and 75%, 63% and 21% for patients after liver resection. The difference was not significant (p = 0.61 and 0.11). In a subset of patients within Milan criteria 1-, 3- and 5-year overall and disease-free survival rates were 90%, 90%, 79% and 86%, 79% and 74% in the transplant group and 89%, 89%, 67% and 78%, 67% and 0% for resected patients. The results were not statistically different (p = 0.90 and 0.13). In patients with solitary tumour and in patients with multiple lesions, the overall survival was not statistically different between transplantation and resection in both groups (p = 0.49 and 0.41). In patients within UCSF criteria the overall survival does not depend on the size of the lesion (p = 0.57, Cox proportional regression model).

Conclusion: Our data show that there is no statistically significant difference in survival of patients with HCC within UCSF criteria between liver resection and transplantation either for patients with solitary or multiple lesions. The study shows higher recurrence-free survival in the transplantation group, however, we were not able to prove the statistical significance due to the small number of patients.

P618

LIVER TRANSPLANTATION IN NONALCOHOLIC STEATOHEPATITIS IS ASSOCIATED WITH HIGHER OPERATION TIMES AND POSTTRANSPLANT INFECTIOUS COMPLICATIONS – A SINGLE CENTER EXPERIENCE

Barbara Kern, Robert Sucher, Ivo Graziadei, Benedikt Feurstein, Claudia Boesmueller, Felix Aigner, Robert Oellinger, Matthias Biebl, Johann Pratschke, Stefan Schneeberger Innsbruck Medical University

Background: Nonalcoholic steatohepatitis (NASH) is prone to become one of the leading indication for liver transplantation in the future. The aim of this study was to describe the clinical post-transplant outcome of NASH patients compared to patients with other common indications for liver transplantation.

Methods: We conducted a retrospective analysis of a prospectively collected single center database of 370 patients who underwent orthotopic liver transplantation between 2005 and 2011. Outcomes were compared between NASH patients and the remaining study group.

Results: The incidence of NASH as primary indication for liver transplantation was 15.4% (57/370). The average MELD score was 22, the average BMI 25.1. NASH patients with HCC were associated with a significantly higher BMI compared to NASH patients with no evidence of HCC (28.3 vs. 26 p = 0.02). NASH patients had significantly longer operative times (p = 0.01) and higher infectious complications (p = 0.01). Patient survival was 3.28 years (3.16 years for NASH patients).

Discussion: Our center performed a significant number of liver transplantations in patients with NASH. Transplantation in this cohort was associated with longer operation times and higher infectious complications most likely due to obesity and presence of metabolic syndrome. Weight reduction prior transplant could therefore lead to better postoperative outcomes.

P619

OUR EXPERIENCE OF SPLENIC ARTERY STEAL SYNDROME AFTER ORTHOTOPIC LIVER TRANSPLANTATION

Young-Dong Yu, Sung-Won Jung, Sung-Ock Suh Korea Univeristy Medical College

Arterial 'steal' phenomenon after orthotopic liver transplantation (OLT) is an important but often underdiagnosed cause of graft ischemia occurring in about 3–8% of cases. It indicates a decreased perfusion of the hepatic artery (HA) because of diversion of the blood flow into the splenic, gastroduodenal or left gastric artery, which leads to graft dysfunction. Splenic artery steal syndrome (SASS) usually occurs within days or weeks after transplantation. Its clinical spectrum is highly variable from a mild disorder to graft failure or ischemic biliary injury cases. We report the case of a liver transplant recipient who developed SASS successfully treated by partial splenic embolization. A 45-year-old man received cadaveric liver transplantation in our center as treatment for HBV-LC decompensated cirrhosis. After the third postoperative day, the patient showed increasing levels of bilirubin and prolongation of the prothrombin time. Doppler sonogram revealed sluggish hepatic arterial flow. After evaluation for other causes for graft dysfunction we performed splenic artery embolization. After splenic embolization, the hepatic artery flow markedly improved and the patient recovered without sequelae. In conclusion, since it can be successfully treated with splenic artery embolization, SASS should be considered following liver transplantation when there is no other cause for graft dysfunction.

P620

ACUTE CHOLECYSTITIS: AN OVERLOOKED CAUSE FOR DECOMPENSATION OF THE LIVER FUNCTION IN PATIENTS AWAITING LIVER TRANSPLANTATION

Sung-Won Jung, Young-Dong Yu, Sung-Ock Suh
Korea University Medical College

Background/aims: Acute-on-chronic liver failure is an increasingly recognized entity encompassing an acute deterioration of liver function in patients with cirrhosis, either secondary to superimposed liver injury or due to extrahepatic precipitating factors such as infection culminating in the end-organ dysfunction. In order to improve survival in these patients, it is imperative to preserve them in suitable condition till transplantation.

Methods: The medical records of patients who received liver transplantation due to acute on chronic liver failure were reviewed.

Results: There were three patients whose condition deteriorated due to acute cholecystitis. All patients were child class C and presented with fever and abdominal pain. The average model for end stage liver disease (MELD) score was 18. Although initial imaging revealed diffuse wall thickening of the gallbladder in all of the patients, it was considered a finding related to liver cirrhosis. Due to persistent symptoms and without evidence of spontaneous bacterial peritonitis, acute cholecystitis was suspected and antibiotic therapy was initiated. Also, percutaneous cholecystostomy was performed in two patients. All patients showed improvement of patient condition and symptoms and received timely liver transplantation with two patients receiving deceased donor liver and the remaining patient receiving living donor liver transplantation.

Conclusions: Since timely intervention for acute cholecystitis can prevent further deterioration of liver function, acute cholecystitis should be considered when finding a precipitating cause for acute decompensation of liver function in patients with liver cirrhosis, especially if imaging studies reveal diffuse gallbladder wall thickening.

P621

TECHNICAL GUIDELINES FOR PORCINE LIVER ALLO-TRANSPLANTATION

Arash Nickkholgh, Majid Esmaeilzadeh, Mohammadreza Hafezi, Mohammad Golriz, Hamidreza Fonouni, Arianeb Mehrabi
Ruprecht-Karls University, Heidelberg

Background: Porcine model is an optimal model in the field of experimental liver transplantation (LTx) research. Here, we present the various techniques of experimental LTx in the porcine model in detail.

Materials/methods: Analysis of Medline-cited studies dealing with different techniques of SBTx in porcine models with particular focus on surgical aspects.

Results: Different methods and modifications have been described. The following major steps have been discussed in detail: donor liver preparation, recipient operation including recipient hepatectomy, and reconstruction phase, including the reconstruction of suprahepatic inferior vena cava (SHIVC), portal vein (PV), infrahepatic inferior vena cava (IHIVC), hepatic artery (HA) and bile duct (BD). IHIVC and SHIVC are anastomosed end to end directly or with the use of prosthesis anastomosed side to side. The PV anastomosis is performed end to end between donor and recipient PV, Cuff method or Stump method. Arterialization has been accomplished via carrel patch or donor HA end to end with recipient HA. There are three major methods for reconstruction of BD: end to end or end to side choledochcholedochostomy and choledojejunostomy with Roux-en-Y jejunal loop.

Conclusion: Each method has advantages and disadvantages regarding the objectives of the study; the most physiological techniques may be preferred for long-term survival studies, while the faster techniques may be selected for experimentations aiming the direct postoperative phase.

P622

NEONATAL HEMOCHROMATOSIS LIVER TRANSPLANT. A CASE REPORT AND LITERATURE REVIEW

Rebeca Sanabria Mateos, Alejandro Manrique Municio, Naim Fakh Gomez, Oscar Caso Maestro, Alberto Marcacuzco Quinto, Sandra García Aroz, María García Nebreda, Cristina Alegre Torrado, Edurne Alvaro, Jorge Calvo, Manuel Abradelo, Felix Cambra, Alvaro García-Sesma, Carmelo Loinaz, Carlos Jimenez
H.U. 12 de Octubre

Background: Neonatal hemochromatosis (NH) is a rare disease of iron metabolism that starts at intrauterine period causing liver failure and extrahepatic siderosis. The etiology has not been understood exactly, it is accepted that is a maternofetal alloimmune disorder. The prognosis of NH is generally bad and death is inevitable if left untreated. The efficiency of chelation-antioxidant cocktail used in medical treatment is between 10% and 20% and these patients frequently need liver transplantation (LT).

Materials and methods: We report a sixteen days old female infant LT secondary of NH diagnosis without medical treatment response.

Results: A sixteen days old infant, with 2.225 grams weight, was diagnosed of NH based on clinical, laboratory (high ferritin and transferrin saturation),

radiological (decreased T2 signal intensity of hepatic parenchyma) and liver biopsy (hepatic nonreticuloendothelial iron deposition). Chelation-antioxidant cocktail was established without response, with severe coagulopathy and encephalopathy, because of she required LT, which made with II-III cadaveric split liver. She had a postoperative torpid with hepatic artery thrombosis and secondary aortic thrombosis caused death, probably related to low weight of infant and technical difficulties with vessel diameter in one of smallest weight liver transplant made. Discussion NH is a rare condition but the most common cause of acute liver failure and LT in the neonatal period. LT, with 50% long-term survival, remains the treatment of choice and should be promptly offered to those infants who do not improve with supportive medical treatment.

P623

EFFECT OF NUTRITIONAL MANAGEMENT ON IMMUNOLOGICAL STATUS IN LIVING DONOR LIVER TRANSPLANTATION

Ayaka Kinoshita, Akihiko Soyama, Mitsuhsa Takatsuki, Yasuhiro Torashima, Amane Kitasato, Tomohiko Adachi, Izumi Yamaguchi, Tamotsu Kuroki, Susumu Eguchi

Department of Surgery, Nagasaki University Graduate School of Biomedical Sciences

Background: Liver transplant recipients are frequently in malnutrition status. Even after the transplantation, oral-intake often does not increase as expected even in cases with ideal recovery of liver function. Postoperative malnutrition is considered high risk of infection as a result of immune deficiency.

Aim: To clarify the association of total nutritional management including symbiotics, early enteral feeding and bile replacement and postoperative infection or immunological status in living donor liver transplant recipients.

Methods: Among 168 patients who underwent living donor liver transplantation between Jan 1997 and Dec 2012, consecutive cases during the certain time period were evaluated as to following parameters: incidence of postoperative infection ($n = 50$), diamine oxidase (DAO) activity as a marker of villous integrity of small intestine ($n = 13$), and CD4+ adenosine triphosphate (ATP) activity (ImmuKnow assay) ($n = 24$).

Results: Incidence of postoperative infection was significantly low in patients with symbiotics compared to patients without symbiotics (1/25, 4% vs. 6/25, 24%, $p < 0.05$). Patients with early enteral feeding with bile replacement tended to show higher DAO increment ratio (DAO of postoperative day 28/day 7) ($p = 0.07$). Low ATP activity was significantly correlated with levels of preoperative retinol binding protein ($p < 0.05$).

Conclusions: Early enteral feeding, bile replacement was considered effective to prevent postoperative infection probably due to the effect on enterobacterial flora and villous integrity of small intestine. In addition, preoperative nutrition status such as retinol binding protein seems to effect even postoperative immunological status.

P624

THE SIMPLIFIED TECHNIQUE OF BILIARY RECONSTRUCTION UNDER MICROSCOPIC FIELD IN RIGHT LOBE LIVING DONOR LIVER TRANSPLANTATION

Young Seok Han, Dong Lak Choi, Joo Dong Kim

Division of Abdominal Organ Transplantation, Department of Surgery, School of Medicine Catholic University

Background: Biliary complications still remain the most common cause of morbidity in living donor liver transplantation (LDLT). According to recent reports, the application of a microsurgical technique in biliary reconstruction has been shown more excellent results. However, many transplant surgeon fear the acceptance of unfamiliar microsurgical technique. Hence, we introduce the simplified microsurgical technique for biliary reconstruction and present our results.

Methods/materials: Forty-seven right lobe LDLTs who underwent biliary reconstruction under microscopic field were enrolled for this study. Transplantations were performed between December 2010 and March 2012. External stent in all patients was inserted and tailored telescopic technique was also used.

Results: We have not experienced biliary complications including bile leak and early biliary stricture at anastomotic site in enrolled LDLTs for 1 year follow-up period. Five ABO-incompatible LDLTs was included and biliary complications were not demonstrated in clinical presentations including imaging and laboratory studies.

Conclusion: Our Simplified biliary reconstruction technique under microscopic field will allow easier access to many transplant surgeons. And, our good results recommend the routine use of microsurgical biliary reconstruction in right lobe LDLT.

P625

SEVERE EARLY POST-TRANSPLANTATION Rhabdomyolysis and Liver Damage Associated to Lamivudine in Autoimmune Cirrhosis with Hepato-pulmonary Syndrome

Rita Gaspari¹, Paolo M. Soave¹, Massimo Siciliano², Francesco Tafuni¹, Brigida E. Annicchiarico², Ciro D'Alò¹, Maria C. Lirossi³, Salvatore Agnes³, Alfonso W. Avolio³

¹Department of Anaesthesiology and Intensive Care Unit; ²Division of Hepatology, Department of Medicine; ³Division of Organ's Transplantation, Department of Surgery

Rhabdomyolysis is a syndrome characterized by skeletal muscle's lesion, resulting in release of intracellular contents into circulation. The most common potentially lethal complication of rhabdomyolysis is acute renal failure. Although episodic cases of rhabdomyolysis have been reported after lamivudine (LAM) administration, none was associated with liver dysfunction in the transplant (LTx) setting. A 32-y.o. Caucasian female, underwent LTx for autoimmune cirrhosis and hepato-pulmonary syndrome with severe hypoxemia. Due to an anti-HBc liver graft, HBV reactivation prophylaxis with i.v. anti-HBV immunoglobulins (10000 U during the anhepatic phase of LTx and 1000 U/day for 7 days thereafter) and oral LAM (100 mg/day from the 1st post-operative day, POD) was administered. In the 4th POD serum potassium (7.1 mEq/l), ALT (1983 U/l) and CK (31 672 U/l) increased, followed by oliguria and metabolic acidosis (lactic acid, 11.9 mm) (table). LAM was withdrawn and rehydration, sodium bicarbonate and mannitol were started. Despite therapy, urine output further decreased and continuous venovenous hemofiltration (CVVH) was started. ALT rapidly decreased, whereas the peak of CK (135 752 U/l) was recorded at 6th POD and returned to normal only after several days. Causes of rhabdomyolysis other than LAM (trauma, viral infections) were ruled out. Liver biopsy performed at the 17th POD showed only cytolysis without rejection. At the 45th POD, liver function is almost normal, but the patient is still anuric.

This case has some peculiarities: the very low total dose of LAM (400 mg), that caused rhabdomyolysis, the extreme severity of the muscular damage and the association with acute liver damage. It can be hypothesized that primitive mitochondrial dysfunction (lung, muscle, liver) due to hepato-pulmonary syndrome may be enhanced by toxic mitochondrial damage caused by LAM. This case report raises questions about the safety of LAM in pts with long-lasting chronic hypoxia.

P626

EVALUATION OF IRI PREVENTION IN LIVER TRANSPLANTATION WITH INFLIXIMAB (ANTI-TNF): PRELIMINARY RESULTS IN STUDY GROUP OF PATIENTS WITH MELD>30

Paolo Girotti, Silvio Nadalin
University Hospital

Background: Ischemia-Reperfusion Injury (IRI) represents a complex series of intracellular and extracellular events that results in molecular, cellular and tissue damage. It's induced by the transient deprivation of blood flow and oxygen, with lack of aerobic metabolism, and the return of blood flow during reperfusion with concomitant induction of innate and adaptive immunity, due to a release of oxygen-free radicals (OFR), cytokines/chemokines, and up-regulation of adhesion molecules, with consequent cellular and organ dysfunction. Focused on solid organ transplantation field, IRI is the main physiopathological event, resulting from an activation of TNF (figure 1.), that induce always an initial damage and that potentially could improve the damage and the development of clinical syndromes, (DGF, PNF).

Material and method trial design: Prospective, monocentric, placebo-controlled study to evaluate of Infliximab (one shot) in the early post operative period (72 h) after liver graft reperfusion. Endpoints: Primary Endpoints Evaluation of significant statistical reduction of IRI due to the following laboratory values at 1 POD: -mean ALAT level -mean Bilirubin level -mean CHE level -mean Leukocytes (CD4+) level Secondary Endpoints Statistical reduction of the occurrence of PDF, PNF, Acute rejection, biliary complication.

Results: Study group: seven patients receiving infliximab after 30 min the Control group: seven patient. Results are showed in Table 1. Study group Group control -mean ALAT level 80 U/l 201 U/l -mean Bilirubin direct level 1.2, 1.8 mg/dl -mean CHE level 7010, 1056 U/ml -mean (CD4+) level 800 1/μl 2400 1/μl No PNF and AR were detected in the study group.

Conclusion: Infliximab injection after 30 min after liver graft reperfusion showed good results in term of fast reduction of injury labor liver values. It seem influences a reduction of iperacute complications (PNF and AR) but not t.

P628

LIMITING THE USE OF DCD GRAFTS IN HCV POSITIVE PATIENTS

Naim Fakh Gomez, Manuel Abradelo, Iago Justo, Oscar Caso Maestro, Rebeca Sanabria Mateos, Alberto Marcacuzco Quinto, Alejandro Manrique Municio, Jorge Calvo Pulido, Alvaro Garcia Sesma, Felix Cambra Molero, Carmelo Loinaz, Carlos Jiménez Romero
12 de Octubre Hospital

Background: Hepatitis C virus(HCV) cirrhosis is one of the leading indications for liver transplantation(LT). Due to the shortage of donors nowadays, donation after cardiac death is becoming a more frequent source of organs. However, there is few information of the impact of using DCD livers in HCV patients.

Materials and methods: Between January 2006 and November 2010, 43 patients underwent LT with DCD (MAASTRICHT II) allografts of whom 21 had HCV-related cirrhosis. In the same period of time, 85 HCV(+) adult patients underwent LT from donors after brain death (DBD). A retrospective analysis was performed comparing three groups of liver recipients: HCV(+)-using DCD allografts(Group A), HCV negative using DCD allografts(Group B), and HCV(+) with DBD grafts (Group C).

Results: A total of 43 patients underwent LT using DCD allografts, 19 of whom were HCV+ after excluding two HIV patients (Group A), 22 HCV negative (Group B); and 85 HCV patients from DBD allografts (Group C). The mean age of recipients was 57 years in group A, 59 in group B and 52.7 in group C. The donors were statistically younger in DCD groups. The mean MELD score was 14.44, 15.15 and 15.87 in groups A, B and C respectively. No statistically significant differences were observed with respect to blood transfusion in groups A & B, where as these requirements were higher than in group C (RBC: 16.11 units, 19.22, and 9.76 in groups A, B, and C respectively) The graft survival rates at 1 and 3 years were 72.3% and 59.6% in group A, 55% and 55% in group B, and 85.4% and 70.2% in group C. The patient survival rates at 1 and 3 years were 68.4% and 52.7% in group A, 71.3% and 71.3% in group B, and 85.4% and 70.2% in group C.

Conclusions: There seems to be worse results in DCD allografts used in HCV(+) patients in comparison to HCV patients with DBD grafts or DCD organs in HCV(-) recipients.

P629

THE ROLE OF HEPATIC TRANSPLANTATION IN ADULT LIVER POLYQUISTOSIS

Alberto Marcacuzco Quinto, Naim Fakh Gomez, Oscar Caso Maestro, Rebeca Sanabria Mateos, Manuel Abradelo, Alejandro Manrique Municio, Jorge Calvo Pulido, Felix Cambra Molero, Carmelo Loinaz Seguro, Sandra Garcia Aroz, Paula Rioja conde, Carlos Bermello Meza, Luis Carlos Jimenez Romero
HU 12 de Octubre

Background: Adult liver poliquistosis(ALP) is a rare congenital disease, of dominant autosomic transmission, characterized by the presence of multiple bilateral hepatic cysts,variable in number and size, and is associated in more than 70-90% of the cases with renal poliquistosis. It affects mostly women between 40-60 years old, growing through the reproductive period and reaching their maximum in the fifth decade of life. They start as a massive hepatomegaly resulting in abdominal tenderness, vena cava obstruction and hemorrhage. Surgical treatment has very poor results and must be considered especially in sintomatic patients. Liver transplantation (LT) is a valid option for this disease.

Materials and methods: Between April 1986 and January 2012, 1580 LT were performed at our center. Ten cases of ALP were found.

Results: Ten patients underwent LT for ALP, of whom seven were women. The mean recipient age was 54 + 10 years and the mean donor age 40 + 19 years. The mean cold ischemia time was 351 + 153 min and that of warm ischemia time was 64 + 12 min. The mean transfusional requirements during surgery were 21 units of red blood cells, 16 units of fresh frozen plasma and 6 pools of platelets. The mean MELD score was 20 + 4. In 90% of the cases, there was concomitant renal insufficiency, requiring a simultaneous renal transplant. The recipient survival rates were 75%, 75% and 60% at 1, 3 and 5 years respectively.

Conclusions: ALP is a rare indication for LT, usually accompanied with renal insufficiency requiring a simultaneous liver and kidney transplantation.

P630

ONCE- VERSUS TWICE-DAILY TACROLIMUS: SAFETY AND EFFICACY ANALYSIS IN LIVER TRANSPLANT RECIPIENTS

Fabio Melandro, Barbara Lattanzi, Manuela Merli, Valerio Giannelli, Michela Giusto, Vincenza Di Gregorio, Nicola Guglielmo, Giovanni Battista Levi Sandri, Gianluca Mennini, Pasquale Bartolomeo Berloco, Massimo Rossi
Sapienza Universita' Di Roma

Background and aim: Tacrolimus is one of the most important immunosuppressive agent in the prevention of organ rejection following liver transplantation. While in the past was typically administered the twice-daily formulation (BID), a

modified-release once-daily formulation (QD) has been developed and licensed for use. This study aims at analyzing the safety, efficacy and blood levels of QD in comparison with BID formulation.

Methods: All patients liver transplanted from January 2010 to December 2012 who assumed tacrolimus de novo as immunosuppressive therapy were considered for the study. Population was divided in two groups. The QD group included liver transplant patients who received initial immunosuppression with tacrolimus QD. This group was compared with the group who received equivalent immunosuppression with twice-daily tacrolimus administration (BID).

Results: We retrospectively analyzed 40 liver recipients. Of these 24 QD (60%) and 16 BID (40%). Patient characteristics were similar between groups except Hepatocellular Carcinoma ($p = 0.09$) Levels of TAC during the first week (5.2 ± 4.2 ng/ml in QD group vs. 5.6 ± 3 ng/ml in BID group; $p = 0.6$) and the first month (5.3 ± 1.8 ng/ml in QD group vs. 5.4 ± 1.6 ng/ml in BID group; $p = 0.9$) after liver transplantation were well-adjusted in both groups. There was not significant difference in number of patients requiring change of immunosuppressive drug due to an inadequate tacrolimus blood level ($p = 0.6$). The rejection rate in the QD group was low, and only 2 patients experienced biopsy-proven acute rejection versus 0 in the BID ($p = 0.23$). Adverse events profiles were similar for both tacrolimus BID and QD. Diabetes Mellitus ($p = 0.24$), Arterial Hypertension ($p = 0.5$), Dyslipidaemia ($p = 0.8$), Acute Renal Failure ($p = 0.2$) Chronic Renal Failure ($p = 0.8$). There was no difference in graft and patients survival between the groups.

Conclusions: Tacrolimus QD have an excellent patient adherence and, in our study, a good efficacy and safe.

P631

EVALUATION OF IRI PREVENTION IN LIVER TRANSPLANTATION WITH INFLIXIMAB (ANTI-TNF): PRELIMINARY RESULTS IN STUDY GROUP OF PATIENTS WITH MELD >30.

Paolo Girotti, Silvio Nadalin
University Hospital

Background: Ischemia-Reperfusion Injury (IRI) represents a complex series of intracellular and extracellular events that results in molecular, cellular and tissue damage. It's induced by the transient deprivation of blood flow and oxygen, with lack of aerobic metabolism, and the return of blood flow during reperfusion with concomitant induction of innate and adaptive immunity, due to a release of oxygen-free radicals (OFR), cytokines/chemokines, and up-regulation of adhesion molecules, with consequent cellular and organ dysfunction. Focused on solid organ transplantation field, IRI is the main physiopathological event, resulting from an activation of TNF, that induce always an initial damage and that potentially could improve the damage and the development of clinical syndromes, (DGF, PNF).

Material and method trial design: Prospective, monocentric, placebo-controlled study to evaluate of Infliximab (one shot) in the early post operative period (72 h) after liver graft reperfusion. Endpoints: Primary Endpoints Evaluation of significant statistical reduction of IRI due to the following laboratory values at 1 POD: -mean ALAT level -mean Bilirubin level -mean CHE level -mean Leukocytes (CD4+) level Secondary Endpoints Statistical reduction of the occurrence of PDF, PNF, Acute rejection, biliary complication Results Study group: seven patients receiving infliximab after 30 min the Control group: seven patient.

Results: Study group Group control -mean ALAT level 80 U/l, 201 U/l -mean Bilirubin direct level 1.2, 1.8 mg/dl -mean CHE level 7010 U/l/ml, 1056 U/l/ml -mean (CD4+) level 800 $1/\mu$ l 2400 $1/\mu$ l No PNF and AR were detected in the study group.

Conclusion: Infliximab injection after 30 min after liver graft reperfusion showed good results in term of fast reduction of injury labor liver values. It seem influences a reduction of iperacute complications (PNF and AR) but not the risk of de.

P632

WHEN THE LIVER KILLS THE PATIENT: TIMING AND ROLE OF PRE-EMPTIVE HEPATECTOMY IN PATIENTS WITH ACUTE LIVER FAILURE

Doerte Wichmann¹, Ruth Ladurner¹, Alexandra Heinger², Jens Mayer², Marcus Mueller², Alfred Koenigsrainer¹, Silvio Nadalin¹

¹Department of General and Transplant Surgery, University Hospital Tuebingen; ²Department of Anaesthesiology, University Hospital Tuebingen

Background: Acute liver failure (ALF) is often associated with toxic liver syndrome (TLS) with consequent multiorgan failure (MOF) and death before transplantation. Through pre-emptive hepatectomy (PHE) the patient may be successfully transplanted. Indication and timing for emergency PEH remain controversial.

Material and methods: A PEH with temporary porto-caval shunt was performed in 8 patients with TLS and MOF secondary to ALF. Indication to PEH: 1. MOF, 2. hemodynamic instability with high dose of vasopressor 3. Therapy-refractory lactate acidosis. The clinical, metabolic and hemodynamic aspects of each patient and their outcome were analyzed.

Results: Etiology of ALF: acute liver transplant failure in two cases, acute on chronic liver failure in 5 and postoperative liver failure in 1. After a mean time of anhepatic phase of 24.5 h (range 4-46), five out of eight patients were successfully transplanted. Two of them died at mean 110 days and 3 are still alive 627 days after LT (153-1415 days). Three patients died without LT because of MOF 6 to 14 h after PEH.

Conclusion: In case of ALF with TLS a PHE should be performed in case of MOF with severe haemodynamic instability and therapy refractory lactate acidosis. This may allow the patient to be successful transplanted.

P633

CHANGING TREND OF INDICATION FOR LIVER TRANSPLANTATION FOR HEPATITIS B FROM DE-COMPENSATION TO HEPATOCELLULAR CARCINOMA

Hussien Elsiey¹, Waleed Alhamoud², Faisal Abaalkhail¹, Mohammed Al-Sebayel³, Hamad Al Bahill³, Almoutaz Hashim³

¹KFSH&RC; ²King Saud University; ³King Faisal Specialist Hospital & research Center

Background: The indication for liver transplantation for hepatitis B (HBV) infected patients are hepatic de-compensation, fulminant liver failure or development of hepatocellular carcinoma. Currently, adequate control of viral replication can be achieved with potent antiviral therapy. We suggest that with better control of viral replication using potent medication (entecavir and tenofovir) compensation, but now with control of viral replication, less de-compensation and more hepatocellular carcinoma (HCC) is the reason for liver transplantation.

Method: We retrospectively reviewed 133 liver transplantation performed for HBV from 1990 till 2012 at our institution. We divided them into two eras, the first era from 1990 till 2006 and the second era from 2007 till 2012, we looked at the number of HCC in each group and the hepatic de-compensation among HCC patients.

Result: Among 133 patients transplanted for HBV, 43 patients has HCC (32.3%), 66 patients were transplanted between 1990 to 2006 of which 18 patients has HCC (27%), hepatic de-compensation was seen in 60 out of 66 patients in this group with only one third of the HCC group being transplanted for MELD exception without de-compensation. While 67 were transplanted between 2007 to 2012 of which 26 patients has HCC (39.4%), hepatic de-compensation was seen in 48 out of 66, 73% of patients with HCC transplanted with MELD exception without de-compensation. In our cohort there was 40% overall increase in transplantation for HCC from the first era to the second with more than 4 fold increase in HCC cases without de-compensation done with MELD exception.

Conclusion: Due to use of highly potent antivirals against hepatitis B (tenofovir or entecavir) with sustained viral suppression, there is a changing trend of indication for liver transplantation for Hepatitis B from hepatic de-compensation to hepatocellular carcinoma.

P634

ASSOCIATION BETWEEN DELAYED GRAFT FUNCTION AND PATIENT SURVIVAL AFTER LIVER TRANSPLANTATION

Nicolas Meurisse, Ina Jochmans, Wim Laleman, Raymond Aerts, Frederik Nevens, Jacques Pirenne, Diethard Monbaliu
University Hospitals Leuven

Background: Delayed graft function (DGF), the immediate consequence of Ischemia Reperfusion Injury (IRI) severity, is characterized by a poor graft function after Liver Transplantation (LTx). DGF is defined by one of the following: peak AST/ALT > 2000 IU/l during the first 7 days post-LTx, total bilirubin > 10 mg/dl on day 7 or INR > 1.6 on day 7 post-LTx (Olthoff). We (i) identified risk factors of DGF and (ii) studied its impact on patient survival.

Methods: Between 01/2000 to 12/2010, we performed 541 LTx. Donor/recipient demographics, procurement/preservation/LTx data and patient survival were analyzed retrospectively.

Results: Of 137 patients developed DGF (26%). Univariate and multivariate analyses revealed cold ($p = 0.01$) and intra-operative warm ischemia ($P = 0.02$) times as independent risk factors of DGF. Recipient ICU/hospital stay and death were significantly associated with DGF. The 1 and 5-years patient survival (81.8% and 66.3%) in recipients with DGF was lower compared to recipients without DGF (94.5, 81.9%), $p < 0.01$).

Conclusion: Cold and intra-operative warm ischemia times were identified as independent risk factors for DGF post-LTx in our series. DGF is associated with a lower patient survival. Whenever possible, cold and intra-operative warm ischemia times should be kept as short as possible whilst strategies to further decrease IRI and DGF are needed.

P635

ARTERY FIRST REPERFUSION OF GRAFTS FROM DONORS AFTER CARDIAC DEATH (DCD); A COMPARATIVE MATCHED PAIR ANALYSIS

Irene Scalera, Glenn bonney, Giorgia Catalano, Simon Bramhall, Hynek Mergental, John Isaac, Darius F. Mirza, Thamara Perera, Paolo Muiresan Queen Elizabeth Hospital

Background: A recent systemic review analysing three previous trials in hepatic artery first reperfusion of DBD grafts concluded there remains a scarcity of data in this area. DCD grafts are subject to functional warm ischaemia and it is in these organs that there may indeed be a benefit of early reperfusion with arterialised blood. We aim to perform a matched pair analysis of grafts with artery first reperfusion compared to portal venous reperfusion.

Methods: Using a prospectively held database we compared all DCD grafts that underwent artery first reperfusion (AR) against a matched cohort of portal venous reperfusion (PVR). Matching was based on donor age, donor BMI, recipient MELD and cold ischaemic time; blinded to outcome. A comparative analysis of the donor and recipient factors between groups were performed. Post operative liver function, in-hospital and patient/graft survival was undertaken.

Results: A comparative analysis was performed on 11 matched pairs. There was no significant difference in donor and recipient characteristics between the AR and PVR groups. There was no significant difference in recipient WIT, acute kidney injury, in-hospital mortality, patient and graft survival. However, there was a trend towards a lower peak ALT and a significantly lower peak bilirubin in the AR compared to the PVR group (71 vs. 124 mm; $p = 0.03$).

Conclusion: This small retrospective analysis has demonstrates that outcomes following AR in DCD grafts are comparable to conventional PVR with a trend towards improved post-operative liver function following AR in DCD liver transplantation. A prospective randomised trial in this area is warranted.

P636

AORTO-HEPATIC CONDUITS IN LIVER TRANSPLANTATION – SHORT AND LONG TERM OUTCOMES

Satheesh Iype, Andrew Butler, Chris Watson Cambridge University Hospital

Objective: Early graft loss secondary to arterial inflow problems remains a major challenge in liver transplantation. Revascularisation of the liver using donor iliac artery conduits is a well-recognised procedure. This study analyzes the outcomes of aorto-hepatic conduits in adult deceased donor liver transplantation.

Methods: We retrospectively reviewed 702 orthotopic liver transplants (OLT) from January 2000 to September 2010. The data on indication, type of graft, complications and survival were obtained from the transplant database and patient case notes. We compared the outcomes of the liver transplants with aorto-hepatic conduits to those without conduits.

Results: Aorto-hepatic conduits were required in 54(7.6%) liver transplants. The median age of the recipients with conduits was 50 years (Range: 19–69). The male to female ratio was 1.5:1. Three (5%) of the recipients received the liver from DCD donor. Four patients had supracoealic conduits. A higher 30 day mortality of 11% compared to those without conduits(4%) was noted. Five out of six deaths were following hepatic artery thrombosis and retransplantation. The conduit patency at 3 years was 81%. Higher incidence of postoperative renal failure and need for renal support was noted in those requiring aorto-hepatic conduits. Five year graft survival of the liver transplants with conduits and those without conduits were 63% and 70% respectively.

Results: Aorto-hepatic conduits in liver transplantation have good long term results and has no negative impact on graft survival. In the short term, there is increased incidence of renal failure and 30 day mortality.

P637

THE LIMAX TEST AND MRT BASED VOLUMETRIC ANALYSIS IN LIVING DONOR LIVER TRANSPLANTATION – A CASE REPORT

Maximilian Jara, Sabine Gebhardt, Maciej Malinowski, Antje Schulz, Gero Puhl, Peter Neuhaus, Martin Stockmann Department of General, Charité, Campus Virchow Clinic, University Hospital, Berlin Visceral and Trans

Background: Due to the perpetual shortage of donor organs living donor liver transplantation (LDLT) has emerged as an option to perform liver transplantation independent from the current deceased donor allocation system. However, donor safety is imperative and new methods need to be explored to improve the safety of LDLT. Beyond that, the fine pathophysiological mechanism of regeneration of liver function after partial resection and partial transplantation remains unclear. Methods

In this case-report data of two donor-recipient pairs was used. LiMAX (Liver Maximum Capacity) test and MRT examinations are routinely performed for donor evaluation. Based on volumetric analysis future remnant liver function (FRLF) is estimated to ensure maximal donor safety. LiMAX tests are performed on postoperative day (POD) 1, 3, 5 and 10 in both, recipients and

donors. We reviewed the accuracy of preoperative estimated future remnant liver function and the pace of liver function recovery.

Results: Volumetric analysis accurately predicted intraoperative measured graft weight. (Pair 1: 1136 ml vs. 1107 ml respectively; pair 2: 1365 ml vs. 1175 ml respectively). Preoperative donor FRLF showed good correlation to measured liver function on POD 1 (Donor 1: 227 vs. 244 $\mu\text{g}/\text{kg}/\text{h}$ respectively; donor 2: 110 vs. 99 $\mu\text{g}/\text{kg}/\text{h}$ respectively). Preoperative liver function was decreased in LDLT recipients ($155 \pm 102 \mu\text{g}/\text{kg}/\text{h}$) compared with donors ($440 \pm 183 \mu\text{g}/\text{kg}/\text{h}$). After surgery LiMAX values dropped in donors but liver function seems to recover within 10 days after surgery ($566 \mu\text{g}/\text{kg}/\text{h}$). Also recipients showed constant improvement in liver function after successful transplantation reaching normal values ($329 \pm 34 \mu\text{g}/\text{kg}/\text{h}$) on POD 10.

Conclusion: In conclusion LiMAX and MRT based volumetric analysis might provide accurate estimation of postoperative liver function of the donor. Liver function seems to recover rapidly within the first postoperative days in both, donors and recipients, after successful LDLT.

P638

RISK FACTORS TO DEVELOP NON-ANASTOMOTIC STRICTURES AFTER LIVER TRANSPLANTATION

Nicolas Meurisse¹, Ina Jochmans¹, Wim Laleman¹, Raymond Aerts¹, Steffen Fieuws², Frederik Nevens¹, Jacques Pirenne¹, Diethard Monbaliu¹

¹University Hospitals Leuven; ²Leuven Biostatistics and Statistical Bioinformatics Centre

Background: Non Anastomotic Strictures (NAS) are often referred to as the 'Achilles heel' of Liver Transplantation (LTx). We aimed to (i) identify risk factors to develop NAS and (ii) study its impact on patient survival.

Methods: Between 01/2000 to 12/2010, 535 LTx were performed in our center. Donor/recipient demographics, procurement/preservation/LTx data and patient survival were analyzed retrospectively.

Results: Of 68 patients developed NAS (13%). Univariate analysis revealed acute liver failure (ALF) ($p < 0.01$), donor height/weight ($p = 0.04$), imported livers (vs. locally procured) ($p < 0.01$), donation after circulatory death (DCD) ($p = 0.02$), Histidine-Tryptophan-ketoglutarate (HTK) ($p < 0.01$) and cold ischemic time (CIT) ($p < 0.01$) as significant risk factors to develop NAS. The total bilirubine (mg/dl) at day 7 in recipient was significantly associated with risk to develop NAS (0.01). Upon multivariate analysis, ALF, imported livers, DCD and CIT remained significantly associated with the risk to develop NAS. The risk of death was not increased in case of NAS.

Conclusion: We identified ALF, imported livers, DCD and CIT as risk factors to develop NAS post-LTx in our series. The development of strategies to decrease the incidence of NAS especially with the increased use of less than ideal liver grafts remains warranted.

P639

IMMUNOSUPPRESSION SWITCH DOES NOT INFLUENCE THE HERNIA RECURRENCE AFTER INCISIONAL REPAIR POST LIVER TRANSPLANTATION

Jun Li¹, Alexandros Kantas², Martina Koch², Eike Achilles², Lutz Fischer², Martina Sterneck², Björn Nashan²

¹University Medical Center Hamburg-Eppendorf; ²Hepatobiliary Surgery and Visceral Transplantation, University Medical Center Hamburg-Eppendorf

Background: Incisional hernias (IHs) are common complications after liver transplantation (LT) with a reported incidence of 1.7% to 34.3%. The traditional repair techniques have been refined because of the high rate of incisional hernia recurrence up to 20%. Perioperative, mTORi or MMF are usually omitted to reduce wound healing complications. The purpose of this retrospective study was to evaluate the risk factors for hernia recurrence with focus on the role of immunosuppressive therapy at the perioperative phase.

Patient and methods: The study included the patients with incisional hernia repair consecutively between 2008 to 2012. Risk factors such as type of incision for liver transplantation, time to hernia repair after transplantation, maintenance immunosuppressive therapy, age, gender, BMI, ascites, diabetes, hernia size, complication within 1 month after hernia repair were collected retrospectively from the database. The recurrence of incisional hernia was diagnosed by clinical and sonographical examination. Univariate and multivariate analysis were performed.

Results: There were 142 hernia repair carried out in our department. Among them, 48 were after liver transplantation. The surgical repair consisted of laparoscopic IPOM, open sublay, open onlay technique. Immunosuppression was changed perioperatively in 19 patients (12 had MMF, 7 had mTORi), and not changed in 29 patients (10 had MMF, 8 had mTORi). Four patients had an impaired wound healing or infectious complications. During the follow-up of (4–43 months), 9 patients developed recurrent hernia. The multivariate analysis failed to identify the immunosuppression switch to be a risk factor for hernia recurrence.

Conclusion: Perioperative switch of immunosuppression, such as MMF or mTORi, is not justified.

P640

HCC: EXCELLENTS OUTCOMES IN 10 YEARS OF EXPERIENCE IN LIVER TRANSPLANTATION AT THE VIRGEN DE LAS NIEVES UNIVERSITY HOSPITAL, GRANADA, SPAIN

Ylliam Fundora Suárez, Karim Muffak-Granero, Andrea Vilchez, Javier Valdivia, Natalia Zambudio, Trinidad Villegas, Antonio Becerra, Daniel Garrote Lara, Jose Antonio Ferron Orijuela
Virgen de las Nieves University Hospital

Objective: To describe our experience in HCC liver transplantation.

Material and methods: The study included recipients on the waiting list including diagnosed with HCC who met Milan criteria, between 2002 and 2012 at the Hospital Virgen de las Nieves, Granada, Spain. We analyzed the diagnostic studies performed at enrollment (US-TAC-MRI) and pathological study of liver after explant. The embodiment of TACE and pathological results in the liver explant. We analyzed the use of TACE in HCC recipients and the incidence of arterial thrombosis. Analysis of survival in this group of patients. The study was performed using SPSS version 15 for Windows.

Results: Between March 2002 and 2012 there were a total of 250 liver transplants, including 58 recipients included on the waiting list with a diagnosis of HCC. The mean age was 56.7 years, 82% were men. The average time on the waiting list was 187 ± 167 days. At inclusion 18 patients were diagnosed by CT + US, whereas in 12 patients MRI was also performed. In 25 patients underwent TACE. Two patients were included after making downstaging after TACE. In two patients underwent FNA pretransplant tests being inconclusive (one negative and one inconclusive for HCC). In analyzing the results of the explant was found embolized 1 lesion with complete necrosis in 10 patients and incomplete necrosis in 6. While in three patients were completely embolized two lesions and two with incomplete necrosis. In a patient with three lesions were found to include three completely necrotic lesions. The degree of differentiation had the following distribution: 24% good, 25.9% moderate and 3.4% poorly differentiated. In a patient cell nests were found in necrosis. In 15% of patients diagnosed with HCC were no found lesions. Only one patient who had undergone TACE file an arterial thrombosis. At the end of the study, with a mean follow-up through 51 ± 33 months, 62% of the patients was alive.

Conclusions: The results of our study are comparable with those pu.

P641

HYPERBARIC OXYGENATION AND LIVER RESECTION FOR HEPATIC ARTERY AND PORTAL VEIN THROMBOSIS AFTER LIVER TRANSPLANTATION

Georg Werkgartner¹, Doris Wagner¹, Daniela Kniepeiss¹, Freyja Maria Smolle-Jüttner², Hans Jörg Mischinger³

¹Division for Transplantation, Department of Surgery, Medical University of Graz; ²Division for Thoracic and Hyperbaric Surgery, Department of Surgery, Medical University of Graz; ³Division for General Surgery, Department of Surgery, Medical University of Graz

Background: Late hepatic artery thrombosis (HAT) is a very rare phenomenon after whole graft liver transplantation (OLT). A combination of HAT and portal vein thrombosis (PVT) has not been reported yet. We would like to present the successful management of a patient with HAT and PVT after OLT.

Case: A 59 years old male presented in 09/2012 after his OLT 02/2011 with right sided abdominal pain and episodes of fever. Liver and biliary enzymes were elevated, inflammatory signs were moderately higher. A CT scan showed HAT of the right hepatic artery branch and PVT of the right portal vein branch in combination with a complete necrosis of the right lobe. As no radiological intervention was possible hyperbaric oxygenation (HBO) was installed to ameliorate oxygenation for 3 months. The follow up CT scan showed no progression of the necrosis or signs for abscesses. The right lobe was resected completely and the patient continued with postoperative HBO therapy. He recovered; liver enzymes restored until normal with an uneventful follow up for 3 months.

Discussion: This surely is a unique case of HAT and PVT after OLT. Surgical management in combination with HBO therapy worked well for our patient.

P642

IN-HOSPITAL AND FOLLOW-UP OUTCOMES OF PATIENT UNDERGOING ORTHOTOPIC LIVER TRANSPLANTATION AFTER HEPATIC ARTERY RECONSTRUCTION WITH ILIAC INTERPOSITION GRAFT

Jiang Hua Ran, Sheng Ning Zhang, Jing Liu, Yi Ming Chen, Lai Bang Li, Li Li
Liver Transplant Center of The First Hospital of Kunming City

Background: Orthotopic liver transplantation (OLT) is the only definitive therapeutic modality for patients with end-stage liver diseases. Hepatic artery (HA) reconstruction is considered as the key to the success of liver transplantation and reducing postoperative complications, due to maintain good hepatic arterial blood supply. To explore the indications, surgical method, and postoperative treatment by studying in-hospital and follow-up outcomes of

Chinese patients undergoing orthotopic liver transplantation (OLT) after hepatic artery (HA) reconstruction with iliac interposition graft.

Methods: Of 17 patients underwent conventional OLT (non-bypass group) and 17 patients underwent OLT with hepatic artery reconstruction by iliac interposition bypass (bypass group). Complications were evaluated by the clinical presentations, liver function changes, and hepatic artery ultrasound findings.

Results: There were no differences between groups in terms of age, sex, and primary disease. The average surgery time of bypass group was longer than that of non-bypass group (82.29±22.00 vs. 48.47±11.86 min, $p < 0.01$). Recipients of bypass had more blood loss than non-bypass group (7047.06±976.04 vs. 4841.18±1268.39 ml, $p < 0.01$). One patient was suffered from biliary fistula and one patient experienced biliary infection combined with intrahepatic bile neoplasia. The rest 14 patients were doing well postoperatively. The hepatic function of two groups was recovered well. In postoperative continuous 10 days, there was no significantly difference of HA peak blood flow velocity between bypass group and non-bypass group. The bypass patients had been followed up for an average time of 45.2 months (20–56 months). The patients had no complications such as artery stenosis and arterial thrombosis. And no one died of artery complications.

Conclusion: Iliac arterial interpositional graft is an effective and reliable method of HA reconstruction in OLT when the use of hepatic artery is not possible.

P643

PYOGENIC SPONDYLODISCITIS CAUSED BY METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS (MRSA) AFTER LIVING DONOR LIVER TRANSPLANTATION. A CASE REPORT

Joo S. Kim, Beong H. Sohn, Jang Y. Jeon
Hallym University

Methicillin-resistant *Staphylococcus aureus* (MRSA) infection frequently complicates the postoperative course of liver transplant recipients. It has been well described that MRSA associated bacteremia, pneumonia and surgical site infection are common. But, MRSA infection manifesting as pyogenic spondylodiscitis is very rare. To our knowledge, pyogenic spondylodiscitis due to MRSA in lumbar spine after living donor liver transplantation (LDLT) has not been previously reported. Here, we report a 50-year-old man who developed pyogenic spondylodiscitis caused by MRSA after LDLT. Our patient underwent LDLT for HBV related cirrhosis using modified right lobe. Immunosuppressive treatment was administered with basiliximab, tacrolimus, corticosteroids and mycophenolate mofetil. He discharged on postoperative 28th day with uncomplicated course. At one week after discharge the patient was readmitted for abdominal pain and high fever. Bile leakage at the anastomosis site was found by endoscopic retrograde cholangiopancreatography (ERCP) and managed successfully with endoscopic nasobiliary drainage (ENBD). The culture of drained fluid showed MRSA and the patient was treated with vancomycin for 4 weeks, and resulted in resolution of the infection. However, one month later the patient presented with severe back pain. At this time, MRI showed massive spondylodiscitis of lumbar 2–3 spine and paraspinous abscess formation. Our patient was treated by surgical debridement and primary bone graft. MRSA was cultured from the abscess specimen. Postoperatively, the patient received intravenous vancomycin for 2 weeks and revealed satisfactory outcome without any neurological sequelae. Presently the patient is followed up without rejection and other complications.

P644

VIROLOGIC BREAKTHROUGH FOR HBV AFTER LIVING DONOR LIVER TRANSPLANTATION ON ENTECAVIR: A CASE REPORT

Iman Montasser
Ain Shams Center for Organ Transplantation

Introduction: In Egypt, where LDLT is the only available option, most transplanted cases are due to HCV related ESLD or HCC. However, other etiologies co-exist as hepatitis B virus (HBV). Without preventive therapy, HBV recurrence after liver transplantation was common and can lead to graft failure and death. The antiviral regimen should be robust and minimize the risk of breakthrough mutations.

Patients and methods: In the period from March 2008 till April 2013 we transplanted 124 cases of LDLT, 4 of them were due to HBV related end stage liver disease and/or HCC and 2 were combined HCV and HBV. According to our protocol all patients were HBV DNA negative before transplant and received intra and postoperative IM anti HBV immunoglobulin and lifelong post transplant nucleos(t)ide analogue. We recorded a single case of virologic breakthrough on Entecavir after 32 months in male patient 45 years who was transplanted for HBV related ESLD and on strict and adherent follow up on entecavir. Breakthrough was documented pathologically by liver biopsy; unfortunately genetic mutation analysis was not available. Patient was treated by adding Adifovir for 2 weeks then shifted to Tenofovir when became available in Egyptian market with normalization of liver enzymes and negative HBV DNA PCR up till now (13 months).

Conclusion: Liver transplantation for HBV carries risk of recurrence even with drugs with high genetic barrier. Regular follow up and early detection of breakthrough is mandatory. Rescue therapy is life saving before graft failure.

P645

CHANGING TRANSFUSION PRACTICE IN LIVER TRANSPLANTATION FROM 1996 TO 2009 – A SINGLE CENTRE RETROSPECTIVE REVIEW

Rebecca Campbell¹, Anneliese Rigby², Thomas Bishop³, Zoka Milan²
¹St George's Hospital; ²King's College Hospital, London; ³Whipp's Cross University Hospital

Background: The impact of blood component transfusion in liver transplantation has significance for both patients and health care economics (Feltracco et al. World Journal of Hepatology 2013;27:5 (1): 1–15). Therefore we decided to review the practice of intraoperative blood component and fluid transfusion in our tertiary liver transplant centre.

Methods: A database of adult liver transplants undertaken at King's College Hospital, London, was retrospectively reviewed for two three-year periods since 1996. Data was analysed using Sigma Stat v3.0.

Results: Results are displayed in the table below.

Conclusion: Though not statistically significant there has been a decrease in blood loss. There is a decrease in RBC and colloid use over the examined period but an increase in use of FFP and platelets. The change in use of clotting products is not reflected in a change in final INR. However, there are improvements in final pH, lactate and base excess.

P646

HEPATIC BLOOD FLOW IN LATE SEPSIS PATIENTS

Amany AbdelMaqsood¹, Abir Zakaria², Fayroze Shokry³
¹Cairo University; ²Faculty of Medicine Cairo University; ³Alayat central hospital

Background: Systemic inflammatory response syndrome (SIRS), sepsis, and severe sepsis influence total hepatic blood flow. However there are conflicting data on the time of its assessment, methodology, study design, and differentiation in terms of whether the condition is an experimental SIRS, sepsis, or a human clinical syndrome. The aim of this study was to define hepatic blood flow changes in SIRS, late sepsis, and severe sepsis patients, aiming to predict mortality in this vulnerable group.

Methods and materials: Assessment of the total hepatic blood flow and the contribution of hepatic arterial blood flow (HABF) and portal venous blood flow using a Doppler vascular ultrasound in 44 individuals divided into four groups; SIRS, sepsis, severe sepsis patients, and control group, aiming at a clear prognostic parameter that can predict the patient's outcome.

Results: There was a clear cutoff point of 16.09 ml/min for HABF, above which the hazard ratio for death was 5.6046, with a 95% confidence interval of 2.0078–15.6451 and a p-value of 0.0011 in late sepsis patients. The predictive potential for this HABF cutoff for patient mortality showed a sensitivity of 80%, specificity of 73.7%, positive predictive value of 70.6%, negative predictive value of 82.4%, 95% confidence interval of 0.612–0.907, and p-value of less than 0.0004. There was a significant positive correlation between the HABF and APACHE II scores ($p = 0.023$). Cox regression analysis showed that only the APACHE II score and HABF were independent predictors for patients' outcome.

Conclusion: Duplex ultrasound assessment was a useful bedside method for predicting mortality in late sepsis patients through estimation of HABF, with a reasonable predictive potential at a definite cutoff level. The study defined for the first time a cutoff point for HABF above which mortality increased significantly (about 5.6 times).

P648

ADAPTING LIVER TRANSPLANTATION FOR HILAR NON RESECTABLE STAGE I-II CHOLANGIO CARCINOMAS ACCORDING TO MAYO CLINIC'S PROTOCOL TO A SINGLE CENTER WITH LOW WAITING LIST TIME – THE OSLO EXPERIENCE

Morten Hagness¹, Svein Dueland², Jon Solheim¹, Pål-Dag Line¹, Aksel Foss¹
¹Section for Transplantation Surgery, Oslo University Hospital; ²Department of Oncology, Oslo University Hospital

Background: The Mayo Clinic's protocol (MCP) for treating unresectable hilar cholangio carcinomas (CCA) with aggressive neoadjuvant treatment, staging procedures and liver transplantation (Lt) yields 5 year overall survival (OS) rate of about 70%. Oslo University Hospital directly adopted the protocol in 2009 as an institutional protocol. We here report the Norwegian experience.

Materials/methods: Medical records were retrospectively reviewed.

Results: Since 2009, six patients underwent Lt for unresectable hilar CCA according to MCP. Three of these have died from cancer, one from graft dysfunction and one is terminally ill from cancer disease. Median OS was 25.9 months (95% CI 14.6–37.2 months); 3 years OS rate was 42%. Median disease free survival was 20.1 months (95% CI 13.9–26.3 months). Median time on waiting list was 15 days (Range 4–29 days).

Discussion: The outcome seems inferior to the published results from Mayo Clinic and US. Generally, Oslo has excellent survival rates after Lt, mainly due to short waiting list. The dropout rate on waiting list in US for this indication is 25%, one could speculate on whether the short waiting time in Norway influence survival negatively.

Conclusion: Adaption of the MCP for CCA in Oslo seems to result in inferior outcome. Further investigation is needed.

P649

THE SYNERGIC EFFECT OF N-(3,4-DIMETHOXYCINNAMONYL)ANTHRANILIC ACID WITH CYCLOSPORIN A IN MURINE ORTHOTOPIC LIVER TRANSPLANTATION MODEL

Jinyan Zhang, Junming Xu, Zhihai Peng
 Shanghai Jiaotong University Affiliated 1st People's Hospital

Tryptophan-derived metabolites, such as 3-hydroxyanthranilic acid, 3-hydroxykynurenic acid and quinolinic acid, induce activated T cell apoptosis, which is an important mechanism in indoleamine 2,3-dioxygenase (IDO)-mediated T cells uppression. In this research, the murine orthotopic liver transplantation model was utilized to investigate the immunosuppressive effect of 3,4-DAA on allogeneic graft rejection. The DA-Lewis rat orthotopic liver transplantation model was established and divided into four groups: group A, negative control group, treatment with normal saline 2 ml/day; group B, treatment with 3,4-DAA (400 mg/kg/day); group C, treatment with cyclosporin A (CsA) (2.5 mg/kg/day); group D, treatment with cyclosporin A (CsA) (5 mg/kg/day); group E, treatment with 3,4-DAA (400 mg/kg/day) and CsA (2.5 mg/kg/day). We found that 3,4-DAA possesses immunosuppressive function, moreover, the regimen (3,4-DAA plus CsA) could reach equal clinical outcome by only half the normal dosage of CsA, which indicated that 3,4-DAA may be used as an adjunct drug in the recipients treated with CsA-based immunosuppressive regimen.

P650

RADIOLOGICAL AND PATHOLOGICAL CORRELATION FOR HCC TREATED WITH LIVER TRANSPLANTATION

Mohamed Abdelfattah, Hadeel Al-manea, Mohamed Neimatallah, Hussien Elsiesy, Mohammed Al-Sebayel, Dieter Broering
 King Faisal Specialist Hospital & Reasech Center

Introduction: Early detection Hepatocellular carcinoma (HCC) is clearly critical to patient outcome. Although many CT and magnetic resonance (MR) imaging studies have reported high diagnostic accuracy for HCC and Dysplastic Nodules (DN) in patients with cirrhosis, most of these have been limited by study design, incomplete pathologic correlation and suboptimal imaging techniques. Correlation between explant pathology and pretransplant radiology is of prime importance to choose the suitable line of treatment for liver nodules in cirrhotic patients.

Methods: Of 100 patients who underwent liver transplantation for the presence of HCC were retrospectively reviewed. Radiological diagnosis for HCC was performed using one or two contrast enhanced dynamic imaging studies including Multidetector computed tomography (MDCT) and MRI. Pathological examination was made using whole liver explant examination by senior pathologists who have experience in liver pathology. Pathologists had knowledge about the pretransplant radiological findings. Radiological and pathological correlation was made between explant pathology and radiological findings. Correlation was made on per nodule level including size, location and nature.

Results: A total 230 nodules were identified in explant pathology from 100 liver transplant patients. Overall; 208 nodules were radiologically identified before transplant (90.4%), while pretransplant imaging modalities failed to show 22 nodules (9.6%). Out of the identified nodules 59 were misinterpreted. 114 nodules were found to be more than or equal to 2 cm in maximum dimensions by pathology (group 1) compared to 67 between 1 and 2 cm (group 2) and 49 less than 1 cm (group 3). percentage of missed or misinterpreted nodules was significantly less in first group as compared to the other two groups, ($p = 0.000$).

Conclusion: Pretransplant imaging modalities are very reliable in diagnosis of cirrhotic liver nodules specially in small lesions.

P651

LIVER ENZYMES ABOVE 5000 U/L AFTER LIVER TRANSPLANTATION: ALWAYS RETRANSPLANT?

Dieter Paul Hoyer, Fuat H. Saner, Georgios C. Sotiropoulos, Jüergen Treckmann, Andreas Paul, Zoltan Mathé
 University Hospital Essen

Background: Preservation induced organ injury is assumed to induce elevation of alanine aminotransferase and aspartate aminotransferase after liver transplantation (LTx). Values above 5000U/l usually are regarded as extreme hepatic preservation injury (EHPI). Some patients and organs recover from this critical condition. The aim of the study was to evaluate factors contributing to graft and patient survival after EHPI.

Methods: From chart review we identified 64 out of 917 LTx adult patients (mean age 51.1 years; 68.8% males) transplanted between 11/2003 and 2/2012, who presented EHPI after OLT. Standard donor and recipient factors

were analyzed and correlated with graft and patient survival by univariable/multivariable logistic regression and cox proportional hazards.

Results: After adjustment by multivariable cox proportional hazards recipient's BMI ($p = 0.0100$), labMELD before OLT ($p = 0.0233$) and labMELD pop1 ($p = 0.0062$) were independently associated with patient survival. 30-days and 12 months-survival in patients with a labMELD pop1 higher than 30.8 was 21.4%, respectively, while patients with a labMELD pop1 lower than 30.8 displayed 30-days and 12 months survival rates of 80% and 71.8%, respectively ($p < 0.0001$).

Conclusion: Listing for Retransplantation in the setting of EHPI after LTx should be based on bedside clinical assessment. Factors associated with survival after EHPI might be considered additionally.

P652

EXPERIENCES OF ADULT LIVING DONOR LIVER TRANSPLANTATION IN THE REPUBLIC OF KAZAKHSTAN

Zhetkergen Arzykulov, Manas Seisembayev, Manas Ramazanov, Daniyar Toksanbayev, Nariman Sadykov
Syzganov's National Scientific Center of Surgery

In the Republic of Kazakhstan the problem of liver diseases complicated with terminal liver failure is an actual one. The only way of radical treating of these patients is to provide a Liver Transplantation. This kind of service was unavailable in Kazakhstan before 2011. The main problem was the country's lack of cadaveric donation, due to specific mentality of the population and imperfect legislation. Liver Transplantation program of the Republic of Kazakhstan is now in its initial stage, but it develops. First case of Liver Transplantation was performed in 2011, 9th December. For today, three Centers in two big cities have made 11 cases of Living Donor Liver Transplantations for adult recipients. Six of them (54.5%) had liver cirrhosis caused viral hepatitis, another five – liver cirrhosis of non-viral etiology: primary biliary cirrhosis – two cases (18.2%), autoimmune hepatitis – two cases (18.2%), idiopathic liver cirrhosis – one case (9.1%). The patients' age ranged from 20 to 52 years. MELD score ranged from 13 to 25. By relation degree, most of the donors of liver fragments were siblings (brothers or sisters) – nine cases (81.8%). In one case, donor was mother of the patient (9.1%), in another one case – patients' wife (9.1%). The preliminary findings based on a small experience showed a good perceptiveness of developing of Living Donor Liver Transplantation program in Kazakhstan. Despite the numerous problems, Liver Transplantation Program tends to its development, as only way of radical treatment of patients with end stages of the liver diseases. There is reason to believe that the number of such operations in the Republic of Kazakhstan will increase in the future.

P653

MODIFIED HEPATICO-JEJUNOSTOMY FOR SEVERED BILE DUCT: A HYBRID TECHNIQUE

Ahmed Nabil, Hesham Amer, Amr Nassef, Sayed Marei
Faculty of Medicine, Cairo University

Background: Advances in surgical techniques and management have decreased the morbidity and mortality after hepatobiliary operations, however, bile duct injuries remain a major cause of postoperative morbidity and mortality. Early recognition and adequate multidisciplinary approach is the cornerstone for the optimal final outcome.

Patients and methods: A prospective study including 10 cases with severed bile duct injuries (post cholecystectomy). The suggested hybrid technique involves preoperative insertion of percutaneous transhepatic draining (PTD) catheter and intraoperative introduction of these catheters into a suitable jejunal conduit. Percutaneous cholangiography is done one week postoperative to assess the anastomosis. A Follow up magnetic resonance cholangiopancreatography (MRCP) was done at 6 and 12 months.

Results: The technique showed significant improvement in the outcome of biliary reconstruction. Eight patients showed rapid recovery post operatively. One patient needed a redo surgery after migration of the stent and leakage from the anastomosis. Another patient in the follow up MRCP revealed dilated intrahepatic biliary radicles, however with no rise in bilirubin and cholestatic enzymes.

Conclusion: This technique provides a safe and sound bilio-enteric continuity with early rehabilitation of the patients, low incidence of complications and long term patency of the bilio-enteric anastomosis.

P654

CAVAL REPLACEMENT LIVING-DONOR LIVER TRANSPLANT: FIRST ARAB WORLD CASE REPORTS

Firas Zahr Eldeen, Mohamed R. Abdelfattah, Yasser Alsheikh, Yehia Saleh, Bandar Alqahtani, Hamad Al Bahili, Mohammed Al Sebayel, Dieter Broering
King Faisal Specialist Hospital and Research Center

Introduction: Living-donor liver transplant (LDLT) for hepatocellular carcinoma (HCC) located on hepatocaval confluence or in contact with Inferior Vena

Cava (IVC) is technically challenging. Additionally; it poses considerable risk for tumor recurrence and risk of thrombosis related to IVC reconstruction.

Methods and results: We report two cases of LDLT combined with IVC reconstruction using cryopreserved iliac vein graft (CPIVG) after en bloc resection of the liver with all or part of retrohepatic IVC for a case of hepatoblastoma and hepatocellular carcinoma respectively. The first patient is 10 years old boy with history of right hepatectomy followed by adjuvant chemotherapy for hepatoblastoma, he had local recurrence and he was subjected to non-anatomical resection of segment IV followed by adjuvant chemotherapy. Unfortunately, patient had 2nd local recurrence and he was referred to our institution for management, he received pretransplant chemotherapy followed by LDLT using left lateral segment from his father. During the procedure completion hepatectomy was done with total resection of retro hepatic IVC. Reconstruction was done using CPIVG. The second patient is 59 years old female patient who had HBV related cirrhosis with HCC at segment VII abutting IVC (Fig 1). Total hepatectomy was performed along with partial resection of IVC (7 cm in length and around 50% of IVC circumference). Reconstruction of IVC was done utilizing CPIVG. Postoperative course was uneventful for both patients. Patency and no evidence of tumor recurrence were demonstrated at short term follow up.

Conclusion: Caval replacement using CPIVG during LDLT is safe and feasible for treatment group of patients with tumors abutting IVC. However long term follow up results should be reported.

P655

EXCESS MORTALITY BEYOND 1 YEAR AFTER LIVER TRANSPLANTATION – A NORDIC MULTICENTER POPULATION-BASED STUDY

Fredrik Åberg¹, Mika Gissler², Tom Hemming Karlsen³, Bo-Göran Ericzon⁴, Aksel Foss⁵, Allan Rasmussen⁵, William Bennet⁶, Michael Olausson⁶, Helena Isoniemi¹

¹Helsinki University Hospital, Finland; ²National Institute for Health and Welfare, Finland and Nordic School of Public Health, Sweden; ³Oslo University Hospital, Rikshospitalet, Norway; ⁴Karolinska University Hospital, Sweden; ⁵Rigshospitalet University of Copenhagen, Denmark; ⁶Sahlgrenska University Hospital, Sweden

Background: A major challenge in liver transplantation (LT) is shifting towards improving survival beyond the first year. Understanding the causes for premature death is a prerequisite for improving long-term outcome.

Methods: Overall and cause-specific mortality rates among all LT patients in the Nordic countries transplanted in 1985–2009 and survived 1 year post-LT were divided by expected rates in the general population adjusted for age, sex, calendar time, and country to yield standardised mortality ratios (SMRs). Patient data came from the Nordic LT Registry, and general population data from national cause-of-death statistics.

Results: Among 3299 patients (23 691 person-year follow-up, mean 8.2 years), 763 deaths occurred. Patient survival >1 year remained unchanged over time and a gap of 20% at 10 years was noted to the expected survival in the matched general population. SMR >1 year post-LT was 2.4 (95% CI 2.2–2.6), and SMR for death before age 75 was 5.8 (95% CI 5.4–6.3). Significantly elevated cause-specific SMRs were noted for infection, malignancy, liver disease, genitourinary disease, and suicide and intentional self-harm, but not for cardiovascular disease (Table). According to primary LT indication, all-cause SMR for death before age 75 was highest in HCC (SMR 33, 95% CI 26–41), followed by alcoholic liver disease (SMR 18, 14–22) and HCV (SMR 12, 10–16). Acute liver failure and HCV showed highest SMRs for infection, HCC for malignancy, and ALD for liver disease (mostly disease recurrence). SMR from cardiovascular disease was significantly elevated only in PBC, alcoholic disease and patients aged 45–59 at LT.

Conclusions: Mortality >1 year after LT is considerable higher than in the general population and has not improved over time. High relative mortality from infection, genitourinary disease, liver disease, suicide, and malignancies merits increased attention in clinical practice and future research.

P656

INTERLEUKIN 28 B GENOTYPE AS A PREDICTOR OF RESPONSE TO THERAPY WITH PEGYLATED INTERFERON PLUS RIBAVIRIN IN HCV INFECTED EGYPTIAN PATIENTS

Mohammad El Sherbiny¹, Wael Mohammad Aref², Mona Mohammad Fathy², Mohammad Sherif El Hawary²

¹Kasr Al Aini Hospital, Faculty of Medicine, Cairo University; ²Faculty of Medicine, Cairo University

Background: Hepatitis C virus (HCV) infection is a major health problem throughout the world. Egypt has the highest worldwide prevalence of HCV (10–20%). (Kamal, S.M. and Nasser, I.A. Hepatology 47 (4): 1371–1383). Pre treatment predictors of response are useful when assessing the benefits and risks of therapy with patients. The ability to respond to interferon-based therapy may be genetically determined. Recent genome-wide association studies have identified genetic determinants of treatment response in HCV-infected patients treated with pegylated interferon and ribavirin. A single nucleotide polymor-

phism near the Interleukin 28B gene on chromosome 19 coding for interferon-lambda-3 is associated with an approximately 2-fold difference in sustained virological response (SVR) rates among patients. (Thompson, et al. Gastroenterology; 139:120–129).

Methods: The study performed on a total number of 100 patients infected with HCV who are candidate for treatment with pegylated interferon plus ribavirin for 48 weeks (after written consent) at Kasr Al Aini Hospital. * Pre-treatment evaluation of patients with HCV: (i) Complete history taking and thorough clinical examination. (ii) Laboratory testing: ♣ Complete liver function tests. ♣ Renal profile. ♣ Complete blood count. ♣ Thyroid profile. ♣ Fasting and post prandial blood sugar. ♣ Antinuclear antibody (ANA) and alpha fetoprotein (AFP). ♣ Hepatitis B surface antigen. ♣ Quantitative HCV RNA level by PCR. ♣ Interleukin 28 B genotyping by Real Time PCR technique using TaqMan SNP assay. (iii) Abdominal ultrasound. (iv) Liver biopsy: to determine the degree of inflammation and stage of fibrosis.

Result: Patients with C/C genotype had higher rates with SVR than non C/C (85.1% vs. 44.1%, $p < 0.001$).

Conclusion: The IL28B polymorphism of HCV were significant pre-treatment predictors of response to pegylated interferon plus ribavirin in Egyptian patients.

P657

SYNTHETIC BIOABSORBABLE STENT FOR DUCT-TO-DUCT BILIARY RECONSTRUCTION IN LIVER TRANSPLANTATION

*Libor Janousek, Jiri Fronek, Martin Oliverius
IKEM, Transplant Surgery*

Background: Biliary stricture remains a significant cause of morbidity after liver transplantation. The incidence of biliary strictures in patients who have undergone liver transplantation (LT) with duct-to-duct biliary reconstruction ranges from 10% to 30%. Most of the initial experience on self-expandable biodegradable stents has been in urological applications. Encouraging experience in these medical fields led to the trial of these stents in experimental liver surgery also. In the past, some authors achieved encouraging results with the biodegradable stent in pancreatic and biliary applications.

Methods/materials: On preliminary group of the five patients we investigated the role of absorbable biliary stent with aim to proof patency of duct-to-duct biliary anastomosis and toxicity of a stent. The stents are made of machine-knitted polydioxanone monofilaments. The recipients of the liver graft were followed up for 12 months.

Results: Our first results demonstrate that duct-to-duct biliary reconstruction using an absorbable internal stent had good patency in all four patients. The anastomoses were not accompanied with signs of biliary leakage or stricture in any of the cases. There was no stone formation or pancreatic irritation caused by stent degradation observed after liver transplantation. The biliary stent was absorbed completely without any adverse effects. Nobody developed primary non function of the liver graft.

Conclusion: The novel stent seems to be easy to insert, nontoxic, disappears safely from the anastomosis Further prospective randomized study is needed to estimate the efficacy of the bioabsorbable stents.

P658

LIVER TRANSPLANTATION (LT) FOR HEPATOCELLULAR CARCINOMA (HCC) FOLLOWING BRIDGING TREATMENT WITH TRANS ARTERIAL CHEMOEMBOLIZATION (TACE)

*Yaacov Goykhman¹, Alex Birenbaum¹, Ido Nachmani¹, Richard Nakache¹,
Isac Kori¹, Oren Shibolet², Elena Kazman², Menachem Ben Haim¹, Joseph Klausner¹*

¹Surgery Department, The Tel Aviv Sourasky Medical Center; ²The Tel Aviv Sourasky Medical Center

Background: LT is curative for patients with cirrhosis and HCC. The tumor control to avoid dropout is one of the challenging issues of the patient's maintenance on the waiting list. TACE before LT ('bridge') is not well established and provides a unique opportunity to evaluate the actual pathological response in the explants.

Methods: LT was within Milan criteria. Allocation was national and according to UNOS principles. Surveillance was with periodic imaging and tumor markers (AFP). Diagnosis of HCC was based on typical imaging without biopsies. Bridging treatment with radio frequency ablation (RFA) or TACE according to the number, size and location of the tumors. TACE was with Lipiodol, Adriamycin and Gelfoam.

Results: Of 104 HCC patients were treated with TACE (2003–2012). In 24 TACE was a bridge for LT. 20 underwent LT, 19 from cadaver donors and one from living donor. Mean age was 58 (range, 43–66). Frequent etiologies of cirrhosis were HCV and HBV, 85%. Mean MELD was 13 (range, 7–34). Perioperative mortality was 10%. Detailed pathological data was available in 17 cases. Mean degree of tumor necrosis was 75% (range, 15–100%). In nine patients (45%), the degree of necrosis was >95% and in 20%, >60%. Pathological review of the explants revealed clinical understaging in two cases (12%). In a mean follow up of 30 months, the overall patient survival is 61%.

Non cancer related mortality was 17% (sepsis or recurrent HCV cirrhosis). The cancer related mortality was 22% with mean disease free and overall survival 10 and 20 months.

Conclusions: TACE is an effective and safe bridging procedure. The issues that required upcoming investigations are possibilities to use of HCC response to TACE for oncological outcome prediction and better patient's selection before LT.

P659

SUBNORMOTHERMIC MACHINE PERFUSION FOR RECOVERY AND VIABILITY TESTING OF THE DISCARDED HUMAN LIVER

Paulo Martins¹, Bote Bruinsma², Adam Farmer², Tim Berendsen², Maria Louisa Izamis², Heidi Yeh², Korkut Uygur²

¹UMass Memorial; ²Massachusetts General Hospital

Background: *Ex vivo* machine perfusion holds the potential to strongly increase the quality of a donor liver and improve post-transplantation function and reducing complications. *Ex vivo* machine perfusion holds the potential to strongly increase the quality of a donor liver and improving post-transplantation function and reducing complications.

Methods: We received 15 discarded human donor livers and machine perfused them in our acellular subnormothermic machine perfusion (SNMP) system for 3 h. Livers are monitored in perfusion for metabolic function and hepatic injury to assess the feasibility of this system for preserving and even recovering discarded human livers. Oxygen consumption and metabolite fluxes are measured as indicators of metabolic function, while AST/ALT and LDH are used to assess hepatocyte injury. Additionally, to assess the function of the biliary system, bile flow, biliary pH and bicarbonate were measured. H&E and EM was performed on the liver and the common bile duct.

Results: Resistance on the portal vein and arterial system decrease during perfusion. During perfusion we observe an increasing oxygen uptake, which coincides with the increase of ATP content. pH normalized after an initial acidosis and lactate normalized after a steep initial increase. Bile production is nearly immediate in most livers and production increases with the duration of perfusion. Biliary pH increases as well as biliary bicarbonate. Histologically the liver maintains its architecture during perfusion. The bile ducts retain a normal looking stroma.

Conclusion: This study demonstrates the first use of SNMP for the preservation and recovery of human livers. Our results show that SNMP sustains hepatic metabolism and improves the energy status of the liver and improves the function of the biliary system. These findings are instrumental in the clinical translation of SNMP in liver transplantation.

P660

CLINICAL ANALYSIS OF THE HEPATITIS B VIRUS RECURRENCE AFTER LIVING DONOR LIVER TRANSPLANTATION

*Dong Goo Kim, Gun Hyung Na, Jae Hyun Han, Young Kyoung You
Department of Surgery, Catholic University of Korea*

Background: Without effective prophylaxis, liver transplantation for hepatitis B virus (HBV) related liver disease is frequently complicated by severe and rapidly progressive HBV recurrence. Advances in the prevention and treatment for recurrent HBV infection resulted HBV recurrence rates are consistently <10%. The aim of this study was to analyze the combination with long-term hepatitis B immunoglobulin (HBIG) and nucleos(t)ide analogues as prophylaxis for HBV recurrence after living donor liver transplantation (LDLT).

Methods/materials: From Jul. 2003 to Dec. 2011, 315 hepatitis B surface antigen (HBsAg)-positive patients received LDLT at our transplant center. 244 of the patients were men (77.5%) with a mean age of 50.4 years. Our protocol for post-transplantation HBV prophylaxis is combination with low-dose HBIG and nucleos(t)ide. We reviewed (i) HBV recurrence rate and contributing factors, (ii) relationship between HBV recurrence and hepatocellular carcinoma (HCC) recurrence (iii) treatment and outcome of HBV recurrence.

Results: During a median follow-up of 49 months post-transplant, 10 patients (3.2%) had HBV recurrence. The HBV recurrence was significantly related to HCC at transplantation ($p = 0.041$) and post-LT antiviral agent ($p < 0.001$) in a multivariate analysis. The level of HBV DNA and HBe Ag state at transplantation were not significant factors for HBV recurrence ($p = 0.342$ and $p = 0.802$ respectively). In 170 patients with HCC at LDLT, HCC recurrence was significantly related HBV recurrence ($p < 0.001$). Also Correlation analysis confirmed a strong correlation between HBV and HCC recurrence times ($R^2 = 0.96$, $p = 0.004$). Of 10 patients with HBV recurrence, three patients are alive and two of them had lost HBsAg. The remaining seven patients died of HCC recurrence.

Conclusion: The combination of low-dose HBIG and nucleos(t)ide analogues are safe and effective for HBV prophylaxis after LDLT. As Post-LT antiviral prophylaxis, Entecavir is more effective than lamivudine.

P661

IMPACT OF TUMOR STAGING, MICROVASCULAR INVASION, AND MELD SCORE ON THE SURVIVAL BENEFIT OF LIVER TRANSPLANTATION IN RESECTABLE HCC

Alessandro Vitale¹, Alessandro Vitale¹, Teh-la Huo², Alessandro Cucchetti³, Umberto Cillo¹

¹Liver transplant unit Padova; ²National Yang Ming University; ³Liver Transplant Unit

Background: There are no studies measuring the impact of tumor morphological staging, microvascular invasion (mVI), and model-for-end-stage-liver-disease (MELD) score on the benefit of liver transplantation (LT) over hepatic resection (HR) for hepatocellular carcinoma (HCC).

Methods: Exclusion criteria: very large (>10 cm) tumours, macrovascular invasion and extra-hepatic metastases.

Study population: 1106 HCC cirrhotic patients undergoing HR from one Eastern ($n = 424$) and two Western ($n = 682$) surgical units. We identified three tumor stages: I (within Milan, $n = 806$), II (beyond Milan within Up-to-7, $n = 123$), III (beyond Milan and Up-to-7, $n = 177$). Patient survival observed after HR by proportional hazard regression model was compared to that predicted after LT by the Metroticket calculator. The benefit obtainable from LT compared to resection was analyzed in relationship with staging, mVI, and MELD using Monte Carlo simulation.

Results: MELD score had the most important effect on transplant benefit independently from tumor characteristics: mean 5-year LT benefit was -2.22 months (95% CI, -2.45 to -1.98) for patients with MELD score <10 , and 6.32 months (95% CI, 6.08 - 6.60) for those with MELD ≥ 10 . mVI significantly decreased LT benefit only in patients staged I-II with MELD <10 ; this subgroup had already a negative benefit independently from mVI, however. Staging significantly increased LT benefit only in patients with MELD ≥ 10 with a stage III tumor; this subgroup had an unacceptable 5-year post-LT survival ($<50\%$), however.

Conclusion: From a transplant benefit perspective, MELD score is the only variable with the potential to influence the therapeutic decision between LT and HR.

P662

THE FIRST PAIRED EXCHANGE LIVING DONOR LIVER TRANSPLANTATION IN EUROPE: CASE REPORT

Murat Dayangac, Murat Akyildiz, Levent Oklu, Necdet Guler, Onur Yaprak, Arzu Ozelik, Fisun Yuzer, Tulay Erkan, Yildiray Yuzer, Yaman Tokat Florence Nightingale Hospital

The success of donor exchange programs for kidney transplants has stimulated interest in similar arrangements for liver transplantation (LT). The concept of donor exchange is proposed mainly to avoid blood type incompatibility problems in adult living donor LT (LDLT). However, inappropriate graft and remnant liver volume is the main reason for donor exclusion in both pediatric and adult LDLT. To cope with living donor incompatibility, we started an exchange living donor program for LDLT in 2012. The first recipient was a 6-month-old baby with a PELD score of 18, who had a history of failed Kasai operation for biliary atresia 5 months ago. Her potential donor was her 25-year-old mother, who was rejected because of the large-for-size status of her left lateral segment with a graft-to-recipient weight ratio of 5.8%. The second recipient was a 69-year-old male patient with a MELD score of 14, who had a history decompensated cryptogenic cirrhosis. His potential donor was his 32-year-old son, who was rejected because the future liver remnant was estimated to be less than 30%. After having been informed of all aspects of donor exchange, both pairs consented to participate in exchange LDLT program. The recipients and their potential donors were blood group O. Further studies showed that, the 735 g-left liver of the first donor would be suitable for the 63 kg-second recipient, and the 147 g-left lateral segment of the second donor would be suitable for the 6.6 kg-first donor. To prevent potential conflicts, both pairs of LDLT operations were performed simultaneously on April 10, 2013. Both procedures were successful; the donors were discharged on the seventh postoperative day. The adult and the pediatric recipients were discharged 20 and 45 days after the operation, respectively. To our knowledge, no other institution in Europe has yet reported on exchange LDLT program. We therefore present the first pair exchange LDLT cases at our institution.

P663

UNRESECTABLE HEPATIC ALVEOLAR ECHINOCOCCUSIS TREATED BY COMBINED LIVING DONOR LIVER TRANSPLANTATION AND RESECTION OF THE RIGHT ATRIUM

Michelle Deoliveira, Pierre-Alain Clavien, Mario Lacht, Beat Müllhaupt, Olivier De Rougemont, Philipp Dutkowski University Hospital Zurich

Background: Hepatic alveolar echinococcosis (HAE) is a slow-grow parasitic disease lethal in absence of the treatment. Radical surgical resection for HAE is

the only chance for cure. However most of patients are diagnosed in advanced stage and resection is performed in less than 35% of the cases. Thus, liver transplantation (LT) associated with bezimidazole may be the only chance for long-term survival and cure.

Objective: To present a case of unresectable HAE extent to the heart (atrium) treated by combined living donor liver transplantation (LDLT) with cardiac surgery in a young female patient.

Methods: We present a first worldwide case about liver transplantation using right hemiliver from a 26 years old donor associated with cava replacement by allograft iliac vein from a cadaveric donor with same blood type. Because of diaphragm and right atrium were infiltrated, both were resected under extracorporeal circulation.

Results: Donor presented an uneventful recovery. Recipient presented Stage IV disease (P4, N1M0), evolved with 3a Clavien grade complication, but recovered well, while liver graft function remained excellent in absence of immunosuppressant.

Conclusion: Liver transplantation should be considered for unresectable HAE without spread disease. The alternative of LDLT offers the possibility of overcome waiting list issues offering a chance of cure for patients with advanced HAE.

P664

PORTAL VEIN THROMBOSIS IN THE SETTING OF LIVER TRANSPLANTATION

Marta Hernández, Elba Llop, Jose Luis Calleja, Juan De la Revilla, Fernando Pons, Fernando Pons, Valentín Cuervas-Mons, Víctor Sánchez Hospital Universitario Puerta De Hierro Majadahonda

Introduction: The prevalence of portal vein thrombosis (PVT) in patients that have been undergone liver transplantation (LT) is $9.7\% \pm 4.5\%$. The factors associated with its presence and involvements in post-transplant prognosis are unknown. The aim of our study was to determine the prevalence, assess the factors that are associated with its presence as well as to clarify their association with the prognosis in patients with liver cirrhosis (LC) and LT.

Methods: From 2005 to 2013, different data were retrospectively collected from patients with LC who had undergone LT in our center for the first time.

Results: Of 165 patients who had (46.7%) or had not been diagnosed of hepatocellular carcinoma (HCC) were included, all of them without tumoral thrombosis. Mean age was 55(SD9), male 73.3% and HVC 44.8%. Child-Pugh was (A/B/C:31.5/40.6/21.2%) and MELD15 (SD6). Previous decompensations were: ascites 61.2%, hepatic encephalopathy 33.9%, variceal bleeding 26.1%, spontaneous bacterial peritonitis (SBP) 15.2%. Post-transplant follow-up was 36 months (0-100). TVP was diagnosed while LT in 16 (9.7%) patients. TVP was previously diagnose with image tests in four patients (25%) (1 [0.1% by Doppler ultrasound [DU] and 4 (43.8%) by computed tomography [CT]). All patients had a DU in a mean time of 4 months prior the LT (0-10) and 7 (43.8%) had a CT in a median time of 1 month before the LT (0-45). TVP was significantly related to the presence of SBP (37.5% vs. 13.1%; $p = 0.01$), high levels of creatinine (1.4 [SD 1.8] vs. 1 [SD 0.6]; $p = 0.04$), and low levels of albumin (3.1 [SD 0.9] vs. 3.5 [SD 0.6]; $p = 0.03$). MELD was higher in patients with TVP (16(SD6) vs. 14(SD5); $p > 0.05$). TVP was correlated with the mortality in the first 30 days (18.8% vs. 8.4%; $p > 0.05$).

Conclusions: TVP is a common complication in patients with cirrhosis undergoing LT. Its presence is correlated with suffering from SBP, high levels of creatinine and low levels of albumin. The pre-transplant diagnosis rate is very low and its presence may have implications for short-term mortality.

P664A

TRANSCUTANEOUS AORTIC VALVE IMPLANTATION (TAVI) BEFORE OLT: A CASE REPORT

Andrea de Gasperi, Giovanni Bruschi, Federico De Marco, Silvio Klugmann, Luciano De Carlis, Andrea Corti, Ernestina Mazza Ospedale Niguarda

Background: Heart valve disease is not common in OLT candidates. Moderate end stage liver disease (MELD >13) contraindicates surgical correction because of poor outcome. Severe aortic regurgitation (AR) with cardiac decompensation constitutes a contraindication to OLT.

Material and methods: We report the case of a 48 yo man, CHILD Pugh 14, MELD 32, with acute cardiac decompensation secondary to AR (jet diameter/LVOT diameter $>60\%$) who was considered for Trans Aortic Valve Implantation (TAVI, TF core valve 31) as a bridge to OLT (Jan 2012). The pt underwent an uneventful TAVI procedure, recovered from the acute heart decompensation without residual AR and one month later (February 2012), underwent under ASA, a successful OLT. Intraoperative hemodynamic stability was acceptable: blood loss were close to 6000 ml, transfusion requirements included PRC 12, FFP 16, PLT 2 apheresis units. The pt was extubated on POD 1, was discharged from the ICU on POD 6 and from Hospital on POD 30.

Conclusion: As far as we know this is the first case of TAVI used as a bridge to OLT in a ESLD pt. Combined surgery was in the past considered as an option, but results were poor. Instead, TAVI might be considered a feasible option for severe aortic valve disease in OLT candidates.

PS13-INTESTINE

P665

REVIEW OF VARIOUS TECHNIQUES OF SMALL BOWEL ALLO-TRANSPLANTATION IN PIGS

*Arash Nickkholgh, Sandra Weih, Markus Kessler, Mohammad Golriz, Stefan Holland-Cunz, Arianeb Mehrabi
Ruprecht-Karls University, Heidelberg*

Background: To present a review of different surgical techniques of SBTx in the porcine model.

Materials/methods: Analysis of Medline-cited studies dealing with different techniques of SBTx in porcine models with particular focus on surgical aspects.

Results: With regard to graft procurement and enterectomy, the reported techniques vary widely. Arterial reconstruction is mainly conducted by performing the anastomosis between the superior mesenteric artery (SMA) of the donor and SMA or infrarenal aorta of the recipient. Alternatively, an aortic segment of the donor can be anastomosed to the infrarenal aorta of the recipient. Venous anastomosis is frequently performed between the superior mesenteric vein (SMV) of the donor and SMV or the inferior vena cava (IVC) of the recipient. Some studies also report venous anastomosis between the portal vein of the donor and the recipient. Bowel continuity is then restored by end-to-end or end-to-side anastomosis. Remarkable results were generated thanks to improved techniques which include proximal side-to-side ileo-ileal anastomosis with double-barrel ileostomy, or so-called "Paul-Mikulicz-Ileostomy". Most frequently used were jejunostomy and the "Bishop-Koop-Ileostomy" – where the proximal part of the bowel is anastomosed end-to-side to the distal part, which is then exteriorized as a Stoma.

Conclusion: Based on the techniques presented in this review, one must select the most suitable surgical technique of porcine SBTx among those various models.

P666

MODELS OF SHORT BOWEL SYNDROME IN PIGS: A TECHNICAL REVIEW

*Arash Nickkholgh, Sandra Weih, Markus Kessler, Giovanni Frongia, Mohammadreza Hafezi, Stefan Holland-Cunz, Arianeb Mehrabi
Ruprecht-Karls University, Heidelberg*

Introduction: In Short Bowel Syndrome (SBS), the absorptive capacity of the intestine is not sufficient due to anatomic or functional reasons. Porcine models of SBS are used to simulate anatomical and physiological conditions similar to those in humans for the purpose of research.

Material/methods: Through a Medline literature search, this work presents an overview of different techniques used to induce the SBS-model and outline the differences between various models regarding surgical procedures, monitoring, and methods of assessment.

Results: Generally, female pigs or piglets 3–8 weeks weighing 10–30 kg were used. The percentage of the resected small bowel ranged from 75% to 100%. The majority of researchers performed a mid-intestinal resection in which the remaining small bowel comprises equal parts of jejunum and ileum. End-to-end anastomoses with single-layer technique with interrupted monofilament absorbable sutures were usually performed. Besides extended bowel resection, small bowel transplantation, bowel lengthening procedures, bowel dilatation, or pharmaceutical treatments for SBS, often in the course of weeks after the extended bowel resection were performed. The period of observation varied widely from 7 days up to 19 weeks. Nutrition was provided parenterally or enterally, according to the objectives of the study. Body weight, food intake, stool output, the general condition of the animal and blood tests were used for monitoring. Functional assessment, morphological assessment, molecular assessment, immunoblotting and immunohistological methods have been also performed.

Conclusion: There are very heterogeneous, and sometimes not exact, definitions of SBS. Also, there are no standardized methods of animal monitoring and outcome analysis once a SBS model is successfully created. This work evaluates the advantages and disadvantages of each model and facilitates the selection of the best suitable SBS model according to the objectives of research.

P667

REMOTE SYNCHRONOUS REVASCULARISATION TECHNIQUE FOR ABDOMINAL WALL TRANSPLANTATION: THE OXFORD EXPERIENCE

*Georgios Vrakas, Henk Giele, Srikanth Reddy, Sanjay Sinha, Peter J. Friend, Anil Vaidya
Oxford Transplant Centre*

Background: We introduce a microsurgical technique of remote re-vascularisation to reduce cold ischemia time (CIT) of the abdominal wall allograft.

Methods/materials: The technique involves primary remote vascularisation of the abdominal wall graft via the vessels of the non dominant forearm (ulnar or

radial artery with corresponding venae comitantes). This process is synchronous with the visceral transplant. The graft is transferred onto the recipient's inferior epigastric (IE) artery after the visceral transplant is done.

Results: Between April 2012 and May 2013, six patients underwent small bowel transplantation and synchronous remote revascularisation of their abdominal wall grafts. Mean cold ischaemia time (CIT) for the abdominal wall graft was 338 min (range 320–360 min). Mean primary warm ischaemia time (PWIT) was 46 min (range 43–55 min). Mean secondary warm ischaemia time (SWIT) was 73 min (range 62–86 min). In five cases the abdominal wall graft was inset orthotopically on the recipient's inferior epigastric vessels at the end of the visceral transplant. In one case the graft was reconnected to the ulnar artery. Subsequently a saphenous loop graft from the internal mammary artery (IMA) was used for vascularisation. All six recipients preserved function of the non-dominant hand.

Conclusion: Remote synchronous re-vascularisation of the composite abdominal wall allograft reduces the CIT for the abdominal wall graft. In addition it allows flexibility in the timing of inseting the graft onto the IE or IMA of the recipient.

P668

CHARACTERISTICS OF ABDOMINAL WALL GRAFT REJECTION AFTER COMBINED INTESTINAL AND ABDOMINAL WALL TRANSPLANTATION: THE OXFORD EXPERIENCE

*Georgios Vrakas, Genevieve Casey, Olivia Espinosa, Henk Giele, Srikanth Reddy, Sanjay Sinha, Peter J. Friend, Anil Vaidya
Oxford Transplant Centre*

Aim: To report our experience of abdominal wall graft rejection after combined intestinal and abdominal wall transplantation with regards to diagnosis, management and relationship to bowel function.

Methods: Retrospective study of all patients undergoing intestinal and abdominal wall composite tissue allograft transplantation was undertaken. Clinical presentation of rejection was correlated with histology, stoma output, citrulline levels and endoscopy findings.

Results: We have performed six combined intestinal and abdominal wall transplants. Abdominal wall and bowel were obtained from the same donor. Remote synchronous revascularisation microsurgical technique (non-dominant forearm) was used for the abdominal wall whilst the intestinal graft was placed intra-abdominally. Two patients presented to hospital around post-operative day 60 with neutropaenia and a peri-follicular, micro-papular pink rash limited to the abdominal wall graft. Histology revealed grade II-III rejection in each case. Both patients were systemically well, had normal stoma output (<20 ml/kg/24 h), citrulline levels >25 μm and endoscopically healthy bowel. Ileal biopsies revealed histologically normal mucosa. Treatment in each case was with a single dose of 20 mg Basiliximab IV, three pulses of 500 mg methylprednisolone IV and mycophenolate sodium or azathioprine. The rash improved within 48 h and neither patient suffered further rejection.

Conclusion: Around post-operative day 60 is the high-risk period for abdominal wall rejection, and presentation is with neutropaenia and rash. CD25 down-regulation with Basiliximab, combined with methylprednisolone is effective in treating acute rejection. Abdominal wall grafts appear to reject whilst underlying bowel remains healthy.

P669

TACROLIMUS (FK 506) ASSOCIATED RENAL DYSFUNCTION AFTER ISOLATED PAEDIATRIC INTESTINAL TRANSPLANTATION

*Cezar D. Nicoara, Paul Davies, Carla Lloyd, Evelyn P. Ong, Paolo Muesan, Darius F. Mirza, Jane Hartley, Khalid Sharif, Girish L. Gupte
Diana Princess of Wales Children's Hospital, Birmingham, UK*

Introduction: Tacrolimus related renal dysfunction has not been reported exclusively following isolated small bowel transplant (ISBTx) in children.

Aim: Review of renal dysfunction in ISBTx patients surviving more than 2 years after transplant.

Material and methods: Retrospective review of database from 1993 to 2011. Liver inclusive grafts were excluded. Renal dysfunction was defined as reduction of cGFR compared to the pre-transplant values. cGFR was assessed with modified Counahan-Barrat formula. Mean cGFR and FK506 trough levels at 1, 2, 3, 6, 12, 18 and 24 m were calculated. Median cGFR changes from the pre-transplant values were assessed with Wilcoxon signed rank test.

Results: 16 children received 18 grafts (15 isolated and three modified multi-visceral) at median age of 62 months (23–164). Induction agent was Basiliximab (n = 14) and maintenance drugs were FK506 and steroids. After ISBTx, cGFR dropped sharply in 3 months. Some recovery was noted by 1 year, but at 2 years is still significantly lower than the pre-transplant value (p = 0.024). No linear relationship between the changes in cGFR and Tacrolimus levels reduction was noted. In MMF group (nine children received MMF +FK506), a 23% reduction in cGFR at 2 years from the pre-transplant values, while in non-MMF group the reduction was 44% (p = 0.270).

Conclusions: Renal dysfunction is uniformly present after isolated intestinal transplantation and shows a partial recovery to pre-transplant level by 2 years. MMF may be useful as nephroprotective agent in ISBTx.

PS14-LUNG

P670

INFLUENCE OF CANNABIS SMOKING DONOR HISTORY ON OUTCOME AFTER LUNG TRANSPLANTATION

Diana Garcia Saez, Prashant Mohite, Anton Sabashnikov, Bartlomiej Zych, Fabio De Robertis, Toufan Bahrami, Mohamed Amrani, Anna Reed, Martin Carby, Andre R. Simon
Royal Brompton & Harefield NHS Foundation Trust, UK

Purpose: Cannabis smoking (CS) can cause chronic bronchitis and airflow obstruction. There is little evidence about utilization of lungs from CS donors. This study evaluates the results of lung transplant (LTx) using organs from this group.

Methods: Retrospective analysis of all lung offers between 01.2007 and 10.2012. Reasons for declining the organs were analyzed. If procured, the recipient outcomes were compared.

Results: Of 2662 offers were received. 136 donors were CS of which 27 offers were accepted but later declined due to retrieval findings. 13 LTx were performed, comprising 5.45% of the total LTx at our centre ($n = 237$). There were no differences in PaO₂/FiO₂ ratio at 24, 48, 72 h, duration of mechanical ventilation or ICU/hospital stay. There was no difference in survival between the groups (Log rank test $p = 0.223$).

Conclusion: LTx from CS donors have comparable results to those from non-CS donors. Our results suggest that these offers should not be excluded from the donor pool.

P671

DOES FEMALE TO MALE DONATION IN LUNG TRANSPLANTATION AFFECT OUTCOME?

Prashant Mohite, Bartlomiej Zych, Anton Sabashnikov, Diana Saez, Massimo Cappocchia, Mohamed Amrani, Toufan Bahrami, Fabio DeRobertis, Martin Carby, Anna Reed, Andre R. Simon
Royal Brompton and Harefield NHS Trust, London

Background: Donor-recipient gender mismatch has got an influence on transplantation outcome however, published data are conflicting. We analysed LTx outcome with regards to donor-recipient gender matching.

Methods: Effect of different gender combinations: male to male (MM), MF, FM and FF on short and mid-term outcome was analysed.

Results: Of 237 lung transplants were performed between 01.2007 and 09.2011. There were 76MM transplants, 17MF, 43FM and 101FF transplantations performed. Baseline donor characteristics were comparable among the groups. Preoperatively FM group had significantly larger population of pulmonary fibrotic recipients as compared to other groups combined. Donor/recipient predicted TLC ratio was significantly lower in FM vs. other groups combined. There was a trend towards decreased 90-days survival in FM vs. other groups combined reaching statistical significance at 1 year.

Conclusions: FM donor-recipient gender mismatch may adversely influence the outcome of LTx.

P672

IMPROVEMENT OF LEFT LUNG FUNCTION IN A PATIENT WITH AIRWAY-CENTERED INTERSTITIAL FIBROSIS AFTER RIGHT-SIDED LUNG TRANSPLANTATION

Hamidreza Abtahi, Hamidreza Davari, Setareh Davoudi, Sahar Latifi
Imamkhomeini Medical Center, Tehran University of Medical sciences

Right sided lung transplantation (RLTx) was done at Feb 2010 on a 29 year old male with airway-centered interstitial fibrosis (AIF) and class IV dyspnea and hypoxia despite prednisolone and azathioprine use. He developed bronchial anastomotic stricture and malacia and RUL bronchial stenosis after aspergillus infection of the bronchial anastomosis extending to RUL bronchi. Repeated episodes of RUL collapse and abscess occurred which were treated with balloon dilatation, bronchoscopic drainage and antibiotic. Repeat HRCT showed hypo vascularity of the right lung and Lung V/Q scan revealed 86% ventilation and perfusion of the left and 16% of the right lung. Pulmonary artery angiography showed little perfusion of the right pulmonary artery. Right pneumonectomy of the transplanted lung was done at Feb 2012 with discontinuation of immunosuppression except prednisolone 5 mg /day. The patient was well during the first week after pneumonectomy. However, the spirometric parameters decreased and HRCT showed patchy ground glass opacity in the left lung that was not responded to increasing prednisolone dose. The patient's dyspnea, spirometric parameters, 6 min walk test and HRCT findings were improved after restarting of mycophenolate, although the indexes were lower in comparison with the early post-pneumonectomy period.

Conclusion: AIF is a rare life-threatening form of non-reversible obstructive lung disease that usually doesn't respond to treatment and progressive cases may require lung transplantation. The mechanism of increased naive left lung function is unknown. However, as it was initiated after right sided lung

transplantation, it could be due to post-transplant immunosuppression. The improvement of post-pneumonectomy left lung function after restart of mycophenolate supports this assumption.

P673

NEGATIVE CONSEQUENCES OF IMMUNOSUPPRESSIVE THERAPY ON BRONCHIAL HEALING FOLLOWING LUNG TRANSPLANTATION (LTx)

Anne Olland, Sandrine Hirschi, Jérémie Reeb, Stéphane Renaud, Nicola Santelmo, Anne Roche, Pierre-Emmanuel Falcoz, Romain Kessler, Gilbert Massard
Lung Transplantation Group

We studied the impact of different immunosuppressive combinations on bronchial healing in LTx. We conducted a retrospective study on all LTx performed in a single center between January 2004 and May 2012. We focused on denutrition, graft ischemia, mechanical ventilation support, lung infection, and the combination of immunosuppressive therapy. Bronchial complications was defined as symptomatic dehiscence or symptomatic stenosis. We found 35 bronchial complications leading to death in seven patients. Of 134 patients remained unharmed. Both groups received overall the same amount of steroids. Patients with the combination basiliximab/steroid/tacrolimus/mycophenolate had significantly more bronchial complications ($p = 0.03$) in comparison to patients with the combination steroid/ciclosporin/azathioprine. The combination basiliximab/steroid/tacrolimus/mycophenolate has a negative effect on bronchial healing. The effects of immunosuppressive drugs should be studied when given in a combination.

P674

CHRONIC LUNG ALLOGRAFT DYSFUNCTION (CLAD): A COLLABORATIVE APPROACH WITH PALLIATIVE CARE

Carine Berutto¹, Claudia Mazzocato², John-David Aubert³, Murielle Pott⁴
¹CHUV/Organ Transplantation Center; ²CHUV/Palliative Care Unit; ³CHUV/Pneumology; ⁴Unité de Recherche En Santé, Lausanne

Background: CLAD is the leading cause of late mortality following lung transplantation. Studies show a 26–32% survival at 5 years after developing CLAD. In the Lausanne-Geneva lung transplantation program about three patients a year die of CLAD. Our experience shows that patients with CLAD suffer not only from physical symptoms but also from psychological, social and spiritual distress.

Method: We made the hypothesis that quality of life of these patients can be improved by incorporating palliative care early in the management of CLAD. As in the literature there are no reports about CLAD/palliative care and in order to better take the patients in charge we have to explore their needs through a qualitative study. We will make interviews that will be recorded and analyzed through a framework approach. The evolution of symptoms and quality of life will be evaluated by (ESAS/SF36).

Results: We will present the first results of the interviews in September and expose the strategies of collaborative management based on these data.

Conclusion: Later we will evaluate the impact of the management on the quality of life and symptoms as well as explore new approaches of care.

P675

FIRST PHARMACOKINETIC EVALUATION OF EVEROLIMUS QD IN THORACIC TRANSPLANT PATIENTS

Romain Guillemain, Vianney Poinsignon, Catherine Amrein, Christian Woloch, Veronique Boussaud, Eliane M. Billaud
CHU Paris Ouest HEGP, Paris Descartes University

Introduction: The use of everolimus (ERL) once daily (QD) is favoured by: a long half-life (30 h); the availability of Afinitor[®] (a similar formulation as Certican[®] developed once daily in oncology); Advagraf[®] with tacrolimus despite the sustained release form. In transplantation, the switch from Prograf[®] to Advagraf[®] is often realized to improve compliance and simplify the treatment of young/difficult patients. We therefore proposed to assess the feasibility of using Certican[®] QD in thoracic transplant patients during their switch to Advagraf[®] for treatment harmonization and simplification to improve compliance.

Methods: Over the 2008–2012 period, the pharmacokinetic of a Certican[®] QD regimen in our centre has been documented in nine patients (four heart transplants, five lung including three cystic fibrosis): four were obtained via a switch QD, two when prescribing initial QD et 3 already with a Certican[®] QD follow-up. Pharmacokinetics (PK) [0, 0.5, 1, 1.5, 2, 3, 4, 8, 12, 24 h] prospectively collected are corresponding to the four switches and two ERL QD straightaway. Therapeutic Drug Monitoring (TDM) results were available in five patients receiving Certican[®] QD including 2 from the PK study. Whole blood ERL samples were assayed by LCMSMS.

Results: TDM data are in favour of maintained trough concentration (C₀) (5 to 10 ng/ml with the usual variability of 25%). The exposure, assessed by the PK data, is adequate and consistent, respectively 331 ± 70 and 155 ± 80 ng.h/ml

for a 3.1 ± 1.1 dose and 1.7 ± 0.9 mg/day with the QD (24 h) versus BID (12 h) schedule. Three patients with a TDM follow-up treated with azole antifungals while ERL QD initiating did not present any particular issues.

Conclusion: The feasibility of using Certican® QD is documented by adequate exposure levels with doses comparable to the standard BID schedule resulting of individual adaptations, susceptible to maintain efficacy performance. Further investigations are needed to confirm the good tolerance observed in these few patients.

P676

OUTCOMES OF LUNG TRANSPLANTATION IN IRAN

Shadi Shafaghi¹, Abolghasem Daneshvar¹, Shahabedin Mohammad Makki¹, Mohammad Behgam Shadmehr¹, Azizollah Abbasidezfuli¹, Zargham Hossein Ahmadi¹, Badiozaman Radpay¹, Shideh Dabir¹, Tahereh Parsa¹, Payam Tabarsi¹, Majid Marjani¹, Babak Shadi Shafaghi¹, Mohammad-Reza Masjed², Ali-Akbar Velayati², Zahra Ansari¹, Kambiz Sheikhly¹, Neda Behzadnia¹, Sareh Parto¹, Jamileh Faeghi¹, Hamid Reza Khoddami Vishteh¹, Fariba Ghorbani¹, Katayoun Najafzadeh¹

¹Lung Transplantation Research Center, Masih Daneshvari Hospital, Shahid Beheshti University of Medic; ²Masih Daneshvari Hospital, Shahid Beheshti University of Medical Sciences

Background: The major limitations for expansion of lung transplantation are shortage of donors and complexity of the procedure. This study was conducted to describe our 12-year experience in lung transplantation.

Methods: We used the database of lung transplantation research center of Masih Daneshvari Hospital affiliated to Shahid Beheshti University, Tehran and extracted all cases since 2000.

Results: Lung transplantation undergone in 65 patients. Fifty patients (75%) were male and the mean age was 36 ± 12 years. The causes of transplantation were pulmonary fibrosis (42%), bronchiectasis (23%), COPD (15%), cystic fibrosis (9%) and the others (11%). One and five year survivals of patients were 52% and 40% respectively. In patients who were alive after three weeks of transplantation, one and five year survivals were 71% and 56%.

Conclusion: Although lung transplant is a complex procedure, our experience shows that it can be performed in developing countries such as Iran. Better donor and recipient selection and more improvement of the surgical aspects of the transplantation by using more specialized equipment can reduce the early mortality and let the survival of lung transplant get close to the international results in Iran.

Keywords: Lung transplantation, Survival.

P677

EVALUATION OF PATIENTS WHO ARE REFERRED FOR LUNG TRANSPLANT IN IRAN

Katayoun Najafzadeh, Shadi Shafaghi, Sareh Parto, Shahabedin Mohammad Makki, Omid Ghobadi, Hamid Reza Khoddami Vishteh

Lung Transplantation Research Center, Masih Daneshvari Hospital, Shahid Beheshti University of Medic

Background: The result of the transplant is highly dependent to the correct recipient selection. We conducted this study to evaluate referred patient's condition.

Methods

We evaluated 960 visited patients in our transplant clinic in 2012 for their general condition, Body Mass Index (BMI), Pulmonary artery pressure (PAP), socioeconomic status and compliance to treatment.

Results: Although % 41 of referred patients were suitable for transplant, 22% were referred early and 37% were unsuitable for transplantation. They were considered unsuitable because of severely high PAP in 33%, severe deconditioning and low BMI in 21%, too old for transplant in 16%, very poor socioeconomic status of 15% and not having enough compliance to follow the treatment in 8%. In 7% of the patients thickening in the pleura was so significant that our surgeons didn't accept them for transplant.

Conclusion: Most Patients referred for lung transplant were in poor condition because of late referring for transplantation and not having a suitable rehabilitation. Establishing the rehabilitation program in different parts of the country and informing the pulmonologists about the referral criteria and managing the patients with end stage lung disease are necessary.

P678

ASSESSMENT OF NUTRITIONAL STATUS IN PATIENTS ON LUNG TRANSPLANT WAITING LIST IN IRAN

Rahleh Sadegh, Katayoun Najafzadeh, R. Sami, M. Rezaei, Diba Tabatabaei

Lung Transplantation Research Center, Masih Daneshvari Hospital, Shahid Beheshti University of Medic

Background: The aim of this study was to evaluate the characteristics of nutritional status in end stage respiratory patients waiting for lung transplant.

Method: Eighty-six patients were visited in lung transplant clinic of Masih Daneshvari hospital from October 2011 to January 2012. Nutritional status was evaluated using anthropometric measurements, FFM1, height, weight, Body Mass Index (BMI), Triceps Skinfold (TSF), mid-arm muscle circumference (MAMC) and FFM1.

Results: Mean recipients age was 37.59 ± 13.73 . Mean of BMI, TSF, MAMC and FFM1 were 21.1 ± 5.12 kg/m², 11.76 ± 7.79 mm, 21.41 ± 3.93 cm² and 16.69 ± 2.35 kg/m² respectively. The highest and the lowest mean of the anthropometric measures were in the ILD and CF group respectively. There were sensitivity of 0.844; specificity of 0.842, Youden Index of 0.686 and Shortest of 0.0493 for cut-off 19.4 in BMI of patients.

Conclusion: Many of patients, who are candidate for lung transplant, suffer from malnutrition. Its prevalence is dependent to the type of lung disease. CF patients are at the highest risk. Results show that the cutoff point of 19.4 kg/m² of BMI predispose malnutrition in chronic pulmonary disease.

P679

HOW OLD IS TO OLD? EARLY AND MID TERM RESULTS OF LUNG TRANSPLANTATION (LTX) FROM THE DONORS OVER 55 YEARS OF AGE

Bartlomiej Zych, Diana Garcia-Saez, Anton Sbashnikov, Prashant Mohite, Fabio De Robertis, Toufan Bahrami, Mohamed Amrani, Anna Reed, Martin Carby, Andre R. Simon

Harefield Hospital, Royal Brompton and Harefield NHS Foundation Trust

Background: Current recommendations for an "ideal lung donor" suggest age of 55 as an upper limit. There are the some data available suggesting that utilisation of older donors does not adversely influence LTx outcome. We retrospectively evaluated our experience with lung donors over 55 years of age.

Methods: 233 LTx were performed in our institution between 01.2007 and 08.2012. Group I ($n = 207$) received organs from donors ≤ 55 years and group II ($n = 26$) from donor > 55 years. Recipient and donor demographics and preoperative variables as well as postoperative outcome were compared between the groups.

Results: Donors from group I were significantly younger (median [interquartile range]): 43(31;49) vs. 59(57;61) year. ($p < 0.01$) with higher partial arterial oxygen pressure/fraction of inspired oxygen ratio ($\text{PaO}_2/\text{FiO}_2$): 58.4 ± 14.2 vs. 50.9 ± 13.9 kPa ($p < 0.01$), more frequent history of smoking: 52.5 vs. 18.5% ($p < 0.01$) and abnormal chest radiogram: 27.5 vs. 7% ($p < 0.05$). Other parameters were comparable. Recipients in group I were younger: 45(29;54) vs. 53(46;58) years. with lower percentage of females: 47 vs. 70% ($p < 0.05$). Diagnosis, percentage of recipient: operated on pump and received double LTx were comparable. There were no significant differences in recipients' postoperative: $\text{PaO}_2/\text{FiO}_2$ ratio: on arrival to intensive care unit (ICU), 24, 48 and 72 h after LTx, duration of mechanical ventilation, ICU and hospital length of stay, and prevalence of acute rejection (AR). 1, 3, and 5 years survival estimated using Kaplan-Maier method were comparable: 86.3% vs. 77.6%, 72.9% vs. 73% and 66.8 vs. 60.9% (log rank = 0.336) as well as freedom from bronchiolitis obliterans syndrome (BOS): 90% vs. 95%, 77.8% vs. 71.6% and 71% vs. 71.6% (log rank = 0.738).

Conclusion: Carefully assessed lungs from donors over 55 years of age can be safely use for transplantation and may decrease a gap between a number of patients awaiting Ltx and number of organs available.

P680

VORICONAZOLE TOLERABILITY IN LUNG TRANSPLANT RECIPIENTS: IS THE N-OXIDE METABOLITE THE MAIN CAUSE OF PHOTOTOXICITY? PRELIMINARY RESULTS OF A SINGLE CENTRE EXPERIENCE

Simona Soresi, Dhruva Dhar, Neil Leaver, Anna Read, Andre R. Simon, Martin Carby

Transplant Unit, Royal Brompton and Harefield Foundation Trust

Background: Voriconazole has been largely demonstrated to be, alone or in combination with other agents, an effective treatment for invasive fungal infections among lung transplant recipients (1-2). Unfortunately its usage is often limited by several adverse reactions including acute and chronic cutaneous effects, mainly due to a phototoxicity mechanism (3). The most likely mechanisms of phototoxicity is directly related to either voriconazole or to its N-oxide main metabolite (NOX), and an interaction with retinoid metabolism (3). There are currently no studies available to state that the presence of higher level of NOX is definitively associated with increase photosensitivity.

Methods: Of 73 lung transplant recipient in treatment with voriconazole have been tested for voriconazole and NOX levels from September 2011 to January 2013. All the patients were asked to complete a surveillance questionnaire specifically generated to assess the presence of photosensitivity. Patients admitted in to hospital during the treatment and patients for whom treatment was suspended for other reasons (liver toxicity, persistent visual hallucinations, etc) were excluded from the study.

Results: Of 33 patients were included in the study. 20 patients had normal NOX levels and none experienced photosensitivity; 61.5% of patients had photosensitivity associated with high level of NOX (despite voriconazole levels being within the therapeutic range); five patients had high NOX level but none experienced photosensitivity (four Cystic Fibrosis and one with $\alpha 1$ antitripsin deficiency).

Conclusion: The preliminary results of the study suggested that there is a correlation between the presence of high level of NOX and photosensitivity. We believe that increased levels of NOX could be associated with a particular subgroup of patients having an "intrinsic susceptibility" to voriconazole. The potential to identify this sub-group could improve short and long term outcomes especially in prolonged treatment.

P681

EFFICACY OF IMMUNOGLOBULIN IN TREATMENT OF COMMUNITY-ACQUIRED RESPIRATORY VIRUSES INFECTION AFTER LUNG TRANSPLANTATION: SINGLE CENTRE EXPERIENCE

Simona Soresi, Haifa Lyster, Anna Read, Anne Hall, Andre R. Simon, Martin Carby
Transplant Unit, Royal Brompton and Harefield Foundation Trust

Background: The incidence of respiratory viruses associated community-acquired pneumonitis (CARVs) is increasing in lung transplant recipient population. In particular virus members of the Paramyxoviridae family (PV) such as respiratory syncytial (RSV), parainfluenza virus (PIV), human Metapneumovirus (hMPV) play an important role in the etiology of this infection. PV infections are also a well recognized risk factor for the development of bronchiolitis obliterans syndrome (BOS) (2-3). The use of intravenous immunoglobulin (Ivlg) for an increasing number of conditions has more than doubled in the last decade (4) and in transplant recipient for treatment of antibodies mediated rejection and viral pneumonitis resistant to antiviral treatment (mainly CMV related). There are very few data about the use of Ivlg in CARVs. We retrospectively reviewed data in our population of lung transplant recipient over a period of 64 months.

Methods: Of 35(36 treatment) lung transplant recipients presenting with drop in lung function and flu-like symptoms were tested with chest imaging, bronchoscopy with bronchoalveolar lavage and biopsy and/or nasal pharyngeal swab/aspirate. Patients with positive PCR for respiratory viruses and biopsy consisted with interstitial viral pneumonitis and/or radiological changes consistent with pneumonitis were treated with Ivlg for 5 days.

Results: PCR was positive for PIV in 11 patients, Hmpv in 9, RSV in 6, H1N1 in 1, Adenovirus in 2, negative in seven patients. In 24 of 36 treatment episodes the respiratory symptoms resolved completely, with RFTs returning to baseline. Nine patients died post-treatment and three patient developed BOS. There were minor adverse drug reactions in four patients: bradycardia (1), headache (3) and nausea (1), none necessitated treatment discontinuation.

Conclusion: CARVs incidence is increasing in lung transplant recipient and is a well established risk for the incidence of BOS. Treatment with Ivlg effective and generally well tolerated

P682

THREE CASES OF HYPERAMMONEMIA AFTER LUNG TRANSPLANTATION: LESSONS LEARNT

Siddiq Anwar, Diptesh Gupta, Syed Khalid, Muhammad Ashraf, Brent Miller, Daniel Brennan

Washington University School of Medicine in St. Louis

Background: Hyperammonemia related encephalopathy (HRE) post orthotopic lung transplantation (OLT), is a rare but fatal complication. Various interventions affecting ammonia generation, pathways of nitrogen excretion, and methods for removing ammonia have been described.

Methods: We describe three cases that developed HRE immediate post OLT. (i) 67 year male with idiopathic interstitial lung disease, day 7 following OLT, became drowsy. Serum ammonia (NH4) level was 302 μM (normal <40). In addition to renal replacement therapy (RRT), rifaximin, arginine, and levocarnitine were commenced. (ii) 46 year male with a1-antitrypsin on day 9 following OLT became agitated, progressing to coma. NH4 level was 269 μM . In addition to RRT, neomycin, lactulose, arginine, sodium benzoate, sodium phenylacetate and acetohydroxamic acid were commenced. (iii) 59 year male with Idiopathic Pulmonary Fibrosis on day 7 developed agitation. NH4 level was 155 μM . In addition to RRT, levocarnitine, arginine, phenylbutyrate, lactulose and rifaximin were commenced.

Dosage and modality for RRT in the three cases are illustrated in figure 1, 2 and 3 respectively.

Discussion: NH4 clearance depends on rate of ammoniogenesis, volume of distribution, and rate of removal. However, even at Continuous veno-venous hemofiltration doses of 40 ml/kg/h and Sustained low-efficiency dialysis (SLED) doses of 250 ml/kg/h, NH4 clearance was not significant. Intermittent hemodialysis (IHD) using a large surface area dialyzer (2.1 m²) and maximum tolerated blood flows (450-500 ml/min) is the most effective RRT. Case 1 died due to development of brain edema and retrospectively, with use of more aggressive RRT to reduce NH4 as with the other cases might have altered the outcome.

Conclusions: Prompt and aggressive ammonia reduction with prolonged daily IHD in conjunction with early weaning of steroids and other therapeutic measures may prevent HRE. We also recommend discontinuation of drugs which impair urea cycle.

P683

LUNG TRANSPLANTATION IN JEHOVAH'S WITNESS

Harish Seethamraju¹, Karolina Chmielowiec², Pawel Kolodziejcki², Scott Scheinin¹, Matthias Loebe¹

¹The Methodist Hospital; ²Baylor College of Medicine

Persons of Jehovah's Witness (JW) faith present complex and challenging surgical cases due to their religious belief preventing use of blood and blood products transfusions. Lung transplantation (LTX) is now recognized treatment for many end stage lung diseases. However, LTX still presents a difficult surgical case as patients can sustain significant blood loss requiring transfusions. Consequently, patients of JW faith with end stage lung disease present a particularly difficult surgical case and management of immune suppressants for LTX where blood transfusion is not possible. We present our experience in caring for a lung LTX recipient who is of JW faith. Patient is a 69 year old Caucasian male with IPF, who was referred to our center for LTX evaluation with a 2 years history of progressively worsening SOB especially with exertion. Patient's FEV1 was 2.17 L and FVC was 2.6 L (82%, 78% predicted) 1 month prior to transplant. Patient was NYHA 3, had noncontributory surgical and family history, and a 20 pack year history of smoking. Because he was unwilling to consent for blood transfusion during LTX, he was given weekly 100 μg SQ darbepoetin injections, premedication with pentoxifylline and methylprednisolone, and 324 mg ferrous fumarate TID. Hemoglobin/hematocrit levels were measured regularly while he awaited transplantation. Patient was listed for single left LTX and a donor became available 6 months after listing. He was admitted to the hospital with hemoglobin/hematocrit at 14.9 g/dl/43.2%, he received 125 mg sodium ferric gluconate in 110 ml NS at 100 ml/h and 200 μg of darbepoetin 6 h prior to surgery. He underwent surgery without CPB. Estimated blood loss was 400 mL. He received two units of Cell Saver intraoperatively. Hemoglobin/hematocrit after LTX measured 13.7 g/dl/40%. Post operatively results remained low for the first two days and returned to normal levels on day five. At discharge, patient's hemoglobin was 14 g/dl. At one year post transplant, patient was classified as NYHA 1. Patient's hemoglobin/hematocrit were 14.6 g/dl/44.1%, with immensely improved lung function: FEV1 of 3.07 L and FVC of 3.76 L (117%, 114% predicted).

P684

LUNG TRANSPLANTATION IN HIV INFECTED PATIENTS: A SINGLE-CENTER CASE SERIES

Neeraj Sinha, Harish Seethamraju, Thomas Kaleekal, Soma Jyothula, Babith Mankidy, Scott Scheinin

The Methodist Hospital

Background: As HIV (human immunodeficiency virus) infected patients have lived longer with the use of effective combination antiretroviral treatment (cART), chronic illnesses including advanced lung diseases have increasingly affected them.

Methods/materials: Study design was a single-center case series.

Results: Since April, 2010, two HIV infected patients (on cART with negative viral load) have received lung transplantation at our hospital. Both patients were Caucasian males in their early sixties with idiopathic pulmonary fibrosis. Both had positive hepatitis B core IgG antibodies without viremia. One patient had hepatitis C antibodies without viremia. Both had pulmonary arterial hypertension. Both patients are alive, well and free of bronchiolitis obliterans syndrome (BOS) at 38 and 13 months post bilateral and right single lung transplantation respectively. Both of them had only one episode of acute rejection each (both A1 grade) in the first year. Both have remained without HIV, hepatitis B, CMV (cytomegalovirus) and EBV (Estein-Barr virus) viremia. Both have remained free from hepatocellular dysfunction/cirrhosis. Except for pseudomonas aeruginosa pneumonia in the third year post transplant in one patient, no significant infectious complications were noted. Significant drug-drug interactions were noted, especially with protease inhibitors.

Conclusion: Lung transplantation can safely be performed and prolong survival in HIV infected patients with advanced lung diseases. Drug-drug interactions pose a significant, but surmountable, challenge.

P685

ONCE-DAILY TACROLIMUS INCREASES FLEXIBILITY IN IMMUNOSUPPRESSION(I/S) OPTIONS POST LUNG TRANSPLANTATION

Bronwyn Levvey¹, Adam Cunningham², Lauren Mitchell¹, Steven Ivlic², Greg Snell¹

¹Lung Transplant Service, The Alfred Hospital; ²Pharmacy Department, Alfred Hospital

Background: Prolonged-release once-daily Tacrolimus (OD-TAC) can improve safety by avoiding toxic peak levels, as well improving adherence to I/S regime, compared with twice-daily Tacrolimus (BID-TAC). However, published data on use of OD-TAC post lung transplantation (LTX) has been minimal to date.

Methods: From June 2011 at our institution, OD-TAC was approved for use in selected LTX recipients with a 1:1 conversion from BID-TAC to OD-TAC. Data

including demographics, indication for conversion, mean TAC doses and trough drug levels, adverse effects, length of treatment were recorded prospectively.

Results: Of 91 LTx recipients [mean age 48 yrs (range 13–69), 56% male, median days post LTx = 362 (range 9–6915); indication for LTx = 32% CF, 35% COPD, 27% ILD] were converted to OD-TAC. Main indications for conversion: antifungal therapy (63%) requiring TAC dose reduction and renal impairment-RI (11%) due to toxic TAC levels, or poor BID-TAC adherence (11%). Mean daily TAC dose and trough level pre and 1 month post conversion were 4 mg, $9 \pm 3.6 \mu\text{g/l}$ vs. 3 mg, $6 \pm 2.1 \mu\text{g/l}$ respectively. Although 14/91 patients are now deceased (primarily due to chronic rejection) only seven patients ceased OD-TAC therapy due to adverse effects: $n = 3$ rash, oedema and $n = 4$ patients with worsening RI ceased TAC completely. Of 75% remain on OD-TAC with a median length of treatment of 358 days (range 18–722) despite 30% having now ceased antifungal therapy. Patients reported adherence to OD-TAC regime was easier and overall frequency of TAC level monitoring was reduced.

Conclusion: OD-TAC has thus far proven to be an additional, safe, effective, long term I/S option in the majority of selected LTx recipients.

P685A

DE NOVO ANTI-HLA IMMUNIZATION AFTER LUNG TRANSPLANTATION: IMMUNOLOGICAL AND CLINICAL SIGNIFICATIONS

Jérémy Reeb¹, Pierre-Emmanuel Falcoz¹, Anne Parissiadis², Anne Olland¹, Nicola Santelmo¹, Daniel Hanau², Romain Kessler¹, Gilbert Massard¹

¹Lung Transplantation Team Strasbourg University Hospital; ²Tissue Typing Laboratory, Etablissement Français du Sang, Alsace

Background: This study assesses the influence of de novo (DN) anti-HLA immunization after lung transplantation (LTx).

Methods: Retrospective study including 66 patients classified into 3 groups: patients with DN anti-HLA donor-specific antibodies (Abs) (DSA) (group 1, $n = 17$), patients with DN anti-HLA non-donor-specific Abs (NDSA) (group 2, $n = 7$), and non-immunized patients (group 3, $n = 42$). After immunological analysis, we compared FEV1 monitoring curves, and survival with and without bronchiolitis obliterans syndrome (BOS).

Results: DSA and NDSA were diagnosed 25 and 36 days after LTx respectively. Abs rates increased in group 1 compared to group 2 ($p < 0.05$). FEV1 decreased earlier in groups 1 and 2 than in group 3. FEV1 decreased in group 1 compared to group 3 ($p = 0.03$). BOS incidences increased in group 1 compared to group 3 ($p < 0.05$). DN Abs does not affect survival.

Conclusion: DN anti-HLA Abs is related to early onset of FEV1 decline. DN anti-HLA DSA lead to humoral rejection.

PS15-PANCREAS

P686

THE PANCREATIC TRANSPLANT PROGRAM QUALITY ASSESSMENT

Tadeusz Grochowicki, Zbigniew Galazka, Krzysztof Madej, Sławomir Nazarewski, Sławomir Frunze, Tomasz Jakimowicz, Amro Alsharabi, Jacek Szmidt
 Department of General, Vascular and Transplant Surgery, Medical University of Warsaw, Poland

Methodology of assessment of the pancreatic transplant program to improve the quality after spktx was established. Complications after 112 spktx were classified by Dindo-Clavien scale and divided into: complications due to transplanted pancreas ($n = 66$), transplanted kidney ($n = 23$) and general surgical complications ($n = 31$). Risk adjusted model using multivariable logistic regression and the observed to expected ratio of mortality (O/E RM) was assessed for three eras of transplant program. Mortality due to complications originated from transplanted pancreas, kidney and general surgery complications were: 12.5%, 1.7% and 1.7% respectively. The model for mortal complications of transplanted pancreas is: $p = 4.08 + 0.064 \times \text{donor age} + 1.37 \times \text{transplanted pancreas vascular anastomoses pancreas above 35 min} - 1.93 \times \text{duration of dialysis therapy above 24 months}$. O/E RM for three eras of pancreatic transplant program were: 0.89, 1.69, 0.92 respectively. This methodology objectively evaluated our program.

P688

ARTERIAL-GRAFT DUODENAL FISTULA AS A CAUSE OF MASSIVE, LONG-TERM GASTROINTESTINAL BLEEDING AFTER PANCREAS TRANSPLANTATION

Katarzyna Baumgart¹, Katarzyna Baumgart², Marta Matejak-Gorska², Aleksandra Poplawska², Marek Durlik², Marek Durlik¹
¹Department of Surgical Research and Transplantology, Polish Academy of Sciences Medical Research Center; ²Clinical Department of Gastroenterology Surgery and Transplantation, Central Clinical Hospital M.O.I.

Background: Pancreas transplantation is still one of the transplantations with the highest rate of postsurgical complications. The risk in the early posttransplant period is crucial for patient and graft survival but some of the complications are life-threatening even a long time after surgery.

Methods/materials: All recipients who underwent deceased donor pancreas or pancreas and kidney transplantation from January 2005 to December 2012 at the Central Clinical Hospital MSW in Warsaw were enrolled in this study.

Results: We performed eighty-seven pancreas or pancreas and kidney transplantations (83 SPK, 1 PAK, 3 PTA). We present three cases of massive bleeding from the gastrointestinal tract in the 2nd, 6th and 10th months after transplantation. Each of these patients required an urgent operation as a result of arterial-graft duodenal fistula. Medical records of these patients were analysed.

Conclusion: Massive gastrointestinal bleeding with concomitant rapid general health state collapse in patients after pancreas transplantation may be the result of an arterial-graft duodenal fistula. Immediate diagnosis and endovascular treatment involving stenting the artery are crucial for the patient's survival. In every case the patient required resection of the pancreatic allograft.

P689

THE ROLE OF NUTRITIONAL ASSESSMENT FOR SIMULTANEOUS PANCREAS KIDNEY TRANSPLANT CANDIDATES AND EARLY ENTERAL NUTRITION

Sally Finlay, Elijah Ablorsu, Argiris Asderakis, Dawn Chapman
 Cardiff and Vale ULHB

Introduction: There is limited research into the role of nutrition within Simultaneous Pancreas Kidney Transplant (SPK) candidates. Malnutrition is considered one of the late complications of chronic kidney disease and type-1 diabetes. It is important to actively manage these patients prior to transplantation and provide adequate, intense nutrition after surgery. Early Enteral Nutrition (EEN) has been proven to improve the postoperative course after major surgery.

Method: Prospective data was gathered from 23 consecutive SPK recipients who underwent transplantation between Jan-2010 and Jul-2012. All candidates received nutritional assessment prior to activation on the WL and post-transplant nutrition was planned according to their nutritional status (early oral intake with supplementation [O] or early jejunal feeding, via NJ tube inserted during surgery [J]). The end-point was to assess nutritional intake between the two groups: achievement of $\geq 60\%$ energy requirements by day-7 (7d-60%) and at the time of discharge (total-60%).

Results: From 23 recipients, 13 received J-feed and 10 O-feed. We found no difference between these groups in demographics. However J-group had lower

BMI (24.17 vs. 24.9, $p = 0.14$) and lower pre-transplant Albumin (30.4 vs. 35.1, $p = 0.05$). Despite features of malnutrition in J-group, they reached 60% energy requirements significantly faster (7 vs. 15 days, $p = 0.02$); with higher 7d-60% (87% vs. 60%, $p = 0.31$) and shorter period of reinstitution of pre-transplant albumin levels (56 vs. 69 days, $p = 0.55$). Only one patient in each group required TPN.

Conclusion: Results suggest both types of EEN provide sufficient nutritional intake for SPK recipients; and more importantly minimize need of TPN. Furthermore, careful pre-transplant nutritional assessment can identify malnourished candidates and recommend early jejunal feeding.

P690

THE IMPACT OF THE METHOD ON KIDNEY GRAFT AND PATIENT SURVIVAL IN KIDNEY-PANCREAS TRANSPLANTATIONS FOR TYPE I DIABETES MELLITUS

Ayhan Dinçan¹, Ibrahim Aliosmanoglu², Huseyin Kocak², Ayhan Mesci², Veysi Bahadır², Hasan Altunbas², Necmiye Hadimioglu², Alihan Gurkan²
¹Akdeniz University Transplantation Institute; ²Akdeniz University Organ Transplantation Institute, Antalya, Turkey

Patients who develop end-stage renal disease (ESRD) associated with Type I Diabetes Mellitus may receive kidney alone (KA) transplantation from a living donor or a cadaver, simultaneous pancreas-kidney (SPK) transplantation, or a pancreas after kidney (PAK) transplantation. The goal of the study is to examine the long-term impact of pancreas transplantation on the kidney graft and patient survival rates. A total of 85 cases, consisting of 30 that received living donor KA, 21 that received SPK, and 34 that received PAK transplantation between February 2003 and June 2010 at Akdeniz University Organ Transplantation Institute were retrospectively screened. The average follow-up duration was 55 months; 33, 65, and 65 months respectively. There was a graft loss in four cases (three chronic rejection, one early acute rejection) from the KA group, and in 1 case (chronic rejection) from each of the SPK and PAK groups ($p = 0.252$). The five-year kidney graft survival rates were 86.7% in KA, 95.2% in SPK, and 97.1% in PAK ($p = 0.252$). There was a single patient loss in both KA (myocardial infarction in the 5th month) and SPK (cardiovascular failure in the 6th year), and there was no patient loss in the PAK group ($p = 0.34$). In this series, the kidney survival was higher in SPK and PAK groups compared to the KA group, after the long-term follow-ups. However, there were no differences observed in terms of patient survival rates. Therefore, SPK should be the primary preference in patients with ESRD associated with Type I DM; however, for the cases that have a living donor, pancreas transplantation should be considered after kidney transplantation, or the patients can be followed-up on with close blood sugar control.

P691

THE USE OF "RESCUE ORGANS" FOR PANCREAS TRANSPLANTATION

Hans-Michael Tautenhahn¹, Hans Michael Hau¹, Dirk Uhlmann², Mehmet Morgül¹, Peter Fellmer¹, Moritz Schmelzle¹, Felix Krenzien¹, Michael Bartels¹, Sven Jonas¹
¹University of Leipzig; ²Klinikum Döbeln

Background: Due to the ongoing shortage of cadaver organs the use of extended criteria donors for pancreas transplantation should be considered. The use of organs after "rescue allocation" within EUROTRANSPLANT region, could be a possibility to expand the donor pool.

Material and methods: Between 2007 and 2010, 31 pancreas transplantations were performed at our centre. Among these, in seven cases (six SPKs, 1PTA) "rescue organs" (RO) were used. These organs had been officially offered to and rejected by at least three consecutive centers for medical reasons (donor instability, medical history of the donor and/or logistical problems). Donor, recipient and clinical/laboratory transplantation/post-transplantation outcomes from patients receiving "rescue organs" were collected and compared with organs from conventional (CONV) donors.

Results: The mean donor age was higher in the RO-group than in the CONV donor-group (28.3 ± 10.7 years vs. 23.0 ± 12.5 years). With a similar mean follow-up period (2.3 ± 0.6 years RO-group vs. 3.9 ± 1.2 years CONV-group), patient, kidney and pancreas graft survival rates were 85% in all three categories in the RO-group respectively, whereas outcomes for CONV donors were 88%, 85% and 83%, respectively. Incidences of pancreatic graft thrombosis, delayed graft function, acute and late rejection episodes such as relaparotomy rates and infections were comparable between both groups. There were no differences between mean Hb1Ac levels between both groups 2 years after transplantation. Whereas, mean serum creatinine levels (RO-group: $78.8 \pm 21.0 \mu\text{M}$ vs. $114.3 \pm 28.4 \mu\text{M}$ in the CONV donor-group $p < 0.05$) 2 years postoperative showed significant differences between both groups.

Discussion: Long-term outcomes of transplanted pancreas from the RO-group were comparable to organs from the CONV -group. Based on the good results, the use of organs from donors with extended criteria's could be a good possibility to expand the donor pool.

P692

USE OF URINARY AMYLASE AS A MARKER FOR REJECTION IN PANCREATIC ALLOGRAFTS?

Michiel D. Voskuil¹, Shruti Mittal¹, Peter J. Friend¹, Rutger J. Ploeg¹, Edward J. Sharples²

¹Nuffield Department of Surgical Sciences, Oxford Transplant Centre, University of Oxford; ²Nuffield Department of Medicine, Oxford Transplant Centre, University of Oxford

Introduction: In pancreas transplantation alone (PTA) monitoring of rejection remains elusive impacting significantly on survival. Exocrine bladder drainage allows assessment of urinary amylase (UA) as surrogate marker. Unfortunately, gold standards for UA collection and interpretation are not well defined.

Methods: From Jan. 2011 to Jan. 2013, 24/92 pancreas recipients received a bladder drained PTA. During in-hospital stay and follow-up, values for UA were determined. All clinical graft events were documented using radiological evidence for thrombosis, rejection or graft pancreatitis, and/or by histologically proven rejection in the duodenal donor segment. Significant drops in UA were defined as a decrease of >25% from baseline. Daily values for UA and urine creatinine (Creat) concentration were determined in both urine spots and 24-h collections.

Results: In this series a large interpatient variability was seen for UA (range 24.5 to 200, 100 IU/l). UA values increased posttransplant and reached stable levels by 15 days. We defined baseline as the median UA concentration after day 15. A strong correlation between UA concentration from 24 h collection and spot urine samples was found ($r = 0.79$, $p < 0.001$). Also, we observed a strong correlation between total 24 h UA production and spot UA/Creat ratio ($r = 0.80$, $p < 0.001$). The UA/Creat ratio showed less variation during episodes of impaired renal function, and appears to be a useful method to assess changes in UA. Of 13 major clinical events occurred in this cohort. A > 25% fall in UA level predicted 9/13(69%) events whilst a >50% fall was found to be less predictive.

Conclusion: Spot UA/Creat ratio is useful and the most accurate method of monitoring following bladder drained pancreas transplants. It correlates well with the most common used method of total 24 h UA production and with clinical events. The large inter-patient variability in UA requires comparison to each patient's individual baseline, that should be set once the values have been stabilized. A drop in UA should be defined as a decrease of >25%. This study reports a reliable measure of pancreas graft function that is simple, accurate, practical and patient-friendly. We conclude that no urine collections but spots should be taken to determine UA values as a marker for events in PTA.

P693

BOVINE PATCH REPAIR OF AN ARTERIAL MYCOTIC PSEUDOANEURYSM FOLLOWING PANCREATIC TRANSPLANTATION

Petros Yiannoullou, David van Dellen, Bence Forgacs, Afshin Tavakoli, David Murray, Titus Augustine
Manchester Royal Infirmary

Background: Arterial mycotic pseudoaneurysms are rare complications of pancreas transplantation. Life threatening haemorrhage results from rupture into the peritoneum, adjacent bowel or bladder and as such the condition is synonymous with mortality. Vascular techniques using synthetic tube graft or endovascular stents frequently fail due to graft infection whilst primary repair results in arterial stenosis.

Case: A 41 year old male, with type 1 diabetes mellitus and end stage renal failure, underwent successful simultaneous kidney pancreas transplantation. He presented, 9 months later, with copious fresh rectal bleeding secondary to an ileo-enteric fistula resulting from a mycotic pseudoaneurysm located at the anastomosis between the native external iliac artery and Y-iliac conduit to the graft pancreas. This was successfully managed with a bovine pericardial patch (BPP) repair of the arterial defect following graft pancreatectomy. He remains well with no vascular insufficiency 12 months following the procedure.

Conclusions: BPP offers good handling technique, excellent haemostatic properties and a favourable profile of infection risk in comparison to synthetic patches. Its use in arterial reconstruction within infected fields has been reported. This case highlights its use as a treatment for a post transplant mycotic pseudoaneurysm.

P694

CONSERVATIVE TREATMENT OF ENTERIC FISTULA (EF) AFTER SIMULTANEOUS PANCREAS AND KIDNEY TRANSPLANTATION (SPK)

Valeria Valli, Lucrezia Furian, Cristina Silvestre, Alessandra Bertacco, Andrea Geron, Paolo Rigotti
Kidney and Pancreas Transplantation Unit, University of Padova

Introduction: SPK is associated with an incidence of pancreatic graft loss up to 10% in the first 6 months. Surgical complications are the most relevant causes of early graft loss. We present a case of a SPK complicated by an EF healed with conservative treatment after failure of surgical repair.

Clinical case: A 57 years old man received a SPK with enteric esocrine drainage with duodeno-ileal mechanical anastomosis. Post operative course was complicated in 8th PO by leakage of the duodenal-ileal anastomosis. The patient underwent two surgical procedures with reconstruction of the duodenal-ileal anastomosis and, due to a further leakage, suture of the anastomotic hole. Nevertheless, the persistence of high flow fistula (800 ml/die with amylase of 40 000 U/l) led to an alternative approach with peri-anastomotic abdominal drainages placed by interventional radiologist. The patient was discharged and underwent serial contrastographical controls for the following months, showing a progressive resolution of the fistula. After 7 months peri-anastomotic drainages were removed; the patient has always had optimal renal function and normal glycaemia with no need of insuline therapy.

Conclusions: Healing of a EF in a SPK transplantation recipient is a slow process which can be obtained with conservative treatment, allowing to preserve graft function.

P695

THROMBOSIS IN PANCREAS TRANSPLANTATION, SINGLE CENTRE, 5 YEAR EXPERIENCE

Karim Wahed, Sophie Shilston, Shruti Mittal, Peter J. Friend, Rutger J. Ploeg, Anil Vaidya, Shrikant Reddy, James Gilbert, Isabel Quiroga, Edward J Sharples, Sanjay Sinha
Oxford Transplant Centre

Introduction: Simultaneous Pancreas Kidney (SPK) and Pancreas Transplant Alone (PTA) transplants are now standard treatment for patients with Diabetic Nephropathy and those with severe hypoglycaemic unawareness. Thrombosis is one of the leading non-immunological causes for early graft dysfunction often resulting in graft loss.

Methods: This was a retrospective single centre study reviewing patients who had SPK or PTA transplants between 2007 and 2012. All patients received a Thromboelastogram (TEG) directed anticoagulation which comprises of intravenous low molecular weight Dextran, subcutaneous Heparin and 75 mg Aspirin. Cross-sectional imaging of the pancreas was carried out in the setting of graft dysfunction or sepsis. Patients who had post-operative thrombosis were identified using an electronic data storing system. Clinical notes and flow charts were reviewed. All those with proven thrombus on imaging were started on therapeutic anticoagulation.

Results: Of 462 patients underwent pancreas transplantations between 2007 and 2012. 73 (15.8%) were reported to have thrombi in the pancreatic blood vessels. 19 (26%) were identified incidentally, however, 54 (74%) cases had demonstrated clinical manifestation of pancreatic insufficiency such as fluctuating blood sugars, failed oral glucose tolerance test, or decrease in urinary amylase for those with bladder drainage pancreas transplant. Thrombosis was reported in the following vessels; 41 (56%) were arterial, 20 (27.4%) were venous and 12 (16.4%) were mixed.

Conclusion: Thrombi formation after pancreas transplantation has been widely reported in the literature. These are seen in spite of an anticoagulation protocol. Some are detected in the background of graft dysfunction, others are identified incidentally when patients are scanned for other causes. Our data suggests that imaging helps detect thrombi in most settings and therapeutic anticoagulation after thrombus detection results in graft salvage in 71.2% cases.

P696

LAPAROSCOPIC SLEEVE GASTRECTOMY IN A OBESE PATIENT WITH A FUNCTIONING PANCREATIC GRAFT: CASE REPORT

Carlo Socci, Luigi Totaro, Elena Orsenigo, Diego Massimini, Danilo Parolini, Paola Maffi, Antonella Lometti, Alessandro Saibene, Francesca Muffatti, Vittorio Giardini, Antonio Secchi, Carlo Staudacher
Ospedale San Raffaele, Milano

Background: It is well established the association between obesity and diabetes, metabolic syndrome, pancreas insufficiency and progression of chronic kidney disease. Recent evidences showed the improving of renal and pancreatic function after bariatric surgery. We reported a single case of obese patient with a functioning pancreatic graft subjected to sleeve gastrectomy. **Clinical case:** A 49 year-old obese man of 118 kg, BMI 35.5, underwent pancreas transplantation in 2004 owing to uncontrolled type 1 diabetes came to our attention. He was affected by mildly chronic kidney disease (Serum creatinine: 1.39 mg/dl, Plasma filtration rate: 61 ml/min) with the evidence of microalbuminuria (55.5 mg/l), arterial hypertension, dyslipidemia. There was a good metabolic control (Hb1ac: 41 mmol/mol, Fasting plasma glucose: 107 mg/dl). Current immunosuppressive therapy was mycophenolate and FK 506. The patient underwent to gastroscopy, gastrografin swallow, abdominal ultrasound before surgery, with the finding of hepatic steatosis. To improve metabolic control and kidney function a laparoscopic sleeve gastrectomy was planned. The section of the stomach was started at 6 cm from pylorus, with a gastric calibration of 12.7 mm (42 French), all fondus of the stomach was then completely removed, with cardias distance from the end staple-line of 1.5 cm. The patient is currently recovered with no complication.

Conclusion: Laparoscopic sleeve gastrectomy is a feasible procedure for diabetic obese patients bearing a functioning pancreas graft.

P697

IN VITRO DIFFERENTIATION OF WHARTON'S JELLY DERIVED MESENCHYMAL STEM CELLS INTO INSULIN-PRODUCING CELLS

Masomeh Nekui¹, Negar Azarpira², Mahdokht Aghdai²

¹Azad University of Arsenjan; ²Transplant Research Center, Shiraz University of Medical Sciences

Background: Diabetes mellitus is one of the major chronic metabolic diseases affects at least 200 million people worldwide. Pancreas and Islet cell transplantation is an effective way for treatment of diabetes. The aim of this study is to produce insulin-producing cells (IPC) from umbilical cord Wharton's jelly mesenchymal stem cells.

Methods: The isolated MSCS from Wharton's jelly were positive for CD44 and CD90 and CD105 and negative for CD133, CD45 and CD34. The cells were cultured in Dulbecco Modified Eagle Medium-F12 (DMEM-F12) with retinoic acid (RA), Epidermal Growth Factor (EGF), exendin-4 and 10% FBS in three step protocol for 20 days.

Results: HUMSCS morphology changed from fibroblast like cells in to round epithelioid cell clusters. The IPCs expressed the insulin, PDX1 and Ngn3 mRNA in RT-PCR method. DTZ staining was employed and the red granule was observed in clusters. The insulin secretion was measured by ELISA assay.

Conclusion: Although we produced the IPC cells, but our yield was low. However, HUMSCS could be considered as the cell of choice for cell-based treatment of type 1 diabetes.

P698

QUALITY OF LIFE AFTER PANCREAS TRANSPLANTATION

Nisheeth Kansal, Louise Johnson, Colin Wilson, Derek Manas, Steve White
Institute of Transplantation

Aim: There is limited evidence currently available to explain the psychosocial aspects of pancreas transplantation especially after graft failure. The aim of this study was to investigate different aspects of patient well being relevant to pancreas transplantation.

Methods: Questionnaires were sent out to patients who had undergone Simultaneous Pancreas Kidney (SPK) transplantation along with those on the waiting list (W/L). Questionnaires included The Hospital Anxiety and Depression Scale (HADS), Clinical Outcomes in Routine Evaluation (CORE-10), Generalised Anxiety Disorder Assessment 7 (GAD-7), Roland Morris Disability Questionnaire Abbreviated (RMDQ-A), work and social adjustment scale (WSAS) and WHO Quality of Life- BREF (WHO-QOL BREF) within four domains. Results are expressed as mean \pm SD and p value \leq 0.05 (ANOVA) was considered significant.

Results: Overall response rate was (45%) including those on the W/L ($n = 6$), functioning SPK (FSPK) ($n = 24$) and non-functioning SPK (NFSPK) ($n = 6$). The HADS responses did not reveal any significant difference between the three groups (p values of 0.078 and 0.079 for anxiety and depression scores respectively). The scores for CORE-10 questionnaires revealed significantly higher levels of psychological distress in patients with NFSPK (17.83 ± 3.0) compared to FSPK group (9.44 ± 6.5) ($p = 0.014$). A similar pattern was noted with the RMDQ-A questionnaire which revealed higher levels of disability in FSPK group (6.1 ± 6) compared to NFSPK group (14.4 ± 3.2) ($p = 0.028$). Scores were similar in all groups for GAD-7 ($p = 0.069$), WSAS ($p = 0.061$) and Domains 1, 2 and 3 in WHOQOL-BREF ($p = 0.054$, 0.066 and 0.087 respectively) with better indices in post transplant group for domain 4 ($p = 0.001$).

Conclusion: This study demonstrates that despite correction of uraemia those patients with a failed pancreas graft do experience significantly reduced impairment in some aspects of their quality of life which should be addressed during their rehabilitation.

P699

OUTCOMES FOLLOWING PANCREAS TRANSPLANTATION IN PATIENTS WITH A RAISED C-PEPTIDE

Carlo Ceresa, Murali Somasundaram, Shruti Mittal, Edward J. Sharples, Srikanth Reddy, Anil Vaidya, Peter J. Friend, Sanjay Sinha
The Oxford Transplant Centre

Background: Simultaneous pancreas and kidney (SPK) transplantation is a recognised treatment for Type I diabetes mellitus (DM) but suitability as a treatment for Type II DM remains controversial. C-peptide levels are used to aid differentiation between Type I and II diabetics. We identified patients with a raised c-peptide prior to pancreas transplantation and assessed post-transplant outcomes.

Methods: All patients undergoing pancreas transplantation at a single centre between January 2008 and September 2012 were identified. Patients with a pre-operative c-peptide >0.02 ng/ml were extracted from this group and analysed. Patient demographics and pre-operative data specific to DM were

recorded. Post-operative outcomes including incidence of complications and short and long term graft and recipient survival were assessed.

Results: Three-hundred-and-sixty-five pancreas transplants were performed during the study period. Twenty five (6.8%) patients had a pre-operative c-peptide >0.02 ng/ml with a median level of 0.49 ng/ml (range = 0.04–4.51 ng/ml). All patients underwent SPK transplantation. Median age at diagnosis of DM was 16 years (range = 2–51 years) and mean body mass index (BMI) was 24.6 kg/m². In the immediate post-operative period, 3 (12%) patients developed vascular complications and 2 (8%) patients developed infected pelvic collections requiring surgical and percutaneous drainage. One (4%) patient required a laparotomy for small bowel obstruction and 1 (4%) patient died 66 days post-operatively following graft pancreatectomy. Twenty four (96%) patients had a functioning graft at time of discharge and at last follow-up (range 0.25–4.5 years), 22 (88%) patients had functioning grafts.

Conclusion: We report favourable early late outcomes in this patient population that are comparable to patients without pre-operative c-peptide production.

P700

NUTRITIONAL SUPPORT IN SIMULTANEOUS PANCREAS AND KIDNEY TRANSPLANTATION: A SINGLE CENTRE EXPERIENCE

Hussein Khambalia, Je Song Shin, Zia Moinuddin, Rauri Greer, Rosalind Campbell, Titus Augustine, David van Dellen
Manchester Royal Infirmary

Background: Simultaneous pancreas and kidney (SPK) transplantation provides insulin and dialysis independence. However, the recipient may have comorbidities contributing to malnutrition and a chronic catabolic state, strong predictors of adverse outcome. Current trends favour early enteral feeding. However, in SPK patients, concerns exist due to perceived risks of gastroparalysis, ileus and a fragile enteric anastomosis. Total parenteral nutrition (TPN) is therefore routine therapy in some units. We aimed to assess outcomes of this nutritional modality.

Methods: A retrospective study was performed of SPK recipients in a single centre over 2 years (11/10–11/12) focusing on nutritional therapies and subsequent clinical outcomes. Nutritional parameters included TPN duration, time to enteral diet, and complications directly attributed to TPN. Clinical outcomes included critical care and total hospital stays. Post-operative nutritional biomarkers were assessed. Results 52 patients were included (32 male, 20 female; mean age 42.9, [SD = 7.9]; mean BMI 24.0 [SD = 2.8]). 77% started TPN on day 1 post-transplant and mean duration was 9.8 days (range 3–23; SD = 4.2). Mean ITU and total lengths of stay were 6 (SD = 6) and 30 days (SD = 26) respectively. Complications attributable to TPN included sepsis (5.8%), feeding catheter leak (3.8%), fluid overload (1.9%) and hyperglycaemia (9.6%) which normalised after a TPN break. Serum albumin dropped by $>30\%$ immediately and remained below normal in the first week post-surgery. Alkaline phosphatase levels increased above normal range after 6 days with no long term sequelae.

Conclusions: TPN appears to provide a safe modality of nutritional support for early post-SPK nutrition with a low rate of reversible complications. However, its potential advantages remain unclear. Further randomised comparative studies against enteral nutrition are required to clarify the optimal approach in this challenging group of patients.

P701

IMPACT OF RECIPIENT BODY MASS INDEX IN SHORT AND LONG TERM SURVIVAL OF PANCREATIC GRAFTS

Benoit Bédard, Nadja Niclauss, Axel Andres, Anne-Sophie Jannot, Christian Toso, Philippe Morel, Thierry Berney
University Hospital of Geneva

Background: The prevalence of obesity is rising in the surgical population. In pancreas transplantation, the impact of recipient BMI on short and long term pancreas graft survival has not been studied.

Methods: We analyzed data from all individuals who underwent a first pancreas transplant from October 1, 1987 to August 30, 2011 and recorded in the Scientific Registry of Transplant Recipients. Recipients were categorized into BMI classes. Long-term graft failure was defined as return to insulin therapy and therefore includes post-transplant diabetes mellitus (PTDM). Patient and graft survival were analyzed by Kaplan-Meier. Groups were compared using the logrank test for univariate analysis and Cox proportional hazard regression for multivariate analysis.

Results: Of 21 075 individuals were included in the analysis. Median follow-up was 4 years. Subjects were overweight or obese in 39%. Early pancreas graft loss increased with recipient BMI ($p < 0.001$). Compared to normal or low BMI, risk of early graft failure at 90 days increased by 21%, 50% and 74%, for overweight, obese class I and obese class II recipients, respectively. Early mortality was similar in all groups, except for class II obese recipients in whom risk of death increased by 84% as compared to other groups. Compared to normal or overweight BMI, risk of graft failure at 4 years increased by 23%, 15% and 35%, for underweight, obese class I and obese class II recipients, respectively. The low

graft survival in underweight recipients was associated with a risk of death increased by 67% as compared to normal BMI recipients at 4 years.

Conclusion: Increased BMI is associated with an increased risk of early graft loss and early mortality. Increased BMI does not seem to be associated with an increased incidence of PTDM. Underweight is associated with an increased risk of death in the long term.

P702

OPTIMAL USE OF PANCREATIC GRAFTS

Edurne Alvaro, Manuel Abradelo, María García, Alejandro Manrique Municio, Felix Cambra Molero, Cristina Alegre Torrado, Sandra García Aroz,

Jorge Calvo Pulido, Oscar Caso Maestro, Alvaro García-Sesma, Carmelo Loinaz Seguro, Enrique Moreno, Carlos Jiménez Romero

Hospital Universitario 12 de Octubre

Background: Pancreas graft is a fragile organ that requires optimal conditions to be retrieved. If we also consider organ shortage, we observe that the number of patients on the waiting list is growing. That is why we must make a special effort to maximize the use of donor pancreas.

Methods: We report three cases of pancreatic harvesting in challenging circumstances. One of them in a donor with a previous splenectomy and the other two cases in two different donors in which we found an annular pancreas (AP). Two of the cases were simultaneous pancreas-kidney transplantation, and the other one was a pancreas after liver transplantation.

Results: The average age of the recipients was 40 years and 66% of them were male. All patients had a graft normal function after transplantation and were discharged without insulin requirements. Only one case transplanted with an AP, suffered a graft thrombosis a year after transplantation and nowadays is in the waiting list for retransplantation.

Conclusions: Pancreas grafts retrieval in donors with previous surgeries and AP grafts are challenging from a technical point of view, but do offer good results in recipients. There are no association between AP transplantation and a higher rate of graft thrombosis. Given the limited numbers of donors, we must evaluate every pancreas graft with these features.

P703

SIMULTANEOUS PANCREAS AND KIDNEY TRANSPLANTATION IS A SUITABLE OPTION FOR TYPE I DIABETICS PATIENTS. RESULTS AFTER FOUR YEARS OF THE PROGRAM

Guadalupe Tabernero Fernández, Marc H. Blanc, Josepa Sebastiá Morant, Cristina Lucas Álvarez

Hospital Clínico Universitario de Salamanca

Background: We studied 28 patients who had received simultaneous pancreas and kidney transplants from 27th February 2010 to 1st of February 2013. Creatinine, amylase, lipase and glycosylated hemoglobin were collected, at discharge and again after 1 month, 6 months, 1 year and 2 years. All patients were treated with Thymoglobulin, corticosteroids, calcineurin inhibitor and mycophenolate mofetil.

Methods and material: We studied the evolution of creatinine at discharge and at two years, also how long cold ischemia and laboratory parameters were at discharge. Pancreatic and renal functions were assessed using Student's t test and are presented as mean and standard deviation. The analysis was conducted using SPSS (v15.0). We determined a confidence level of 95% and the results were considered statistically significant, the differences if $p < 0.05$.

Results: During this period 28 patients received pancreas-kidney transplants in our service. The average cold ischemia time of the pancreas was 11 h 57 min and of the kidney was 14 h 58 min. The mean creatinine, amylase and lipase at discharge were 1.31 mg/dl, 74 and 32.5 U/l respectively. We observed no statistically significant changes between values of creatinine, lipase and amylase at discharge and at six months, one, two, three and four years. However, HbA1c showed a statistically significant decrease between the values at the time of transplant and three months being the average of 7.41% and 5.03% respectively. Four years later after the start of our program, all our patients are alive. One patient (a woman) died in the operating theatre and because of that, she was excluded from the study. Considering this, our survival is 96.4% at 4 years, with all the allografts working.

Conclusions: Pancreas and kidney transplantation is a very suitable treatment option for type I diabetes patients, who need renal replacement therapy, with improvement evident in the levels of glycosylated haemoglobin.

P704

PANCREAS TRANSPLANTATION WITH ENTEROANASTOMOSIS AGAINST NATIVE DUODENUM IS SAFE – AND OFFERS IMPROVED ENDOSCOPIC ACCESS FOR SCHEDULED BIOPSIES AND THERAPEUTIC INTERVENTIONS

Tor J. Eide, Ole Øyen, Rune Horneland, Aksel Foss, Vemund Paulsen, Jørn P. Lindahl, Knut Lundin, Lars Aabakken, Trond Jenssen
Oslo University Hospital Rikshospitalet

Background: To further improve on rejection surveillance after pancreas-Tx (PTx), we have now performed a series with enteroanastomosis against native duodenum (END; at the junction of pars descendens/horizontalis), allowing endoscopic transduodenal ultrasound-guided biopsies of the pancreas (EUS-BP).

Material and methods: From sep. 2012 to may 2013, 27 PTx's have been performed by END. Scheduled biopsies of the duodenal segment and pancreas were planned at weeks 3 and 6, and 1 year post-Tx.

Results: This PTx-END material, which represents the largest series published so far, has been divided into an early (first 13) and late (last 14) era, to demonstrate the experience gained. The PTx-END was easy to perform, without tension, and none of the complications were directly attributable to the END. In the patients with graftectomy, the duodenotomy was closed without complications. The case with exocrine leakage was solved by endoscopic stenting of the pancreatic duct. Fig. 1: Endoscopic stenting of the PTx-END duct. Guide-wire and contrast in duct (right). Final placement of stent (left); Tx-duodenal segment below; distal duodenum below.

However, the more "retrovisceral positioning" of the pancreas gave rise to tension on the portal vein/caval anastomosis – reflected in the high rate of reoperations during the first era. Through this series, we have adjusted several technical details, and do think we are about to "crack the code". The portal vein should be elongated in the majority of cases. The END was easy to access endoscopically – preferably by 0–30° optique. Biopsies were easier and faster to obtain than by Double balloon enteroscopy.

Conclusions: By technical adjustments, our PTx-END results have improved through this series.

The PTx-END and EUSBP seem safe, and may provide improved rejection surveillance – as well as improved therapeutic options towards exocrine leakage. However, the procedure is still considered "under evolution".

P705

ROLE OF ABDOMINAL ULTRASOUND, ENDOSCOPIC ULTRASOUND (EUS) AND FINE NEEDLE ASPIRATION (FNA) IN DIAGNOSIS OF CYSTIC PANCREATIC LESIONS

Reem Ezzat¹, Hussein Okasha², Hala Moustafa¹, Mahmoud Ashry¹, Mohamed Naguib², Emad Elgemeie³

¹Assuit University Hospital; ²Cairo University Hospital; ³National Cancer Institute

Background: Recently, many imaging techniques helped in increasing frequency of detection of pancreatic cystic lesions. The addition of fine needle aspiration for the used imaging methods has raised the accuracy a lot for early detection of neoplasm.

Aim: To differentiate between benign and neoplastic pancreatic cystic lesions by evaluating cyst fluid CEA, mucin stain, amylase and CA19-9 compared to conventional cytopathologic examination.

Subjects and methods: This prospective study included 61 patients with pancreatic cystic lesions. After having written consents, the patients were subjected to US-FNA or EUS-FNA according to the accessibility of the lesion. The aspirated specimens taken from the cysts were subjected to cytopathological examination (including mucin staining), tumor markers (CEA, CA19-9) and amylase level.

Results: Using the appropriate statistical tools, specificity, sensitivity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy were calculated. Mucin stain alone in cystic fluid showed sensitivity 86%, specificity 94%, PPV 90%, NPV 92% and accuracy 92% for neoplastic detection. Cytopathological examination alone showed sensitivity 83%, specificity 91%, PPV 89%, NPV 85% and accuracy 87% for detecting neoplastic lesions. CEA level had sensitivity of 69%, specificity 59%, PPV 55%, NPV 73% and accuracy 64% for neoplastic detection. Adding CEA level to mucin level with cytopathological examination of the aspirate showed sensitivity 97%, specificity 50%, PPV 63%, NPV 94% and accuracy 72% for neoplastic detection. Endoscopic ultrasound had sensitivity 40%, specificity 100%, PPV 100%, NPV 10% and accuracy 44% but abdominal ultrasound was inconclusive. CA19-9 did not show statistical significant difference between neoplastic and benign cysts.

Conclusion: The combination of CEA, mucin and cytopathology in fine needle aspiration of pancreatic cystic lesions showed better sensitivity than each analysis when done alone and are suggestive but not diagnostic.

P706

BLOOD TRANSFUSION IN SIMULTANEOUS PANCREAS AND KIDNEY TRANSPLANT AND PANCREAS ALONE TRANSPLANT PROCEDURESTim Sparkes*Oxford University Hospitals Trust*

Little information is available to advise patients during the consent process about the necessity for- and likely quantities of packed red blood cell transfusions for pancreas transplants. In 2012, 77 pancreas transplant procedures were performed in Oxford, (15 pancreas alone transplants PAT and 62 simultaneous pancreas and kidney SPK transplants). The actual

quantities of packed red blood cells used, both intra-operatively and during the admission were recorded. Pancreas transplant patients received an average of 4.77 units of packed red blood cells (5.29 for SPK, 2.6 for PAT). On average, of 1.46 units (1.58 SPK, 0.93 PAT) was transfused on the day of operation and a further 3.31 units (3.71 SPK and 1.67 PAT) were given during the rest of the admission to hospital. Only 24.68% of patients did not require a blood transfusion (16% SPK, 60% PAT). Admission haemoglobin and dialysis technique were the only predictors demonstrated for transfusion quantity for each procedure (age, BMI, HbA1C, cold ischaemic time also assessed). Information is now available to better advise pancreas transplant patients on the need for blood transfusions both intra- and post-operatively.

PS16-PEDIATRIC TRANSPLANTATION

P707

PEDIATRIC VERSUS ADULT KIDNEY TRANSPLANTATION ACTIVITY IN ARAB COUNTRIES

Bassam Saeed
Kidney Hospital

Objective: To evaluate the current status of pediatric kidney transplantation (PKT) activity in the Arab world. **Methods:** A questionnaire was mailed to all kidney transplant centers in Arab countries to collect data on kidney transplant activity in a recent single year.

Results: Of 3309 kidney transplants were performed in one year with a transplant rate of 9.5 per million populations (pmp); 298 were performed for children with a PKT rate of 0.87 pmp. The pediatric share of all transplants is 9% 0.93.5% of all transplants were from living donors. Deceased transplant activity in Arab countries accounts for 14–31% of all transplants in the three countries with deceased donor programs. Out of 212 adult and pediatric transplants that were performed from deceased donors in 8 countries; only 29 cases were for pediatric recipients.

Conclusion: PKT is still inactive in most Arab countries and mostly relying on living donors. The lacking of well developed deceased programs is the main issue to be addressed.

P708

DESIGN OF A RANDOMIZED STUDY EVALUATING EVEROLIMUS IN PEDIATRIC RENAL TRANSPLANT RECIPIENTS

Dhaval Gupta
XXXXXX

Background: Early introduction of everolimus (EVR) may address the concern with long term use of calcineurin inhibitors and steroids in pediatric renal transplant recipients (pRTxR).

Methods: This is a 12-month (mo) study with 24-mo additional safety follow-up in pRTxR (i_T 1 and <18 years). Following a 4–6 weeks run-in period post-Tx, pRTxR (eGFR >50 ml/min/1.73 m²) treated with tacrolimus (TAC) + mycophenolate mofetil + steroids will be randomized (RND) to either continue this regimen or start EVR + reduced TAC + steroid withdrawal at month 6 (figure). Co-primary objectives at Mo12 are to estimate the rate of composite efficacy endpoint of biopsy proven acute rejection, graft loss or death and to evaluate the renal function.

Results: Approximately 106 pRTxR will be RND in 2012 and 2013 across 30 sites in 12 countries. Till date, nine patients were enrolled of whom four were RND. Mo12 results are expected in Q4 2014.

Conclusions: This study will validate the benefits with early introduction of EVR to reduced TAC exposure and steroid withdrawal at Mo6 in pRTxR.

P709

THE FACTORS AFFECTING THE LONG TERM GRAFT SURVIVAL IN PEDIATRIC KIDNEY TRANSPLANTATION

Ismail Sert, Önder Yavascan, Cem Tuđmen, Selçuk Kılınc, Orhan Deniz Kara, Alkan Bal, Sait Murat Dođan, Caner Aksu, Cezmi Karaca, Nejat Aksu Tepecik Training and Research Hospital

Although short-term renal allograft survival in children has improved over the years, long-term graft outcomes remain unclear. We report the characteristics and other variables that impact long-term kidney graft survival in children. Records of 61 pediatric kidney transplant recipients performed at our institution between 1995 and 2011, were evaluated. Patients were divided into two groups (functional and non-functional grafts) to investigate the factors that impact graft survival. The groups were compared in terms of recipient characteristics, underlying disease, HLA status, immunosuppressive therapy, donor characteristics as well as acute rejection and delayed graft function (DGF). Overall graft survival at 1, 5, 10 and 15 years were 93%, 74%, 55% and 41%, respectively. The median graft survival was 128.4 months. Donor age, acute rejection and DGF strongly predicted the chance of graft survival. We consider that several modifiable risk factors can partially account for poorer graft survival in pediatric kidney transplant recipients.

P710

NEONATOLOGY AND ORGAN DONATION – REALITY OR UTOPIA?

Angelika Eder, Jutta Weiss, Carl-Ludwig Fischer-Fröhlich, Thomas Breidenbach
Deutsche Stiftung Organtransplantation

Introduction: Although the number of recipients under 12 months on the waiting-list is small, children often die before transplantation due to the

limitation of size-match. To estimate the potential of donors and the need of organs from that group we investigated the situation in Germany.

Methods: We reviewed the DSO-data-base for donors realized and recipients transplanted under 12 months in Germany from 2007 to 2012. We analysed the number of donors, causes of brain-death and number of organs transplanted.

Results: We identified about 5 organ donors under 12 months per year. In total 27 donors provided 62 grafts, mostly livers (24), hearts (20) and kidneys (17). Of 174 organs were transplanted into recipients under 12 months. Liver-transplantations dominated (135), followed by heart-transplantations (33) and kidney-transplantations (5).

Conclusion: Brain-death on a neonatological ICU is a rare but realistic event. When focusing on the organs donated mostly to be sized-matched more organs were transplanted than donated in Germany (despite liver-splitting). Demand for such organs exceeds the supply provided within the country. Consequently organ donation on neonatological ICUs is an very important issue. In spite of the difficult setting there should be a clear commitment of the whole staff towards organ donation.

P711

SURGICAL COMPLICATIONS IN PEDIATRIC RENAL TRANSPLANTATION; SINGLE INSTITUTION EXPERIENCE

Hakan Sozen, Kibriya Fidan, Necla Buyan, Oguz Soylemezoglu, Enver Hasanođlu, Ayдын Dalgic
Gazi University

In Gazi University Transplantation Center between 1996 and 2013; out of 240 recipients; sixty one pediatric kidney transplantation were performed to fifty nine pediatric recipients ages between 4.5–17 years old (27 female, 34 male). There were 18 (30%) deceased donors and 43 (70%) living related donors. Among 61 pediatric renal transplantations, totally 12 (19.6%) surgical complications were seen. While 8 of them were early, 4 were occurred as a late complication. In the early period of transplantation, five (8%) surgical, two (3.2%) vascular and one (1.6%) urologic complications were seen. Among 5 surgical complications, there were 3(4.9%) lymphocele and 2(3.2%) bleeding. Totally 8(13%) grafts were lost in 15 years of follow-up. These are as follows: chronic allograft nephropathy in 4, BK virus nephropathy in 3 and thrombus of renal artery in 1 patient. Re-transplantation was applied to 2 patients. Total 2 recipients have died. The reasons were familiar mediterranean fever (FMF) associated multi-organ failure and traffic accident. Now, 50 patients go on their lives with normal graft functions in 2–177 months follow-up period. The overall 1, 5, 10, 15 year graft and patients survival rates were 100%, 85%, 78%, 78% and 100%, 98%, 95%, 95% respectively for all recipients. For cadaveric donors, 1, 5, 10, 15 years graft and patient survival rates were 100%, 95%, 78%, 78% and 100%, 85%, 85%, 85% respectively. Our datas in 15 years time have got advantages in comparison to datas of international developed centers. Renal transplantation is accepted as the most suitable treatment in our center for end stage renal disease patients in all age groups and it is applied successfully.

Key Words: Pediatric, Kidney Transplantation, Surgery, Outcome.

P712

DESIGN OF CRAD001A2314: A RANDOMISED STUDY EVALUATING EVEROLIMUS IN PAEDIATRIC RENAL TRANSPLANTATION

Burkhard Tönshoff¹, Lars Pape², Luca Dello Stroligo³, Robert Ettenger⁴, Patrick Niaudet⁵, El-Djouher Martzloff⁶, Marcela Vergara⁷, Alison Balfour⁸, Catherine Cornu-Artis⁶

¹Universitätsklinikum Heidelberg, Heidelberg, Germany; ²Medizinische Hochschule Hannover, Hannover, Germany; ³Responsabile UOS Clinica del Trapianto Renale, Roma, Italy; ⁴UCLA Center for the Health Sciences, Los Angeles, United States; ⁵Université Paris-Descartes, Hôpital Necker-Enfants malades, Paris, France; ⁶Novartis Pharma AG, Basel, Switzerland; ⁷Novartis Pharmaceuticals Corporation, East Hanover, United States

Background: Early introduction of everolimus (EVR) may allow to reduce the exposure to calcineurin inhibitors and steroids, without loss of efficacy, in paediatric renal transplant recipients (pRTxR).

Methods: This is a 12-month study with a 24-month additional safety follow-up in pRTxR (1 to <18 years). After a 4–6 weeks run-in period post-Tx, pRTxR on tacrolimus (TAC) + mycophenolate mofetil + steroids will be randomised to either continue the regimen or start EVR + reduced TAC with steroid withdrawal at month 6 (figure). Co-primary objectives at month 12 are to estimate rate of composite efficacy failure events (biopsy proven acute rejection, graft loss or death) and to evaluate renal function. Approximately 106 pRTxR will be randomised in 2012 and 2013 across 30 sites in 13 countries.

Results: Month 12 results are expected in Q4 2014.

Conclusions: This study will evaluate the benefits of early introduction of EVR to reduce TAC exposure and withdraw steroids at month 6 in pRTxR.

P713

CHANGES IN CORE TEMPERATURE DURING GRAFT WARM ISCHEMIA AND REPERFUSION PHASES DURING LIVING DONOR LIVER TRANSPLANT: ADULT VERSUS PEDIATRIC

Ibrahim Abdelkader Salama, Mohamed Abdulla
National Liver Institute, Menophya University

Background: Maintaining normothermia essential during liver transplant. Serious adverse outcomes from perioperative hypothermia are well documented. Objective: Evaluation of the core temperature changes during graft warm ischemia and reperfusion periods in adult and pediatric cases. Method: 30 recipients, (adult $n = 15$ and pediatric $n = 15$) enrolled in this study. Nasopharyngeal core temperature (NCT) was recorded at the following points: 5:30 min after induction of anesthesia (temp1 and 2), the Lowest NCT during dissection phase (temp3), the Lowest NCT during the anhepatic phase and before implantation of the graft (temp4), Lowest NCT during warm ischemia (putting the graft at its bed till reperfusion) (temp5), also at 5 (temp6), and 30 min (temp7 after reperfusion, then before the end of surgery (temp8).

Results: Significant decrease in core temperature during the anhepatic phase (temp4), warm ischemia time (temp5), 5 min after reperfusion (temp6) and 30 min after reperfusion (temp7) with mean values of $36.4 \pm 0.47^\circ\text{C}$, $35.4 \pm 0.45^\circ\text{C}$, $35.2 \pm 0.50^\circ\text{C}$ and $35.2 \pm 0.52^\circ\text{C}$ respectively in the pediatric group, while in adult group the mean values $36.3 \pm 0.33^\circ\text{C}$, $36.1 \pm 0.38^\circ\text{C}$, $36.1 \pm 0.61^\circ\text{C}$ and $35.9 \pm 0.34^\circ\text{C}$ respectively.

Conclusion: Significant drop in NCT was observed at the beginning of the warm ischemia period that persists through the reperfusion phase in both adult and pediatric recipients. Children with a body weight <14 kg had their core temperatures affected more than adult patients because of receiving relatively large grafts with a greater GRWR.

Key Words: Hypothermia -ischemia reperfusion-living liver transplant.

P714

COMBINED LIVING DONOR LIVER AND KIDNEY TRANSPLANTATION IN CHILDREN

Burak Kocak, Emre Arpali, Yucel Yankol, Cihan Karatas, Turan Karatas, Ahmet Nayir, Koray Acarli, Munci Kalayoglu
Organ Transplantation, Istanbul Memorial Hospital, Istanbul, Turkey

CLKT is a treatment modality in pediatric patients with severe liver and kidney disease. Simultaneous CLKT from living donors (LD) is entirely a different procedure bringing other issues specific to living donation. Most of the transplantations are performed from two different LDs simultaneously. This is a major surgery in children with extremely difficult technique requiring high level of expertise in order to perform two LD procedures on two adults and a major LD transplantation of two adult organs in a sick child. Six LD CLKT were performed in children between 2007 and 2012 in our department. Patient demographics are given in Table 1. Case 3 had roux en y anastomotic bleeding requiring surgical exploration. Graft nephrectomy was performed due to graft thrombosis arising secondary to severe hypovolemia from vascular leak syndrome. She died on POD43 secondary to sepsis. Case 5 had bile leakage from roux en y anastomosis requiring surgical exploration twice. He died on POD29 secondary to sepsis. Case 1 required surgical exploration due to abdominal hematoma. He had bile duct stenosis treated with percutaneous dilatation in the long-term. Case 2 required surgical exploration due to abdominal hematoma. Case 4 had de novo HUS in the transplanted kidney treated with plasmapheresis and medication switch from Tacrolimus to Sirolimus. 4 cases had good liver function with mean serum cr level of 0.4 mg/dl. In midst of cadaveric organ shortage, simultaneous combined LKT from a LD may be a reasonable therapeutic alternative in children with severe liver and kidney disease. One should remember that this is a major procedure with considerable mortality and morbidity requiring high level of expertise.

P715

ROLE OF PARENTAL SOCIAL, ECONOMIC AND EDUCATIONAL STATUS AFTER PEDIATRIC LIVER TRANSPLANTATION FROM DECEASED DONOR: THE ISMETT EXPERIENCE

Duilio Pagano¹, Calogero Ricotta¹, Davide Cintorino¹, Marco Paci¹, Pasquale Bonsignore¹, Marina Romano¹, Silvia Riva², Stefania Milito², Bruno Gridelli¹, Marco Spada¹

¹Division of Abdominal and Transplantation Surgery, Istituto Mediterraneo per i Trapianti e Terapie a; ²Pediatric Hepatology and Liver Transplantation Unit, ISMETT, UPMC, Italy

Backgrounds: Nowadays, the main focus of pediatricians, pediatric transplant hepatologists and transplant surgeons taking care of children with end-stage liver disease is not only to find a way to get these children transplanted, but is the long-term follow-up with prevention of immunosuppression-related complications, adherence and promotion of a growth as normal as possible. We aimed to determine whether parental education level, social and economic status in a cohort of pediatric liver transplant recipients in the south of Italy were potential predictors of graft and children survival.

Materials and methods: This retrospective study included 116 consecutive liver transplant recipients younger than 18 years at ISMETT between 2001 and 2012. Donor gender and age, extended criteria donors, recipient age, gender, primary aetiology, retransplantation, Pediatric end-stage liver disease score, co-morbidities, patient growth and development assessed on the basis of clinical follow-up, highest parental level of education achieved, social and economic status were collected and analyzed.

Results: Kaplan-Meier analysis measured by parental higher education level, social and economic status showed a better survival rate without significant associations, for patients ($p = 0.07$, $p = 0.12$, $p = 0.31$), and graft survival ($p = 0.23$, $p = 0.22$, $p = 0.76$), respectively. After adjusting for co-variables, results of the multivariate Cox regression analyses confirmed that parental educational level or socioeconomic status are not independent or significant predictors of patients and graft survival.

Conclusion: ISMETT optimization of adherence with the pediatric transplant medical and nursing management enhanced the chances for a successful outcome from liver transplantation in children, reducing the impact of the lack of access to quality health care. Prospective clinical studies are necessary to fully identify the impact of parental connection between the care of the child and his/her family.

P716

RENAL TRANSPLANTATION TO CHILDREN WITH DIFFERENT ORIGINATED URINARY TRACT DYSFUNCTION

Hakan Sozen¹, Kibriya Fidan², Utku Yılmaz³, Necla Buyan², Oguz Soylemezoglu², Sevcin Bakkaloğlu², Enver Hasanoglu²

¹Gazi University; ²Gazi University Pediatric Nephrology; ³Gazi University Transplantation

Renal transplantation in patients with lower urinary tract dysfunction (LUTD) of various origins is a challenging issue in the field of pediatric transplantation.

Aim: To evaluate patient and graft survivals as well as the risks of the surgery and immunosuppressive therapy pediatric patients of LUTD at Gazi University Transplantation Center.

Patients and methods: Among 61 pediatric transplantation recipients since 1996, LUTD was displayed in 6 (9.8%) pediatric recipients. The cause of urologic disorders were as follows; PUV ($n = 4$), PUV+neurogenic bladder ($n = 1$) meningiomyocele+neurogenic bladder ($n = 1$). Clean intermittent catheterization (CIC) was needed in two patients to empty the bladder. Three out of three patients received kidneys from cadaveric and three from living donors. All patients were received calcineurine-based triple immunosuppressive therapy. None of patients had pre-transplantation augmentation. Only one patient whom has VUR + neurogenic bladder had augmentation operation during transplantation surgery. Haberal's corner saving suture technique was used with ureteral stenting for ureteroneocystostomy anastomosis.

Results: The mean age at transplantation was 10.7 ± 3.8 years old (4–15 years old). The median follow-up after transplantation was 53.7 months (1.8 to 168 months). Two patients who have neurogenic urine bladder had recurrent symptomatic curable urinary tract infections. Two out of 6 recipients had BK virus nephropathy (BKVN). One out of two graft was lost due to BKVN and other one has normal graft functions. None of the recipient had urologic or surgical complications after transplantation. No patients died after transplantation during follow-up. Three grafts were lost (BKVN, immunologic, traffic accident), but remaining patients are doing well with mean creatinine 1.5 ± 1.1 mg/dl (median 1.2 mg/dl).

Conclusion: Renal transplantation is a safe and effective.

P717

DESIGN OF H2305: A PROSPECTIVE STUDY EVALUATING EVEROLIMUS IN PAEDIATRIC LIVER TRANSPLANTATION

Rainer Ganschow¹, Lutz Fischer¹, Giuliano Torre², Robert Langer³, Bo-Göran Ericzon⁴, Andrea Brunati⁵, Carole Sips⁶, Alison Balfour⁶, Guido Junge⁶

¹University Medical Centre Hamburg-Eppendorf, Hamburg, Germany;

²Bambino Gesù Children's Hospital, Rome, Italy; ³Department of

Transplantation and Surgery, Semmelweis University, Budapest, Hungary;

⁴Karolinska University Hospital, Stockholm, Sweden; ⁵Liver Transplantation

centre, San Giovanni Battista Hospital, University of Turin, Italy; ⁶Novartis

Pharma AG, Basel, Switzerland

Background: Nephrotoxicity due to calcineurin inhibitors (CNIs); cyclosporine and tacrolimus is a major concern in paediatric liver transplant (LTx) recipients (pLTxR). Reducing CNI dosing to ameliorate renal function in pLTxR is an important goal.

Methods: H2305 is a 24-month (mo) study with a target to enrol 75 pLTxR aged ≥ 1 month and <18 years with a body weight >5 kg. Eligible patients will start everolimus (EVR) with reduced CNI between mo1 and mo6 post-LTx and continue treatment for 24 month (Figure). The primary objective is to assess the change in renal function (Schwartz formula) from start of EVR to month 12. Other objectives are to assess the rate of efficacy failure events (treated

biopsy-proven acute rejection, graft loss or death), safety and tolerability at mo12.

Results: The study is still open for enrolment. The 12 month results are expected in November, 2015.

Conclusion: This is the first prospective study assessing the renal function, efficacy, safety and tolerability of EVR plus reduced CNI regimen in pLTxR.

P718

SPLIT LIVER TRANSPLANTATION: A SINGLE CENTRE EXPERIENCE AT KFSH AND RC IN SAUDI ARABIA

Yasser El Sheikh, Hamad Al Bahili, Firas Eldeen, Martin Burdelski, Mohammed Al Sebayel, Dieter Broering

King Faisal Specialist Hospital and Research centre

Background: Organ shortage resulting in delisting and mortality on the waiting list due to deterioration of patients condition remains a challenge; more exaggerated in pediatric patients. The option of living donor liver transplantation, size reduction of an adult cadaveric liver or the use of segments was implemented to overcome the size mismatch in pediatric recipients. However, the remaining liver was discarded, which led to donor organ shift from adults to children. Split liver transplantation allowed the whole liver to be divided into two allografts; hence, the total number of grafts was increased.

Patients/methods: We report two *ex situ* and two *in situ* split liver transplantation performed in at KFSH & RC in Riyadh, Saudi Arabia. Between May 2011 till March 2013, four livers harvested from heart beating hemodynamically stable brain dead donors. Two *ex situ* and two *in situ* splits were performed. Four adult patients received an extended right grafts and three children received four left lateral lobes (one child required a re transplant for hepatic artery thrombosis). The demographic data and diagnoses for both recipients and donors were described including: the donor liver graft condition, cold, warm and total ischemia time, the operative technique, the aetiology of the liver disease in the recipients, ICU and hospital stay, morbidity and complications, patient and graft survival.

Results: Three adult females and one male with ESLD received an extended right lobe graft. Two female and one male children received four left lateral lobe grafts. We report 75% graft & patient survival in the adult population and 100% patient survival with 75% graft survival in the pediatric age group. No major events were encountered during their hospital stay; apart from one adult mortality due to pulmonary embolism.

Conclusion: Split liver transplantation can be performed for non-urgent recipients with ESLD with good results. Increasing the organ pool for pediatric recipients, without affecting the adult recipient outcome.

P719

RISKS ASSOCIATED WITH THE PROCESS OF TRANSITION OF PEDIATRIC KIDNEY TRANSPLANT RECIPIENTS TO ADULT HEALTHCARE SERVICE

Silvie Bloudíčková-Rajnochová¹, Ondřej Viklický¹, Tomáš Seeman²

¹Institute for Clinical and Experimental Medicine; ²Motol University Hospital

Background: Transfer of pediatric kidney transplant recipients to adult care is considered as a risk factor of graft failure because of higher incidence of rejections and problematic compliance with therapy. The goal of our study is to evaluate kidney graft survival after transition from the only Czech pediatric transplant center (Motol University Hospital) to adult transplant center in Institute for Clinical and Experimental Medicine (IKEM).

Methods: We retrospectively analyzed a group of 64 pediatric kidney transplant recipients, who underwent kidney transplant surgery in Motol

University Hospital between 1987 and 2006, and after reaching adulthood were transitioned to adult transplant center in IKEM. The complete laboratory and clinical data over the period of 12 month before and 36 months after transition were obtained in 42 (65.6%) patients.

Results: At the time of transplantation, the mean age of patients was 13.2 years (6–18 years), three patients underwent two kidney transplantations. At the time of transition, the mean age of patients was 20.6 years (17–24 years). In nine patients (21.4%) the renal graft failed during the first 36 month and in 6 patients (14.2%) during the first 12 months after transition. In analyzed period, we observed graft failure in 7/13 (53.8%) patients with serum creatinine levels above 200 μM and in 3/29 (10.3%) patients with serum creatinine levels below 200 μM /l at the time of transfer. Chronic rejection was the main cause of graft failure with the mean graft survival of 12.5 years (6–18 years). The non-compliance with therapy was clearly demonstrated in 3 (7.1%) patients. In one patient, non-compliance led to graft failure during 5 months after transition.

Conclusion: The transfer of pediatric kidney transplant recipients to adult care is one of risk factors of graft failure. Regarding the specific attributes of this group of patients, the transition process should comprise both special medical and psychosocial care.

P720

ACUTE ANTIBODY-MEDIATED REJECTION IN PAEDIATRIC RENAL TRANSPLANT RECIPIENTS: SINGLE CENTRE EXPERIENCE

Osama Gheith, Torki Al-Otaibi, Narayanan M.R. Nampoory, Ahmed Mosaad, Salah Alwaheeb, Medhat Halim, Tarek Said, Mohamed Balaha, Waleed Hosni, Hasanein Aboatteya, Prasad Nair

OTC

Introduction: Acute antibody-mediated rejections (aAMR) after renal transplantation are defined as rapidly deteriorating graft function, donor-specific antibodies and characteristic histology. Anti-rejection strategies among children with aAMR are lacking.

Aim of the work: To evaluate pediatric renal transplant recipients who experienced at least one episode of antibody mediated rejection and received different modalities of treatment protocols.

Patients and methods: Out of 105 pediatric renal transplants performed in Hamed Al-Essa organ transplant center, 21(20%) experienced at least one episode of biopsy proven antibody mediated rejection. Most of these episodes occurred within 1st two years after their 1st renal transplantation (20 ± 2.6 months). Pre-transplant cross matches were negative. Basic immunosuppression comprised Tacrolimus, MMF and steroids. The diagnosis was made according to Banff classification 2007 and cases were subdivided into 2 groups: aAMR ($n = 10$) and mixed rejection ($n = 10$).

Results: Mean patients age was 12.5 ± 4.9 and 13.5 ± 2.3 in both groups respectively and both were matched regarding donor source and age, original kidney disease, HLA mismatches, type of immunosuppression, basal graft function and hemogram. The majority of our patients received PE, IVIG and rituximab, however we found that graft outcome was significantly better only in those who received rituximab ($p = 0.002$). On the other hand, graft survival was significantly worse in those who received lymphocyte depleting agents ($p = 0.036$). Graft function-at last follow up- in both groups were comparable as measured by serum creatinine (132 ± 33 vs. 143 ± 65 , $p = 0.88$ respectively). Patients with mixed rejection received significantly more steroid pulses but without significant impact on graft survival. Patient survival was comparable.

Conclusion: Combined therapy of IVIG, plasmapheresis and rituximab is effective in the treatment of aAMR in pediatric renal transplants.

PS17-ISCHEMIA/REPERFUSION INJURY/PRESERVATION

P721

PARICALCITOL ATTENUATES INFLAMMATION IN ISCHEMIA-REPERFUSION VIA UPREGULATION OF CYCLOOXYGENASE-2

Hyeon Seok Hwang¹, Keum Jin Yang², Ki Cheol Park², Hyun Soo Cho², So Hee Kim², Yoon Kyung Chang¹, Cheol Whee Park¹, Suk Young Kim¹, Sang Ju Lee¹, Chul Woo Yang¹

¹Division of Nephrology, Department of Internal Medicine, The Catholic University of Korea, Seoul, Ko; ²Clinical Research Institute, Daejeon St. Mary's Hospital

Background: The effect of paricalcitol on renal ischemia-reperfusion injury (IRI) and its mechanism has not been investigated. Methods. Paricalcitol was administered to mice 24 h before IRI. Bilateral kidneys were subjected to 23 min of ischemia, and mice were killed 72 h after IRI.

Results: Paricalcitol improved renal function, tubular necrosis and apoptotic cell death in IRI-mice kidneys. The infiltration of inflammatory cells, and production of proinflammatory cytokine were reduced in paricalcitol-treated mice with IRI. Paricalcitol upregulated cyclooxygenase (COX)-2 expression and prostaglandine E2 (PGE2) synthesis in postischemic renal tissue. The cotreatment of selective COX-2 inhibitor with paricalcitol restored functional injury and tubular necrosis in paricalcitol-treated mice with IRI.

Conclusions: Our study demonstrates that paricalcitol pretreatment prevents renal inflammation in IRI, and upregulation of COX-2 and PGE2 is one of the protective mechanism of paricalcitol.

P722

PRETREATMENT WITH RITUXIMAB PREVENTS SUBSEQUENT ISCHEMIA-REPERFUSION INJURY IN MICE KIDNEY

Hyeon Seok Hwang¹, Ki Cheol Park², Keum Jin Yang², Hyun Soo Cho², So Hee Kim², Yoon Kyung Chang¹, Sang Ju Lee¹, Suk Young Kim¹, Chul Woo Yang¹

¹Division of Nephrology, Department of Internal Medicine, The Catholic University of Korea, Seoul, Ko; ²Clinical Research Institute, Daejeon St. Mary's Hospital

Background: There is growing evidence of the roles of B-cell after Ischemia-reperfusion (IRI) renal injury, and we investigated pretreatment effects with rituximab against subsequent IRI injury in mice kidney. Methods. Rituximab (10 mg/kg) was administered to mice 7 days before IRI injury by clamping both renal pedicles for 22 min.

Results: Rituximab decreased serum creatinine and tubular necrosis scores in post-ischemic kidney. The infiltration of CD19+ B-cells and CD40+ tubular cells were decreased in the rituximab-treated kidneys, which was accompanied with decreased production of interleukin (IL)-12. Rituximab inhibited the infiltration of T-cells and macrophages, and decreased production of IL-1 β , interferon- γ and tumor necrosis factor- α in mice kidney with IRI. Conclusion. Rituximab has a protective effect on renal IRI and that this effect is associated with reduced antigen-presentation and decreased activation of inflammatory cytokine associated with Th1-pathway.

P723

IL-6 CONCENTRATION IN THE EARLY PERIOD AFTER KIDNEY TRANSPLANTATION

Alexey Zulkarnaev, Andrey Vatazin
M.F Vladimirsky Moscow Regional Research Clinical Institute

Background: Kidney transplant always has ischemic injury. Ischemic injury causes the release of many mediators. One of the inflammatory mediators is IL-6. We have studied the dynamics of its concentration in the early postoperative period after kidney transplantation, and the factors that influence on it.

Methods/materials: The study included 28 patients. The selected time points: T0 – before surgery, T1 – 10–15 min after reperfusion, T2 – 4–6 h after reperfusion; T3 – in 12–14 h after reperfusion; T4 day after reperfusion. **Results:** Found that most of the patients showed a significant increase in IL-6 levels. We have identified four groups of patients, depending on the shape of the concentration curve of IL-6. Though the baseline, all patients had normal levels of IL-6 – <10 pg/ml.

Conclusion: The study of IL-6 profile and the role of cytokines in the postoperative period in recipients of renal graft may identify new targets for specific therapy.

P725

TLR4 PATHWAY REGULATION BY PPAR IN STEATOTIC LIVER TRANSPLANTATION

Mónica Bibiana Jiménez-Castro¹, Arani Casillas-Ramírez¹, Mariana Mendes-Braz¹, Maria Elias-Miró¹, Marta Massip-Salcedo², Juan Rodés¹, Carmen Peralta¹

¹Institut D'Investigacions Biomediques August Pi i Sunyer (IDIBAPS), Barcelona, Spain; ²Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas, Barcelona, Spain

Numerous steatotic livers are discarded for transplantation because of their poor tolerance to ischemia/reperfusion. Toll-like receptor 4 (TLR4), signaling is mediated by two distinct intracellular adaptor proteins: myeloid differentiation factor 88 (MyD88) and TIR domain-containing-adaptor inducing IFN β (TRIF); both activate intracellular signaling cascades that ultimately trigger an inflammatory response. Herein we evaluated the role of TLR4 in steatotic liver grafts under cold ischemia. We also investigated whether TLR4 pathway could be regulated by PPAR γ in steatotic liver transplantation. This was based in our previous results indicating the benefits of PPAR γ agonists in steatotic liver grafts and the changes in TLR4 expression induced by PPAR γ regulators in non-steatotic livers undergoing warm ischemia.

Methods: Steatotic liver transplantation was induced in Zucker rats. PPAR γ and TLR4 were altered pharmacologically.

Results: The PPAR γ antagonist treatment protected steatotic livers grafts and this was associated with higher TLR4 levels than those observed in the Transplantation group. Protein levels of MyD88 were unchanged. A pattern similar to that observed for TLR4 protein levels were observed for TRIF protein levels. When TLR4 action was inhibited, PPAR γ antagonists did not protect steatotic liver grafts. TLR4 agonist treatment reduced damage in steatotic liver grafts. The benefits of TLR4 induction might be not explained by changes in the mechanisms potentially involved in the vulnerability of steatotic liver to I/R damage including neutrophil accumulation, TNF, IL-1 and IL-6 levels.

Conclusions: We describe the role of the TLR4 pathway in steatotic liver transplantation. A reduction in PPAR γ can up-regulate the TLR4 pathway, specifically the TRIF pathway, thus protecting steatotic liver grafts. Strategies based on TLR4 signaling pathway induction may improve the outcome of patients receiving marginal grafts that would not otherwise have been transplanted.

P726

HEAVY WATER AND HYDROGEN AMELIORATE COLD PRESERVATION (CP) AND REPERFUSION INJURY IN RAT LIVER

Shingo Shimada¹, Moto Fukai¹, Kenji Wakayama¹, Taichi Kimura¹, Kenichiro Yamashita¹, Masahiko Taniguchi², Tomomi Suzuki¹, Tsuyoshi Shimamura¹, Toshiya Kamiyama¹, Hiroyuki Furukawa², Satoru Todo¹, Akinobu Taketomi¹
¹Hokkaido University Graduate School of Medicine; ²Asahikawa Medical University

Background: We previously reported the stronger ability of modified UW with 30%-D2O (Dsol) than UW, in rat hearts. The present study was designed to assess the ability of Dsol against hepatic CP, and combination effect of hydrogen gas (H2) against reperfusion injury.

Methods: Livers were subjected to 48-h CP in UW or Dsol, and were reperused with or without H2, using isolated perfusion apparatus for 90 min. Groups; UW, Dsol, UW+H2, and Dsol+H2. Perfusion kinetics, liver functions and injury, and cytoskeletal integrity were assessed.

Results: The highest portal resistance, LDH leakage, 8-OHdG and endothelin-1 staining, cytoskeletal degradation (Fodrin, dephosphorylated-Sling-shot), and the least bile production and oxygen consumption were shown in UW group, whereas significantly improved in UW+H2 and Dsol groups. Further drastic improvement was shown in Dsol+H2 group.

Conclusion: Distinct therapy with D2O during CP and H2 during reperfusion conferred protection in CP of rat liver.

P727

RECOMBINANT C1 INHIBITOR LIMITS ISCHEMIA REPERFUSION INJURY AND IMPROVES GRAFT OUTCOMES

Raphael Thuillier¹, Sylvain LePape¹, Thibault SaintYves¹, Jerome Danion¹, Edwin van Amersfoort², Beatrijs Oortwijn², Thierry Hauet¹
¹InsermU1082; ²Pharming Technologies BV

Background: Ischemia reperfusion injury (IRI) remains a critical issue in transplantation. C1 inhibitor (C1INH) regulates complement and contact system activation, but also has protease-independent anti-inflammatory functions.

Methods/materials: We investigated functional outcomes using a recombinant human C1INH (rhC1INH) in a preclinical pig model of kidney autotransplantation ($n = 7$).

Results: Serum creatinine (Fig 1) measurements showed that while Vehicle animals could never recover proper kidney function, rhC11NH animals recovered quickly, reaching pretransplant levels by D11 ($p < 0.05$ AUC comparison). In regards to chronic graft outcome (Fig 2) rhC11NH treatment prevented chronic loss of function and fibrosis development compared to vehicle ($p < 0.05$).

Further data on modulation of complement activation and markers of inflammation will be presented.

Conclusion: RhC11NH offers a high degree of protection against IRI and preserves graft integrity, significantly improving outcomes.

P728

TARGETING THE UNFOLDED PROTEIN RESPONSE TO IMPROVE GRAFT PRESERVATION: A MECHANISTIC ANALYSIS

Le Pape Sylvain, Thuillier Raphaël, Hauet Thierry
IRTOMIT, INSERM UMR 1082

Background: We investigated the Unfolded Protein Response (UPR) in Ischemia-reperfusion injury (IRI), a critical issue in transplantation.

Material and methods: *In vitro* evaluation of cold storage (24 h of hypoxia in UW at 4°C) and reperfusion (6 h in culture medium at 37°C) in human aortic endothelial cells. Interconnections between cell survival and UPR were studied by fluorometry, RT-qPCR and Western-Blot (WB).

Results: RT-qPCR analysis showed that UPR pathways are activated during hypoxia, proportionally to duration. We thus targeted the UPR during hypoxia (IRE1 α or ATF6 inhibition and PERK activation) and significantly improved cell survival. Moreover, WB analysis showed that IRE1 α inhibition fostered an early activation of the PERK pathway. siRNA modulation and protective mechanisms will be discussed.

Conclusion: PERK appears to be the main protective pathway during cold storage and could represent an important therapeutic target towards improving organ preservation.

P729

AMNIOTIC FLUID-DERIVED STEM CELLS PRESERVE RENAL GRAFT FUNCTION IN A PRECLINICAL PORCINE MODEL MIMICKING DECEASED AFTER CARDIAC ARREST DONOR

Edouard Baulier¹, Frédéric Favreau¹, Amelie Lecor², Christophe Jayle¹, Fabrice Schneider¹, Jean Michel Goujon¹, Olivier Feraud³, Annelise Bennaceur-Griscelli², Ali Turhan², Thierry Hauet¹

¹Inserm U1082, Université de Poitiers, CHU de Poitiers; ²Inserm U935, Université de Poitiers, CHU de Poitiers; ³Inserm U935

Background: It is well known that ischemia/reperfusion injuries (IRI) strongly impact the success of organ transplantation (Eltzschig, H.K. & Eckle, T. Nat Med 2011; 17: 1391–1401). Stem cells are a promising therapeutic tool already developed in various ischemic diseases (Koehler, A.A. et al. Nat Med 2001; 7: 430–436). Amniotic fluid stem cells (AFSC), a subpopulation of multipotent cells identified in amniotic fluid, are known to secrete growth factors and anti-inflammatory cytokines. We expect that AFSC could limit IRI consequences in renal graft.

Methods/materials: To determine the efficiency and safety of AFSC infusion in a preclinical porcine model of renal auto-transplantation mimicking deceased after cardiac arrest donor conditions and specifically targeting IRI, we injected autologous AFSC in renal artery 6 days after transplantation.

Results: AFSC injection improved graft viability with full renal function recovery and abrogated fibrosis development up to 3 months. The reduction of tubular atrophy and proteinuria observed in AFSC treatment group was associated with a drastic decrease of inflammatory cell infiltration in graft. Conclusion

The strong proof of concept supported by this work could be the first step before evaluation of AFSC-based therapies in human kidney transplantation.

P730

COMPUTER MODELING OF RENAL ISCHEMIA-REPERFUSION INJURY: 1. CORTICAL OXYGENATION

Vivien Aubert, Nathalie Quellard, Beatrice Fernandez, Jean-Michel Goujon, Thierry Hauet, Patrick Hannaert
INSERM U1082, IRTOMIT

(i) For a clinically relevant description of transplantation renal IR injury, here we validate a quantitative model of cortical (CTX) oxygenation (O_2). (ii) NetLogo(R) agent-based platform is used. CTX (10 μm thick) consists in 1024 patches (100 μm^2) able to diffuse and/or consume O_2 (vascul./epith./lumin./interst.). Values are taken within reported range (eg. 6% interstitium). Model is fed for blood (Hb 15 g/dl, 40–70 mmHg O_2 , dissolved and Hb-bound, Ht 0.45, FF 0.3) via transverse peritubular capillaries PTC (20–70 ml/min); tubules flow rate 10–50 ml/min. Inputs: RBF (2–10 ml/min) and efferent arteriole O_2 (40–60 mmHg); consumption $M(O_2) = 2–10$ ml/min; output: mean PO_2 . (iii) At steady-state, model is sensitive to diffusion constant and consumption. Model reproduces

CTX PO_2 values of both normo (38 vs. 42 mmHg) and hypertensive (32 vs. 31 mmHg) rats by Welch et al. 2001. (iv) Human and pig renal IR injury will be next addressed via the influence of oxygenation on inflammatory and fibrogenic processes.

P731

EXPERIMENTAL HYPOTHERMIC MACHINE PERFUSION OF DISCARDED DONOR LIVERS WITH HTK SOLUTION

Aliaksei Shcherba¹, Andrew Minou¹, Evgeni Santotski¹, Sergei Korotkov¹, Olga Lebedz², Alexander Dzyadzko¹, Oleg Rumo¹

¹RSPC for Tissue and Organ Transplantation; ²Minsk City Pathology Bureau

Hypothermic machine perfusion (HMP) is a promising field in liver transplantation (Guarrera JV et al. Liver Transplantation. 2012; S31–3).

Objective: To compare the results of HMP and cold static storage (CSS) with HTK in the same donor organ.

Methods: Five discarded donor livers were submitted for the study. The mean steatosis rate was 30% (20–45). Organs were procured with standard technique using 10 l of HTK. After transporting to the center HMP of RL was performed through a cannula in the main p.v. with biopump (Medtronic) and free venous outflow. Volume of perfusate was 2000 ml. No active oxygenation was used. CSS of left lobe (LL) was achieved by clamping of the left portal vein (p.v.). P.V. pressure was monitored (Draeger Infinity Delta XL) in the inflow line and maintained at 7–9 mmHg. The flow was maintained at 25–30 ml/100 g of liver parenchyma. Cooling was achieved with ice packing of the liver and lines. Temperature was monitored (Philips Intelli Vye MP 70) with a probe inserted in hepatic veins. Pre and postperfusion effluents and serial tissue samples from both lobes were taken.

Results: HMP was started since 4.6 ± 1.5 h and lasted till 15.1 ± 0.8 h after procurement. Mean temperature dropped from initial 8.1–5°C after 2 h of HMP but increased to 7.6°C after 11 h. AST, ALT, LDH levels were decreased in RL compared to LL post-perfusion effluent, but only AST reached statistical significance (2430 vs. 3940). PH of perfusate changed from 6.62 at 3 h to 6.48 at 8 h of HMP and cLac of perfusate changed from 7.5 at 3 h to 15.7 at 8 h of HMP. A trend toward lower mean necrosis rate was found in HMP compared to CSS lobe at 8 and 11 h of perfusion, 1.6% and 6.3% vs. 5% and 12.3% correspondingly.

Conclusion: HMP with HTK seems to be safe in terms of liver function tests and histology.

P732

LIVER ALLOGRAFT PRESERVATION FLUIDS: A SYSTEMATIC REVIEW AND META-ANALYSIS

John O'Callaghan, Robert Morgan, Simon Knight, Peter Morris
Centre for Evidence in Transplantation

Background: Cold storage of livers for transplantation requires the flush-out of blood with a chilled preservation fluid before storage on ice. Our aim was to appraise the evidence for the efficacy of available preservation solutions.

Methods: A systematic literature search was performed using MEDLINE, EMBASE, the Cochrane Library, the Transplant Library, and the International Clinical Trials Registry Platform. Inclusion criteria specified any Randomised Controlled Trial (RCT) of preservation solutions for liver allografts from deceased donors. Studies were assessed for methodological quality. Outcomes analysed were: early dysfunction, primary non-function, re-transplantation rate, patient survival, graft survival, and peak serum ALT in the first week. Fixed effects (FEM) were used where appropriate. Summary effects are presented as Relative Risk (RR) for binary outcomes and Relative Log Survival (RLS) for survival outcomes. Both are presented with 95% confidence intervals (95%CI).

Results: 3364 unique abstracts were retrieved and from these, 16 RCTs met the full inclusion criteria (1620 liver transplants). The majority of trials were of poor quality. Comparing University of Wisconsin Solution (UW) with Celsior Solution, there was no evidence of a difference in early dysfunction (FEM RR = 1.08, 95%CI = 0.63–1.08, $p = 0.77$), in patient survival (FEM, RLS = 0.86, 95%CI = 0.58–1.28, $p = 0.46$) or graft loss (FEM, RLS = 0.85, 95%CI = 0.59–1.21, $p = 0.39$). No other significant differences were demonstrated between Celsior Solution, Histidine-Tryptophan-Ketoglutarate Solution (HTK) and UW in terms of the outcomes of interest.

Conclusions: The best available studies show no evidence for a superiority of Celsior, HTK or UW Solutions. The quality of available studies also means that we have only moderate evidence of equivalence. An adequately powered and well conducted RCT is required to establish the most cost effective solution for liver preservation.

P733

PREOPERATIVE FASTING PROTECTS AGED OBESE MICE AGAINST RENAL ISCHEMIA-REPERFUSION INJURY

Franny Jongbloed¹, Ron de Bruin¹, Sandra van den Engel¹, Luc J.W. van der Laan¹, Harry van Steeg², Jan N.M. Ijzermans¹, Martijn E.T. Dollé²

¹Laboratory for Experimental Transplantation and Intestinal Surgery (LETIS), Erasmus Medical Center; ²Laboratory of Health Protection Research, National Institute of Public Health and the Environment, t

Introduction: Renal ischemia-reperfusion injury (IRI) is inevitable during kidney transplantation leading to oxidative stress and inflammation and is a risk factor for delayed graft function, rejection and transplant loss. Our previous research showed protection of preoperative fasting against IRI in young-lean male mice. Because of heterogeneity and (co)morbidities in patients, we investigated the effects of fasting on oxidative stress induced by IRI in mice of another age, sex, bodyweight and genetic background.

Methods: Male and female F1-FVB/C57BL6-hybrid mice, mean age 73 weeks and weight 47.4 respectively 47.1 grams, were randomized in preoperative normal food or 72 h fasting. Induction of renal IRI was performed by clamping both renal pedicles: in males 37 min, in females 60 min. Wellbeing, bodyweight, kidney function and survival of the animals were monitored until day 28 postoperatively.

Results: Preoperative fasting improved survival after renal IRI in both sexes compared with normal fed mice. All normal fed males died or were sacrificed because of morbidity indicative of irreversible kidney failure, whereas 88% of the fasted males survived. Of the ad libitum fed females, 82% died or had to be sacrificed, whereas 70% fasted mice survived. Both fasted groups had a better kidney function shown by lower serum urea levels after IRI. Histopathology showed less necrosis and more regeneration in kidneys from fasted mice. In the first week after IRI, bodyweight declined followed by recovery in the weeks thereafter.

Conclusions: Similar to young healthy male mice, preoperative fasting protects against renal IRI in male and female aged obese mice. These findings suggest a general protective response of dietary restriction against renal IRI regardless of age, sex, bodyweight and genetic background. Therefore, dietary restriction could be a non-invasive intervention inducing increased oxidative stress resistance in older and obese patients as well.

P734

MEASUREMENT OF RENOVASCULAR CIRCULATING VOLUME DURING HYPOTHERMIC ORGAN PERFUSION

Eva de Vries¹, Tim van Smaalen², Jorine Boer³, Pieter Hoogland², Nikolai Krivitski⁴, Maarten Snoeijis⁵, Ernest van Heurn²

¹Medisch Centrum Alkmaar; ²Maastricht University Medical Center; ³University Medical Center Nijmegen; ⁴Transonic Systems Inc.; ⁵Atrium Medisch Centrum Heerlen

Background: Kidney donation after cardiac death leads to vascular damage as a result of warm ischemia, affecting renovascular circulating volume. Novel ultrasound dilution techniques may be used to measure renovascular circulating volumes during hypothermic machine perfusion of donor kidneys.

Methods: Renovascular circulating volumes of machine perfused porcine kidneys were repeatedly measured by ultrasound dilution at different perfusion pressures (30, 40, 50, and 60 mmHg), durations of perfusion (1 and 24 h) and warm ischemia times (15 and 45 min). Validity of ultrasound dilution was assessed by comparing volume changes after clamping of renal artery branches.

Results: Repeatability of ultrasound dilution measurements of renovascular circulating volumes was good (mean coefficient of variation: 7.6%). Renovascular circulating volumes significantly increased with higher perfusion pressures, remained constant over time, and significantly decreased with longer warm ischemia times. Changes in ultrasound dilution measurements after renal artery branch clamping did not correlate with changes in actual perfused volumes.

Conclusions: Ultrasound dilution is a reproducible method to assess renovascular circulating volumes in machine perfused kidneys, which is susceptible to changes in warm ischemia times. Future studies should evaluate the value of renovascular volume in pretransplantation kidney viability testing.

P735

IMPACT OF REWARMING MACHINE PERFUSION PRESERVATION FOR DCD LIVER GRAFTS IN PIGS

Naoto Matsuno¹, Hiroyuki Kanazawa², Ikuko Hamano³, Hajime Uchida³, Seisuke Sakamoto³, Mureo Kasahara³, Hiromichi Obara⁴, Shin Enosawa¹

¹National Center for Child Health and Development, Innovative Surgery and Transplantation; ²National Center for Child Health and Development; ³National Center for Child Health and Development, Transplantation Surgery; ⁴Tokyo Metropolitan University

Utilization of grafts from donors after cardiac death (DCD) would greatly contribute to the expansion of the donor organ pool. However, the implemen-

tation of such a strategy requires the development of novel preservation methods to recover from changes due to warm ischemia. To assess potential methods and effect, livers procured after 60 min of warm ischemic time (WIT) were perfused and preserved.

Methods: Porcine livers were perfused with newly developed machine perfusion preservation (MPP) system. Each system for the portal vein or the hepatic artery has a roller pump, a flow meter and a pressure sensor. The livers were perfused with modify UW-gluconate (UW-G) or amino solution (JPS). All grafts were procured after acute hemorrhagic shock and ventilator off. Group 1 ($n = 4$): grafts were procured after WIT of 30 min and preserved by hypothermic MPP (HMPP) for 4-5 hrs with UW-G. Group 2 ($n = 4$): grafts were procured with WIT of 60 min and preserved by HMPP for 4-5 hrs with UW-G. Group 3 ($n = 4$): preserved with 2 hrs. simple cold storage (CS) and HMPP with JPS for 2 hrs. Group 4 ($n = 4$): preserved with 2 hrs CS and rewarming up to 25°C by MPP with JPS for 2 hrs. The preserved liver grafts were transplanted orthotopically.

Results: The AST and LDH levels in the 2 hrs after reperfusion were significantly lower in Group 4 than Group 2 and 3 (421 vs. 889 and 1203 IU/l in AST, 634 vs. 1417 and 2132 IU/l in LDH). Histologically, the necrosis of hepatocytes were less severe in Group 4. Survival rate in Group 1 and 4 was 3/4 and 3/4 respectively, but 0/4 in Group 2 and 3.

Conclusion: Rewarming MPP is expected to facilitate the recovery and resuscitating function of DCD liver grafts.

P736

ACTIONS OF RBP4 INDEPENDENT OF RETINOL TRANSPORT IN STEATOTIC AND NON-STEATOTIC LIVERS UNDER LIVER SURGERY. STEATOSIS REDUCTION BY RETINOL

Maria Elias-Miro¹, Marta Massip-Salcedo¹, Jeans Raila², Florian Schweigert², Mariana Mendes-Bras³, Fernando Ramalho³, Monica Bibiana Jiménez-Castro¹, Arani Casillas-Ramírez¹, Raquel Bermudo¹, Antoni Rimola⁴, Juan Rodés¹, Carmen Peralta¹

¹IDIBAPS; ²University of Postdam; ³Universidade de Sao Paulo; ⁴Hospital Clínic de Barcelona

Background: Hepatic steatosis is a risk factor for liver surgery in conditions that require both, partial hepatectomy under ischemia-reperfusion, including hepatic resections and reduced-size liver transplantation.

Methods/materials: We examined whether modulating RBP4 and/or retinol could protect steatotic and non-steatotic Zucker rats subjected to partial hepatectomy under ischemia.

Results: Decreased RBP4 levels were observed in both liver types whereas retinol levels were reduced only in steatotic livers. RBP4 administration exacerbated the negative consequences of surgery on damage and regeneration in both liver types. The injurious effects of RBP4 were not due to changes in retinol. Indeed, the administration of RBP4 with or without retinol, resulted in similar results of damage and regeneration in steatotic livers. Actions of RBP4 independent of retinol transport were observed. Indeed, retinyl ester but not retinol levels were increased in steatotic livers and circulating retinol levels were reduced in steatotic livers undergoing surgery and treated with RBP4 when compared with the untreated group. Retinol treatment was effective only in steatotic livers. Indeed, retinol reduced damage and improved regeneration in steatotic livers and increased survival rate in obese animals undergoing liver surgery. However, retinol increased hepatic injury and impaired liver regeneration in non-steatotic livers. In steatotic livers, retinol administration resulted in MDA and nitrotyrosine levels similar to those detected following liver surgery, indicating that retinol did not modify oxidative stress. The benefits of retinol in steatotic livers were associated with reduced hepatocellular fat accumulation.

Conclusion: Thus, in surgical conditions that require liver regeneration, modulating RBP4 levels in either directions worsens the surgical outcome and is therefore not advised. However, retinol pre-treatment could be a useful strategy in steatotic livers.

P737

BENEFITS OF HEMO2LIFE SUPPLEMENTATION DURING MACHINE PERFUSION PRESERVATION OF PORCINE KIDNEY GRAFTS SUBJECTED TO WARM ISCHEMIA

Chatauret Nicolas¹, Delpech Pierre-Olivier¹, Hebrard William², Duthell Delphine³, Polard Valérie³, Zal Franck³, Hauet Thierry¹

¹Inserm U1082, Faculté de Médecine et Pharmacie, Univ de Poitiers, Poitiers, France; ²Ibisa Domaine expérimental du Magneraud, Surgères, France; ³HEMARINA, Morlaix, France

Background: Benefits of the supplementation with HEMO2life[®] during kidney cold static storage have been reported in a optimal donor porcine model. Implementation of this strategy to machine perfusion (MP) solutions may improve kidney graft functions from donors deceased after cardiac death (DCD).

Methods: Kidneys were cold-preserved after 60 min of warm ischemia for 24 h in Lifeport[®] machine (ORS) with KPS-1 ± HEMO2life[®] (0.5, 1 and 2 g/l). We quantified the level of lactate and ASAT(Aspartate amino transferase) in

the perfusion liquid. Then, kidneys were transplanted and creatininemia assessment was performed.

Results: MP preservation with KPS-1 alone induced an increase in extracellular lactate and ASAT levels in liquid perfusion. In HEMO2life[®] treated groups, 2 g/l dose reduced lactate release and 0.5 g/l dose level led to about 3 fold reduction in ASAT release after 24 h of preservation. A benefit was also observed in 1 g/l treated group in comparison to MP control group with a weaker creatininemia peak (about 1100 vs. 400 μM respectively) and a faster return to pre-surgery values.

Conclusion: This pilot study reported that HEMO2life[®] supplementation protected kidney cells during MP preservation.; Creatininemia follow-up in Ctrl MP and MP+ HEMO2life[®] groups.

P738

PULSATILE MACHINE PERFUSION ALLOWS EFFICIENT KIDNEY TRANSPLANTATION FROM DCD EVEN AFTER 20-MIN NO-TOUCH PERIOD. PRELIMINARY ITALIAN RESULTS

Massimo Abelli, Elena Ticozzelli, Mladen Lucev, Jacopo Ferrario di Tor Vajana, Vincenzo Sepe, Benedetta Maiga, Alessandro Patanè, Alessio Vinci, Ilaria Benzoni, Carolina Bianco, Eduardo Castillo
Fondazione IRCCS Policlinico San Matteo

Background: The Italian legislation provides a mandatory 20-min no-touch period after cardiac arrest before organ retrieval in Donor after Circulatory Death (DCD); for this reason doubts on viability of these organs discouraged Italian surgeons to perform DCD transplants. However, in 2008 we started the "Alba" DCD programme using the most performing tools for preservation of these organs including normothermic regional perfusion (NRP) and pulsatile machine perfusion.

Methods/materials: Initial experience using only NRP and cold storage (CS) led to a transplantation of 4 kidneys from 3 donors, and 2 of them are still functioning grafts with an acceptable 1-month SCR (2.6 ± 0.1). After the inclusion of machine perfusion (MP), 10 kidneys were transplanted from 7 donors. Histology and cold ischemia time (15.7 vs. 15.9 h, NS), were similar between the CS and MP kidneys, although significantly the longer cold ischemia time (CIT) reached 23 h in MP group.

Results: From the 4 CS kidneys, 2 showed DGF and 1 PNF and 1 graft loss due to renal vein thrombosis (IX day postop), while in the MP group 3 didn't show DGF, no PNF was observed and DGF time was significantly shorter (9.7 vs. 20.5 days, $p < 0.05$). CS kidneys showed extremely difficult reperfusion in all cases when compared to MP kidneys. MP kidneys demonstrated better function (Scr mg/dl) at 1 month (2.5 ± 1.16 vs. 4.4 ± 2.55) and improved at 3 months (1.65 ± 0.61 vs. 3.2 ± 1.98). Out of 10 MP kidneys only 1 kidney was discarded due to high resistances during MP.

Conclusion: DCD kidney transplantation is feasible even after a 20-min no-touch period with the use of pulsatile machine perfusion, increasing the number of transplants with good graft function. MP gives us additional information of the quality of the organs that allows a more efficient use for transplantation.

P739

RENAL GRAFT RECONDITIONING FROM "NON HEART BEATING DONORS" BY IGL-1 SOLUTION. AN EXPERIMENTAL STUDY IN RATS

Jacopo Ferrario di Tor Vajana¹, Andrea Peloso¹, Ilaria Benzoni¹, Carolina Bianco¹, Benedetta Maiga¹, Federico Costanzo², Giulia Meroni², Mariacaterina Canepa¹, Annalisa Gaspari², Elena Ticozzelli¹, Massimo Abelli¹, Marcello Maestri¹

¹IRCCS Policlinico San Matteo Pavia; ²Università degli Studi di Pavia

Introduction: The shortage of available organs is a major problem for a wider access to kidney transplant. Recently Non Heart Beating Donors (NHBD) have been proposed as a new resource and proven clinically effective. The Italian law requires a prolonged "no touch period" to declare one dead. Thus NHBDs come with an abnormally long warm ischemia. Graft reconditioning is mandatory in such situation. IGL-1 is an effective rinse solution to perfuse damaged organs. Several studies have demonstrated that measurement of flow and trend of resistance are reliable parameters to predict the graft outcome prior to perform the transplant.

Methods: Of 21 male Lewis rats were stratified into three groups and euthanized to collect the kidneys under non heart beating status (Table 1 shows the induced ischemia and solutions used). The grafts were perfused on the bench by a hydrostatic device fixed at 40 mmHg, with real time evaluation of renal flow and resistance.

Results: Data were analyzed by ANOVA. As expected, Group 1 had a much better performance than group 2 and 3. However, the use of IGL-1 (Group 3) was beneficial, with a significantly better flow and resistance than in Group 2 (ANOVA, $p < 0.05$). These data were confirmed at histologic evaluation that showed less thrombosis and glomerular sclerosis in kidney perfused with IGL-1, while tubular necrosis was similar in Group 2 and 3.

Conclusions: While kidneys from NHBD show a significant damage compared to HBD, new approaches to the treatment of ischemic damage demonstrate a promise of salvage for a pool of grafts. Modern solutions like

IGL-1 are effective. Further studies will demonstrate the long-term beneficial effect of reconditioning and the overall survival of such graft after KTx.

References: 1. Thuillier R, Renard C, Badet L et al. Effect of polyethylene glycol-based preservation solutions on grafts injury in experimental kidney transplantation. *Br J Surg* 2011 Mar; 98(3): 368-78.

2. Kosieradzki M, et al. Ischemia/reperfusion injury in kidney transplantation: mechanisms and prevention. *Transplant Proc* 2008.

P740

DONOR PRE-TREATMENT WITH THE HEAT SHOCK PROTEIN-INDUCER GERANYLGERANYLACETONE REDUCES BRAIN DEATH-ASSOCIATED INFLAMMATION IN THE KIDNEY AT ORGAN RETRIEVAL

Leon F A Van Dulleman, Dane Hoeksma, Petra J. Ottens, Susanne Veldhuis, Rutger J. Ploeg, Henri G.D. Leuvenink
University Medical Center Groningen

Brain dead-derived kidney grafts have inferior transplantation outcomes compared to living donated kidneys. The protective heat shock proteins (HSP) are known to be up-regulated, but at the end of the brain death period. To reduce the brain death-related kidney injury, we want to increase the Hsp72 expression at the start of brain death. We investigated whether geranylgeranylacetone (GGA), an Hsp72 inducer, can reduce the pro-inflammatory changes and improve kidney donor quality in an *in vivo* brain death rat model.

Male F344 rats (275-300 g, $n = 15$) underwent slow induction of brain death and were kept brain dead for 4 h. We administered GGA (400 mg/kg orally) or a saline vehicle 20 h and 1 h prior to brain death induction. Sham-operated animals ($n = 14$) received the same treatment.

At the moment of organ retrieval, the expression of Hsp72 is not increased by GGA. However, kidney interleukin-6 mRNA levels in GGA pre-treated brain dead rats were lower compared to saline-treated controls. Systemic ASAT levels were also reduced by GGA, indicating decreased inflammation. These results suggest that GGA reduces pro-inflammation during the brain death period, despite the unchanged expression of Hsp72. To further explore the effects of GGA on HSP expression, we want to assess expression of HSF-1 and other stress-induced HSP: Hsp90, Hsp32.

P741

AN INNOVATE, NOVEL HYPOTHERMIC STORAGE SYSTEM FOR DONOR HEARTS

Lisa Anderson¹, William Edelman¹, Steven Tsui²
¹Paragonix Technologies Inc.; ²Papworth Hospital

Background: The cornerstone of cold ischemic storage of donor hearts is immediate electro-mechanical arrest of the donor heart with a preservation solution and maintenance of hypothermia. The current practice of cold storage using an "Igloo" cooler relies on crushed ice to maintain hypothermia. However, clinical experience suggests that these storage temperatures may be highly unpredictable and some donor hearts become frozen solid. These temperature uncertainties are sub-optimal and potentially detrimental on the myocardium due to focal super cooling. This study assesses the temperature profile of donor hearts stored in the Sherpa Pak Cardiac Transport System (CTS) and those stored in the conventional Igloo with ice.

Methods/materials: The Paragonix Sherpa Pak[™] CTS is a single-use device that utilizes cold chain shipping technology and FDA cleared organ cold storage solutions. This portable device weighs 15 kg and is designed to transport donor hearts with transport times of up to 4 h. In one set of test, temperature profiles ($n = 3$ runs) were recorded for the Paragonix Sherpa Pak[™] CTS. In a second test, a 500 g pig heart was placed in plastic bags with 2 l of storage solution in an igloo with 15 kg of crushed ice, and a second 500 g pig heart was placed inside the Sherpa Pak[™] CTS. Two temperature probes (ESCORT iMiniPlus) were placed inside the left ventricle and at the cardiac apex. Temperatures were monitored at 5 min. intervals for 12 h.

Results: Temperature performance runs demonstrated that the Sherpa Pak[™] CTS was able to maintain stable cardiac temperatures between 4 and 8°C for over 12 h. Comparable Igloo storage results demonstrated temperatures near and below 0°C following 2 h of static storage.

Conclusion: The Sherpa Pak[™] CTS provides more reliably and clinically acceptable storage temperature for the donor heart compared with conventional storage using an "igloo" cooler and ice.

P742

NOVEL APPROACHES FOR THE PREVENTION OF ISCHEMIA-REPERFUSION INJURY (IRI)

Muhammad Ashraf, Martina Haller, Marion Enthammer, Koziel Katarzynna, Sana Khalid, Jakob Troppmair
Daniel Swarovski Research Laboratory, Department of Visceral-, Transplant- and Thoracic Surgery, Innsbruck Medical University, Austria

Background: The production of reactive oxygen species (ROS) during early reperfusion is a major early contributor to the development of ischemia-

reperfusion injury (IRI). ROS cause impaired function or death of cells through direct damage to biomolecules or the activation of intracellular signaling pathways. Moreover, they play an important part in the amplification of damage through e.g. inflammasome activation. The use of antioxidants provided limited therapeutic benefit in the clinical setting and thus novel strategies for avoiding early ischemia-reperfusion injury (IRI) are essential. Ischemia and in particular also early reperfusion are linked to the activation of intracellular signaling pathways, whose contribution to damage progression is only partially understood. In our work we focused on preventing ROS-induced damage by exploiting intracellular signaling pathways.

Methods/materials: Experimental models used included established and newly derived cell lines obtained from genetically altered animals and kidney clamping in the rat. As stress stimuli we analysed ischemia/reperfusion, hypoxia/reoxygenation, pro-oxidant treatment and growth factor abrogation. Molecular, biochemical, imaging and histological assays were used to quantify damage and function.

Results: Our work demonstrates the activation of p38, ERK, JNK, members of the mitogen-activated protein kinase (MAPK) family, during early reperfusion/reoxygenation, when we also observe most pronounced ROS production. The activation of ERK could be linked to limiting ROS levels and cell survival, while p38 clearly increased ROS levels and enhanced cell death. Consequently inhibiting p38.

P743

MIRNA AND MRNA REGULATION IN HUMAN KIDNEY ALLOGRAFTS WITH DELAYED GRAFT FUNCTION AND REJECTION

Julia Wilflingseder¹, Alexander Kainz¹, Judith Suzenauer², Eva Toronyi³, Robert Langer³, Rainer Oberbauer¹

¹Medical University of Vienna; ²KH der Elisabethinen Linz; ³Semmelweis University Budapest

Post-transplant events such as acute allograft failure and rejection are highly choreographed on the molecular level. Aim of this study was to study the molecular regulation in the human kidney allograft.

We plan for ten samples of each clinical condition, currently eight have been obtained and analysed. The Affymetrix GeneChip human Gene 2.0 and miRNA 3.0 arrays for gene expression and miRNA profiling were used. An integrative bioinformatics approach was chosen to combine differentially regulated mRNA and miRNA targets before and after transplantation. Target genes were further evaluated based on their functional annotation. miRNA target prediction was verified by experimental data.

Allografts with posts ischemic non-function exhibited a distinct molecular pattern compare to acute rejection and protocol biopsies on the mRNA and miRNA levels. T-cell and B-cell activation ($p = 0.002$ and $p = 0.03$, respectively) before transplantation, Integrin signalling pathway ($p = 0.008$) after transplantation and the p53 pathway ($p = 0.02$) and the Ras pathway ($p = 0.04$) were associated with the development of posts ischemic injury.

These data show that distinct miRNA and mRNA signatures are associated with the development of posts ischemic injury. A detailed analysis of the miRNAs and target genes will be presented at the meeting.

P744

GRADUAL REWARMING OF KIDNEYS REDUCES INJURY COMPARED TO IMMEDIATE REPERFUSION

Paria Mahboub, Petra J. Ottens, Henri G.D. Leuvenink
Department of Surgery, Surgical Research Laboratory, University Medical Center Groningen (UMCG)

Background: Reperfusion injury after cold storage (CS) of organs is an inevitable consequence of a transplant procedure. We hypothesize that the sudden warm reperfusion after CS is detrimental for the graft. We therefore evaluated different warming-up temperatures of the organ before reperfusion in order to improve organ quality.

Methods: Rat left kidneys were retrieved and stored in University of Wisconsin solution for 24 h at 4°C followed by immediate reperfusion at 38°C (control $n = 4$) or gradually warming-up (WU) to 10°C ($n = 5$), 25°C ($n = 5$) or 38°C ($n = 5$), using isolated machine perfusion. Renal function (GFR) and renal injury was assessed by isolated kidney perfusion with a modified Williams Medium E solution for a total of 90 min.

Results: Compared to control, rewarming resulted in all groups in reduced AST levels in the perfusate indicating less mitochondrial injury as well as reduced LDH levels indicating cell injury. GFR at the end of the observation period was similar in all groups. Sodium reabsorption tended to be improved in WU groups.

Conclusion: Gradually warming up is associated with less renal injury and better renal function indicating that reperfusion injury might be reduced.

P745

AMPK INVOLVEMENT IN ENDOPLASMIC RETICULUM STRESS AND AUTOPHAGY MODULATION AFTER FATTY LIVER GRAFT PRESERVATION: A ROLE FOR MELANONIN AND TRIMETAZIDINE COCKTAIL

Mohamed Bejaoui¹, Mohamed Amine Zaouali¹, Eleonora Boncompagni¹, Eirini Pantazi¹, Emma Folch¹, Hassen Ben Abdennebi², Joan Roselló-Catafau¹

¹IIBB-CSIC; ²Molecular Biology and Anthropology applied to development and health (UR12ES11)

Background: Prolonged cold storage during transplantation remains a risk factor for the viability of grafts, especially when steatosis is present. Steatotic livers exacerbate endoplasmic reticulum (ER) stress that occurs in response to cold IRI. In addition, a defective liver autophagy correlates with liver damage. This study evaluated how the use of combination of additives, as melatonin (ML) and trimetazidine (TMZ) to IGL-1 preservation solution can increase the sources of AMPK and affect ER stress and autophagy.

Methods: Steatotic livers were preserved for 24 h (4°C) in UW or IGL-1 solutions with or without ML (100 µM) + TMZ (10–6 M) and subjected to 2-h reperfusion (37°C). In a further group, steatotic livers preserved for 24 h in IGL-1 solution enriched with ML+ TMZ+ AraA (AMPK inhibitor) and reperused as previously. We assessed hepatic injury (AST/ALT) and function [bile production, BSP clearance, vascular resistance], as well as oxidative stress (MDA) and nitric oxide. We also evaluated ER stress (GRP78, PERK, CHOP) and autophagy (beclin-1, ATG7, LC3B, P62).

Results: Fatty livers preserved in IGL-1 enriched with ML+TMZ showed lower injury and better function compared to those preserved in IGL-1 alone. Moreover, IGL-1+MEL+TMZ induced a significant decrease in ER stress after reperfusion. This was consistent with a major activation of autophagic parameters and AMPK phosphorylation. The inhibition of AMPK induced an increase in ER stress and a significant reduction in autophagy. These benefits correlated with the generation of nitric oxide (through constitutive e-NOS activation) and the prevention of oxidative stress.

Conclusion: The addition of ML and TMZ to IGL-1 preservation solution improved steatotic liver graft preservation, through AMPK activation which reduces ER stress and increases autophagy.

P746

PROTECTIVE EFFECTS OF HBSP ON ISCHEMIA-REPERFUSION AND CYCLOSPORINE A INDUCED RENAL INJURY IN A 2-WEEK RAT MODEL

Bin Yang¹, Yuanyuan Wu², Cheng Yang³, Feng Liu², Lan Shi², Yajun Wu², Tongyu Zhu³, Michael L. Nicholson⁴, Yaping Fan²

¹University of Nantong/University of Leicester; ²University of Nantong;

³University of Fudan; ⁴University of Leicester

Background: Ischemia-reperfusion (IR) injury and cyclosporine A (CsA), mainstay immunosuppressant, nephrotoxicity are unavoidable in kidney transplantation affecting allograft survival. In this study, a novel tissue protective peptide, helix B-surface peptide (HBSP) derived from erythropoietin, was hypothesized to eliminate IR and CsA induced renal injury in a rat model.

Methods: The right kidney was subjected 45 min ischemia and followed by 2-week reperfusion with the left nephrectomy. HBSP 8 nmol/kg/d was administered daily after reperfusion, together with or without CsA 25 mg/kg/d. The effects of HBSP on IR and/or CsA induced tubulointerstitial damage were evaluated focusing on renal function and structure, caspase-3 activation, apoptosis and inflammation.

Results: The level of blood urea nitrogen was increased by CsA, but decreased by HBSP in the IR+CsA kidneys at 1 week and 2 weeks, while the same changes were revealed in urinary protein/creatinine only at 2 weeks. The caspase-3 mRNA was also decreased by HBSP only in the IR+CsA kidneys. The number of active caspase-3+ cells, apoptotic cells and MPO+ cells was greatly reduced by HBSP in the both IR and IR+CsA groups. In addition, HBSP mainly decreased CsA-increased MPO+ cells in interstitial areas, but reduced apoptotic cells in tubular areas. The tubulointerstitial damage was gradually increased by ischemia alone, IR and CsA; but significantly ameliorated by HBSP treatment.

Conclusions: It has been revealed, for the first time, that HBSP effectively improved renal function and tissue damage induced by IR and/or CsA, which might be through reducing caspase-3 synthesis and activation, apoptosis and inflammation.

P747

CHARACTERISING THE EXPRESSION OF HIF IN DCD AND DBD DONORS; POTENTIAL FOR EXPLOITING PROTECTIVE PATHWAYS IN DECEASED DONORS

Zeeshan M. Akhtar¹, Rosa Lammerts², Maria Kaisar¹, Susan Fuggle¹, Henri Leuvenink², Christopher Pugh¹, Rutger J. Ploeg¹

¹Oxford Transplant Centre, Churchill Hospital, University of Oxford; ²Surgical Research Laboratory, University of Groningen

Background: The hypoxia inducible factor (HIF) pathway has been shown to be able to precondition organs against ischemic injury. The characterisation of HIF in deceased donor kidneys has not yet been reported on.

Methods: We compared the expression of HIF1 α and the HIF target gene HO1 expression in four models: (i) NRK-49 cells (positive control): 24 h of 1% Oxygen. (ii) Renal IRI (Fischer rat; positive control): Left kidney: 30 min of warm ischemia (WI) followed by reperfusion for 4 h, right kidney: control. (iii) DCD model (Fischer rats): Right kidney harvested as control. Subsequently cervical dislocation was performed and rodents exposed to 30 min of WI prior to harvesting of the left kidney. (iv) DBD model (Fischer rats): Brain death induction was performed as previously described. Kidney and liver samples were obtained after 4 h of BD. Sham procedures were performed as controls. Tissues/cells were prepared using a Ureas SDS lysis buffer. Western blots were performed using monoclonal antibodies to HIF1 α (Novus Biologicals NB100-479 1:1000) and HO1 (Assay Designs OSA-111 1:1000) with B-actin as control.

Results: Our results demonstrate: – HIF1 α is detected in the cell culture and IRI models (Image 1). – Less HIF1 α signal detectable compared to controls in a DCD model of 30 min of WI, a HO-1 signal persists (Image 1). – A HIF1 α signal is detectable following 4 h of brain death, although the results are heterogeneous in both kidney (Figure 2) and liver tissues (Figure 3).

Conclusion: In DCD donors HIF1 α appears to be abolished after 30 min of WI, whereas a small HO1 response persists. In DBD donors a HIF1 α signal is detectable, however there is variability in expression between experimental groups. In both DCD and DBD donors up-regulation of HIF1 α and its downstream protective effectors represents a novel therapeutic target to improve the quality of kidney and liver allografts procured for transplantation.

P748

THE TRUTH ABOUT THE RELATIONSHIP BETWEEN FLOW RATES FROM MACHINE PERFUSION AND TRANSPLANT OUTCOME FOR KIDNEYS FROM DONORS AFTER CARDIAC DEATH

Jennifer Johnson¹, Muhammad Arslan Khurram², Susan Stamp³, Neil Sheerin³, David Talbot⁴

¹Newcastle University Medical School, Newcastle Upon Tyne; ²Barnet and Chase Farm Hospital NHS Trust London; ³Institute of Cellular Medicine Newcastle University; ⁴Freeman Hospital Newcastle Upon Tyne

The relationship between parameters determined from kidneys before transplant and their subsequent outcome continues to be controversial with advocates for and against. We initially used machine perfusion to determine which kidneys were 'viable' and we found this useful for Maastricht II donors where the warm ischaemia was particularly protracted. However the majority of DCD's utilised now in the UK are Maastricht III where the relevance of machine perfusion characteristics are more controversial. We have reviewed the outcome of 94 single kidneys transplanted from MIII DCD's where the flow characteristics and GST perfusate levels were known at 3 h after commencing machine perfusion. Follow up data was available for these kidneys up to 7 years post transplantation. The parameters were divided into thirds (good, satisfactory and poor) and these groups compared for glomerular filtration rate, graft and recipient outcome. Findings: there was no correlation with perfusion characteristics or GST with recipient survival. However for both graft function and graft survival there was a significant correlation between flow and outcome particularly flow/mmHg- perfusion flow index ($p < 0.0005$). No such correlation was found with perfusate GST. In a separate analysis of PFI with donor age there was a 2 tailed correlation between the two ($p < 0.01$), though the correlation coefficient was only 0.154. Therefore the flow parameters which correlated with outcome for Maastricht III donor kidneys are likely to be explained by its cause namely donor age (and presumably donor hypertension) which is known to influence graft outcome.

P749

NOVEL REAL-TIME MICRODIALYSIS MONITORING OF TISSUE VIABILITY – A PROMISING NEW TOOL IN MARGINAL KIDNEY TRANSPLANTATION?

Karim Hamaoui¹, Sally Gowers¹, Sotiris Mastoridis¹, Nick Bullocks¹, Samir Damji¹, Martyn Boutelle¹, Ara Darzi¹, Vassilios Papalois²

¹Imperial College London; ²Imperial College Renal and Transplant Centre

Viability assessment during the preservation period is imperative to avoid unnecessary discarding of marginal organs and maximising graft outcomes. To address this need, we have developed a novel system based on a rapid-sampling microdialysis analyser that allows continuous tissue monitoring and measurement of the metabolic markers of cell damage. We report the results from our ongoing study. We aim to develop a new tool that allows for accurate organ viability assessment during preservation.

Methods: Twenty-two kidneys were retrieved from cadaveric pigs, flushed and transported to the laboratory (Warm Ischaemia Time = 15 min, Static Cold Ischaemia Time = 4–5 h). 10 kidneys underwent 24 h of static cold storage (SCS); 12 underwent 10 h of hypothermic machine perfusion (HMP, Waters Medical Systems RM3). Kidneys were monitored for tissue lactate throughout by tunnelling a probe superficially into the parenchyma of the lateral cortex; online measurements of lactate concentrations were made every 60 s. Following preservation monitoring continued while tissue temperature increased passively to ambient temperature.

Results: On commencement of monitoring quantifiable lactate concentrations were successfully detected within 15mins. During the initial 1.5 h lactate

concentrations were similar during SCS (88.0 μ M) and HMP (140.5 μ M, $p > 0.05$). Lactate concentrations were however lower after 10 h of SCS preservation compared with HMP (77.3 vs. 266.8 μ M, $p < 0.01$). Overall lactate levels during SCS remained low and stable during preservation while in HMP lactate increased between 1.5 and 10 h from 140.5 to 266.8 μ M ($p < 0.01$). Warming data suggests a resilience of HMP kidneys to subsequent temperature induced ischaemia compared to SCS kidneys.

Conclusion: This preliminary work provides the baseline ischaemic profile for porcine kidneys whilst validating the technique of microdialysis as a tool for organ viability assessment during preservation with potential for clinical application. Differences can be seen between the preservation methods with cortical lactate progressively increasing in HMP, while remaining stable in SCS. The data here may help elucidate why HMP is clinically superior to SCS, and allow development of further interventions to augment these benefits.

P750

A NOVEL ADENOSINE/LIDOCAINE PRESERVATION SOLUTION FOR RENAL MACHINE PERFUSION – A POTENTIAL ALTERNATIVE TO UNIVERSITY OF WISCONSIN SOLUTION?

Karim Hamaoui¹, Adeel Aftab², Sally Gowers¹, Sotiris Mastoridis¹, Donna Rudd³, Martyn Boutelle¹, Ara Darzi¹, Geoffrey Dobson³, Vassilios Papalois⁴

¹Imperial College London; ²Department of Surgery, Imperial College London; ³James Cook University; ⁴Imperial College Renal and Transplant Centre

The gold standard perfusate for renal hypothermic machine perfusion is University of Wisconsin solution (UW). Adenocaine[®] (AL) is a relatively low-cost novel adenosine/lidocaine composite solution that has proven to exert protective effects in cardiac preservation and resuscitation. Machine perfusion (MP) is beneficial for marginal kidneys with perfusate constituents a potential factor in optimising organs. The optimal solution for MP is yet to be established. Using a porcine MP and normothermic reperfusion (NMR) model, we investigate whether AL's novel characteristics translate favourably to kidney preservation compared to UW.

Methods: Of 12 cadaveric porcine kidneys (warm ischaemia = 45mins) were randomized into two groups (AL, $n = 6$ and UW, $n = 6$). After flushing and transport (transport cold ischaemia=5 h) all kidneys underwent MP with UW or AL at 4°C using clinical protocols for 10 h on Waters Medical Systems RM3 devices. Kidneys then underwent 2 h of NMR at 38°C with modified Krebs Henseleit Buffer solution. Perfusion dynamics, functional parameters, histology, and real-time microdialysis was used to assess kidney responses and viability.

Results: MP: Systolic pressure declined progressively in the UW group at 5–10 h, which was not as evident in the AL group ($p < 0.02$). Flow rates remained persistently higher overall in the AL group vs. the UW group (15.5 vs. 13.3 ml/min/100 g, $p = 0.01$ AUC). Resistance was low, stable, and viable (<0.5 mmHg/ml) from onset and throughout AL perfusion (0.49 mmHg/ml [0.51–0.44]) while time to a viable resistance was 9 h with the UW group (range: 0.7–0.44 mmHg/ml). NMR: Urine output remained stable with UW while trending to increase in the AL group. There were no differences in creatinine clearance, oxygen and glucose consumption between the two groups. Lower perfusate lactate 4.07 vs. 5.45 mm was evident during NMR in the AL group ($p = 0.03$). Histology showed similar degrees of reperfusion injury.

Conclusion: MP with AL solution is feasible and produces a more rapid stabilisation of perfusion dynamics to viable levels, with higher flow rates and lower resistance compared to UW potentially allowing earlier viability categorisation. NMR shows similar kidney function and viability profiles (AL versus UW) with a trend of increasing urine production in the AL versus UW group. Development of AL as an alternative MP solution is a step towards maximising the benefits of MP, improve marginal graft viability assessment, and the delivery of potential cost-savings in relation to current techniques, while potentially expanding donor pools.

P751

HYPOTHERMIC MACHINE PERFUSION CAN AMELIORATE PROLONGED STATIC STORAGE INJURY IN PORCINE KIDNEYS?

Anna Rizzello¹, Karim Hamaoui², Sotiris Mastoridis², Daniel Casanova³, Vassilios Papalois¹

¹Imperial College Renal and Transplant Centre; ²Imperial College London; ³University of Cantabria

Introduction: Hypothermic preservation has formed the mainstay for organ maintenance in transplantation, with static cold storage (SCS) constituting the commonest and simplest method. Prolonged static storage is associated with deleterious graft outcomes, especially in marginal allografts. Hypothermic machine perfusion (HMP) preservation however has been shown to be beneficial for marginal organs. We investigate whether HMP is able to ameliorate the ischemic damage caused by extremely prolonged cold static storage.

Methods: Eight cadaveric porcine kidneys were isolated and randomized into two groups thereby undergoing either 4-h (SCS4, $n = 4$) or 52-h (SCS52, $n = 4$) of SCS. Following SCS all kidneys underwent HMP with UW solution at 4°C over 12 h, and were finally subjected to 2 h of normothermic machine reperfusion (NMR) at 38°C. Perfusion dynamics, perfusate samples, renal

function parameters, histology, and novel real-time microdialysis techniques were used to assess kidney responses.

Results: All kidneys showed stable and viable perfusion dynamics during HMP.

During NMR, flow dynamics and resistance characteristics followed the well-described, within-subject decline over time ($p < 0.001$), however between-group repeated-measures analyses showed no significant difference ($p = 0.230$). Urine output tended to be higher in SCS4 versus SCS52 kidneys ($p > 0.2$), while oxygen and glucose consumption, and perfusate lactate levels were similar between groups ($p > 0.2$).

Conclusion: This early data shows that porcine kidneys, despite exposure to extremely prolonged static cold storage, have similar functional outcomes and viability profiles following optimisation with HMP as those with shortened static cold storage times.

P752

SUCCESSFUL EX-VIVO NORMOTHERMIC MACHINE PERFUSION AND VIABILITY TESTING OF DISCARDED HUMAN DONOR LIVERS

Sanna Op den Dries¹, Negin Karimian¹, Michael E. Sutton¹, Andrie C. Westerkamp¹, Maarten W.N. Nijster², Annet S.H. Gouw³, Janneke Wiersema-Buist⁴, Ton Lisman⁴, Henri G.D. Leuvenink⁴, Robert J. Porte¹

¹Section of Hepatobiliary Surgery, Department of Surgery, University Medical Center Groningen; ²Department of Critical Care, University Medical Center Groningen; ³Department of Pathology, University Medical Center Groningen; ⁴Surgical Research Laboratory, Department of Surgery, University Medical Center Groningen

In contrast to traditional static cold preservation of donor livers, normothermic machine perfusion may reduce preservation injury, improve graft viability, and potentially allows ex-vivo assessment of graft viability prior to transplantation. We have studied the feasibility of normothermic machine perfusion in four discarded human donor livers. Normothermic machine perfusion consisted of pressure and temperature controlled pulsatile perfusion of the hepatic artery and continuous portal perfusion for 6 h. Two hollow fiber membrane oxygenators provided oxygenation of the perfusion fluid. Biochemical markers in the perfusion fluid reflected minimal hepatic injury and improving function. Lactate levels decreased to normal values, reflecting active metabolism by the liver (mean lactate 10.0 ± 2.3 mM at 30 min to 2.3 ± 1.2 mM at 6 h). Bile production was observed throughout the 6 h perfusion period (mean rate 8.16 ± 0.65 g/h after the first hour). Histological examination before and after 6 h of perfusion showed well preserved liver morphology without signs of hepatocellular ischemia, biliary injury, or sinusoidal damage. In conclusion, this study shows that normothermic machine perfusion of human donor livers is technically feasible. It allows assessment of graft function before transplantation, which opens new avenues for organ selection, therapeutic interventions and preconditioning.

P753

IN VIVO ALTERATIONS TO CHOLANGIOCYTE MICROVILLI AND BILE COMPOSITION IN RESPONSE TO HEPATIC ISCHAEMIA-REPERFUSION INJURY

Aimen Amer, Matthew Wright, Steven White
Newcastle University

Introduction: Both ischaemia-reperfusion injury (IRI) and altered bile are implicated in the development of non-anastomotic biliary lesions following liver transplantation. However a causal link between IRI and altered bile composition remains to be proven. Our aim was to examine the effects of IRI on bile homeostasis and on BEC microvilli *in vivo*.

Methods: Sprague Dawley rats were divided into two groups ($n = 30$ /group): IRI group subjected to 90 min of left hepatic ischaemia followed by reperfusion and a sham-operated group. Bile flow was measured and liver tissue harvested at various time-points (5 hrs up to 28 days post-reperfusion) in addition to serum and bile collection. Liver tissue was examined using transmission electron microscopy to assess BEC microvilli morphology.

Results: The IRI group demonstrated significantly raised serum bile acids and alkaline phosphatase which peaked on day 1 and 3 respectively. Bile flow was significantly lower in the IRI group immediately post-reperfusion and normalised by day 3. Biliary bile acid concentration was significantly higher in the IRI group on day 1. A delayed rise in biliary phospholipid concentration was also noted in this group. BECs demonstrated a significant increase in microvillar height, width and density in the IRI group compared to the sham group. These changes persisted at 28 days after reperfusion.

Conclusion: This study demonstrates that IRI results in changes to bile composition which may play an important role in the pathogenesis of biliary strictures. It also results in persistent changes to BEC microvilli suggesting an adaptive response to a prolonged pathological process.

P755

MACHINE PERFUSION WITH A NEW CELL-FREE OXYGEN CARRIER SOLUTION PROVIDES EFFECTIVE EX-VIVO OXYGENATION, MINIMIZES ISCHEMIA REPERFUSION INJURIES AND DOWNREGULATES GENES ASSOCIATED WITH LIVER DAMAGE

Paulo Fontes¹, Wallis Marsh¹, Roberto Lopez¹, Arjan van der Plaats², Rick Light³, Shirish Paranjpe⁴, Sruti Shiva⁴, George Michalopoulos⁴, Yoram Vodovotz¹

¹University of Pittsburgh Medical Center; ²Organ Assist; ³OPK Biotech; ⁴University of Pittsburgh

Background: Machine perfusion (MP) with a newly developed cell-free oxygen carrier solution (CFOCS) was compared to cold storage preservation (CSP) in a porcine model for liver transplantation.

Methods: Two groups of 6 animals (60 kg) underwent orthotopic liver transplantation after a period of 9 h of cold ischemia time (CIT). The liver allografts from the control group were stored with University of Wisconsin solution at 4°C and the study group with MP (dual pressures and full oxygenation with $FI_{O_2} = 60\%$). Extensive clinical and laboratory data were obtained, which included tissue oximetry and mitochondrial function assessment with an oxygraph chamber. Affymetrix gene-arrays (swine oligoarray chip) were performed in both groups in three different time points: baseline, post reperfusion (9 h) and at end-study necropsy (5 days). Additionally, a cytokine profile was obtained from the same specimens using Luminex.

Results: The MP group had 100% survival with excellent allograft function. The CSP group had 33% survival after experiencing moderate to severe ischemia/reperfusion injuries. A significant ($p < 0.004$) benefit of MP was detected after 16 different variables were analyzed in comparison to CSP. Hepatic O_2 delivery (0.78 ml O_2 /g/h) was eight times higher than O_2 consumption (0.096 ml O_2 /g/h) while under MP with the CFOCS. The MP group showed a significant decrease on I/R injuries ($p < 0.05$) when compared to the CSP group. The top 100 most affected genes showed over-expression (fold change > 1.5) of the genes associated with general metabolic functions, anti-inflammatory, regeneration and protective mechanisms against free radicals. Extensive retention of expression of many genes associated with hepatocyte differentiation was observed. Ingenuity[®] pathway analysis of functional groups affected by perfusion revealed that genes associated with liver damage were significantly down regulated in the MP group. The CSP group showed significant upregulation of genes associated with liver pathology when compared to the MP group.

Conclusions: MP with a CFOCS promotes efficient hepatic oxygenation during a prolonged CIT (9 h) and minimizes I/R injuries. Enhanced oxygenation under subnormothermic conditions triggers pivotal regenerative and cell protective gene responses which may have implications for improved liver allograft function after transplantation.

P756

CCL5, HSP70 AND DCN ARE REVEALED AS CANDIDATE BIOMARKERS IN A DCD MODEL OF RENAL WARM ISCHAEMIA

Mohammad Hossain¹, Ayesha DeSouza², Iain MacPhee³, Nicos Kessar⁴, Mohamed Morsy⁵

¹St Georges Hospital NHS Trust; ²Department of Cardiovascular Sciences, St Georges University of London; ³Department of Renal Medicine, St Georges University of London; ⁴Department of Renal Transplantation, Guys & St Thomas' Hospital NHS Trust; ⁵Department of Renal Transplantation, St Georges Hospital NHS Trust

Introduction: Warm Ischaemia (WI) is a risk factor for delayed graft function after renal transplantation from donation after circulatory death. A tissue biomarker of WI has yet to be validated to quantify donor WI damage.

Methods: Open renal biopsies were taken post termination for up to 3 h in six large white female pigs. Total RNA and protein extracts were subjected to expression microarray and 2-DE differential in gel electrophoresis, with respective qPCR and western blot validation.

Results: 784 genes were differentially expressed ($p < 0.01$, RM-ANOVA). Both CCL5, and HSP-70 increased (+2 fold change) over the 3 h time period. Decorin (DCN), decreased (-2 fold change) over the time period. Forty uniquely identifiable protein spots were differentially expressed across all time points. Differential increased expression of PRX3, PRX6 and HSP-70 were found (+2 fold change) throughout the time points ($p < 0.05$).

Conclusions: CCL5, HSP70 and the antioxidants (PRX3, PRX6) demonstrated positive correlation while DCN showed negative correlation over 3 h of WI. These expression profiles are novel in a large animal model. This study suggests that these biomarkers could facilitate viability testing.

P758

TLR2 RECEPTOR UPREGULATION IN PATIENTS UNDERGOING RENAL TRANSPLANTATION WITH A HIGH RISK OF DELAYED GRAFT FUNCTION (DGF)

Mary Reilly¹, Jacques Sennesael², Andreas Pascher³, Pdraig O'Grady¹, Robert Miller¹, Dirk Kuypers⁴

¹Opsona Therapeutics; ²UZ Brussels Hospital; ³Charité, Campus Virchow-Klinikum, Berlin; ⁴UZ Leuven, Brussels

Background: Up-regulation of TLR2 plays a critical role in the mediation of inflammation ischaemia/reperfusion tissue damage (1). OPN-305 is the first humanised IgG4 MAb against TLR2 in development for the prevention of reperfusion injury in renal transplantation. TLR2 receptor occupancy (RO) and OPN-305 pharmacokinetics (PK) in healthy volunteers (HVs) may not truly reflect the situation in transplant recipients receiving kidneys at high risk of DGF who may have an increased TLR2 gene expression. To avoid under-treating patients in the planned Phase II study, the RO and PK of OPN-305 administration in HVs and transplant patients were compared.

Methods: As part of a Phase I dose escalation study four HVs were given a single intravenous dose 1.5 mg/kg OPN-305 over 2 h. In a subsequent study eight patients receiving high risk kidneys (five Expanded Criteria Donors [ECD] and three Donation after Cardiac Death [DCD]) were administered 1.5 mg/kg of OPN-305 over 1 h prior to reperfusion of the allograft. PK and TLR2 RO, on circulating monocytes, were measured in both populations.

Results: In HVs, 100% TLR2 RO was seen for at least 28 days returning to baseline by Day 56. In the patients, 100% RO was only retained for at least 14 days in 6/8 patients. In both populations the PK was correlated with the RO duration but not with allograft function. The geometric mean C_{max} and AUC_{0-t} were 43.5 ng/l and 7.511 ng*h/l respectively in HVs and 23.9 ng/l and 2440 ng*h/l in patients; the mean half-life for HVs at this dose was 181 vs. 110 h for the patients. There were no related serious adverse events.

Conclusions: TLR2 receptors appear to be up-regulated in patients receiving ECD or DCD kidney transplants which resulted in a reduction in AUC to approximately 30% of that seen in HVs and consequently a shortening of 100% receptor occupancy duration. 1. Anders HJ, Banas B, Schlondorff D. 2004. *J Am Soc Nephrol* 15: 854–67.

P758A

ASSESSMENT OF BLOOD SUPPLY TO HAND ALLOGRAFTS

Rafał Malecki¹, Małgorzata Gacka², Maria Boratyńska³, Ilias Dumas⁴, Jerzy Jablecki⁵, Adam Chelmoński⁵, Rajmund Adamiec¹

¹Department of Angiology, Systemic Hypertension and Diabetology, Wrocław Medical University; ²Department of Angiology, Systemic Hypertension and Diabetology, Wrocław Medical University; ³Department of Nephrology and Transplantation Medicine, Wrocław Medical University; ⁴Department of Physiotherapy, Wrocław Medical University; ⁵Microsurgery Center for Limb Replantation, Surgery of Hand and General Surgery, Trzebnica

Background: The development of vasculopathy in the limb allograft can result in amputation. A routine assessment of blood supply may reveal early stages of ischemia. The aim of the present study was the evaluation of blood supply to hand allografts using noninvasive modalities.

Methods/materials: Five patients with 6 hand allografts transplanted in Microsurgery Center for Limb Replantation in years 2006–2010 were included in the study. The mean time from the procedure was 44 months. Two persons underwent transplantation of the right forearm, two patients – transplantation at the level of the arm, and one person had bilateral forearm transplantation. Doppler ultrasonography (DUS), impedance plethysmography (IP), Doppler measurement of segmental pressures (DSP), optical pulse oscillography (OPO), and thermography were performed in all patients.

Results: There was no difference in the mean temperature of the fingers and wrists, with the exception of one native hand, which was significantly cooler. In DUS a tendency for higher resistance of the flow in grafts was observed, that appeared statistically significant with respect to the ulnar arteries (RI 0.87 and 0.72, $p < 0.05$). In the patient with bilateral transplantation stenosis of the right ulnar artery and decline in the flow in both radial arteries were found. IP showed the worsening of the flow in grafts (ABF 28.27% vs. 40.64%/min, $p < 0.05$). DSP revealed significant pressure reduction in two patients. OPO showed flattening of the flow curve in one graft.

Conclusion: In patients without clinical symptoms of ischemia non-invasive methods revealed slight abnormalities in blood supply to hand grafts. A comprehensive assessment of the regional circulation can be useful in monitoring of patients after hand transplantation.

PS18-XENOTRANSPLANTATION

P759

DIFFERENT IMPLANTATION SITES OF SODIUM CELLULOSE SULFATE MICROENCAPSULATED PORCINE ISLET CELLS IN FIVE BEAGLE DOGS

Karlheinz Tscheliessnigg¹, Philipp Stiegler¹, Georg Haimef², G. Dupre², F. Zeugswetter², Vanessa Stadlbauer-Köllner³, Michael Sereinigg¹

¹Department for Surgery, Division for Transplant Surgery, Medical University Graz; ²Department for Small Animals and Horses, University of Veterinary Medicine Vienna; ³Department for Gastroenterology and Hepatology, Medical University Graz

Purpose: Whole pancreas transplantation or human islet cell transplantation are alternatives but limited due to the organ shortage and lifelong immunosuppression. The use of immune isolated porcine islet cells (PIC) could offer a feasible alternative. In this study, the safety and applicability of three possible implantation sites for Sodium Cellulose Sulfate (SCS) microencapsulated PIC were evaluated in five healthy beagle dogs.

Methods: Five healthy, male castrated Beagle dogs were used for this study. SCS microencapsulated PIC were implanted in the subcutaneous tissue, the omentum and the gastric submucosa. Surgery time and intraoperative complications were monitored. Implantation in the omentum and gastric submucosa was performed laparoscopic assisted. All animals were continuously monitored including clinical examinations and complete blood counts for possible occurring side effects. On day -3, 30 and 90 a glucagon stimulation test was performed to assess β -cell function and glucose metabolism. On day -3, 1, 3, 12, 30, 60 and 90 fasting glucose and insulin were measured. Blood samples were taken to check a possible porcine endogenous retrovirus (PERV) transmission. Biopsies of all implantation sites were obtained for histopathology on day 90.

Results: No technical complications occurred at the subcutis and omentum site. At the gastric submucosa only a limited amount of cells could be implanted. Delayed wound healing at the subcutaneous implantation site was observed in three out of five dogs. No further side effects occurred during the study period. Transmission of PERV was not detected. Glucagon Stimulation Tests showed a trend towards a faster response to a glucagon stimulus and an

increased insulin peak. Histopathology results have not been completely evaluated yet.

Conclusion: First results show that SCS microencapsulated PIC do not cause any harmful side effects to the recipients concerning application. No transmission of PERV was detected. The outcome of

P760

WHAT IS THE FUTURE OF XENOTRANSPLANTATION?

Constantinos S. Mamas¹, Georgia Kostopanagiotou², Nicolaos Arkadopoulos¹, Vasileios Smyrniotis¹, Ismene Dontas¹

¹Surgical laboratory Prof. C.Tountas; ²Attikon University Hospital

Background: Scientific analysis needs data for description of a class of events, for their explanation and for prediction. Current xenotransplantation (X) research status is monitored for clarification of its level of evidence.

Material and methods: A bibliographical study based on the immunological, coagulation dysregulation (CD) and on xenozoonosis (XZ) barriers of (X) was applied after a research in the PUB MED by typing the key words or their combinations: (X), immunological barriers, (CD) and (XZ). Ninety five articles were first selected and twenty five of them were finally studied dependently on their up to date information, their source and on their future prospect analysis.

Results: The majority of articles (24/25) reported results from multiple genes modified porcine based (X) basic studies. None referred to a porcine or primate to human (X). Progress has been variable, and several obstacles, e.g., immunobiology of pig-to-nonhuman primate transplantation, Hyperacute rejection, acute humoral xenograft rejection, acute cellular rejection chronic rejection, and (CD), have been identified as barriers to (X). Currently, the hyperacute xenograft rejection, can be controlled by various strategies, including the use of organs from transgenic pigs expressing human regulators of complement such as decay accelerating factor. The delayed xenograft rejection and T-lymphocyte-dependent xenograft rejection are now the major remaining immunological barriers. The (CD) defined as thrombotic microangiopathy and systemic consumptive coagulopathy is recognized as a barrier to (X). Multiple-gene transgenic pigs, systemic medication such as statins, and anti-platelet agents are considered among the solutions. The potential for the development of a (XZ), is now considered less significant.

Conclusion: Current (X) research level of evidence, seems to be "stuck" to the safety and understanding level (I). The levels II, III and IV of research evidences seem to be the future of (X).