Poster Presentations

Poster Session 1: Sunday, 30 August 2009 – Monday, 31 August 2009

Cell transplant

P-1 TISSUE FLUID/LYMPH CYTOKINES AND GROWTH FACTORS REGULATE HUMAN KERATINOCYTE PROLIFERATION AND DIFFERENTIATION

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Introduction: Our previous studies revealed presence of a number of growth factors and cytokines in human skin tissue fluid/lymph (TF/L) at levels higher than in serum. This prompted us to study whether TF/L may have a regulatory effect on keratinocyte (KC) growth.
Aim: To study the effect of TF/L on proliferation and differentiation of KC and their stem cell markers expression.
Material and methods: KC were isolated from lower limb skin and were cultured for 1 to 7 days in TF/L. Phenotypes were identified using antibodies against p63, CD29, Ki67 and PCNA. Blocking of cytokines with antibodies helped to estimate which cytokine stimulated KC proliferation and differentiation.
Results: KC cultured in TF/L showed higher than in controls percentage of dividing and elongated cells from basal layer as well as lower percentage of differentiated cells from upper layers. Higher percentage of p63 and CD29 positive cells was also observed. Neutralization of IL -1β, IL -6, TNF-α, KGF caused decrease in percentage of mitotic cells. Neutralization of KGF decreased percentage of p63 and CD29 positive cells.
Conclusion: TF/L cytokines have a stimulating effect on proliferation of basal KC but not on their differentiation. KGF turned to be a strong stimulator.

P-2 INDUCTION OF LETHAL GRAFT-VERSUS-HOST DISEASE (GVHD) BY ANTI-CD137 MONOCLONAL ANTIBODY IN MICE WHICH ARE PRONE TO CHRONIC GVHD

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Chronic graft-versus-host disease (cGVHD) is an increasingly frequent complication of allogeneic stem cell transplantation. We previously showed that anti-CD137 monoclonal antibody (mAb) can cure advanced cGVHD by inducing activation-induced cell death of donor T cells. In this study, we examined whether administration of anti-CD137 mAb can prevent the development of cGVHD after bone marrow transplantation (BMT) in mice conditioned with total body irradiation. The Balb/c (H-2d) minor histocompatibility antigen-mismatched model, which◇B10.D2 reflects clinical and pathological symptoms of human cGVHD, was used in this study. A single injection of anti-CD137 mAb was done immediately after BMT. Contrary to the results obtained from the curing model of cGVHD, anti-CD137 resulted in lethal GVHD when treated simultaneously with BMT. Histopathological evaluation revealed inflammation and damage of target organs for acute GVHD (aGVHD) in anti-CD137-treated mice. Anti-CD137-induced acute lethal GVHD required host cells as well as irradiation and mature donor T cells. It seemed that anti-CD137 mAb rapidly induced activation of donor T cells and sustained their activation status under the inflammatory condition triggered by irradiation. When treated on day 12, but not on day 30, after irradiation and BMT, anti-CD137 mAb could still exacerbate GVHD. Our data demonstrate that anti-CD137 mAb can amplify inflammation induced by host preconditioning, subsequently resulting in acute lethal GVHD. Thus, it is critical to alleviate irradiation-induced toxicity in order that anti-CD137 mAb might be used as a GVHD prophylaxis.

P-3 CHARACTERIZATION, CRYOPRESERVATION AND EXPERIMENTAL TRANSPLANTATION OF THE HETEROGENOUS POOL OF STEM CELL IN HUMAN FETAL LIVER

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Fetal liver contains hemopoietic, hepatic and mesenchymal stem and progenitor cells which may assist in regenerative medicine.
Aim: To characterize the main cellular populations in human fetal liver and assess their cryopreservation and potential for regeneration after transplantation in different experimental chronic diseases.
Fetal liver cells (FLC) were isolated from human fetuses of 8-10 weeks gestation under guidelines of Consent and Ethical Approval of Ukraine Ministry of Health and cryopreserved by slow cooling. The phenotypes of haematopoietic and mesenchymal stem/progenitor cells were assessed by flow cytometry. To characterize cells of hepatic lineage, FLC were cultured in monolayer and stained against albumin and alfa-fetoprotein (AFP). The ability of FLC to stimulate hepatic function was studied in the model of CCl_4-induced cirrhosis in rats. Recovery processes were evaluated by blood indexes, hepatic detoxification function and liver morphology. The effects of FLC–derived mesenchymal cells were also assessed in a model of osteoarthrosis in rats. Samples of articular cartilage of the knee joint were studied by electron microscopy.
The majority of FLC suspension was presented by hemopoietic cells. Cells of hepatic lineage expressed albumin and AFP. Primary suspension of human FLC contained 2-3 CFU-Fs per 10^5 seeded cells. Ex vivo expanded fibroblast-like FLC demonstrated the phenotype of mesenchymal stem cells (MSC) and ability for osteogenic and adipogenic differentiation.
FLC transplantation to cirrhotic rats reduced mortality of animals, increased synthetic and detoxification liver functions and stimulated regenerative processes in liver. Electron microscope data showed that transplantation of FLC into defects of articular cartilage in rats with a model of osteoarthritis stimulated regenerative processes in cartilage.
Primary FLC suspensions contain haematopoietic, hepatic and mesenchymal precursors. Each cell lineage demonstrates specific therapeutic potential in xenograft models.
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P-4 NON-COMMERCIAL CLINICAL TRIALS IN ADVANCED THERAPIES PROMOTED AND SPONSORED BY GOVERNMENT OF ANDALUSIA (SPAIN)

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Purpose and methods: To facilitate the development of Clinical Trials (CT) in Advanced Therapies (AT), the Government of Andalusia has created the Andalusian Advanced Therapies Initiative (AATI) which represents a new organizational model to facilitate the clinical translation.
The AATI includes a network of research centers dedicated to cell therapy, gene therapy and nanomedicine as well as infrastructures and biobanks. The AATI gives financial support for research projects and develops different recruitment and training programs. In order to help the development of CT, we have designed a model in which the Andalusian Public Health System (APHS) promotes clinical research in AT by sponsoring CT.
Results: AATI works to comply with the FDA/EMEA requirements and AATI facilitates to the researchers the access to authorised GMP facilities, supporting in the elaboration of the Investigational Medicinal Product Dossier. Finally, the AATI localizes teams of clinicians to develop a clinical protocol. As a result of this work, the AATI is promoting the creation of GMP facilities in 9 centers for cell- and gene-therapy as well as tissue engineering. Moreover, in 2008 we were recruiting patients for 4 CT in cardiology, neurology and peripheral vascular diseases. On 2009, the drug agency has approved 2 more CT and in another 2 we are pending the drug agency's approval.
Conclusion: There is a big gap between the research results and their everyday application in patients. The involvement of the Health Authorities, acting as sponsor and consulting agency, can help to translate the results into treatments as soon as possible, giving support in every step of the process between knowledge and innovation, especially facilitating the access to the GMP labs and the performance of legal requirements to carry out CT.

P-5 CD4+CD25+ T REGULATORY CELL MOBILISATION FOR THERAPEUTIC PURPOSES

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Objective: CD4+CD25+ T regulatory (T reg) cells play important role as antigen-specific suppressors of autoimmune and allogeneic reactions. Therapeutic potential of T reg cells has recently been recognised. We investigated CD4+CD25+ cell mobilisation during haemopoietic stem cell (HSC) mobilisation.
Material and methods: Peripheral blood (PB) CD4+CD25+ cell dynamics was monitored during HSC mobilisation in four allogeneic HSC donors and six patients who underwent autologous HSC mobilisation. All donors received intermediate doses of G-CSF, and in some patients G-CSF was used in combination with chemotherapy
Results: The relative numbers of CD25+ expressing cells increased 10-20 times that, in combination with PB leucocytosis, resulted in high absolute contents of CD4+CD25+ cells. The absolute numbers of circulating CD4+CD25+ cells in all patients and donors increased significantly ($p<0.01$) from 1.5-25 cells/ul baseline to 20-100 cells/ul during mobilisation. The magnitude of increase ranged from 3-6 folds to 20-70 folds while higher T reg cell increase was generally observed in patients with lower baseline levels.
No difference in CD4+CD25+ T cell mobilisation was revealed on comparison of the G-CSF alone and G-CSF plus chemotherapy mobilisation regimens. Circulating T reg cell contents were also elevated in patients in whom mobilisation procedures did not result in any increase of PB white cell count and even in cases when the total T cell counts were depressed by chemotherapy.
There was no correlation between the numbers of CD4+CD25+ cells and CD34+ cells. A similar increase in circulating T reg cell pool was observed in both good and poor mobiliser groups, as defined by CD34+ cell mobilisation.
Conclusions: A substantial release of CD4+CD25+ T regulatory cells into circulation is observed on HSC mobilisation. T reg mobilisation occurs in various mobilisation regimens and is independent on CD34+ cell mobilisation efficacy. This provides opportunities for T reg cell collection for therapeutic applications.

P-7 HUMAN UMBILICAL CORD BLOOD AND UMBILICAL CORD MESENCHYMAL STEM CELLS CAN CONTRIBUTE TO LIVER REGENERATION IN AN ANIMAL MODEL OF CHEMICAL-INDUCED INJURY

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Purpose: To evaluate the contribution of Mesenchymal Stem Cells (MSCs) from Umbilical Cord Blood (UCB) and cord to liver regeneration in an animal model of acute chemical-induced liver injury.
Materials and methods: Liver injury was induced by intraperitoneal injection of CCl_4 (1ml/kg) into 17 male Lewis rats. After 48 hours from the injury, 6 animals received 10^6 MSCs from UCB or cord in the peritonean, 5 animals received physiological buffer as control, while 6 animals died before the treatment. Animals were sacrificed at different times; liver, kidneys, lungs, heart were harvested, fixed and paraffin embedded. Samples were treated for hematoxilyn-eosin staining and for immunohistochemical analysis for human HLA1 expression.
Results: 7 days after MSCs injection, the liver presented a level of steatosis and sinusoids dilatation lower than the control, while at 14 days from injection liver appeared almost completely regenerated in both animals treated with cells and in control animals. Immunohistochemical analysis revealed some positive cells to human HLA1 in the liver treated with MSCs from UCB after 7 days from the injection, while there was no positive evidence to human HLA1 in other investigated organs.
Conclusions: MSCs from human UCB and umbilical cord seem to contribute to liver regeneration by enhancing the reparative activity of hepatocytes that spontaneously occurs in case of injury. Liver damage specifically attracts MSCs as human cells were detected into the organ and not in the other ones. Nevertheless, the modality of MSCs contribution to liver regeneration remains to be investigated.

P-8 STUDY OF THE USE OF ICG FOR RAPID ASSESSMENT OF ISOLATED HUMAN HEPATOCYTE FUNCTION

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Aim: Hepatocyte transplantation is a promising alternative to liver transplantation. Currently, no rapid assays are available to assess the function of fresh hepatocytes prior to transplantation. The aim of this study was to investigate whether the uptake and release of ICG by hepatocytes could be used as a test of hepatocyte function.
Methods: Hepatocytes isolated from donor livers were incubated for 30 min with ICG (0-2 mg/ml) in suspension and culture. Cells were then incubated in medium without ICG for 3 h. The supernatants were collected at 1-3 h for measurement of ICG release. MTT (mitochondrial activity) and SRB (cell attachment) assays were done at 18h after incubation with ICG. Taurine was added to some cells prior to culture.
Results: ICG was taken up and secreted by hepatocytes. In hepatocytes incubated with concentrations of ICG above 1.0 mg/ml, ICG had a toxic effect on hepatocytes with cell death observed. There was a slight increase in MTT (0.053 v.s. 0.045) and SRB (0.67 v.s. 0.59) for plated hepatocytes compared to controls after 18 h incubation post ICG uptake. ICG release peaked at 1-2 h in both cell suspension and in culture and then declined slightly at 3 h. The pattern of ICG release appeared to be related to viability by trypan blue. Higher ICG concentrations caused more detachment of plated cells. Addition of taurine to plated hepatocytes gave greater release of ICG and helped hepatocytes attach better compared to controls at all ICG concentrations (1.36 ± 0.08 v.s. 0.91 ± 0.16, $p=0.011$ at 1.0 mg/ml)
Conclusions: Further refinement of this ICG test may be needed in order to develop a rapid assay for assessment of human hepatocyte function. Taurine was shown to increase cell attachment and let cells endure higher concentrations of ICG.

P-9 AUTOLOGOUS BONE MARROW STEM CELLS IN THE TREATMENT OF CIRRHOTIC PATIENTS

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Liver cirrhosis (LC) is the end stage of chronic liver diseases. Liver transplantation is one of the only effective therapies available to such patients.
However, lack of donors, surgical complications, rejection, and high costs are it's serious problems. The potential for stem cells in bone marrow (BM) to differentiate into hepatocytes was recently confirmed. In this study we evaluated safety and feasibility of autologous bone marrow mononuclear (BM -MNC) and enriched CD133+ hematopoietic stem cell transplantation through the portal vein in patients with decompensate cirrhosis.
Seven patients with decompensated cirrhosis were included in two groups (CD133 or BM-MNC). Approximately 200 ml of the bone marrow of the patients was aspirated, and CD133+ or BM-MNC cells were selected and the cells were slowly infused through the portal vein under sonography monitoring. All patients were monitored for side effects, toxicities, and changes in the clinical, hematological, and biochemical parameters. All patients tolerated the procedure well, and there "were no treatment-related side effects or toxicities observed. Totally, all patients showed marginal improvements in serum albumin level and MELD score, but not in each group. Other markers did not improve significantly. However, we could not find any difference between CD133 and BM-MNC groups. This early experience with portal vein application of CD133+ or BM-MNC could suggest this novel therapeutic approach for cirrhotic patients.

P-10 AN "IN VITRO" MODEL FOR EVALUATION OF ENGRAFTMENT ENHANCERS IN LIVER CELL TRANSPLANTATION

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Cell therapy is an emergent technology that promises to help in the regeneration of damaged organs and tissues. The liver is one of the organs where these techniques must be implemented because the supply of organs is scarce.

The liver is an excellent organ for cell transplantation, as the sinusoids do not have a basal membrane, and in an intraportal cell perfusion the unique physical barrier between transplanted cells and the liver parenchyma is endothelium. However, at present, hepatocyte transplantation has not been very successful as most cells do not bind to the receptor parenchyma and die soon after perfusion.
Our work is focused in identifying engraftment enhancers, substances that improve the efficiency of cell transplantation in a reversible mode, modifying vascular tissue, in order to permit the outflow of transplanted cells into liver parenchyma and allow liver regeneration.
We have developed an "in vitro" model of two assays to test drugs and select the best strategy to achieve effective forms of intraportal infusion of hepatocytes, so they migrate to damaged tissue and become engrafted.
First assay, in a confluent endothelial cell culture we tested diverse drugs and measured their effect in generating "in vivo" gaps allowing cell outflow from the blood. The loss of confluence was confirmed through image analysis.
In the Second test, mouse stem cells were seeded on a pretreated HUVEC layer to confirm the activity of the molecules selected in the first assay, and to quantify the number of cells engrafted.
Our preliminary results using different drugs, have allowed us to identify 2 molecules that could potentially have the capacity to function as engraftment enhancers.

Composite tissues

P-11 INVESTIGATION OF THE ROLE OF ISCHEMIA AND REPERFUSION IN LIMB TRANSPLANTATION

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Introduction: Acceptable ischemia times in hand transplantation and the effect of preservation solutions remain undefined. We herein investigate the effect of cold tissue storage and preservation with HTK and UW in a rat hindlimb transplant model.
Methods: LEW rat limbs were flushed and stored for 0, 2, 10, 30 and 40h in HTK or UW preservation solution. After transplantation, limbs were analyzed for morophological and functional (muscle) alterations by histomorphology and high resolution respirometry at 0h, 24h and 10 days. Muscle damage was assessed using a previously established scoring system evaluating injury in individual myocytes. Skin was scored: 0, no necrosis; 1, less than 50% necrosis; 2, more than 50% necrosis. Reperfusion after transplantation was validated with angiography on pod 10.
Results: Appearance and histology of all tissues remained unaltered during preservation. Two hours of cold ischemia and 24h reperfusion did not cause alterations in histomorphology, regardless of the preservation solution used. At 10 days, however, limbs flushed and stored in HTK showed significantly less tissue damage when compared to UW (p= 0.0498). Angiography at postoperative day 10 showed no occlusion of the vasculature. High resolution respirometry of permeabilized muscle fibers demonstrated significant decline in mitochondrial respiratory capacity (state 3 respiration and respiratory control ratio) after cold ischemia-reperfusion, indicating damage to complex I, whereas complex II respiration was well preserved. No damage to the mitochondrial phosphorylating system was observed.
Conclusions: Histomorphological alterations after limb ischemia and transplantation can be observed at 10 days. Preliminary results suggest an advantage of HTK over UW for tissue preservation. Analysis of muscle mitochondrial function, reflects a substantial functional deficit after cold ischemia.

P-12 ROLE OF ALLOTRANSPLANTATION IN REHABILITATION OF THE PATIENTS WITH TRAUMATIC INJURY OF SKELETAL SYSTEM AND ORTHOPEDIC DISORDERS

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Purpose: To define the indications of bone allotransplantation in clinical practice, with respect to type and localization of the abnormality and to shape and sizes of the grafts.
Material and methods: Small-sized cortical bones and gross grafts (including joint fragments and semijoints), conserved in 1% formalin were used. The study involved 1600 patients, with age range 5-70 years.
Results and discussion: The outcomes of allotransplantation procedures were studied from the very first day after operation up to 20 years, applying neurologic, radiologic methods, CT and the methods of evidence-based medicine. Statistical analysis provided by the package XSPSSX2 criterion (PEARSON). The results of the study demonstrated that in small-sized cortical bone transplantation settings, absorption and substitutional processes occur simultaneously, providing the true regeneration – restitution of the bone.
Conclusion: Bone allotransplants can be successfully used in the settings of unhealed fractures of long bones and/or congenital and acquired false joints, requiring intra- and extra medullar osteosynthesis, in combination with metal constructions; also, in case of benign bone abnormalities (bone cysts, osteoblastoma, fibrotic dysplasia, echinococcus, Brod's abscess etc.), for repairing defects, developed after resection of pathological sites; in the settings of osteochondrosis, spondylolisthesis, grave forms of scoliosis, when posterior spondylosyndesis in combination with distracter is needed; Along whith anterior spinal fusion (anterior spondylosyndesis) in case of fragmented vertebral fractures; In addition, it can be applied in plastic surgery of various types of foot deformations too including: varus, valgus, equinovarus, calcaneo-valgus types, wandering foot etc.

Donation & allocation

P-13 WEB BASED NATIONAL TRANSPLANT DATABASE & APPLICATION. A COMPLETE SOFTWARE SOLUTION FOR ORGANS, CELLS AND TISSUES

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After deployment of National Transplant Database and Applications for United Kingdom (UKT)we have implemented the new for central Europe region (Slovakia). This solution covers the hospitals, TX units, FUP, HLA labs, eye banks and external users in the field of solid organ transplantation plus covers the tissues and cells allocation and procurement mechanism as a whole.
Solution provides transplant centres, OPOs, HLA labs and eye & tissue banks the ability to:
- Manage their patient's waiting list.
- Access, complete and submit transplant data forms.
- Add donor information and run donor-recipient matching lists.
- Access various transplant data reports and policies.
- Maintain an organ donor register
- Interact with other national transplant systems online
- Manage processes in Eye and Tissue banks
- Manage all processes in tissue typing HLA laboratories
- Compare individual national transplant practices between information systems and exports reports to the relevant international bodies.

Helps guarantee the safety of organs and the ethical standards.
Connects multinational transplant services for sharing surplus organs into one virtual database
Provides the complete national solution for an individual country.

- The fastest Matching Run I have seen so far. Impressive performance. (Sfalvey, Duty Office Manager, UKT.)
- Chosen Web technology applications proved to be a visionary solution connecting external users to National Transplant Database from all over the UK and Republic of Ireland. Applications are extremely user friendly and remarkably stable. (Shashmi, Head of IT, UKT.)
- Comprehensive validation of all records prior to their being committed to the database is in place and the applications are designed to ensure that the management has complete control over all aspects of the validation process. (Dshute, MD, UKT.)
- Absolute accuracy of data stored in the database is of paramount importance to our work and the design of the applications ensures that this objective is achieved. (AMaxwell, DEManager, UKT).

P-15 MODULATION OF BRAIN-DEAD INDUCED INFLAMMATION BY VAGUS NERVE STIMULATION

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Because the vagus nerve is implicated in control of inflammation, we tested in the present study the hypothesis that brain death causes impairment of the parasympathetic nervous system, hence contributing to inflammation. Stimula-

tion of the vagus nerve would therefore reduce the expression of inflammatory mediators during brain death.
Brain death (BD) was induced in rats. Heart rate variability (HRV) was assessed by ECG. In the intervention group the vagus nerve of BD rats was electrically stimulated (BD+STIM). Intestine, kidney, heart and liver were harvested after 6h and processed for further analysis. Affymetrix chip- analysis was performed on intestinal RNA. Quantitative PCR was performed and serum was collected. Renal transplantations were performed to address the influence of vagus nerve stimulation on renal function.
HRV was significantly lower in the BD group compared the ventilated non-brain-dead (NBD) group, suggesting a change in parasympathetic activity. Vagus nerve stimulation inhibited the increase in serum TNFα concentrations. Affymetrix analysis and consecutively qPCR (intestine) revealed that vagus stimulation resulted in down-regulation in a number of pro-inflammatory genes including cytokines, adhesion molecules and signalling molecules.

qPCR analysis on intestinal RNA

	Group	Intestine		Group	Intestine
TNFα	BD	4.2±0.6	ICAM-1	BD	1.7±0.2
	BD+STIM	2.1±0.4**		BD+STIM	0.7±0.2**
	NBD	1.7±0.2**		NBD	0.7±0.1**
IL-1α	BD	0.7±0.1	MyD88	BD	1.2±0.1
	BD+STIM	0.2±0.02**		BD+STIM	0.9±0.03*
	NBD	0.2±0.03**		NBD	0.7±0.04**
IL-1β	BD	2.1±0.2	C1R	BD	0.7±0.06
	BD+STIM	0.5±0.08**		BD+STIM	0.3±0.1**
	NBD	0.7±0.06**		NBD	0.5±0.02*
E-sel	BD	8.4±3.1	CXCR4	BD	1.9±0.1
	BD+STIM	2.0±0.3*		BD+STIM	0.5±0.**
	NBD	3.1±1.6*		NBD	0.8±0.1**
VCAM-1	BD	1.4±0.1			
	BD+STIM	0.9±0.2*			
	NBD	0.7±0.1*			

*P<0.05 vs. BD; **P<0.01 vs. BD.

In renal tissue vagus stimulation significantly decreased the expression of E-selectin and IL1 beta. In liver/heart IL-6, VCAM-1, TNF-a and E-selectin expression was higher in the BD group but this was not influenced by vagus stimulation. Iso-/Allogeneic renal transplantation revealed a significantly better renal function in recipients and a tendency for reduced renal inflammation.
Our study demonstrates impairment of the parasympathetic nervous system during BD. Stimulation of the vagus nerve reduces the expression of pro-inflammatory genes. Renal function was significantly improved after transplantation when vagus nerve stimulation was performed in BD donors. Hence, vagus nerve stimulation might be a new approach in donor management to avoid inflammation in the course of brain death.

P-16 DECEASED DONOR MANAGEMENT AND DEMOGRAPHIC FACTORS RELATED TO KIDNEY ALLOGRAFT REJECTION AND GRAFT SURVIVAL

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Background: There is agreement that the number of organ donors and the number of organs recovered per donor are not maximized despite promotion of awareness and new guidelines for transplant teams. A single standard for donor management does not exist, in part because there is no consensus with respect to donor factors and management effect on transplant outcomes.
Methods: Retrospective study the long-term outcomes of 402 deceased donor kidney transplant recipients analyzed with respect to donor factors. This study differs from previous studies in that all recipients were treated under the same selection and immunosuppression protocols.
Results: Factors associated with improved graft survival included donor race, more organs donated, and lower peak sodium (p<0.01). Delayed graft function decreased if more organs were donated, but increased when the donor was given dopamine. Donors with a higher peak creatinine were less likely to have delayed graft function; those with a higher final creatinine were more likely (p<0.01). Decrease in acute rejection was seen in patients whose donors had received dopamine, donated more organs, and had a shorter time between incision and clamp (p<0.05). Donors with a higher last creatinine had fewer rejection episodes; those with a higher peak creatinine experienced more rejection episodes (p<0.05).
Conclusion: The effect of donor variables on kidney transplant outcomes is important and may not be consistent with traditional expectations. Additional data collection and assessment of both short and long term transplant outcomes are critical to improving our understanding of the impact of deceased donor factors and management.

P-17 THE ROLE OF THE TRANSPLANT NURSE CLINICAL COORDINATOR FOR LIVER TRANSPLANTATION IN ITALY

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Background: The TNCC is an essential figure supporting the organization and the activity of tranplant centers from listing to transplantation and follow-up.
Aim: To evaluate the coordination of liver harvesting and transplantation by the TNCC in two transplant center in Italy (Palermo and Modena).
Material and methods: Analysis of all the coordination activities in the two centers between April and September 2008.
Results: Sixty-five liver harvesting and transplantation coordination activities have been analyzed, 35 in Palermo and 30 in Modena. The overall duration of the coordination was 15h51min (range 5h30min-33h), respectively 15h40 min (range 6h15min-33h) and 15h45min (range 5h30min-20h) in Palermo and Modena (p=0,25). A median of 38 (range 20-55) contacts (phone, fax and direct) in Palermo and 40 (range 15-80) in Modena (p=0,43) have been performed for every single process of coordination. The Inter-Regional Coordinating Centers (CIRs) was always contacted in Palermo a median of 18 times (range 10-30), while in Modena this figure accounted for only 3% of cases (p<0,0001) reflecting a different approach by the two centers and CIRs. The recipient was alerted by the TNCC in 89% vs 70% of cases (p=0.06) in the two centers respectively, while he was almost always welcomed (97.1% vs 96.6%) in the hospital by the nurse staff on-duty. The TNCC had a role in the transport of the recipient to the hospital respectively in 8% and 16% of cases (p=0,32); 14% and 27% of the recipients were in-patients at the moment of transplantation. In Palermo the TNCC coordinated the transport of the harvesting team in 97% of cases vs 0% in Modena (p<0,0001).
Conclusion: The TNCC is a most relevant figure of the transplant team and should have a very definite and specific formation in this particular field.

P-18 IMPLEMENTING MINIMUM NOTIFICATION CRITERIA FOR ORGAN DONATION IN AN ACUTE HOSPITALS CRITICAL CARE UNIT

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Aims: To increase the number of donated organs through an effective donor identification and referral scheme in a large acute hospital critical care units.
Background: The barrier to successful organ transplantation is a serious shortage of donated organs. In January 2008 the Department of Health officially endorsed all 14 recommendations presented by the Organ Donation Taskforce. Recommendation 5 from the Taskforce is that minimum notification criteria for potential organ donation should be introduced on a UK-wide basis.
Design: A hospital policy entitled Required Referral was developed and implemented into a hospital Trust consisting of 4 critical care units. Support from the Trust board was sought and it was agreed that the policy would be implemented as a 'pilot policy', then a formal review after a 6 month period. An education program was instituted to incorporate 170 clinical staff to ensure the policy was activated with the following criteria: If the plan is to perform brain stem death test on a patient or a clinical decision is made to withdraw treatment, the on call Donor Transplant Co-ordinator is contacted for an assessment of suitability.
Results: A 700% increase in potential donor referrals and a 200% increase in donated organs has been achieved with the policy. A retrospective audit for the six month period prior to the policy launch had shown 4 referrals from the pilot sites. The following six months as the policy was implemented revealed an impressive 53 referrals to the Transplant Co-ordinator. This has resulted in 4 successful multi organ donors and 16 corneal transplants.
Conclusion: The Required Referral scheme has clearly shown an impressive increase in donation activity within the Trust. Donation has been embraced as a normal part of end of life care.

P-19 RELATIONSHIP BETWEEN CLINICAL AND CYTOKINES PROFILE OF BRAIN-DEATH DONORS

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Background: Brain death induces a massive inflammatory response. The majority of transplants are derived from donors who suffered from brain injury. The

possible relation of clinical profile and cytokines in donors has been poor explored
Objectives: To analyze clinical characteristics of brain-dead donors and its correlation with cytokines profile in intensive care unit (ICU) of unique tertiary care hospital
Methodology: We evaluated 120 consecutive potential brain-dead organ donors (mean age 34.9 years, 74.2% males) between July, 2007, and June, 2008. Plasma cytokines (tumor necrosis factor, interleukin [IL]-2, IL- 4, IL-5, IL-6, IL-8, IL-10, INF-gamma, TNF) were measured in 40 donors immediately criteria for brain death (or confirmatory tests) and after obtaining consent from families. Cytokines were assessed by cytometric bead array in the plasma and the all laboratory personnel were blinded to clinical information
Results: The main cause of brain death was cerebral trauma (80%) and cerebral vascular accidents. The use of vasoactive agents was 90.6%. The median time stay in ICU was two days and the mean of the organs transplanted was 2.2. Data (mean pg/ml) of cytokines were IL-2 3.32, IL-4 2.63, IL-5 11.4, IL-10 25.99, INF 9.72 and TNF 2.32. In 35% of donors IL-6 was above 5000 pg/ml and in 15% IL-8 was below the detection limit of analysis. We did not find correlations (nonparametric statistical tests) between cytokines and gender, age, laboratory tests our organs donors. Pearson correlation between IL-6 and TNF was 0.001. IL-2 and IL-4, IL-5, IL-10 and INF presented Pearson correlation $\leq$ 0.00
Conclusions: Levels pro and anti-inflammatory cytokines were increased in brain-dead donors and were correlated. The was no difference between cytokines and clinical and laboratory profiles.

P-20 CRITICAL CARE STAFFS' EDUCATIONAL NEEDS AND THEIR ASSOCIATION WITH COUNTRIES' DONATION PERFORMANCE: DATA FROM THE DONOR ACTION DATABASE

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Study aims: To investigate on the association between Critical Care (CC) staffs' self-reported educational needs re donation related issues and national organ donation performance figures.
Methods: Donor Action (DA) Hospital Attitude Survey (HAS) data was collected from 19,537 CC staff in 245 hospitals in 11 countries (Australia, Belgium, Croatia, Finland, France, Israel, Italy, Japan, Norway, Poland, Switzerland) between November 2006 and October 2008. Medical and nursing staff were asked whether they 'had received' or 'would like to receive' education on donation related issues such as 'clinical donor management', 'explaining brain death to family', 'obtaining consent for donation' and 'donor family issues'. Countries' donation performance was expressed as a Procurement Efficiency Index (PEI) (organs procured and transplanted in 2007/deaths from eligible causes/million population/year)*.
Results: On average, significantly more medical (26.7%) than nursing staff (19%, P=.0008) reported to have received related training, with highest rates in Australia (35.2%), lowest in Japan (4.8%). More nursing (54.3%) than medical staff (43.3%) requested additional training (P=.0025). A significant association was found between national PEIs and medical staffs' educational needs re donor management (R=.613, P=.043), explaining brain death (R=.628, P=.037), obtaining consent (R=.684, P=.018), and donor family issues (R=.596, P=.052).
Conclusions: DA's HAS methodology is a powerful and standardized tool to assess CC staffs' needs re donation related tasks in different environments. HAS outcomes are strong predictors of national donation rates, as demonstrated in this study. Measures to improve countries' donation performance should focus on guidance and education of CC staff so as to ensure that these practitioners have sufficient knowledge and confidence with donation related issues.
References: Countries' Donation Performance in Perspective: Time for more Accurate Comparative Methodologies (Editorial). *L. Roels et al., Am J Transplantation 2007; 7:1439-1441*

P-21 DETECTION OF BILIARY AND VASCULAR ANOMALIES IN LIVING LIVER DONORS: VALUE OF GADOBENATE DIMEGLUMINE ENHANCED MR AND MDCT ANGIOGRAPHY

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Purpose: To evaluate the performance of magnetic resonance (MR) and multidetector computed tomography (MDCT) in the assessment of living donor's vascular and biliary anomalies, having surgical findings as reference standard.
Methods and materials: Thirty-two living liver donors underwent MR cholangiography (1.5-T; standard cholangiography pulse sequences and delayed acquisitions after administration of biliary contrast agent) for biliary anatomy evaluation. MDCT (16-row multidetector scanner, multiphase protocol, 3 mm slice thickness) was also performed in all cases for assessment of vascular anatomy before transplantation. Hepatic veins (<4 mm in diameter) were not considered. MR and MDCT images interpretation was performed by 2 reviewers by consensus, based on source axial images, multiplanar reformats, and three-dimensional (3D) postprocessing images. Surgical intraoperative findings were used as standard of reference.
Results: At surgery, 17 biliary anomalies, 3 portal anomalies, 32 venous and 8 arterial variants were found in the 32 patients. MR correctly identified 15/17 biliary anomalies, with a sensitivity of 88% and a specificity of 93%. MDCT correctly identified 8/8 arterial, 3/3 portal and 29/32 venous variants, with a sensitivity of 100% and 91%, respectively, and a specificity of 100%.
Conclusions: MR and MDCT proved to be efficient in evaluating living liver donor's biliary and vascular anomalies.

P-22 POSSIBLE ERRORS IN HBV AND HCV TESTING DUE TO FLUID ABNORMALITIES IN DECEASED ORGAN DONORS

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To avoid donor-recipient viral transmission anti-HIV, anti-HCV, HBsAg, anti-HBc tests are obligatory. There are limitations to viral determination: detection limit is difficult to define, genotypes react differently. Also donor management is associated with alterations in fluid/electrolytes which, we suggest influence viral testing to provide false-negative or false-positive results.
To explore the potentiality of errant HBV, HCV determination we designed a study of over 2000 donors with aims to assess/compare the incidence of positive and negative anti-HCV, HBsAg and anti-HBc in groups of donors with low (0,11-0,35 l/l), normal (0,36-0,44), elevated hematocrit (0,45-0,56) and groups of donors with low (256-27 9miliosmoles/kg), normal (280-300), elevated osmolality (301-404).
Material, method: Between 2004-2007, 2435 possible deceased donors were referred to Poltransplant. Anti-HCV was tested in 2185, HBsAg in 2200, anti-HBc in 1183. Hematocrit was recorded, osmolality calculated from the equation: $P_{OSM} = 2[NA] + 2[K^+] + [Urea] + [Glucose]$.
Results: 61 (2,8%) donors were anti-HCV(+). In group with low hematocrit we observed a significantly lower incidence (2,2%, p=0,04) of negative tests. In group with hypoosmolarity higher percentage of positive tests were recorded (6,9%), but not significantly.
HBsAg was positive in 15 cases (0,7%). Although in the group with elevated hematocrit, hypo- and normal osmolality numbers of HBsAg(+) were distinctly very low (0 or 1), it was not possible to estimate the significance due to small groups.
Anti-HBc(+) results were obtained in 192 cases (16,2%) and it differs between groups with different hematocrit (from 12,9% to 16,7%) and osmolality (from 13,0% to 20,0%), but not significantly.
Conclusions: 1. In cases of donors with hematocrit of less than 0,35 significantly lower percentage of anti-HCV(+) tests is probably related to hemodilution with possible consequence of false-negative viral determination. PCR-RNA should be considered in this donors.
2. Abnormailities in osmolality do not affect viral determination.
3. The influence of homeostasis abnormalities on HBsAg testing requires further investigation in a larger group of donors.

P-23 DISEASED DONOR WITH THE SUSPICION OF BRAIN TUMOR – CASE REPORT

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Aim: The description of transplantation procedure in the case of brain tumour suspicion.
Methods: Single case analysis and literature review.
Case report: 26 years old female was admitted to neurology department due to intracranial stroke. She suffered from occasional headache and right arm numbness since few months. The day before she also got a fist hit in the occipital region. Despite intensive therapy in the second hospitalization day brain death was suspected and regional transplant coordinator was informed. Although in two subsequent CT scans only intra-cranial haemorrhage was diag-

nosed, a suspicion of bleeding brain tumour aroused. All standard tests results were normal, except for extremely high CMV IgG titer (882 U). Harvesting procedure and very early autopsy were performed. First results of frozen section investigation did not confirm the diagnosis of brain tumour and the transplantation procedures started. During the second kidney implantation the results of next frozen sections revealed some cells of glioma, but without particular histopathology. Glioblastoma multiforme was diagnosed two days later. Both recipients were informed about the risk of tumour transmission but refused proposed graftectomy. Rapamycin was introduced and frequent control examinations (CT and USG) were recommended. 16 months after transplantation both recipients are in good clinical condition with creatinine concentration below 1.3 mg/dl. No signs of any malignancy were found.
Conclusions: Intracranial haemorrhage may be a primary demonstration of the malignant brain tumour. Intracranial bleeding of unknown origin should be an indication for very early autopsy. The microscopic examination of brain tissue performed even after organ implantation should be a standard procedure for all donors with intracranial haemorrhage. High titer of CMV IgG may be an additional diagnostic signal since almost all malignant gliomas are CMV infected.

P-24 MELD-BASED ORGAN ALLOCATION INCREASES TOTAL COSTS OF LIVER TRANSPLANTATION: A SINGLE-CENTRE EXPERIENCE

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Introduction: In December 2006, MELD-based organ allocation replaced the CTP/waiting-time based system. The impact on costs of transplantation has not been evaluated yet.
Methods: Total costs for liver transplantations (LTx) before and after implementation of MELD-based organ allocation were identified (256 of total 283 cases, 01.01.05 – 08.12.07). 49 cases were excluded (re-transplantations, HU-listed recipients and patients with 30-day mortality). For the remaining 207 cases, total costs were compared to their corresponding MELD-scores. Furthermore, 84 cases from the pre-MELD-era were compared to 123 cases of MELD-based organ allocation.
Results: Total costs for LTx correlate (r^2=0.28) to the recipients' labMELD-scores. No significant correlation could be identified for Child-Pugh classification and total costs. MELD-Scores can be stratified in 4 groups (I: 6-10, II: 11-18, III: 19-24, IV: $>$24) representing a difference of 15.672$\pm$2.233 € between each group ($p<0.05$). Recipients' labMELD-scores were significantly higher in the MELD-based allocation system by 9 points and correlated to a median increase of costs by 11.650 €/case ($p<0.05$). The indication for liver transplantation had no influence on total costs. For LTx of HU-listed patients, significantly more resources were needed.
Conclusion: MELD-based organ allocation has led to increased total costs of LTx. In accordance with other studies, sicker patients had higher health-care costs.

P-25 EDUCATION FOR HEALTH IN SCHOOLS PROMOTING BONE MARROW DONATION

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The North Histocompatibility Centre (CHN) is one of 3 Centres that compose the Portuguese Registry of BMDonors CEDACE. The strong activity to create it started in 2003. Portugal reached the third place in 3 years in the European ranking with an exemplar union of efforts involving all society. We developed since 2005 an Educational Program directed to children in basic and secondary schools. The first step was the production of an Interactive CD: "Bone Marrow: The Factory of Life", intended to prepare the future, making today's children future donors. It has basic concepts about BM, Leukaemia, Transplantation and how to become a BMDonor. It is directed to several age groups and has funny games, to test knowledge acquired with it. The CD had an excellent success in children, youth, donors, teachers and parents. The second step was its distribution to all schools in the country to be discussed in Science classes and paint tile panels in art classes, expressing children feelings. Those panels will be part of the walls of our building. We received 101 tile panels and 154 projects, mobilizing children aged from 6 -18 from all the country. The beautiful paintings exhale purity and tenderness and some express the painful knowledge and close proximity to affected colleagues. The nice work of these students is the proof that we can mobilize healthy people to help patients. A book with pictures of all the tile panels, texts coming from several countries and a new CD were produced and translated to English. The panels are shown in an itinerant exhibition. The message of commitment of these children will be known and followed. "I am Francisco! I received Bone Marrow from Mariana that saved my life" (8 years old), is the 1rst panel.

P-26 RESULTS OF THE IMPLEMENTATION OF A MELD SCORE-BASED ALLOCATION SYSTEM IN A EUROPEAN CENTER

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Background: MELD score-based allocation has been proven to be a reliable tool for prioritization of candidates for liver transplantation (LT) since 2002 in the UNS. The aim of this study was to determine the impact of this implementation in a single French transplantation center.
Patients and methods: Between Sept 2005 and Sept 2008, 187 cirrhotic patients listed for a first LT were retrospectively studied. Mean age was 54 years. The cause of cirrhosis was alcohol in 83, HBV infection in 27, HCV infection in 49 and others in 28. Ninety nine patients had HCC (53%). Two groups were considered: Group 1, within 18 months preceding MELD score-based allocation (allocation based on waiting time); Group 2, within 18 months following the implementation of MELD score-based allocation.
Results: Groups 1 and 2 included 79 and 108 patients, respectively. Mean MELD score (independent of HCC) at listing was significantly higher in Group 2 patients compared to Group 1: 14$\pm$5 vs 16$\pm$7 (p=0.01). The proportion of HCC was comparable between groups. The rate of waiting list mortality or removal from the list due to deterioration was significantly lower in Group 2 (7%) than in Group 1 (17%, $p< 0.05$). Proportion of PNF was lower in Group 2 (5%) than in Group 1 but the difference was not significant. Finally, one-year post LT survival tended to be higher in Group 2 than in Group 1 although the difference did not reach a significant level (93% *vs* 80%).
Conclusion: The results of this study confirm that in a European population, MELD score-based allocation system reduces waiting list mortality or dropout without affecting post transplant outcome.

P-27 A PROPOSAL FOR A PORTUGUESE KIDNEY PAIRED DONATION PROGRAM

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The growing disparity between the number of renal patients on the national waiting list for a kidney transplant and the number of deceased donors has compelled transplant programs to seek ways to increase the number of organs available for transplantation. Rapaport formulated the principle of paired exchange in 1986, given it the title 'kidney paired donation'. Individuals who are unable to donate a kidney to a loved one because of immunologic incompatibility are exchanged in order to form compatible pairs; the volunteers thus become living donors for unknown recipients. The aim of this study is to describe a method for an exchange program applicable to the Portuguese reality. We propose a computer match which selects exchange combinations with the following hierarchy: 1) maximum number of matched pairs; 2) blood type O donors preferentially donates to blood type O recipients; 3) combination pairs with the higher donor-recipient average match score.
In our sample we have 5 patients with an incompatible blood type living donor and 8 patients with a positive crossmatch living donor. We used a computer match program for paired kidney and unconventional exchanges. This match program gives us all the exchange possibilities involving two and three donor/recipient incompatible pairs for each one of the incompatible pairs in our sample. The computer takes into account ABO and HLA compatibility to define the possible exchanges. With all the possible exchanges we select the ones that maximize the number of possible transplants.
With a sample of 13 incompatible donor/recipients pairs we were able to define 7 possible transplants.
In conclusion, this program may prevent the current loss of a significant number of suitable living donors, and thereby have a significant impact upon the current acute shortage of organs for transplantation.

P-28 WASTING KIDNEY GRAFTS

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Purpose: In making renal insufficiency highest priority, the model for end-

stage liver disease (MELD) system prefers combined simultaneous liver kidney transplants (SLK). But MELD era outcomes in Europe demonstrate a decline in patient survival and an increase of postoperative morbidity after liver transplantation only. The simultaneously transplanted kidney grafts are sacrificed.
Methods/Materials: Ten recipients of SLK in European MELD era were prospectively observed in a single center. Graft and patient survival according to Kaplan-Meier analysis and the preoperative risk factors, such as high MELD or intensive therapy (catecholamines, ventilator support) are presented.
Results: Four past SLK patients (MELD 33, 37, 36, 40) died of septic complications, one patient due to left ventricular failure (MELD 36). Another patient survived, but the transplanted kidney was removed after primary non-function (MELD 40) due to high dose catecholamine therapy. In summary, 6 kidney grafts have been wasted by simultaneous kidney transplants. Only three recipients with low laboratory MELD Scores (22, 20, 19) and absent risk factors are alive with functioning kidney grafts (SLK). One recipient's death was caused by tumour of unknown origin (MELD 25) with functioning grafts (SLK).

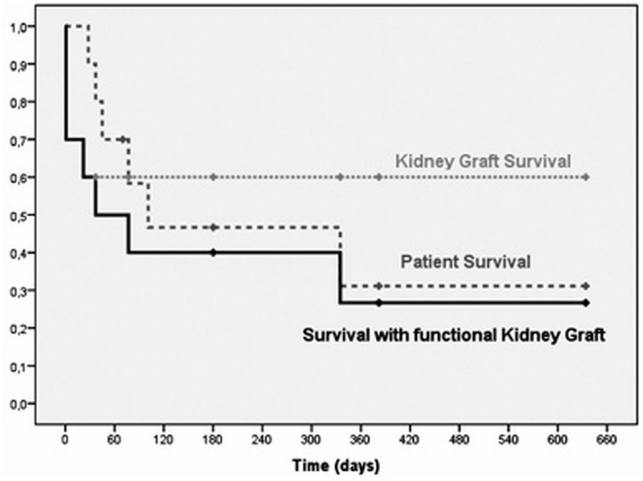

Figure 1. Outcome after simultaneous liver kidney transplantation (SLK); n=10.

Data pre SLK and outcome

Patient	MELD	Ventilator support	ICU	Catecholamines	Dialysis (days)	Kidney graft failure	Death
1	33	no	no	no	70	no	yes
2	22	no	no	no	360	no	no
3	25	no	no	no	150	no	yes
4	20	no	no	no	1000	no	no
5	37	no	no	no	90	yes	yes
6	19	no	no	no	0	no	no
7	36	no	yes	yes	75	yes	yes
8	30	no	no	no	75	yes	yes
9	40	no	yes	yes	60	no	yes
10	40	yes	yes	yes	30	yes	no

Conclusion: Even if high MELD patients survive liver transplantation, the unfavourable conditions in high MELD liver recipients damage simultaneously transplanted kidney grafts (SLK).
Only in low MELD recipients SLK appears to be worthwile. Therefore we suggest additional kidney transplantation in high MELD recipients with additional risk factors not to be performed until liver transplantation moved successful and a stable condition is attained.

P-29 AN EXPERIENCE IN THE HEALTH AUTHORITY IMPLEMENTATION OF A QUALITY ASSURANCE PROGRAM OF THE DONATION PROCESS

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Introduction: In 2005, the European Council strongly encouraged the implementation of Quality Assurance Programs (QAP) of the donation process in member states. The Catalan Department of Health, through the OCATT, chose for Catalonia (Northeastern autonomous region of Spain, 7.4 M inhabitants) the well known QAP from the National Transplant Organization (ONT), which has been used all over Spain since 1999 and currently with more than 100 participating hospitals.
The Catalan Department of Health authorizes organ extracting hospitals, with previous agreement from the OCATT, and also purchases health services through contracts with different health services providers -authorized organ extracting hospitals amongst them.
Methods: A few authorized hospitals had joined ONT's QAP spontaneously in the early 2000s, but no statement of association with ONT's QAP as the official OCATT program had been made till 2005. Later, in 2006, the Catalan Department of Health, following the OCATT's advice, decided to include compulsory participation in the official QAP in authorizing organ extracting centres. Economic conditions were also included in the health services contracts in order to improve QAP participation.
Results: Between 2001-2004 there was an average of 4 participating hospitals (out of 20) each year. 5 participated in 2005 and after the 2006 proactive measures participation increased to 11 in 2006, 13 in 2007 and 15 in 2008.
Conclusions: Scientific and authoritative directives, even coming from the highest level, are not always enough. The involvement of authorized health centre management staff can help the hospital transplant coordinator to achieve time and/or human resources to fulfil all the requirements of his/her demanding job.

P-30 DONOR ACTION PROGRAM IN THE EMILIA-ROMAGNA REGION (ERR)

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Objectives: Donor Action (DA) is an international program utilized to optimize donation practices. In July 1998 DA was adopted in ERR main Intensive Care Units (ICUs), 6 belonging to hospitals with neurosurgical departments.
Methods: The aim of this paper is to analyze the potential donor's identification in ERR (about 4 million inhabitants), with the chart revision of the patients dying in the main ICUs (196 beds) through the regional computer network, whose data are analyzed by CRT-ER.
Results: The results (Table 1) showed that total deaths rised from the beginning to the end of the study, in spite of a decrease in the percentage of deaths with severe brain damages (GCS=3) on total deaths (43.9% vs 23.9%) and a significant increasing brain death assessments (30.2% vs 66.6%). In the last years is reported an increase of family refusals.

Table 1. D.A. results

	1998 (2nd sem)	1999/2000	2001/2002	2003/2004	2005/2006	2007	2008
ICUs Total Deaths	649	1227/1179	1369/1438	1530/1442	1481/1418	1417	1513
Severe Brain Damage (SBD)	285	510/484	486/336	416/398	362/321	349	362
SBD/Total Deaths (%)	43.9	41.1/41.4	35.5/23.4	27.2/27.6	24.4/22.6	24.6	23.9
Brain Death Assessments	86	179/243	252/218	231/214	229/207	182	213
Organ Donors	55	98/116	136/134	137/120	145/118	108	128
Refusals	26	51/86	82/46	65/65	59/61	55	71
Refusals (%)	30.6	30.4/38.4	34.7/23.5	28.1/30.4	25.8/29.5	30.2	33.3

Through the years organ donation improved from 24.1 to 32.1 per million population (p.m.p.) and, in consequence, also organ transplantation rised (Table 2).

Table 2. Activity results

	1998/1999	2000/2001	2002/2003	2004/2005	2006	2007	2008
Organs donor p.m.p.	24.1/25.5	29.9/34.5	33.8/34.7	30.1/36.4	29.6	27.1	32.1
Kidney transplantations	139/152	157/169	151/167	143/191	131	135	160
Heart transplantations	24/33	25/35	41/33	43/42	28	33	35
Liver transplantations	76/95	95/115	114/115	106/156	137	134	141

Conclusions: These results confirm that DA program is an efficient quality control program and helped the ERR system to improve potential donor's identification.

P-31 RECENT EXPERIENCE WITH ORGAN DONATION AFTER CARDIAC DEATH (DCD) IN ONE REGION OF AUSTRALIA

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Introduction: Prior to 2004 there were 1-2 DCD donors per annum in our region. Renewed stakeholder and community interest in 2004 stimulated jurisdictional policy development and implementation - www.health.nsw.gov.au/policies/gl/2007/GL2007_012.html. Here we describe our resulting recent experience with DCD organ donation.
Methods: LifeGift records of all intended/actual DCD donors 1/2004-12/2008 were reviewed. An intended DCD donor is where death is not declared <60 minutes post treatment withdrawal precluding organ donation. Statistics were by SISA.

Results: There were 13 intended and 33 actual DCD donors. All but one donor were Maastricht category 3. The number of actual DCD donors versus donors declared brain dead per annum significantly increased from 2/63 (3%) in 2004 to 10/57 (17%) in 2008 [p=0.008]. Underlying cause of death for actual DCD donors was CVA 15, hypoxia 7, trauma 6, ICH 4, multiple organ failure [on ECMO] 1. Median actual donor age was 44 (9-74) years. Treatment withdrawal was in intensive care in 82% and operating room in 18%. Median time from treatment withdrawal to declaration of death was 16 (5-31) minutes. Median donor warm ischaemic time was 31 (6-62) minutes. A total of 71 organs were retrieved and transplanted (organ utilization rate 2.15) - 62 kidneys, 3 livers and 6 sets of lungs. Organs discarded included 2 kidneys (trauma, +ve virology), and 1 liver [non perfusion]. Multiorgan DCD donation increased from 0% in 2004 to 17% in 2008 [p=NS]. Tissue procured from DCD donors included 16 sets of corneas and 17 heart valves. For the intended DCD donors the mean time to declaration of death post treatment withdrawal was 350 (55-1480) minutes.
Conclusions: DCD organ donation has increased over the last 5 years predominantly form Maastricht category 3 donors. Organ discard rates are low for actual DCD donors. Multiorgan donation is now increasingly common.

P-32 A SINGLE CENTER EXPERIENCE USING EXTRACORPOREAL SUPPORT IN DONATION AFTER CARDIAC DEATH DONORS

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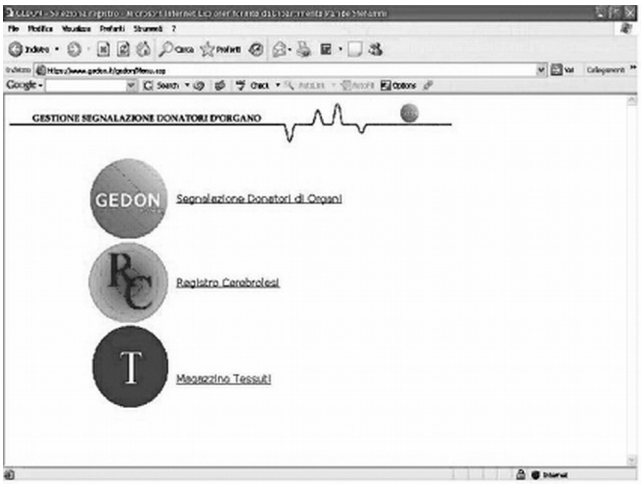
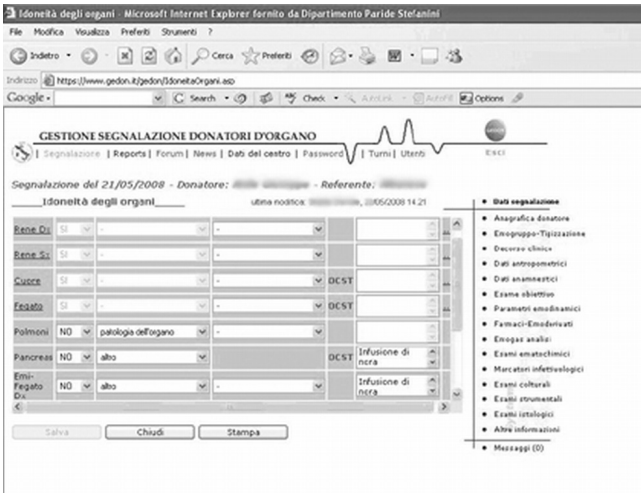
The purpose of this study was to determine if using extracorporeal support (ES) influences outcomes in donation after cardiac death (DCD) deceased donor (DD) kidney transplantation (KT) and simultaneous kidney-pancreas transplantation (SKPT).
Methods: From 4/1/03 to 06/30/08, we performed 70 KTs and 5 SKPTs from DCD donors. All 5 SKPTs and 8 (11%) KTs were recovered from DCD donors with ES initiated after death by cardiac arrest.
Results: With a mean follow-up of 21 months, patient (pt) and graft survival rates were 100% in the 5 SKPTs with no DGF. In the solitary DCD donor KTs, actual pt and kidney graft survival rates were 91% and 83%, respectively, and the death-censored kidney graft survival rate was 89%. The 8 DCD donor KTs with ES had 100% patient and kidney allograft survival rates. Comparison of KTs with (n=8) and without ES (n=62) showed that the former had slightly less DGF (25% ES vs 60% no ES, p=.13) and slightly better graft function at 1 year (mean serum creatinine level 1.4 mg/dl ES vs 2.0mg/dl no ES; mean GFR 58 ml/min ES vs 49 ml/min no ES, both p=.20). Comparison of the 70 DCD donor KTs with 414 concurrent donation after brain death (DBD) DD adult KTs revealed no differences in pt demographics, pt or graft survival rates, readmissions, reoperations, infections, or 1 yr kidney function. The incidences of DGF (56% DCD vs 19% DBD, p<.001) and acute rejection (27% DCD vs 14% DBD, p=.008) were higher in the DCD donor group.
Conclusion: The use of ES after cardiac arrest in DCD donors may improve KT outcomes and permit extrarenal organ recovery and transplantation with excellent short-term results in terms of graft survival and function.

P-33 TELEMEDICINE IN TRANSPLANTATION PROCESS

Francesco Gabbrielli[1], Renzo Pretagostini[1], Davide Stabile[1], Pamela Fiaschetti[1], Alessandra Oliveti[1], Daniela Peritore[1], Benedetta D'Ercole[2]. *[1]Surgery "Stefanini" Dept. OCST Coord. Transp. Centre, Policlinico of Rome Umberto I, Rome, Italy; [2]R&D, Cooperative "La Traccia", Matera, Italy*

The present work aims to show the obtained results on innovative web based synchronous data and images sharing systems and to analyse the possibilities to develop new donation and transplantation dedicated Telemedicine systems in Centre-South Transplant Organization (OCST) area including nine italian Regions.
Methods/Materials: From 2006 to 2008 in OCST the donation processes were performed always using GEDON ICT system for data synchronous sharing between Intensive Care Units (ICUs), Regional Transplant Coordinators (CRTs), Transplantation Centres (CTs) and OCST Centre (CIR-OCST), with the contribution of the InterUniversity Consortium for Organs Transplantation. All the personnel working in ICU on patients with cerebral lesions and organs and tissues donors in OCST can digit or insert new data or images and all they can view them in real time. The CIR-OCST and CRT decide how to manage the information flows from ICUs towards the interested CTs following the national and regional allocation protocols, also for donor risk and organ suitability evaluation. The GEDON donor-history was projected at first to exchange information guaranteeing data traceability with 250 different items and it was designed





in 20 different sections. All the information are treated by Communitarian and Italian laws on privacy.
Results: Information was inserted in GEDON for all the 2153 signalled cadaver donors in OCST to manage 847 allocation procedures and 2585 retrieved organs as well as 2535 successfully transplanted organs. The number of donation processes blocked cause of network organizational or technical problems was limited to 88 cases.
Conclusion: The GEDON ICT system in OCST demonstrated its utility to guarantee the data traceability, to support risk management and allocation procedures as real time operative tool. The improvement of ICT technologies can give us a new possibility to make another advance in donation and transplantation management by remote control developing new dedicated Telemedicine systems.

P-34 ANALYSIS OF PROCUREMENT AND UTILIZATION OF DECEASED CARDIAC DONORS IN MICHIGAN

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Purpose: Deceased cardiac donors (DCD) are an emerging source of organs, but data on their implementation remains lacking. We sought to identify trends in DCD donation in the state of Michigan, as well as factors associated with successful donation.
Methods: We reviewed Gift of Life Michigan records for all in-state deceased donors between 2005 and 2008. Donors were defined as either standard (brain death) or cardiac death. Kidney and graft utilization was measured by transplantation into recipients. Utilization rates were studied with regard to year, donor hospital volume, and time between donor referral, death and cross-clamp.
Results: 1308 donor referrals were made during the study period, of which 291 were for DCD donors. Progression to transplantation was more common for standard (67%) than DCD (50%) kidneys ($p < 0.001$), as well as for liv-

ers (64% vs. 14%, $p < 0.001$). Standard donor referrals and discard rates remained static over the study period, while DCD referrals and rate of utilization of DCD kidneys increased (Figure 1). DCD liver donation and success rates also increased over time. Hospital total donor volume, but not DCD volume or hospital size, was associated with lower discard rates for DCD kidneys (Figure 2). Time between donor referral and death was greater for DCD than standard donors (3.35 vs. 1.49 days, $p < 0.001$). Time intervals between referral, death, and crossclamp were comparable across hospitals, and were not associated with rate of DCD kidney discard.

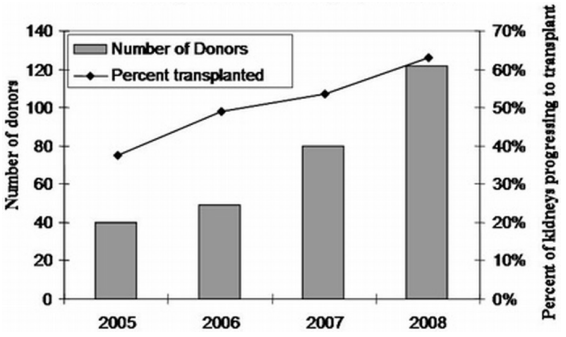

Figure 1. Increase in supply and transplantation of DCD kidney donors in Michigan, 2005–2008.

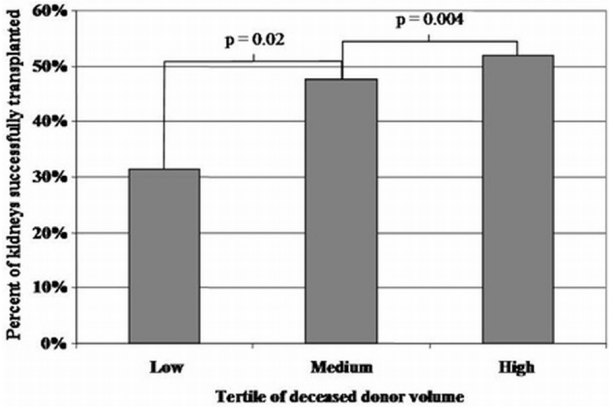

Figure 2. Progression to transplantation in DCD kidneys is associated with hospital total donor volume.

Conclusions: DCD donation increased over the study period without negatively impacting standard donation. Utilization of DCD kidneys also improved over time, with discard rates lowest among hospitals with the highest donor volume. Deceased cardiac donation augments organ supply, and can be effectively implemented even in hospitals with little DCD experience.

P-35 HEPATOCELLLULAR CARCINOMA ON CIRRHOSIS: LIVER RESECTION, LIVER TRANSPLANTATION OR BOTH SURGICAL TREATMENTS? AN INTENTION TO TREAT ANALYSIS

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Background: The management of patients with cirrhosis and early hepatocellular carcinoma (HCC) is controversial especially due to low availability of cadaveric liver donors.
Methods: From January 1996 to November 2008, 360 patients with transplantable HCC according to Milan criteria were treated by liver resection (LR)(n = 128) or liver transplantation (LT) (n = 232 of 426 listed for LT) at our institution.
Results: Among 128 patients eligible for transplantation who underwent LR, 51 (40%) developed HCC recurrence and 38/51 (74%) of these patients presented HCC recurrence into Milan criteria. Only 18 of the 51 patients underwent LT as salvage procedure, with a transplantation rate of 35% of patients with HCC recurrence. According to intention-to-treat analysis of transplantable HCC patients who underwent LR (n = 128), compared to all those listed for transplantation (n =426), 5-year overall survival was 71% in the LR group versus 62% in patients listed for LT, respectively (p =NS); 5-year disease-free survival was 41% in the LR group versus 54% in patients listed for LT (p = NS). The median time from resection to transplantation was 2.1 years (0.8–5.5) in the subgroup of 18 patients with HCC recurrence after LR.
Five-year overall (62% vs. 73%, p = NS) and disease-free (48% vs. 71%, p = NS) survival rates and the mean time on the waiting list was similar (5.5±6.4 vs. 8.2±6.5 months) for salvage LT and primary LT for HCC, respectively.
Conclusion: For patients with early HCC and well-compensated cirrhosis selectively to perform resection as first-line therapy followed by salvage transplantation is the best strategy that spares the use of liver grafts, avoids potential problems with prolonged waiting times, and provides the patient with rapid access to an effective therapy.

P-36 NON TRANSPLANTABLE LIVER OBTAINMET FOR CELL ISOLATION FOR THERAPEUTIC USE

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Liver transplant currently has been shown to be the best option in treating patients with terminal liver illnesses. Unfortunately, there are not enough livers to treat patients on waiting lists which in turn increase the mortality in these patients. Therefore, it is necessary to develop new treatments for these types of patients. The development and use of new clinical cell therapy could be a solution to this kind of problem as cell therapy repairs and improves the biological function of the damaged organ. The treatment of liver illnesses through cell transplant has been studied in different animal models. These results and the first use in humans could offer an option to complement liver transplant. Thus, one donated organ that is rejected from transplant could be used to obtain optimal cells in order to treat patients.
Material and methods: A network was created with defined rules and criteria for organ selection in order to obtain and use livers rejected for transplant. In order to this, was necessary to manage and coordinate all collaborative centers and establish a good logistic and communication process. Two steps were defined in order to link hospitals to the network and to look for non transplantable livers for cell isolation to obtain and send
Results: The network started in 2003 in Europe, It has linked hospitals in Spain, Italy and Portugal. 99 livers have been obtained and 250,29 billons of cell have been isolated. With these cells, it has been possible to start two clinical trials called Safety and Efficacy of Liver Cell Application SELICA I – II

P-37 A MODIFICATION TO HEART TRANSPLANT ALLOCATION TO SAVE MORE CRITICAL PATIENTS: TIME FOR ALLOCATION SYSTEM CHANGE?

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Purpose: Given donors shortage, the heart allocation system ought to be examined to determine whether its distribution is equitable and efficient to save critical patients.
Methods: A national program for heart transplant in cardiac emergency has been activated in Italy since 2005. We have investigated a new allocation policy among the six transplant centres belonging to our organization. This policy prioritizes candidates with the greatest clinical urgency (status 1 or 2A according to the UNOS) not included in very strict clinical criteria defined for National Emergency (NE), allocating non local donors primarily to them, without imbalancing the overall offers to the centres. We present a preliminar analysis comparing this policy with the previous one in which donor hearts were allocated primarily according to a rotation system, clinical urgency and waiting time.
Results: Table 1 shows the distribution of heart transplant recipients according to the previous allocation rules as compared to that under the modified rules. During the observation periods 33/92 heart transplant were performed in urgency status in 2007 (36%), whereas 48/112 (43%) in 2008. The number of priority requests rose by 52%. Median waiting time after priority request decreased from 22 to 12.5 days (-43.2%). The number of patients in the waiting list was not different in the two observation periods. As concerning mortality while on waiting list, 40 patients out of 459 (8.7%) died in 2007 while 7.1% (32/453) died in the same period in 2008.
Conclusion: Urgent candidates high mortality on the waiting list justifies their prioritization. The modified heart allocation system decreased the waiting time

Table 1. Comparison between two observation periods

	2007	2008
No. requests (+NE)	40 (+5)	61 (+11)
% Candidates	8.7	13.5
Urgent HTX	33	48
Median time urgency request to transplant, days	22	12.5
All HTX	92	112
% Urgent HTX	36	43
Death urgent candidates on the waiting list (%)	5 (11%)	10 (13.8%)
Death non-urgent candidates on the waiting list (%)	35 (7.6%)	22 (4.9%)
Average candidates no.	459	453
Deaths on the waiting list (%)	40 (8.7%)	32 (7.1%)
Overall post transplant mortality (%)	6 (6.5%)	7 (6.2%)

for urgent candidates without increasing the overall mortality on the waiting list. Post transplant mortality was the same in the two periods.

P-38 TRAINING OF HEALTH CARE STUDENTS AND PROFESSIONALS: A PIVOTAL ELEMENT IN THE PROCESS OF OPTIMAL ORGAN DONATION AWARENESS AND PROFESSIONALIZATION

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Introduction: Successes in organ donation and transplantation programs are directly evidence-based education. Transplant Procurement Management (TPM) is an international educational project on organ donation and transplantation.
Purpose: The purpose is to evaluate the TPM educational project. The data of 17 years of experience, strategies and methods were compared.
Methods: A retrospective descriptive analysis was done of all the educational activities developed between 1991 and 2008 and 7 crucial points were identified.
Results: In 1991 (1), TPM started under the auspices of University of Barcelona (UB) and the National Spanish Transplant Organization (ONT) (national training, face to face). In 1994 (2), TPM became international (international advanced training and country-based) (Italy 1997, France 2006) (3). TPM implemented short (1-3 days) introductory courses worldwide. In 2000 (4) the e-learning platform program was launched to facilitate the education of professionals. In 2006 (5), the courses were enlarged on the pre-graduate health science faculties (PIERDUB). In 2005 (6), an international master degree was created at UB under the Life-Long Learning Institute (IL3). In 2007, the European funded ETPOD project was started (7). Currently, TPM offers face-to-face, e-learning and blended international courses. Until the end of 2008 TPM has trained 6597 professionals in 91 countries (5 continents).
Summary: TPM has impacted positively the different essential levels in the process of organ donation and transplantation, with a life-long follow-up and international network through the capacity of adapting to specific country needs as well as the continuous quality improvement thanks to the collaboration of expert teachers and consultants.

P-39 ORGAN DONATION IN MOSCOW

Marina Minina. *Organ Donation, Moscow Coordinating Centre for Organ Donation, Moscow, Russian Federation*

Introduction: Up to 2004 in Moscow the main source of organs for transplantation were non – heart beating donors. Most of the procurements were limited by kidneys only.
During the last four years donation and transplantation activities in Moscow have raised in times.
Material and methods: In 2007 the rate of donation in Moscow consisted

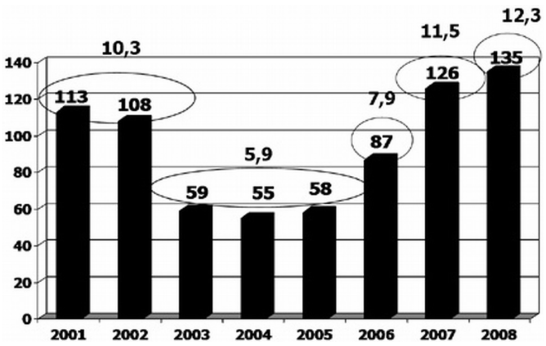

Figure 1. Effective donors: absolute number and pmp/y.

11,5 effective donors/pmp/y what is in 1,5 times higher than in 2006. In 2007 the number of effective donors with brain death exceeded the number of non – heart – beating donors (73 vs 53) with a total number of donors is 126.
The part of multiorgan donation among donors with brain death consisted 75%. The increase in number of donors with brain death was a great stimulus for extrarenal transplantation development. In 2007 in Moscow 54 cadaver livers were transplanted what is in 2 times higher than in 2006. From the end of 2005 in Moscow two programs on "pancreas + kidney" transplantation have started. By now we have 27 "pancreas + kidneys" complexes transplanted. In February 2007 for the first time in Russian Federation the split liver was procured from a cadaver donor and successfully transplanted to one child and one adult recipients.Then three more split liver transplantations were made and for now there are no objective barriers to continue such an important direction of our activity. Kidney transplantation activity per year consists in average 250–260 transplants. Unfortunately in spite of increasing of donors with brain death heart transplantation stays on the level of 20 operations per year.
Conclusion: In order to achieve a better results in organ donation we must concentrate our efforts on improvement of donor's hospital activity on the day-by-day basis using principles of transplant coordination.

P-40 INFLUENCE OF CERTAIN DONOR FACTORS ON THE FUNCTION OF TRANSPLANTED LIVER

Marina Minina. *Organ Donation, Moscow Coordinating Centre for Organ Donation, Moscow, Russian Federation*

Introduction: In the circumstances of organ shortage and extended donor criteria important significance acquire the quality of donor organs.
Material and methods: We have analyzed 50 donor charts from 1 January 2007 until 31 December 2007. All donors undergone multiorgan procurement. By age all donors were divided on four groups: I group 18 – 35 (n= 16), II group 36 – 45 (n= 16), III group 46 – 55 (n= 12), IV group 56 – 65 (n= 6). We analyzed all donors by following factors which: clinical factors included duration of artificial ventilation, arterial hypertension or diabetes existence, dosage of vasopressors, mean arterial pressure; laboratory factors included serum sodium, SGPT and SGOT levels, serum bilirubin; macroscopic factors included color of liver, liver edge, liver swelling, atherosclerosis existence. All factors were scored from 0 to 4 and summarized for each group.
Results: There is a statistically significant difference between sum of scores in I and III groups (p = 0,008) and in I and IV groups (p = 0, 04) for clinical factors. The difference is explained by higher dosage of vasopressors in donors of III and IV groups. There is no statistically significant difference between all groups in the sum of scores for laboratory factors (p = 0, 28). The main contribution to the sum of scores for all groups of donors for laboratory factors belongs to the serum sodium. In groups I, II and III the serum sodium consised half of the sum of scores. We have find statistically significant differences between all groups of donors in macroscopic factors (p= 0, 05) by color of liver parenchyma, atherosclerosis existence, swelling of liver parenchyma.
Conclusion: Donor factors influencing our value of liver condition are dosage of vasopressors, serum sodium and macroscopic appearance of liver.

P-41 RENAL FUNCTION OUTCOMES IN LIVING KIDNEY DONORS

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Live kidney donation still remains the best option for renal function replacement. Although considered safe, donor outcomes are continuously investigated.
Aim: To examine the impact of kidney donation on renal function, 40 live kidney donors (26 female, 14 male, mean age 53.5years, range 33-71, SD ±9,71) were followed up over a mean period of 89,9 month (12-312, SD: ±80,00). Renal function, and proteinuria were accessed before donation and at the end of follow up.
Results: Mean serum creatinine increased from 0,85mg/dL (0,58-1,13 SD ±0,15) before donation, to 1,16mg/dL (0,81-1,61, SD ±0,19) at the end of follow up ($p<0,0001$, 95% CI 0,25-0,38). Mean GFR, measured with $CR^{51}EDTA$ clearance, decreased from 100,69ml/min/1,73mm^2 (73-168 SD ±22,21) before donation to 60,03 (28-103 SD ±16,43) at the end of follow up ($p<0,0001$ 95% CI 32,32 – 43,32). After the first year post donation the rate of GFRdecline ranged from 0,05 to 5,75ml/min/1,73mm^2 per month. The presence of a GFR <60ml/min/1,73mm^2 at the end of follow up was significantly associated with age (p=0,008), serum creatinine (p=0,003) and GFR (p=0,0001) at donation. Newly diagnosed hypertension affected 34% of donors. 18 donors ended up with a GFR between 60 and 30ml/min/1,73mm^2 and two with a GFR of 30 and lower. The later were two out of three, aged 75 or older at the end of follow up. Proteinuria in a 24h urine collection at the end of follow up ranged from 30 to 171mg/24 (mean: 104,47 SD ±39,9). It correlated with (p: 0,005) proteinuria

at donation (22–185 mg/24h, mean: 103 SD ±51,4) but was not significantly increased.
Conclusion: Kidney donation does not seriously compromise donor renal function. A 40% drop of GFR is expected. Older donors with an initial GFR of under 90ml/min/1,73mm^2 may anticipate a decline to a GFR of less then 60ml/min/1,73mm^2

P-42 INTERNATIONAL ORGAN EXCHANGE OR HOW CAN WE INCREASE THE NUMBER OF HEART TRANSPLANTATIONS IN SWITZERLAND

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Swisstransplant, Bern, Switzerland

Introduction: Organ shortening is an important issue in general an especially in heart transplantations (HTX) in Switzerland. International exchange within the European organ exchange organisations (EOEO) is of increasing interest. The aim of the study is to analyse the frequency of foreign heart offers to Swisstransplant and the involved centers and the reasons for acceptance or refusal.
Patients and methods: A retrospective study was conducted between 01/04 and 18/11/2008 to analyse all foreign heart offers. Reaction time (Swisstransplant and transplant center), quality of medical information and decision process were evaluated. The data were collected from the Swisstransplant database and from the EOEO organ offer form sheets.
Results were analyzed in relation to medical decisions and logistic aspects.
Results: Overall 289 foreign donor hearts have been offered. Average age of the donor was 24.4 years. Nearly 60% of the donors were under the age of 30 years. 8 hearts have been accepted and were successfully transplanted, corresponding to 5.8% of the total number of HTX in this time period in Switzerland. In 12 foreign offers decision time was too long and the organs were no longer available at the time of decision, which would have increased the number of HTX of 14.5%. 90% of the accepted organs were within a range of 1000km distance between donor and transplant centre. Logistic refusal was found in 44 offers mainly due to long distances (>1000km).
Conclusion: Fast decision making would allow to substantially increase the number of heart transplants in Switzerland. The introduction of new technologies, such as perfusion machines, must be considered in the close future. Transports over long distances would be tolerable and high quality organs could be obtained.

P-43 EDUCATIONAL SYSTEM FOR TRANSPLANT COORDINATORS IN POLAND. POSTGRADUATE STUDIES IN WARSAW MEDICAL UNIVERSITY; 2 YEARS OF EXPERIENCE

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Local coordinators in donor hospitals play key role in donation. These coordinators in Poland are only few while there are about 400 hospitals with ICU's. This will change, when there will be in every hospital coordinator appointed.
Coordinators must be professionals in organization, legal issues, donor identification and evaluation, brain death diagnosis, family approach, donor care, allocation and distribution, quality and safety standards. These skills coordinators acquire during Transplant Coordinators Postgraduate Studies in Warsaw Medical University. The project, initiated by Polish Union for Transplantation Medicine began in 2007. Seminars and exercises (99 hours, 6 weekends) are run by experienced experts. Studies end with an examination and diploma. The cost per person is 1000 Euro, the trainee should pay 25 Euro, the remaining amount come from the Ministry of Health. The main criterion of acceptance for candidate is employment in key department for donation. The aim of studies is to educate coordinator for each hospital in the country. Four editions were completed; 123 graduates, 71 persons (60%) employed in strategical departments of 48 hospitals.
Graduates' activity – preliminary results: Activity in donor detection was compared in period before the course (2005-2006) and in period during the course (2007-2008) in hospitals where graduates are employed and where not. In years 2007-2008 in Poland averall transplant activity droped to 79% of the 2005-2006. This ratio for hospitals with graduates was 82% and in hospitals without -76%.
Of the 48 hospitals that employ the graduates: improvement in donation was observed in 14, in 12 both periods there were no donations, in 11 number of donations was much lower (>20%), in 5 numbers of donors were the same, in 6 was lower but in line with the national trend.

P-44 A PRIORITIZATION MODEL FOR LIVER TRANSPLANTATION BASED ON A DUAL WAITING LIST: A PROSPECTIVE CONTROLLED STUDY

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Purpose: The aim of this prospective-controlled study was to validate the impact of an objective and reproducible prioritization model for liver transplantation (LT), on 2-year patient intention-to-treat survival.
Materials and methods: A prioritization model based on 2 sub-lists: non hepatocellular carcinoma (N-HCC) cirrhotic patients in the waiting list (WL) classified according to MELD score (MELD WL) and cirrhotic patients with HCC in WL according to a targetted score without extra-points based on response to downstaging treatment (stable/progression=6;untreatable=5; partial response=4; new tumor recurrence> 6mo last therapy awaiting therapy=3; new tumor awaiting therapy=2;complete tumor necrosis=1), tumor stage and time from diagnosis (N-MELD WL). We compared the prospective cohort of adult patients enlisted for LT from 01/07/2006-31/12/2008 (study group) versus an historical cohort of patients enlisted from 01/01/2003 to 31/12/2005 (control group) listed in a single WL according to time-dependent rules.
Results: Three-hundred thirty one patients (mean age 55 years, F 27%) were enrolled in the study group, whereas 327 (mean age 56 years, F 37%) in the control group. In the study and in the control group, the N-HCC MELD at listing was 14 vs 13 (p<.01) respectively and at transplant was 20 vs 15 respectively (p<.01).

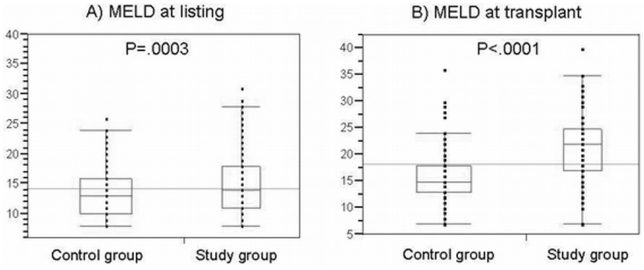

Figure 1. MELD score in N-HCC patients at listing (A) and at transplantation (B) in study vs control groups.

The percentage of listed (35% vs 26%, p<.01) and transplanted (49% vs 32%, p<.01) HCC patients was significantly higher in the study than in the control group. The 2-year intention-to-treat survival rates were similar in the study and in the control group, overall (80% vs 82%, p=ns), and again similar both in N-HCC (82% vs 83%, p=ns) and in HCC patients (75% vs 80%, p=ns).

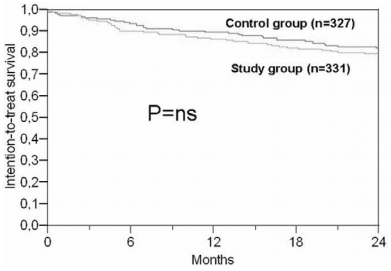

Figure 2. Intention-to-treat survival Kaplan-Meier curves (study vs control group).

Conclusions: We prospectively applied a LT prioritization model, based on objective criteria, favouring patients most in need, without impairing overall LT outcome.

P-45 TPM ON-LINE COURSES: THE E-LEARNING PLATFORM ON PROFESSIONAL TRAINING AND EDUCATION FOR HEALTH PROFESSIONALS TAKING PART IN THE ORGAN DONATION PROCESS

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Introduction: Insufficient education on organ doantion causes system failures such as detection of potential donors being one of the main causes of the gap between organ demand and offer. Thorough knowledge and advanced training are required to modify and professionalize the pro-active attitude to make donor detection possible.
Aim: TPM created an e-learning training platform for professionals involved in the organ donor process. It is aimed to bring education opportunities closer to the health care professional.
Methods: The e-learning method is highly interactive. Time, geographical and professional barriers are overcome, by facilitating individualized and interactive contact between all members including the tutors. Each course develops a core structure based on written and audiovisual support that concentrates on learning by emphasising key concepts. Modules are created for better association of concepts. General and specific debates through a forum help participants to share their points of view and knowledge.
Results: 671 participants from 59 countries were supported throughout their learning process by a trained team of tutors. 7 different modules have been implemented until now, covering the whole organ and tissue donation process: 1. Donor Detection System, 2. Brain Death Diagnosis, 3. Donor Management – Organ Viability, 4. Family Approach, 5. Organ Retrieval Organization, 6. Preservation and Allocation Criteria, 7. Tissue Banking Course and 8. Train the trainers.
Summary: The evaluation of the program was highly positive and this has to be seen in a total training concept of professionals in organ donation. No matter if it is a refresh course, a first training session or a true professionalized training, the e-learning platform of TPM closes the gap in order to bring eduaction to the professional in the need of it.

P-46 CORTICOSTEROID TREATMENT OF DECEASED DONORS IN THE EUROPEAN SENIOR PROGRAM

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In recent studies we observed an initially pronounced immune response in patients of the European Senior Program (ESP). Beside an intensified early immunosuppression, donor treatment may be particularly beneficial when transplanting older grafts into older recipients. Treatment of deceased donors with steroids has been shown to be effective after liver transplantation. We analyzed the impact of steroid treatment on age-adapted immune responses after human kidney transplantation.
In a prospective randomized trial (06/06 to 07/08) donors of the ESP (n=21) and regularly allocated transplants (ETKAS/n=43) were treated with steroids before recovery (250 mg initial, afterwards 100 mg/h). Early immune response was evaluated at day (d)0 before and d7 after transplantation by flow cytometry (peripheral blood) and ELISPOT analysis. Untreated recipients (ESP/n=14, ETKAS/n=91) served as controls.
Donor and recipient age as well as HLA mismatch were significantly higher in the ESP group ($<$0.001 vs. ETKAS), while cold ischemic time was shorter ($p<0.01$). At d7 percentages of activated CD4+ T cells, DCs, and B cells were comparable in all groups. In contrast, ESP patients showed significantly elevated frequencies of activated CD8+HLA-DR+ cells, which were not reduced by steroid pretreatment (ESP vs. ETKAS, control: 6.7$\pm$1.6 vs. 3.3$\pm$0.4%, steroids: 5.8$\pm$0.9 vs. 3.1$\pm$0.4%; $p<0.01$). While steroids reduced CD56+CD16+ NK cell counts in ETKAS patients, treatment increased NK cell frequencies in ESP patients (control vs. steroids, ETKAS: 11.8$\pm$1.4 vs. 6.6$\pm$1.3%, $p<0.05$; ESP: 9.0$\pm$1.8 vs. 12.5$\pm$2.9%, $p<0.05$). Moreover, donor treatment significantly reduced T-cell alloreactivity in ETKAS recipients (IFN-γ+ cells/2.5$\times 10^5$ splenocytes, control vs. steroids, 173$\pm$41 vs. 42$\pm$19, p=0.02), but had no impact on alloreactivity in ESP patients (76$\pm$42 vs. 81$\pm$38, ns).
Donor treatment with steroids significantly reduces T cell alloreactivity and numbers of NK cells in ETKAS patients whereas ESP recipients do not seem to benefit from donor treatment.

P-48 EUROPEAN TRAINING PROGRAM ON ORGAN DONATIO (ETPOD): A NEW COLLABORATIVE EUROPEAN FORMATIVE STRATEGY ON ORGAN DONATION (PROJECT FUNDED BY DG SANCO (2005205)

Martí Manyalich, Gloria Páez, Xavier Guasch, Ricard Valero, Maria del Río. *Transplant Procurement Management (IL3), IL3 - Universitat de Barcelona, Barcelona, Spain*

Introduction: Imbalance in organ demand versus offer together with dramatic differences on deceased organ donor rates between European countries, are one of the biggest future challenges.
Methodology: Two factors were identified to optimize the organ donation process: 1. presence of an organ donation key person at hospital level, 2. quality control program evaluating and improving the donation process. Therefore, a consortium of 20 partners in 17 countries designed the ETPOD project.
Aims: Three training levels were developed to optimize this process
1) *Essentials in Organ Donation*: teaching basic knowledge for ICU and Emergency Room healthcare professionals to promote active donor detection
2) *Professional Training on Organ Donation*: training hospital level professionals (new transplant donor coordinators) efectuating potential organ donors
3) *Organ Donation Quality Managers Training*: training managers active at organizational level in countries or areas with high activity on organ procurement and transplantation. Designed to provide participants with a theoretical, technical and practical framework on the organ donation process management
Results: During 2007, 4 ETPOD working groups defined training needs and designed different courses. During 15 months (01/01/2008 – 31/03/2009), about 3000 professionals from 25 target areas (TA's) in 16 European Union Countries and Turkey, were trained in 1 of 3 levels. The participants' knowledge was evaluated after each course. At the same time they evaluated the courses aspects: contents, activities, faculty and organization. Promising results were reached in both areas.
Conclusion: An important effort was made to create and validate a formative strategy that was applied to a significant number of participants in a heterogeneous group of TA's. The pedagogical goals have been achieved. A second objective, to measure the donation activity impact in the TA's, is ongoing.

P-49 AN AUDIT OF SUDDEN DEATHS IN ACCIDENT AND EMERGENCY UNIT AS AN ON-GOING REVIEW OF POTENTIAL NHBD DONORS

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Aim: Since 1998 the Newcastle renal transplant programme have actively recruited Maastricht category II donors principally from Newcastle Accident and Emergency departments, which initially were the Royal Victoria Infirmary and later Newcastle General hospital. This has provided about 10 donors per year. However over the last 18 months this number seems to have declined for no real reason. We were aware of publications from the Scottish cardiologists on the decline of acute coronary syndrome admissions, which was attributed to the smoking ban in public places and wondered if this could have any bearing on the declining number of donors.
Method: The admission notes were reviewed for all sudden deaths that were brought to the Newcastle General Hospital Accident and Emergency unit. These numbers were correlated with national death rates from IHD.
Results: Sudden Deaths locally follow the seasonal trend seen in death from IHD.

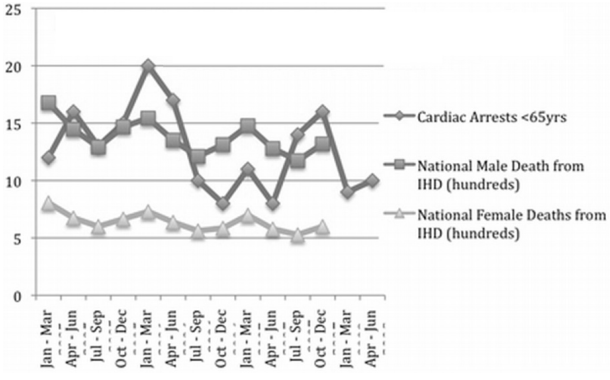

Figure 1. National deaths from IHD compared to local sudden deaths.

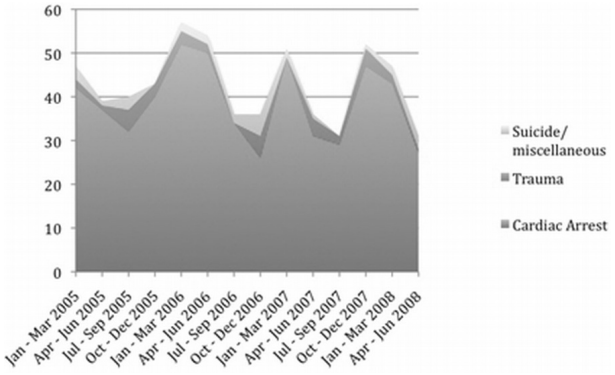

Figure 2. All age sudden death.

Conclusion: It is apparent that sudden deaths are a seasonal phenomenon, as are deaths from IHD. To claim that rates of ACS have fallen 10 months after a smoking ban may be somewhat premature. Particularly as the national figures suggest that there have been a decline in sudden deaths for some time; which predates the smoking ban. No information on smoking history was available from the sudden deaths; therefore the cardiologists claim that the non-smoking group is the main beneficiary remains to be determined.

P-50 TWO YEARS OF MELD ALLOCATION SYSTEM IN SÃO PAULO – BRAZIL

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Background and methods: MELD score has been implemented as the new liver organ allocation system for Liver Transplantation (LT) since July 2006 in Brazil. Currently, in São Paulo State, more than 2400 patients are waiting for a liver transplant and the aim of this study was to evaluate the impact of MELD score in liver transplantation waiting list. Meld score allocation was initiated in 17th July 2006 and, in this study we compared two periods: two year before (07/17/2004 to 07/16/2006) and two year after (07/17/2006 to 07/16/2008) this new allocation policy according to list admission and mortality, transplantation, transplantation with living donor liver transplants (LDLT) and the enhancement of the waiting list.
Results: The results are presented in table

Results

	Pre-MELD	Post-MELD
Living Donor LT	274	195
List Admission	3674	2239
Mortality in List	17,50%	20,11%
List enhancement	27,44%	-19,57%
6-month patient survival rate	74,66%	71,34%
1-year patient survival rate	72,41%	68,12%

P-51 A REVIEW OF RENAL TRANSPLANT LIVING DONORS ATTENDING INKOSI ALBERT LUTHULI CENTRAL HOSPITAL, DURBAN, SOUTH AFRICA

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The shortage of cadaver organs has increased the reliance on living donor related transplants. The incidence of end-stage renal disease is increasing worldwide. The wellbeing of the living kidney donor is essential for a successful living donor transplant program.
Methods: This is a retrospective study of kidney donors attending the donor clinic at Inkosi Albert Luthuli Central Hospital. Medical records of 50 donors were examined over a three year period. Mean arterial pressures, creatinine clearances and 24 hr urinary protein excretion collections were recorded at the first visit and at the last visit. The patients' ages and racial demographics were also recorded. Chi-square test using Instat 3 statistical program (Graphpad^R, San Diego, CA, USA) was used to analyse results.
Results: The average age of the renal donor was 44.92 years (±1.32 yrs). Forty- one of the donors were female and nine were male. The donors were divided in terms of racial demographics as follows: forty Indians, six Whites, two Blacks, and two Coloureds. The average mean arterial pressure at the 1st visit was 91.3 mm Hg and was 91.2 mm Hg at the last visit. The average creatinine clearance at the 1st visit was 88.1 ml/min. The average creatinine clearance at the last visit was 87.4ml/min. No statistically significant difference was found between the average 24 hour urinary protein excretion at the 1st visit (0.16g/24hrs) and at the last visit (0.2g/24hrs) [p=0.16].
Conclusions: There was no significant decrease in creatinine clearances nor significant increase in 24 hr urinary protein excretion rates, and mean arterial pressures in the donors within the three year period. Renal organ donation is the most common in females, and the Indians race groups.

P-52 LONG TERM OUTCOME OF LIVING KIDNEY DONORS. RETROSPECTIVE ANALYSIS

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Introduction: Living kidney donation is widely and increasingly used in order to meet the need of kidney transplantation. We assess the impact of donor nephrectomy on renal function and development of hypertension and proteinuria with median follow-up of 8 years.
Methodology: We performed a retrospective analysis of 284 donors who were kidney donors between 1986 and 2007. We obtained the serum creatinine, BMI, proteinuria and blood pressure during the follow-up.
Results: At donation the mean age of examined donors was 42±12 (20-67) years. The donors were 167 female and 117 male. We found hypertension in 23 donors before donation and in 50 donors (26%) after transplantation but the age – adjusted prevalence among donors was not higher than in general population. Mean proteinuria in pre – transplantation was 0.14 g/day and 0.73 ± after donation. Mean creatinine clearance in pre – transplantation was at 114±29in male and 105 ± in female and respectively after transplantation at 90±25 and 82±27. Two donors developed an end stage renal disease and required dialysis. In the two cases was diagnosed a familial focal and segmental glomerular sclerosis The BMI was before donation at 25±4 in male and 27±5 in female and respectively at 26±4 and 29±6 after donation. Two donors died during the period of follow- up.
Conclusion: Kidney transplantation with living donors is a great option to promote kidney transplatation activity but we must be more cautiously on evaluation and the follow – up of the donors. After this study we decided to setup a registry for the follow-up of the living kidney donors.

P-53 ACTIVE SEARCH IN ORGAN DONATION: INCREASING RESULTS THROUGH EDUCATION PROGRAMS

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Brazil ranks second in terms of absolute number of transplantations and launches the most extensive public campaigns to encourage donations. The current progressive increase in the waiting list for an organ indicates the need for new recruiting measures to increase donation rate. The *active search* for organ donors has the aim to encourage the activities and actions towards recruiting organ donors, warranting the exams and procedures required to determine brain death, assistance to the family of potential organ donors, and following of organ removal and conservation. This work contain data collected from the Organ Recruiting Organization of Hospital of the State University of Campinas, which covers 124 cities. This study includes Celso Pierrô Maternity Hospital, Dr.Mario Gatti Campinas District Hospital and Dr Leandro Franceschini" Sumaré State Hospital. Low notification rates represent a great difficulty in transplantations using organs from deceased donors. The removal of organs from these donors is possible, when brain death is determined; this is characterized by the irreversible loss of brain and brainstem function. This study verified that during 2005 the doctors and nurses of these institutions issued only ten notifications. Of these ten notifications, ten potential donors were included in the Single List System and four resulted in donation. After the implantation of active searching in 2006, there was a significant increase in notifications and organ donations up to 2007. This leads to the conclusion that education is the main factor towards a change of attitude and behavior. When precise information is received there is a transformation in decision-making and actions. After the systematization of active search, together with a process of permanent education, and orientation regarding any questions arising during the donation procedure, there was an increase in the number of notifications issued and transplantations.

P-54 KNOWLEDGE AND ATTITUDES OF MOROCCAN MEDICAL STUDENTS TOWARDS ORGAN DONATION AND TRANSPLANTATION: A PILOT STUDY

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Background: Physicians' knowledge of and attitudes towards organ donation may be a key factor in organ procurement rates.
Aim: This pilot study assesses the knowledge, attitudes and beliefs of Medicine University students related to organ transplantation and organ donation.
Methods: 120 students of Medicine University, Marrakech, Morocco answered the same questionnaire comprised of multiple-choice before and after a training program on organ transplantation. We then analyzed the changes from before to after the educational program in order to assess the program's effectiveness.
The subjects addressed in the document were socio-cultural status, willingness to donate organs, ability to identify major organs and tissues currently being transplanted, and knowledge of the definition of brain-death.
Results: Of the 120 students, 77.5% were women, they were 22.8±0.8 years old. The correct listing of transplantable organs was chosen by 45% of the respondents before training, and by 95% after training ($p<0.0001$). Concerning brain-death, 37.5% of the respondents identified the correct definition of this concept before training, and 97.4% did so after training ($p<0.001$).
Prior to the training program, 70% of the 120 respondents stated that they were willing to donate their organs after death, whereas after training 75% said they would do so ($p<0.87$). Before training, 67.3% of the respondents said they were absolutely opposed to living organ donation, and after the program was completed 23.7% were still hesitant about living organ donation.
Before training 30% believed that their religion is adverse to transplantation, and this rate fell significantly to 5% after the program was completed ($p<0.01$).
Conclusion: Moroccan Medical students possess limited knowledge about organ donation and transplantation. Early special training is essential in order to increase the number of donors and the rate of transplantation in Morocco.

P-55 WITHDRAWAL OF THERAPEUTIC EFFORTS CAN BE A CONDITIONING FACTOR FOR DECEASED ORGAN DONATION?

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Severe Brain Damage (SBD) is the main source of donors after brain death (DABD). In patients with bad neurological prognosis Withdrawal of Therapeutic Efforts (WTE) can impede the follow-up period required to develop brain death, then it is crutial to know the incidence of WTE to avoid lost potential donors.
Objective: To know if the WTE in SBD patients would result in a reduce number of DABD in comparison with cases without WTE.
Material: Retrospective and descriptive medical record review (MRR) between January and December 2007 of all deceased patients in SBD occurred in ICU, emergency, neurological/neurosurgical wards. Patients with absolute contraindications for donation where excluded.
Results: 760/1625 (47%) MRR where done of all deaths and it was found that 179 (11%) died as a consequence of SBD. 102 patients where excluded (57%) with a final sample population of 77 (43%) patients. WTE where applied in 44 cases (57%) and non-WTE in 33 cases (43%). No differences where found between groups in gender, age, GCS at time of hospital entry, duration of hospital stay, indication of mechanical ventilation and associated diseases (HBP, Diabetes or renal insufficiency). Factors associated with WTE where older age, associated diseases, severity of cerebral haemorrhage measured in the cerebral CT (Fisher IV) and GCS at time of hospital entry ($r^2=0.22$ p=0,051). 23 patients (30%) evolved to BD distributed in 11 (25%) in the WTE vs 12 (36%) in the no-WTE group (p=NS). The others 53 patients died after cardiac death.
Conclusions: 11% less of BD cases where found in the WTE group. In front of any bad neurological prognosis during hospital evolution of SBD patients, before the application of WTE the option of organ donation should be evaluated with the physician in charge.

P-56 ORGAN PROCUREMENT AND TRANSPLANT IN VIRAL RISK DONORS IN ITALY – GRAFT AND RECIPIENT SURVIVAL

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Introduction: To minimize the gap between organ supply and demand for transplantation, expanded criteria donors protocols have been implemented over the years. The "calculated risk" protocol has been in use nationwide.
Aim of the study: Aim of this study is to review organ procurement in Italy and related transplantations from 2003 to 2008, then to assess graft outcome and recipients survival among transplants carried out from 2003 to 2006.
Material and methods: "Calculated risk" donors have been divided into 5 categories: 1) HBsAg+, 2) HCV+, 3) HBsAg+ and HCV+, 4) HCV+ and HBcAb+, 5) HBcAb+.
All viral risk effective donors and all organs with related transplants from the 1st of January 2003 to the 31st of December 2008 have been reviewed. Afterwards organ and recipient survival data concerning transplantations which were carried out from the 1st of January 2003 to the 31st of December 2006 have been analyzed and compared with those concerning the sample of all transplanted in the same period.
Results: 1047 "viral risk" effective organ donors with 2631 donated organs in all (251hearts, 863 livers, 1431 kidneys, 19 pancreas and 67 lungs) were reported between the 1st of January 2003 and the 31st of December 2008. Table 1 shows heart, liver and kidney transplants divided according to the risk category.

Table 1

Heart	2003	2004	2005	2006	2007	2008	Total
HBsAg+	1	6	2	1	3	1	14
HCV+	3	1	1	2	4	7	18
HBsAg+ HCV+	0	0	0	0	0	0	0
HCV+ HBcAb+	0	3	1	0	0	1	5
HBcAb+	40	47	38	22	36	31	214
Total	44	57	42	25	43	40	251
Liver	**2003**	**2004**	**2005**	**2006**	**2007**	**2008**	**Total**
HBsAg+	1	10	7	7	9	6	40
HCV+	6	12	11	10	11	14	64
HBsAg+ HCV+	0	0	1	1	0	0	2
HCV+ HBcAb+	2	3	5	6	3	8	27
HBcAb+	113	149	139	80	126	123	730
Total	122	174	163	104	149	151	863
Kidney	**2003**	**2004**	**2005**	**2006**	**2007**	**2008**	**Total**
HBsAg+	2	24	6	9	8	3	52
HCV+	14	28	16	10	16	11	95
HBsAg+ HCV+	0	0	0	0	0	0	0
HCV+ HBcAb+	2	10	6	4	6	3	31
HBcAb+	207	259	251	132	205	199	1253
Total	225	321	279	155	235	216	1431

Graft and recipient survival appears to be comparable to that concerning the sample of all transplanted in the same period of time.
Conclusion: Graft and recipient survival appears to be satisfying in every risk category; whilst data regarding HBcAb+ category are several, those regarding the other categories are quite few. The positive issues of this study, along with the improvements in treating these infections, should encourage to enlarge the range of organ choice in order to increase organ procurement.

P-57 MELD ALLOCATION SYSTEM IN BELGIUM-ET AND OUTCOME

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Higher MELD predicts a reduced expectancy of life while waiting for a suitable organ to be transplanted, but contradictory results are reported regarding its association with outcome. We performed a single center retrospective review to address this issue.
Methods:
Since 2007, when the MELD allocation was started, 102 liver transplantations were performed in our hospital. High Urgency patients were excluded. The patients were divided into two groups according to labo_MELD. The whole series was analyzed also according to allocation group: labo_MELD, exceptional_MELD, and center driven allocation (ECD, NHBD, LDLT).
Results:
Seventy-five adult patients and 9 pediatric patients were transplanted. Mean labo-MELD of the entire series was 18±8.5 range (6-40), while the match-MELD was 22.5±7.3. Ten patients were included in the MELD≥30 group (mean 34.4±3.5), and 74 in the MELD<30 group (mean 15.8±6). Median waitlist time was shorter in the MELD≥30: 5 days, range (1-730) vs. 89 days, range (1-981), p=0.01. Median ICU time in MELD≥30 was longer: 10 days, range (1-60) vs. 4 days, range (1-93), p=0.01. In the whole series 30% of the grafts were allocated according to the labo_MELD, 30% were allocated according to exceptional_MELD and 40% were allocated otherways. The exceptional_MELD has doubled (19.2% in 2007, 46.9% in 2008). Median FU was 10.2 months,

range (0.03-23). No significative differences were found in the incidence of vascular or biliary complications betweengroups. One year graft and patient survivals were 67.5% vs 77.3% and 67.5% vs. 81% respectively, p=n.s.
Conclusions:
The increase in time of exceptional-MELD patients did not increase the labo-MELD needed to receive a liver graft. Patients with higher-MELD received a liver graft sooner and ICU stay was longer, evidencing the more complex management of these patients. In this initial experience, MELD≥30 did not worsen outcome.

Clinical immunosuppression I

P-58 PREFERENTIAL INCREASE IN MEMORY AND REGULATORY SUBSETS DURING CD4+ T-CELL IMMUNE RECONSTITUTION AFTER THYMOGLOBULIN INDUCTION THERAPY IN RENAL TRANSPLANT PATIENTS RECEIVING SIROLIMUS VS CYCLOSPORINE

Emmanuel Morelon, Nicole Lefrançois, Caroline Besson, Julie Prévautel, Marie Nathalie Kollop-Sarda, Maria Brunet, Jean-Louis Touraine, Lionel Badet, Françoise Touraine-Moulin, Olivier Thaunat, Christophe Malcus. *Transplantation Unit & Immunology Unit, Edouard Herriot Hospital, Lyon, France*

Thymoglobulin induction with sirolimus maintenance therapy is effective and may minimize renal injury but no study has compared immune reconstitution with sirolimus vs calcineurin inhibitors following Thymoglobulin induction.
Methods: In a 12-month, randomized, open-label, single-center pilot study, peripheral lymphocyte reconstitution was compared in *de novo* kidney transplant patients receiving sirolimus (n=9) or CsA (n=10). All patients received Thymoglobulin induction, MMF and corticosteroids. Lymphocyte count was recorded at baseline (day 0), during days 1-14, and at months 1, 2, 3, 6 and 12. Cell counts were compared between treatment groups using a Fishers test on a compacted data set, allowing a single comparison across all post-baseline timepoints.
Results: Total lymphocyte reconstitution was greater in the CsA arm vs sirolimus (p=0.004). At baseline, nave T-lymphocytes ($CD4^+$ $CCR7^+$ $CD45RA^+$) were more numerous in the sirolimus cohort vs the CsA arm (p=0.028) but became less numerous vs CsA after Thymoglobulin therapy (p=0.019). In contrast, memory cells ($CD4^+$ CD45RO) were less frequent in the sirolimus group vs the CsA arm at baseline (p=0.006) but were more frequent after Thymoglobulin, a difference that approached significance (p=0.05). Finally, while the number of regulatory T cells ($CD4^+$ $CD25^{bright}$) was similar at baseline in the two groups, this subset was significantly increased after Thymoglobulin in the sirolimus cohort vs the CsA arm.
Conclusion: Homeostatic reconstitution after Thymoglobulin induction is characterized by a disproportionately high recovery of memory and regulatory T-cell subsets during sirolimus versus CsA maintenance therapy in kidney transplant patients. These data suggest that the anticipated beneficial effect of sirolimus that favour T-regulatory cells during immune reconstitution could be counterbalanced by a parallel increase of memory subsets, more resistant to immune regulation.

P-59 EFFECT OF TRIPTERYGIUM ON PROTEINURIA ASSOCIATED WITH SIROLIMUS IN RENAL TRANSPLANT RECIPIENTS

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This is a study comparing with Tripterygium Wilfordii Hook F.(T II) and without T II (valsartan) based immunosuppressive regimens: sirolimus (SRL) + mycophenolate mofetil (MMF) + prednisone (Pred) in renal transplant recipients, to investigate the safety and efficacy of T II on proteinuria associated with sirolimus in renal transplant patients.
Methods: Thirty six (29.0%) cases developed proteinuria (>1.5 g/24-hr.),19.4% (6/31) patients receiving SRL de novo developed proteinuria and 32.3% (30/39) displayed proteinuria (these patients underwent abrupt cessation of a CNI sparing protocol). The mean value of proteinuria was 4.20±1.66 g/24 hr. According to accept T II, 36 recipients were divided into the two groups:T II group (n=21) and valsartan group (n=15). Evaluation of the efficiency: Complete remission: proteinuria decrease by >50%, Part remission: proteinuria decrease by 20%-50%, Ineffective: proteinuria reduces below 20%.
Results: Follow-up 12 month, the two levels of proteinuria both drop in the two groups, but the descending extent of proteinuria in T II group is more obvious than that in valsartan group. The total effective rate in T II group and valsartan group were respectively 95.2% and 86.7%, P<0.001. The ineffective rate were respectively 4.8% and 13.3%, P<0.001. As for the mean serum creatinine at level 3, 6 and 12 months after the follow-up, each of the T II group was clearly lower than that of vaslartan group (1.61±0.45 vs. 1.60±0.33mg/dl,1.50±0.29 vs. 1.82±0.45 mg/dl and 1.44±0.39 vs. 2.03±0.49 mg/dl, P<0.05). All patients tolerated T II well over the 12 months of this study.
Conclusions: It suggested that the use of T II markedly reduces proteinuria associated with sirolimus in renal transplant patients, without any obvious side effects and can be the first choice in the treatment of these patients.

P-60 CLINICAL STUDY OF THE CONVERSION TREATMENT WITH SIROLIMUS AND MYCOPHENOLATE MOFETIL IN THE RENAL TRANSPLANT RECIPIENTS

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We evaluate the efficacy and safety of conversion calcineurin inhibitor to sirolimus in the renal transplant recipients with risk factors. A total of 93renal transplant patients were recruited from the Research Institute of Nephrology, Jinling Hospital,including 59 males and 34 females,aged 38.2±11.1 (22–48) years,including CNI nephrotoxicity,CNI hepatotoxicity,PTMD, CAN and tumor.
Methods: 93 eligible cadaver renal transplant patients treated with CNI as main immunosuppressant were converted to SRL immunosuppressant protocol with quickly CNI withdrawal in 2 weeks.A loading dose of SRL of 6mg was administered with in 48 hours after transplantation, maintained at 2 mg/d thereafter. SRL was titrated to target trough levels of 6.3±2.3 ug/L. Mycophenolate mofetil (MMF,750mg,twice daily) and prednisone (5 mg daily) were administered orally.
Results: At conversion mean time after transplantation was 22-36 months with follw-up 32.5±21.2 (6-36) months, SRL target trough levels were 6.3±2.3 ug/L. The incidence rate of biopsy confirmed acute rejection were 9.1% in the 6 months post conversioninthe SRL 2mg/d. Seventeen of the 33 (51.5%) patients showed improvements in graft function follow up 26±9 months at SRL conversion, fourteen patients showed amelioration in graft function. CNI related nephrotoxicity (n=13), hepatotoxicity (n=26) and PTMD (n=11) were improved after SRL treatment. Eight of 10 patients with malignant tumor (follow-up 21.3±14.9 months) were stable and the rest recurrence. During the study,SRL was well tolerated. Hyperlipidemia and gastrointestinal reaction are the most frequently accounted adverse events. Adverse events attributed to SRL including hyperlipidemia,usually responded to dose reduction. At the end of 36 months, patient and graft survival was 90.9% and 75.8%, respectively.
Conclusion: The conversion treatment with SRL and MMF may be a better option for the renal transplant recipients with CNI with risk factors.

P-61 THE MAXIMUM TOLERATED DOSE OF MYCOPHENOLIC ACID (MPA) IS HIGHER WITH ENTERIC-COATED MYCOPHENOLATE SODIUM (EC-MPS) COMPARED TO MYCOPHENOLATE MOFETIL (MMF) IN KIDNEY TRANSPLANT RECIPIENTS: RESULTS OF A RANDOMIZED, MULTICENTER TRIAL

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No randomized trial has assessed if conversion from MMF to EC-MPS permits an increase in tolerated MPA dose, with the potential for improved long-term outcomes.
Methods: In a randomized, multicenter, open-label trial at 19 UK centers, kidney transplant patients with gastrointestinal (GI) complications, or who had required MMF dose reduction due to GI events, either remained on MMF or switched to an equimolar dose of EC-MPS. EC-MPS 1440mg was considered bioequivalent to MMF 2000mg. At week 2, MPA dose in both groups was adjusted to achieve the highest tolerated dose. Patients were followed to 12 weeks post-randomization.
Results: The ITT population comprised 68 EC-MPS patients and 61 MMF patients. Baseline mean MMF dose (EC-MPS 1283±461 mg/day, MMF 1279±485 mg/day) and concomitant immunosuppression were similar between groups. The primary efficacy endpoint, proportion of patients maintained at 12 weeks on an EC-MPS dose ≥180 mg/day or MMF dose ≥250 mg/day higher than at randomization, was greater in the EC-MPS arm (32/68, 47.1%) vs. the MMF arm (10/61, 16.4%; p<0.001). At week 12, 50.0% (34/68) of EC-MPS patients were receiving the maximum recommended dose vs. 26.2% (16/61) of MMF patients (p=0.007). 16/36 EC-MPS patients (44.4%) with a low baseline dose (1000mg/day MMF) were receiving the equivalent of MMF

>1000 mg/day at week 12 vs. 6/31 MMF patients (18.4%). The decrease (i.e. improvement) in Gastrointestinal Symptom Rating Scale total score from baseline to week 12 was -0.49 in the EC-MPS arm vs. -0.22 in the MMF cohort (n.s.).
Conclusions: Kidney transplant patients receiving reduced doses of MMF due to GI side effects can tolerate a significant increase in MPA dose after conversion to EC-MPS without compromising quality of life.

P-62 HEALTH-RELATED QUALITY OF LIFE MAINTAINED DESPITE INCREASE IN MYCOPHENOLIC ACID (MPA) DOSE FOLLOWING CONVERSION FROM MYCOPHENOLATE MOFETIL (MMF) TO ENTERIC-COATED MYCOPHENOLATE SODIUM (EC-MPS): A RANDOMIZED, MULTICENTER TRIAL IN KIDNEY TRANSPLANT RECIPIENTS

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Poor tolerability frequently leads to MMF dose reduction or discontinuation, adversely affecting efficacy, while gastrointestinal (GI) symptoms impair quality of life (QoL). Conversion to EC-MPS may permit increased dosing but QoL should be preserved.
Methods: In a multicenter, prospective trial, MMF-treated maintenance kidney transplant recipients experiencing GI complications, or who had previously required MMF dose reduction due to GI events, were randomized to continue MMF or convert to EC-MPS (week 1). At week 3, MPA dose was adjusted in both groups to the highest tolerated dose. Patients were followed to 12 weeks post-randomization. Symptom burden and GI-specific health-related QoL were assessed at weeks 1 and 12 using The Gastrointestinal Symptom Rating Scale (GSRS) and the Gastrointestinal Quality of Life Index (GIQLI), respectively.
Results: The ITT population included 68 EC-MPS and 61 MMF patients. Groups were well matched other than more EC-MPS patients <65 years old. Significantly more patients randomized to EC-MPS than MMF were receiving an increased MPA dose (i.e. an increase of EC-MPS ≥180mg/day or MMF ≥250mg/day) at week 13 vs. baseline: EC-MPS 47.1%, MMF 16.4%; p<0.001. At week 3, there was a significantly greater improvement from baseline with EC-MPS vs. MMF for GSRS total score (-0.50 vs. -0.07, p=0.004) and GIQLI total score (8.9 vs. 1.9, p=0.037). At week 13, following MPA dose adjustments, the change from baseline was not significantly different (GSRS -0.49 vs. -0.22, n.s.; GIQLI 8.2 vs. 4.3, n.s.; EC-MPS and MMF, respectively).
Conclusions: Despite almost threefold more EC-MPS patients achieving an MPA dose increase than MMF-treated patients, all health-related QoL measures were similar in the EC-MPS and MMF groups at 12 weeks post-randomization.

P-63 CAMPATH INDUCTION AND SIROLIMUS MAINTENANCE THERAPY, A STEROID FREE AND CALCINEURIN FREE PROTOCOL IN LIVE-DONOR RENAL TRANSPLANT RECIPIENTS: PILOT STUDY

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Purpose: The aim of this prospective study is to develop a new tolergenic immunosuppressive protocol using Campath induction followed by steroid and calcineurin free sirolimus based protocol among our live-donor renal transplant recipients.
Methods: Campath was used as induction therapy (single dose 30 mg) in 20 live related renal allotransplants. All patients received tapering doses of steroids for two weeks. Tacrolimus was given in a dose of (0.1 mg/kg) targeting a trough level 4-8 ng/ml for two months. After two months Sirolimus was given in an initial dose of 5 mg aiming target blood trough level 10-15ng/ml and FK was stopped after reaching that level. MMF was given in a dose of 500 mg/12 H whenever the WBC is ≥ 4000/μL.
Results: Graft and patient survival was 100% after a follow up period of 15±3 months. The mean serum creatinine 1.3±0.2 mg%. Five of the 20 patients have experienced acute rejection, which was successfully treated in all of the patients. None of these patients had pathological evidence of a humoral component of their rejection. Steroids were re added in 3 out of those patients. Rapamycin was generally well tolerated, since there were no wound-healing problems or lymphoceles. Currently, a total of 15 patients are enjoying a steroid-calcinumine-free regimen. Five patients are receiving KF-based therapy, and only three of them are still maintained on steroid. To date no chronic allograft nephropathy has been shown in the biopsies.
Conclusion: This pilot clinical trial provides a good insight into a potentially safe steroid free and calcineurin free protocol with the use of Campath-1H induction in combination with rapamycin.

P-64 IMPROVED LONG-TERM SURVIVAL AFTER AN INTRA-OPERATIVE SINGLE HIGH-DOSE ATG-FRESENIUS INDUCTION IN CADAVERIC RENAL TRANSPLANTATION: A SINGLE CENTER EXPERIENCE

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Purpose: After organ allografting donor-specific sensitization is initiated immediately after re-vascularization. Therefore, in 1990 we changed our immunosuppressive scheme and introduced the intra-operative single high-dose ATG-Fresenius (ATG-F) induction in addition to the standard immunosuppression. This analysis presents data of recipients who received two different ATG-F inductions (1st group: 9 mg/kg body weight as single high-dose intra-operatively, 2nd group: 3mg/kg body weight on 7 or 8 consecutive days as multiple-dose starting also intra-operatively) and standard triple drug therapy (TDT) alone (3rd group: TDT alone).
Methods: Retrospective analysis of clinic records and electronic databases of first cadaveric renal transplantations whose induction therapy regimens did or did not include ATG-F in addition to TDT, dating back to January 1987.
Materials: A total of 778 first renal transplantations that involved TDT in combination with an ATG-F single high-dose infusion (n=484), TDT plus ATG-F multiple-dose therapy (n=78), or TDT alone (n=216) were included in this evaluation.
Results: More than 250 patients had completed a follow-up of at least 10 years. At the individual end of follow-up the patient survival rates were 79.1% (1st group), 80.8% (2nd group) and 67.1% (3rd group; p=0.001), and the graft survival rates with deceased patients counted as graft failures were 62.8%, 52.6% and 36.6% (p=0.001), respectively. A total of 69% of the patients in the two cohorts receiving ATG-F did not experience any transplant rejections compared to 56% in patients undergoing TDT alone (p=0.018). The incidence of infectious complications was comparable across all groups.
Conclusion: According to evidence obtained from the routine documentation of 778 renal transplantations ATG-Fresenius administered as part of immunosuppressive therapy significantly improves patient survival and reduces the risk of graft failure and transplant rejections.

P-65 EXTENDED RELEASE TACROLIMUS IN DE NOVO KIDNEY TRANSPLANT RECIPIENTS. CLINICAL EXPERIENCE OF A SHORT-TERM USE

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The new modified release formulation of Tacrolimus has been developed to enable once daily dosing, to improve compliance. The purpose of this study is to known the behavior of the use of extended release of tacrolimus (XL) in the short-term in de novo transplant recipients, the incidence of adverse evens and assess kidney function.
Methods: We studied 30 patients, during the first 3 months. All subjects received XL-Tacrolimus (0.22 mg/kg), Basiliximab, corticosteroids, and mycophenolate mofetil,only those with high risk of rejection.
We analyzed the characteristics of the donor and recipient, pretransplant cardiovascular risk factors and kidney function, levels of immunosuppressive therapy, side effects and adverse events related to XL-Tacrolimus.
Results: 76% were male and 24% women. The mean age was 57.80 years. Seven cases (28%) was a second transplant. Before trasplant 92% had Hypertension and 16% Diabetes Mellitus.
During follow-up highlights, we found hyperkalemia in up to 36% of patients, as well as hyperuricemia by 44%. Both effects seem to relate to elevated levels of XL-Tacrolimus.
The mean dose of XL-Tacrolimus was 0.22mg/kg at 7 days, 0.19 mg/kg at 30 days and 0.15mg/kg at 3 months, to achieve target blood levels according to our protocol. The mean serum creatinine were 2.3 mg/dl at 7 days, 1.8mg/dl at 30days and 1.9mg/dl at three months.
The most frequent side effect was a tremor (48%).
As we detect adverse events: 20% of acute tubular necrosis, and one acute rejection.
Conclusions: The XL-tacrolimus is well tolerated, although we found a high incidence of hyperkalemia and hyperuricemia, not always associated with high levels of the drug. To prove we should extend the study, both in number of patients and in time.

Abstract P-66 – Table 1. Results of serial soluble CD30 from day 0 up to one year of transplantation

Group	Day 0	Day 3	Day 5	1 Month	1 Year
UC	122.9±88	55.5±37 (p<0.0001)	47.8±55 (p<0.0001)	44.2±58 (p<0.0001)	9.4±8 (p<0.0001)
AR	69.7±33	46.7±15.8	45.8±9.9	15.25 (p0.0005)	6.14 (p<0.0001)
ATN	140.5±86	58.1±44 (p0.011)	47±27 (p0.007)	25.15 (p0.008)	13.214 (p0.04)
O	148±149	47.7±27 (p0.103)	43.5±23 (p0.111)	22.219 (p0.075)	8.38 (p0.014)
Total	118±87.9	52.2±34.5	43.8±43.9	21.7±10.9	9.0±8.2
Live donor	117.1±94	46.9±36 (p<0.0001)	41.7±51 (p<0.0001)	21.1±11 (p<0.0001)	9.2±10 (p<0.0001)
Deceased donor	120.2±73	65.3±28 (p0.001)	48.9±17 (p<0.0001)	20.9±7 (p<0001)	8.8±5 (p<0.0001)

P values are compared with pre-transplantation (Day 0) sCD30 level and expressed as one sided T test.

P-66 SERIAL SOLUBLE CD30 MEASUREMENT AS A PREDICTOR OF KIDNEY GRAFT OUTCOME

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Introduction and aims: Pre and post-renal transplantation high soluble CD30 (sCD30), a marker for T helper 2-type cytokine-producing T cells, is a relevant predictor for development of rejection episodes and may contribute further to the selection of appropriate immunosuppressive regimens in high risk recipients.

We evaluated the accuracy of serial sCD30 post-transplantation as a predictor for acute rejection versus other pathologies which affect graft outcome over one year.

Methods: Fifty renal transplant recipients were randomly selected to check sCD 30 at day 0, 3, 5, 7, 14, 21, 1 month, 3 months, 6 months and 12 months post-transplantation. Results were analyzed for development of acute rejection, ATN or other pathologies and graft outcome at one year.

Results: Compared with pre-transplantation sCD30, there was significant reduction of the average sCD30 immediately post-transplantation from day 3 onwards ($p<0.0001$). Patients were divided into four groups: 1 - Uncomplicated course (UC) (56%), 2 - Acute rejection (AR) (18%), 3 - ATN (16%) and 4 - Other diagnoses (O) (10%). There was significant reduction of sCD30 immediately post-transplantation for group 1, 2 and 3 ($p<0.0001$, 0.004 and 0.002 respectively) but not group 4 (p=0.387).

Patients who developed acute rejection after one month had higher pre-transplantation sCD30 value than others who had rejection before one month (p 0.019) with odds ratio 1.649 for the graft loss. All groups had significant improvement of graft function over one year of follow up without significant difference between them.

Conclusions: Though significant drop of sCD30 post-transplanation is recorded, measuring sCD30 serially post-transplantation did not help to differentiate between acute rejection, ATN and other diagnoses. In this study, higher sCD30 levels pre-transplantation were reported in patients who developed rejection episodes later then one month of transplantation.

P-67 ACTIVE MANAGEMENT OF POST-RENAL TRANSPLANTATION BK VIRUS NEPHROPATHY – A PRELIMINARY REPORT

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Introduction and aims: There is no active treatment for post-renal transplantation BK virus nephropathy (BKVN) proved to be effective so far. Leflunomide, intravenous immunoglobulin, ciprofloxacin and cidofovir are still under investigation as active measures for BKVN treatment and our aim was to assess their efficacy on graft outcome after one year.

Methods: Renal transplant recipients with positive BKV-PCR in urine and blood twice underwent graft biopsy to confirm BKVN. Once BKVN is diagnosed, anti-metabolites (mycophenolate mofetil or azathioprine) were changed to leflunomaide and a course of immunoglobulin and oral ciprofloxacin were given.

Results: Eighteen patients were reviewed, 72% were males, deceased donors were 50%, mean HLA mismatches was 3.56, all patients received induction therapy (61% received thymoglobulin and 39% received basiliximab) and 61% received antirejection treatment before diagnosing BKVN.

Maintenance immunosuppression was mainly prednisolone (93%), MMF as 2gm daily (93%) and Tacrolimus (61%). Baseline mean creatinine clearance (CCl) was 35.6 11.5 which was reduced to 29.3 17.3 ml/min/1.73m^2 at one year (p 0.012). According to baseline CCl value above and below 40, patients were divided into two equal groups; with mean CCl 44.5 and 25.3 ml/min/1.73m^2 for group 1 and 2 respectively. At one year, mean CCl was reduced to 42.6 (p 0.229) for group1 and 16.7 ml/min/1.73m^2 (p 0.009) for group2. Three grafts were lost by the end of the study (16.7%), all were in group 2 (p 0.031).

Table 1. Demographic features and results

	Total	Group 1	Group 2	P (group 1&2)
Number of patients	18	9	9	
Age	46.2±12.8	46.7±15.8	45.8±9.9	0.874
Sex (male/female)	13/5 (72/28%)	8/1	5/4	0.045
Donor (live/deceased)	9/9 (50/50%)	5/4	4/5	0.43
HLA mismatch	3.56±1.1	3.44±1.2	3.67±1.2	0.678
Thymoglobulin induction	11 (61.1%)	4 (36.3%)	7 (63.7%)	0.03
Rejections pre-BKVN	9	5	4	0.894
Time from Tx to BKVN (months)	23.3±31.9	21.2±26.7	25.5±37.9	0.835
BKVN proven biopsy	16/18	7/9	9/9	0.984
Viremia at baseline	13/16	7/8	6/8	0.91
Viremia at 12 months	4/7	3/4	1/3	0.836
Viruria at baseline	15/16	8/8	7/8	0.916
Viruria at 12 months	6/7	4/4	2/3	0.867
Baseline serum creatinine (Cr) (a)	190±56.5	154.4±13.3	225.5±61.4	0.004
Cr at 1 year (b)	339±327	170±47	508±401	<0.0001
	P(a,b) 0.025	P(a,b) 0.148	P(a,b) 0.029	
Baseline estimated Cr clearance (c)	35.6±11.5	44.4±6.6	26.7±7.8	<0.0001
Estimated Cr clearance at 1 year (d)	29.3±17.3	42.6±12.8	16±9	<0.0001
	P(c,d) 0.012	P(c,d) 0.229	P(c,d) 0.009	
Graft outcome	15/18 (83.3%)	9 (100%)	6 (67%)	0.031

Conclusions: Late diagnosis and heavy immunosuppression are predisposing factors for development of BKVN. Early active treatment for BKVN may improve graft outcome at one year.

P-68 DOSAGE REDUCTION OF CICLOSPORIN A IN COMBINATION WITH EVEROLIMUS IN HEART TRANSPLANT RECIPIENTS WITH CHRONIC RENAL FAILURE: A TWO-YEAR FOLLOW UP

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Therapy with the calcineurin inhibitors Ciclosporin A (CSA) is often associated with nephrotoxic side effects. Deduction of CSA dosage in combination with Everolimus, may improve renal function.

Since January 2004 and December 2005, 96 maintenance heart transplant patients have been converted from CsA (n=75) – Monotherapy (60-80 ug/l). CsA dosage was reduced by 50%.

Cholesterol (LDL/HDL) did not differ significantly. There was a significant increase in serum triglycerides (t_0: 187,19±101,83 mg/dL; t_{12}: 204.17±158.26 mg/dL; t_{24}: 242,81±207.83 mg/d). CSA concentrations decreased by 39%. Blood levels of everolimus were 4.1 ng/l at t_{24}. Mean serum creatinine levels decreased from 2,41±0,73 ng/mL at t_0, 2,13±0,82 ng/mL at t_6, 2,25±0,92 ng/mL at t_{12} and was 2,47±1,39 ng/mL at t_{24}, with significance (p=0,001). Mean serum creatinine levels decreased from 2,41±0,73 ng/mL at t_0, 2,13±0,82 ng/mL at t_6, 2,25±0,92 ng/mL at t_{12} and was 2,47±1,39 ng/mL at t_{24}, with significance (p=0,001). This correlates with a decrease of approximately 11,6%.

BUN also decreased by approximately 10,45% post conversion with significance (p=0,044), and is associated with improved renal function In this analysis patient with termination of everolimus were excluded. Adverse effects: peripheral edema (15,6%), dyspnea (15,6%) lingual edema (6,2%), gastrointestinal complications (6,2%), dermatological complications (6,2%)erythropenia (other complications (16,5%). Two year survival: 93,75%. Rejection rate: 4,2%.

Our data indicate that everolimus 1) effectively inhibits cardiac rejections 2) is able to improve kidney function, 3) leads to a massive increase in serum triglycerides levels, and 4) shows an expected spectrum of side effects.

P-69 NONCOMPLIANCE TO TACROLIMUS AND SIROLIMUS IN RENAL TRANSPLANTATION

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Purpose: Measure and compare extent of noncompliance to Tacrolimus-FK and Sirolimus-SRL in renal transplant patients, generating hypotheses on potential risk factors.
Methods/Materials: Observational and prospective study (SRL-140±32 days; FK-125±20 days). Compliance methods: electronic monitoring-EM, pills/capsules counting-PC/C, monitoring of blood levels-MBL and compliance self-reporting-CSR. Operational definitions according to methods and investigators criteria. Compliance rate-CR expressed by median (Percentile$_{25}$-Percentile$_{75}$) except for MBL. Adherents/Non-adherents categorization using 80%-CR-"cut-off". Potential noncompliance risk factors identification (EM-based) using: patients-interview, prescriptions-review, appointments-files, local-database, quality-of-life-questionnaire and EM-report. Statistical analysis (SPSS-11.5) for groups' comparison: Student's-t or Mann-Whitney-U tests and Chi-squared-test or Fisher's-exact-test. Statistical significance threshold $p<0.05$.
Results: Forty-nine patients studied (SRL-31; FK-18). Groups' baseline characteristics similar (mostly males; comparable age-47 (mean)). FK and SRL compliance results comparable using the 4 methods:
EM
CR "according-to-dose":
FK-98.8% (92.4%-100.1%); SRL-99.3% (97.7%-100.7%)
CR "according-to-doses-interval":
FK-88.9% (75.0%-96.5%); SRL-89.7% (83.9%-97.6%)
CR "according-to-days":
FK-91.7% (82.0%-97.0%); SRL-95.0% (88.6%-99.2%)
Non-adherents: FK-33.3%; SRL-16.1%
PC/C
CR: FK-99.4% (97.5%-101.9%); SRL-99.7% (97.7%-100.5%)
Non-adherents: FK-0.0%; SRL-6.5%
MBL
CR: FK-46.6±28.5%; SRL-50.3±26.7%
Non-adherents: FK-88.9% and SRL-90.3% (CR)
FK-50.0% and SRL-41.9% (mean concentrations)
CSR
Non-adherents: FK-5.6%; SRL-6.5%
Noncompliance related to (N=49): more than 3 elements in domestic aggregate, memory compliance barriers, drug addictive behaviours and higher alcohol intake.
Conclusion: Non-compliance estimates varied within each group due to different methods and definitions (as in literature). Based on EM (closest to reference), high CRs were found, probably explained by study design or mostly by patients' perceptions, and 22.4% of total non-adherents were seen, which is in accordance to other studies' findings in this population. Results confirmed that the ideal way of measuring compliance is based on methods association (different/complementary information with congruent compliance results in studied groups). Compliance wasn't associated to any drug, although they were different (ex. daily intake; side effects). Most of potential noncompliance risk factors weren't associated with noncompliance (although small sample size), confirming that noncompliant behaviour is usually unpredictable.

P-70 SUBCLINICAL TOXICITY OF CALCINEURIN INHIBITORS IN REPEATED PROTOCOL BIOPSIES OF TRANSPLANTED KIDNEYS: AN INDEPENDENT RISK FACTOR FOR THE DEVELOPMENT OF INTERSTITIAL FIBROSIS AND TUBULAR ATROPHY

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Purpose: The objective of this prospective study was to evaluate the prevalence of the subclinical nephrotoxicity of calcineurin inhibitors (CI) in repeated protocol renal graft biopsies carried out in the course of the first year following the transplantation and to assess its impact upon the development of interstitial fibrosis and tubular atrophy (IF/TA).
Methods: 424 protocol graft biopsies were carried out in the population of 158 newly transplanted patients, of which: 158 biopsies were performed in week 3, 142 in month 3, and 124 one year after transplantation. Three groups were set off in the population: a control group with normal histological finding, a group with subclinical toxicity and a group with clinically manifest toxicity and graft dysfunction. The groups were monitored for the IF/TA progression using Banff score of chronic changes, and cross comparisons were carried out. The test results were marked as significant at a level of statistical significance of $P<0.05$.
Results: Histological signs of toxicity occurred in week 3 in 33 (20.1%) patients with persisting findings following a reduced CI dose, in month 3 in 27 (19.0%) patients, and in year 1 in 23 (18.5%) patients. As much as 52% of the toxic changes were clinically silent. At the end of the one-year follow-up, both subclinical and clinically manifest toxicity resulted in a similar increase in IF/TA and they significantly differed from the control group ($P<0.05$).
Conclusion: Subclinical toxicity of CI affects a significant percentage of grafts, it is associated with the progression of chronic changes as early as in year one following the transplantation, and it represents an independent risk factor for the development of IF/TA.

P-71 MONITORING THE IMMUNOSUPPRESSIVE EFFECT OF CsA BY NFAT REGULATED GENE EXPRESSION

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Purpose: Therapeutic monitoring of CsA is usually performed by analysis of serum drug levels. We investigated whether CsA drug levels reflect the effect of CsA on inhibition of NFAT regulated cytokine expression in de novo and long term liver transplant (LTx) recipients.
Methods: In 20 de novo (< 3 mo) and 20 long term (3 mo-10 y) LTx patients CsA drug levels (by LC-MS/MS) as well as IL-2, IFN-γ and GM-CSF mRNA levels (by quantitative RT-PCR) were prospectively and repeatedly determined before (C0) and 2h after (C2) CsA intake. Residual cytokine expression at C2 relative to CO was calculated.
Results: Median CsA C0 and C2 levels were 216 and 689μg/l (de novo) and 87 and 552μg/l (long term) LTx patients, respectively. Two hours after CsA intake the residual cytokine expression was comparable in both groups (de novo patients IL-2 18%, IFN-γ 29%, GM-CSF 21%, mean total 23%; long term patients IL-2 15%, IFN-γ 21%, GM-CSF 23%, mean total 20%). There was a significant ($p < 0.01$) correlation between the CsA C2-levels and the mean residual cytokine expression in both de novo (r=0.528 (total); 0.491 (IL-2), 0.511 (INF-γ), 0.516 (GM-CSF)) and long term patients (r=0.783 (total); 0.805 (IL-2), 0.736 (INF-γ), 0.766 (GM-CSF)). In contrast, we found no correlation between CsA C0-levels and residual cytokine gene expression in both groups (mean total de novo r=0.069; long term r=0.282).
Conclusion: There was a significant correlation between the residual cytokine expression and the CsA C2 levels, but not the CSA CO levels in both long term and de novo LTx patients. Therefore only monitoring of C2 levels reflects the immunsuppressive activity of CsA. A potential superior clinical value of monitoring residual expression of NFAT regulated genes as compared to CsA C2 levels should be investigated in further studies.

P-72 THE COST OF SIROLIMUS THERAPY IN KIDNEY TRANSPLANTATION: IS THERE A HIGH PRICE TO PAY?

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Sirolimus is an immunosuppressive agent increasingly used to replace calcineurin inhibitors (CNI) for serious CNI toxicity or CNI withdrawal/avoidance protocols. Currently, clinical and pathologic experience with sirolimus is limited. We retrospectively analyzed the efficacy, severe adverse events (SAEs) requiring readmission and clinical outcomes in 108 kidney transplant recipients treated with sirolimus, MPA and steroids (SG). We compared the SG to 220 patients transplanted in the same period and treated with tacrolimus, MPA and steroids (TG). Pts with less than 3 months graft survival or who had less than one year follow up were excluded. Demographic data including sex, donor type, age, race, HTN, DM, CIT, PRA >30% and HLA matching were similar between groups. Both groups received similar induction therapy: low-dose thymoglobulin (total 3-5 mg/kg) or Simulect. All pts were taking 5 mg/d prednisone by day 30. Average follow up was 32±21 months. The rejection rate was 8% in the RG and 11% in the TG (p=NS). There were 73% readmissions in SG compared to 43% in TG ($p<0.01$). The majority (>90%) of readmissions in both groups were due to drug effects, however, the spectrum of illnesses differed slightly. Both groups suffered from infections, CHF and renal insufficiency. However, only the SG experienced pulmonary emboli, and the TG had anemia and leukopenia were significantly more common in the SG (p=0.006, p=0.02 respectively). Cardiovascular events and average serum creatinine at 1 and 3 years were similar between groups (p=0.12, p=0.62 and p=0.4 respectively).

Table 1. Clinical outcomes

	Pt 1y survival	Pt 3y survival	Graft 1y survival*	Graft 3y survival*	Hospital Stay (days)	CMV infection	Other infections
RG 108 pts	98%	88%	96%	87%	8.3	2 (1.8%)	24 (22%)
TG 220 pts	94%	85%	95%	90%	7.6	2 (0.9%)	39 (17%)
p-value	NS	NS	NS	NS	NS	NS	NS

*Death censored.

Our study shows that sirolimus therapy is associated with significantly higher SAEs and readmissions than tacrolimus therapy. Thus, sirolimus should be used with caution and careful consideration of other alternative immunosuppressive strategies, such as low dose CNI therapy.

P-73 OPTIMIZATION OF TACROLIMUS FOR RENAL TRANSPLANTATION – AN HISTORICAL RETROSPECTIVE FOR 10 YEARS

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Backgroud: Although calcineurin inhibitors led to major advances in the field of transplantation, long-term outcomes remain suboptimal. Recently, Tacrolimus (Tac) remains the main immunosuppressive agent regardless of its well known side-effects, including nephrotoxicy.
We retrospectively compared the outcomes of renal transplantation (RTP) according to tacrolimus trough levels, conventional dose versus low dose. Methods: The medical records of 338 patients who received RTP between Dec 1998 and Dec 2007 were reviewed retrospectively. Two groups of patients were defined based on Tac target levels. In the first group, patients transplanted from Dec 1998 to Dec 2002, target Tac level was was 10-20ng/mL (group A, n=102). In the second group, patients transplanted after Jan. 20036, target Tac level was 5-10ng/mL (group B, n=125). Comparisons were made between two groups.
Results: There were no significant differences between the two groups in the demographic characteristics. However, compared to group A, more group B recipients received triple regimen (Tac, MMF and prednisolone). Compared to group A, group B patients had significantly lower trough Tac levels after RTP. The daily dosage of tacrolimus also was significantly lower in group B than in group A. There was no significant differences between the two groups in serum creatinine after transplantation, however, the incidence of acute rejection was significantly lower in group B than in group A (9.3% vs. 22.3%, p=0.009). The incidence of PTDM was lower in group B than in group A but didn't show the statistically difference (10.9% vs. 19.4%, p=NS)
Conclusions: In conclusion, modest reductions in tacrolimus target trough levels is effective and associated with decreasing adverse effects. Additional clinical trials attempting further optimization in drug levels are needed particularly in patients with lower immunologic risks.

P-74 ASSESSMENT OF THE NEW TACROLIMUS CMIA ASSAY IN HEART, KIDNEY AND LIVER TRANSPLANTATION

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We determined the performances of the tacrolimus CMIA assay on ARCHITECT (Abbott). Inter-run reproducibility was analyzed for the three controls measured in duplicate for 5 consecutive days (n=10). Functional sensitivity was defined using negative blood samples spiked from 0 to 5 ng/ml. A clinical assessment in transplant patients was carried out on heart (14 samples, 9 patients), kidney (66 samples, 49 patients) and liver transplant (36 samples, 19 patients). Results obtained with CMIA were compared to EMIT, ACMIA and LC-MS-MS (TQD). The inter-run reproducibility showed coefficients of variation of 5.7, 3.7 and 3.6% and accuracies of 98, 104 and 104% respectively for the three controls. The limit of quantification defined as the lowest concentration with a CV of 20% was 0.5 ng/ml (95%CI 0.22-1.38 ng/ml) for CMIA and 2.5 ng/ml for ACMIA. 116 samples were assayed (12% heart, 31% liver and 57% renal Tx). For all the organs, the linear regressions were CMIA=1.2LCMSMS+0.14 (r=0.98), CMIA = 0.92EMIT + 0.36 (r=0.98), CMIA = 1.16ACMIA - 0.25 (r=0.99). Regarding the range of 0.5-8 ng/ml concentrations (72 samples), CMIA = 1.091LCMSMS + 0.48 (r=0.86). These results are very important because many transplant patients were treated using low-dosing of tacrolimus. We measured tacrolimus concentrations by ACMIA and CMIA in two patients presenting an interference in ACMIA. In the first renal transplant, tacrolimus concentrations were 12.5 *versus* <0.5 ng/ml using ACMIA and CMIA respectively. In the second renal and HIV patient, tacrolimus concentrations obtained by ACMIA are 1.8- to 43.7-fold higher than CMIA assay. The clinical outcome could be dramatic! The cause of this interference remains unknown but linked to the pretreatment without methanol in ACMIA.
In conclusion, the new tacrolimus CMIA assay is a suitable method in routine laboratory and avoid analytical error observed in some patients with ACMIA method.

P-75 MPA EXPOSURE IN PATIENTS WITH EARLY STEROID WITHDRAWAL: COMPARISON BETWEEN TWO MMF BASED IMMUNOSUPPRESSIVE REGIMENS, CONCENTRATION-CONTROLLED VERSUS FIXED DOSE

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Therapeutic drug monitoring of MPA has been shown to be effective in reducing the inter- and intra-patient variability. In the OPERA study we compared 2 MMF based immunosuppressive regimen in kidney recipients receiving anti IL2R induction and a short course of CS.
Patients in group A (n=130) started at 3g/day of MMF followed by dose adjustment according to MPA exposure at W2, W6, W12 and W26, whereas patients in B group received 2g/day of MMF throughout the 1 year follow-up period. In group A, MMF dose adjustments were calculated according to a therapeutic target of 40mg/h/l.
A starting dose of 3 g provided a higher MPA exposure at W2: mean AUC 36.2±14.8 versus 29.3±12.4 mg.h/L, p<0.001, with 61% of patients of group A in the therapeutic window *versus* 35% in group B. At W6, the mean MPA exposure (mg.h/L) was still significantly higher in group A: mean AUC 44.2±16.1 versus 36.7±18.1 mg.h/L, p=0.002. After W12 MPA exposure was not significantly different between recipients of both treatment arms. Adjustments of the MMF dose in group A were made rigorously according to MPA AUC values for more than 70% of the patients over the study period. The mean MMF doses were 2.9±0.7 g/d at W4, 2.5±0.9 g/d at W12, and 2±0.9 g/d at W26 in group A with dose ranging from 0.5 to 4 g/d at each time period.
MMF 3g/day associated with CsA allows most of the kidney transplant recipients to reach the MPA therapeutic window within 2 weeks. The MMF doses necessary to achieve therapeutic concentrations vary between individuals, suggesting the use of TDM.

P-76 RELATIONSHIP OF CLINICAL MARKERS OF SYSTEMIC ENDOTHELIAL DYSFUNCTION TO THE CALCINEURIN INHIBITOR NEPHROTOXICITY

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Background: The use of the calcineurin inhibitors led to major advances in the field of transplantation. However, the nephrotoxicity of the calcineurin inhibitors (CNIN) is the Achilles' heel of current immunosuppressive regimens.
In our study we have investigated the relationship of several clinical markers of endothelial dysfunction (ED) to the prevalence of CNIN in protocolar biopsy in patients after renal transplantation (RTX).
Methods: In a cohort of 25 patients levels of PAI-1 (63,52±15,44ng/ml), t-PA (2,20±1,65ng/ml), v-Wf (200,27±57,48%), big endothelin-1 (2,71±1,85pg/ml in week 3, 3,01±1,70pg/ml in week 52), FMD (7,40±4,85% in week 3 and 5,07±4,15% in week 52) were compared to the prevalence of CNIN in protocolar biopsies of kidney allografts performed in week 3,15 and 52 after RTX (CNIN was present in 13% ... 23% ... 20% patients and was defined by striped cortical fibrosis or new onset arteriolar hyalinosis). GFR estimated by Cockroft-Gault formula reached average level of 1,0192±0,3346 in week 52.
Results: A significant correlation were revealed between the progression of ED (expressed by the ratio of ET-1 week3/week52 and FMD week 3/week 52 after RTX) and CNI nephrotoxicity in week 3 in case of ET-1 ratio (r= -0,428, p<0,05) and in week 15 in case of FMD ratio (r = 0,454, p<0,05) The relationship of other ED markers to CNIN in protocolar histology during the first 52 weeks after RTX did not reached the statistical significance. GFR did not correlated to ED markers and CNIN after 52 weeks after RTX.

Conclusion: These results documented the significant relationship of the progression of endothelial dysfunction to the CNI nephrotoxicity during the first year after RTX and contribute to the discussion on its systemic versus local nature.

P-77 TREATMENT OF ACUTE ANTIBODY-MEDIATED REJECTION WITH THE COMPLEMENT INHIBITOR ECULIZUMAB

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Patients undergoing antibody-incompatible transplantation (AIT) are at risk of antibody mediated rejection (AMR). Complement activation, via the membrane attack complex C5b-9, is thought to play a major part in the rejection process. A complement factor C5 inhibitor – eculizumab – has recently become available, and has potential benefit in AMR.

Patient 1 was a 33year old man who received a 2nd renal transplant from his father. Pre-treatment non-AHG cytotoxic crossmatch was +ve at titre 1:16 (donor specific antibodies (DSA) HLA A2, DR9, DR53, DQ9) and ABO (A1 to B). Post-operative course was complicated with AMR partially unresponsive to anti-thymocye globulin (ATG) and plasmapheresis. HLA and ABO antibody levels rose markedly above pre-treatment levels. He was treated with two doses of eculizumab. Urine output increased dramatically, and he is currently well at 5 months with serum creatinine 244 umol/l.

Patient 2 was a 29 year old man who received a 4th renal transplant from his mother. After his third transplant he experienced a serious thrombotic microangiopathy with coma, so immunosuppression was calcineurin inhibitor-free. Pretreatment flow crossmatch was +ve (DSA HLA A2, B51, Cw14, DR15, DR51, DQ6). Two days post-transplantation his serum creatinine rose and a renal biopsy was suggestive of AMR. He was treated with eculizumab, but despite this a subsequent biopsy showed marked rejection, and ATG was given. Rejection resolved, but he experienced a CMV infection at 14 days, and subsequently an eosinophilic infiltrate of the graft that responded to steroids, lymphocoele, pneumonia, and urine infection with bacteraemia. He is well with serum creatinine at 4 months of 293 umol/l.

In summary, the availability of an inhibitor of the complement arm of the immune system is potentially an important addition to treatment modalities. Further use of the drug requires careful monitoring for infection.

P-78 EFFICACY AND SAFETY OF SINGLE AND MULTIPLE DOSE ANTITHYMOCYTE GLOBULIN INDUCTION TREATMENT IN LIVING RELATED RENAL TRANSPLANTATION

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Antithymocyte globulins (ATG) have been used as induction agents after organ transplantation for many years, but there are concerns with costs, adverse events, and the inconvenience of repeated dosing via a central vein. The aim of the study was to compare the safety and efficacy of two regimens of induction therapy with ATG-Fresenius in living related renal transplant recipients.

Eighty-seven patients were allocated into group 1 receiving single dose ATG (9 mg/kg b.w, 15 patients), group 2, multiple dose ATG (9 mg/kg b.w intraoperatively plus 3 mg/kg b.w. for the next 4 days=21 mg/kg b.w in total, 53 patients), and group 3 on triple immunosuppression alone (20 patients). Maintenance immunosuppression consisted of cyclosporine (CsA) or tacrolimus (Tac), mycophenolate mofetil, corticosteroids.

Demographic data and immunologic risk were similar for three groups. All the patients from group 1 received a minimum of two units of blood transfusion before transplantation, while one patient from group 3 and fourteen patients from group 2 ($p = 0.03$) were transfusion naïve. One patient from group 1, nine from group 2 and three from group 3 exhibited acute rejection (AR) and five patients delayed graft function (DGF). Mean creatinine clearance, estimated by MDRD, differed insignificantly between the three groups at every point of the 12-month follow-up period. Multiple dose ATG therapy was associated with leucopenia (six patients) and more frequent infections (group 1 vs. 2: $p = 0.03$)

Conclusion: In primary kidney graft recipients with peak PRA above 40% single dose ATG is as safe and equally efficient as multiple ATG doses in the prevention of AR and DGF but the same efficacy was achieved with triple immunosuppression.

P-79 ANGIOTENSINOGEN (AGT) M235T GENOTYPE BUT NOT INSERTION/DELETION (I/D) POLYMORPHISM OF ANGIOTENSIN-CONVERTING ENZYME (ACE) GENE AFFECTS GLUCOSE METABOLISM IN TACROLIMUS TREATED KIDNEY TRANSPLANT RECIPIENTS

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Renin-angiotensin system (RAS) is activated in patient with metabolic syndrome and insulin resistance. Certain genotypes of its components are associated with higher activity of RAS.

Objective: To assess the impact of AGT M235T genotype and I/D polymorphism of ACE gene on glucose metabolism in patients after kidney transplantation.

Patients and methods: Medical records of 80 adult Caucasoid patients covering a period 4th month – 4 years after Tx were included in a retrospective analysis. All Ps received Tac, mycophenolate and 10 mg of prednisone. Evaluated groups did not differ in acute rejection episode incidence and methylprednisolon treatment.

Results: TT: TM: MM genotypes frequencies of AGT were 19%: 44%: 37%; frequencies of ACE gene II: ID: DD genotypes were 36%: 36%: 28%. Highest fasting plasma glucose level was significantly different in TT homozygous individuals in comparison to MM genotype (8.03 ± 0.59 vs 6.2 ± 0.22 mmol/l, $p = 0.001$), differences between I/I vs D/D were not significant (7.26 ± 0.44 vs 7.03 ± 0.41 mmol/l, $p= 0.93$). Seventy seven percent of TT homozygous Ps had fasting plasma glucose $\geq$ 6.1 mmol/l in comparison to 38% of Ps wit MM genotype ($p= 0.01$). HbA1c levels were higher in TT than in MM genotypes (7.59 ± 0.43 vs $6.72\pm0.16\%$, $p = 0.03$), differences between I/I vs D/D were not significant (6.76 ± 0.16 vs 7.11 ± 0.26, $p=0.24$).

Conclusions: We suggest influence of RAS polymorphisms on glucose metabolism in Tac treated Ps after kidney transplantation. Carriage of at least one T allele (M235T) of angiotensinogen gene was linked to increased fasting glycaemia and HbA1c during the follow up.

P-80 RESULTS OF CONVERSION TO EVEROLIMUS IN PATIENTS PRESENTING WITH CALCINEURIN INHIBITOR NEPHROTOXICITY

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Aim: The aim of this study was to analyze the efficacy and safety of conversion to everolimus (Certican) combined with a low Neoral dose in patients with CNI nephrotoxicity.

Materials and methods: This prospective study included 15 maintenance renal transplant recipients (44.6 ± 33.8 months after transplantation) with declining graft function due to CNI nephrotoxicity. All biopsies demonstrated nodular arteriolar hyalinosis combined with nterstitial fibrosis. Mean area of interstitial fibrosis and tubular atrophy was $31\pm12\%$. The target concentrations were as follows: Certican -3 to 8 ng/mL for; Neoral C_0 - 35 to 50 ng/mL and C_2 -300 to 400 ng/mL. The mean dose of cyclosporine was reduced from 3.26 ± 0.98 mg/kg/day to 1.48 ± 0.44 mg/kg/day (by 54% on the average). The mean follow-up is 11.3 ± 3.7 months.

Results: A transient improvement was observed in transplant function in the first month after conversion: the mean GFR increased from 46.4 ± 12.9 mL/min to 54.6 ± 13.8 mL/min while the mean creatinine concentration decreased from 0.184 ± 0.03 mmol/L to 0.161 ± 0.03 mmol/L; afterwards, transplant function stabilized at the previous level: by the end of observation, the mean Pcr was 0.192 ± 0.05 mmol/L and the mean glomerular filtration rate 45.6 ± 12.6 mL/min. In one patient Certican therapy was discontinued after 3.5 months due to proteinuria (3 g/d). No graft loss or acute rejection episodes were observed in any of the cases.

Conclusion: Conversion to Certican in patients with CNI nephrotoxicity developing in the late period after kidney transplantation allows to significantly decrease the dose of cyclosporine without increasing the risk of acute rejection, and to stabilize transplant function, at least in the first year of observation.

P-81 THE POSITIVE EFFECT OF MYCOPHENOLATE MOFETIL ON THE HISTOLOGY COURSE OF HEPATITIS C AFTER LIVER TRANSPLANTATION

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Background: Hepatitis C virus (HCV) recurrence after orthotopic liver transplantation (OLT) is almost universal. The optimal immunosuppression for these

patients is still under discussion. We designed a prospective case-control study to evaluate the effect of mycophenolate mofetil (MMF) monotherapy treatment in patients with recurrent hepatitis C.
Material and methods: Fifteen patients with histologically proven hepatitis C recurrence after OLT were under MMF treatment from 48 months. We matched them with 15 calcineurin inhibitors (CNI) treated liver transplant recipients with the same follow up. Baseline biopsies of both groups were comparable in terms of fibrosis rate. Liver protocol biopsies were obtained yearly during the study. Histological changes were evaluated utilizing the Ishak score.
Results: Comparison of fibrosis showed no impairment of histological findings in the MMF group [2.6±1.5 (baseline) vs 2.7±1.8 (after 48 months MMF treatment), p= 0.6]. In contrast, histological findings of the 15 CNI patients showed a significant increase of fibrosis [2 (baseline) vs 3.2 (after 48 months CNI), p=0.0002]. In addition the MMF group showed a yearly fibrosis progression rate of 0.05±0.44 vs 0.33±0.24 of CNI group (p=0.04).Viral load was similar in both groups when alanin amino transferase (ALT) levels, measured during MMF treatment, showed a significant decrease [74±40.5 UI/L vs 40.3±22.0, p=0.01]. In addition MMF group showed a favourable impact on the cholesterol [162.9±39.3 vs 143.0±34.3 mg/dl, p=0.01], triglycerides [148.9±57.9 vs 116±44.8 mg/dl, p=0.02] and creatinine [1.9±0.9 vs 1.3±0.3mg/dl, p=0.001] course levels.
Conclusion: MMF monotherapy showed a positive effect on fibrosis progression and ALT levels compared to CNI transplant patients. Furthermore this study confirm the favouring impact on metabolic assay in MMF treated patients.

P-82 THE EFFECTS OF CONVERSION FROM CNI (CALCINUERIN INHIBITORS) TO SIROLIMUS IN RENAL TRANSPLANT RECIPIENTS

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Aim: To study effects of conversion from CNI to sirolimus in renal transplant recipients (RTR) in a single centre over a 7-year period.
Method: RTR converted to sirolimus were identified from the Unit's electronic database. The relevant parameters -serum creatinine (SCr), cholesterol, eGFR, blood pressure (BP), haemoglobin (Hb), and EPO dosage – were documented, at 3 monthly intervals for 1 year prior to and after conversion.
Results: 30 patients were switched from CNI to sirolimus during this period. The mean duration between transplantion and conversion was 75 months and the mean age was 48.8 years. Three patients withdrew from sirolimus due to side effects.
The mean SCr at switch was 341 mcmol/L. The mean SCr and the rate of change in SCr (ΔCr) are presented in the Table.

Effects of conversion from CNI to sirolimus

	No	Mean SCr		ΔCr		Change in Hb
		pre-switch	post switch	pre-switch	post-switch	
All Patients	27	305	342	+5.53	+0.52	–0.4
SCr <300 at switch	12	224	226	+1.8	–1.7	–0.7
SCr >300 at switch	15	369	424	+9.0	+2.3	–0.2

SCr in mcmol/l. Hb in g/dl

The rate of change in eGFR pre-conversion was -0.59 improving to +0.28 post-conversion. Patients switched early (SCr <300) had no further rise in SCr after conversion, in contrast to those with SCr>300.
There was a decrease in Hb post-conversion, and an associated increase EPO dose by a factor of 2.15. Serum cholesterol increased from a mean 5.72 to 6.34 mmol/L after conversion. The average BP was unaffected by conversion, and there was no change in number of antihypertensive medications used. The number of patients was too small for any of these these observed changes to reach statistical significance.
Conclusions: In this study, conversion from CNI to sirolimus was associated with improvement in the rate of decline in serum creatinine. Early switch appeared to be more beneficial, with stabilisation of SCr. There was a decrease in Hb and an increased EPO requirement. Our findings are in keeping with previous studies, supporting a switch from CNI to sirolimus in appropriate RTR with SCr <300 mcmol/l.

P-83 EVEROLIMUS AS BASE-THERAPY IN KIDNEY TRANSPLANTATION (KTX)

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Calcineurin-inhibitors (CNI) have a pivotal role in preventing rejection in KTX. However, their dose-related nephrotoxic potential limits their use in the middle-long term. Proliferation signal inhibitors are powerful immunosuppressants as well and are not nehrotoxic; however they are just regarded as ancillary drugs. Herein we report from an immunosuppressive protocol in which everolimus has been employed as base therapy and that foresee minimization/withdrawal of steroids and of CNI.
24 patients have been treated: they were 14 m and 10 f, their age ranged between 35 and 59 years old. They all received KTX from a deceased donor, 21 primary, 3 retransplants. Immunosuppression included Basiliximab (20 mg i.v. POD 0 e 4), everolimus (trough levels 4 – 10 ng/ml) and very low doses of neoral (C2 <400 ng/ml) and steroids (4 mg of 6-MP). Follow up was 3-25 months.
To date all grafts are functioning (creatinine 0.8-2 mg/dl).
We recorded only 1 case of DGF. 3 rejections occurred, all reversed, 1 steroid resistant. Surgical complications included 2 wound healing problems, 2 lymphoceles, 2 urinary leakage, 1 late hematoma. Hematologic toxicity was mild and expressed as 2 episodes of temporary leukopenia. 6 patients required treatment with statins, only 5 patients developed hypertension. Only 1 pt suffered of severe edema requiring everolimus withdrawal. No case of pneumonia or proteinuria.
In 5 pts steroids were withdrawn within a year and neoral reduced to C2 levels <300 ng/ml: in one patient an acute, but reversible, rejection occurred.
Our preliminary data show that excellent results in term of efficacy can be achieved by the use of an everolimus based immunosuppresive protocol. The safely profile appears satisfactory as well and it is likely to be due to the peculiar pharmacokinetics of everolimus compared to other proliferation signal inhinbitors.

P-84 A 6-MONTH, MULTI-CENTER, SINGLE-ARM, PILOT STUDY TO EVALUATE THE EFFICACY AND SAFETY OF GENERIC TACROLIMUS (TacroBell®) AFTER PRIMARY RENAL TRANSPLANTATION

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Purpose: Tacrolimus has been shown to be an important immunosuppressive agent in organ and bone marrow transplantation. As an immunosuppressive drug, tacrolimus is an equal or superior to cyclosporine. Previously, we reported that there were no statistically significant differences between the pharmacokinetic parameters of the oral formulation of generic tacrolimus (TacroBell®) and the conventional formulation (Prograf®). This study was designed to evaluate the efficacy and safety of oral capsules of TacroBell®, in de novo renal transplantation.
Methods: Ninety-six renal transplant patients from 9 transplantation centers were enrolled between November 2005 and July 2007. *De novo* renal recipients ranged from 19- 65 years old were included. This phase 4 clinical trial was a 26 week, open label, non-comparative, multi-center study.
Results: The acute rejection rate was 10.6% (95% CI: 4.4-16.9%) in the full analysis (FA) set and 12.3% (95% CI: 5.2-19.5%) in the per protocol (PP) set. There were no patient deaths during the study. The 6-month graft survival was 96.8% in the FA set and 97.5% in the PP set.
Conclusion: Based on this study, treatment with TacroBell® is considered to be efficient and safe after primary renal transplantation.

P-85 EXRERIENCE WITH MYFORTIC APPLICATION IN RENAL TRANSPLANT RECIPIENTS

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Purpose: To investigate the efficiency, safety and tolerability of myfortic after renal transplantation.
Materials and methods: This study includes the materials of observation over 183 renal transplant (RT) recipients. The 1st group was comprised of 83 pts, who had been receiving myfortic since the tranplantation in combination with prednisolone and neoral. The 2nd group was comprised of 100 pts, who were switched over from mophetyl mycophenolate or azathioprine to myfortic after 57.3±48.6 mo after RT. The duration of observation was 6 mo.The efficiency of immunosuppression was evaluated by the rates of acute rejection (AR), patients' and RT survival. For the analysis of myfortic tolerability, the frequency of detection of adverse effects and frequency of dose reduction/drug withdrawal were taken into account.
Results: In group 1, AR were detected in 8.4% of patients. The 6-month patients and RT survival were 98.7% and 98.7%, respectively. One patientt has died due to sepsis. One RT was removed because of the tumor process. Infections were developed in 44.5% of patients, hepatic disorders in 13%, leucopenia in 12%, gastrointestinal disorders in 7.2% of cases. The myfortic dose was reduced in 7 (8.4%) of patients.
In group 2, AR were not found. The 6-month patient survival was 100%, and survival of RT was 98%. Infections in this group occurred in 27% of patients, liver dysfunction in 6%, gastrointestinal disorders in 10% and leucopenia in

11% of cases. In 13% of patients myfortic dose was reduced, and in 3 of those the drug was cancelled completely thereafter.
Conclusions: Therefore, preliminary results of the study confirmed data by other authors about high efficiency and safety of myfortic as a basic immune suppressive drug after RT. The adverse effects of the drug can restrict its application to only limited number of patients.

P-86 A PHASE 2b, OPEN-LABEL, MULTI-CENTER, PROSPECTIVE, RANDOMIZED STUDY TO COMPARE THE PHARMACOKINETICS AND SAFETY OF LCP-Tacro™ TABLETS ONCE-A-DAY TO PROGRAF® CAPSULES TWICE-A-DAY IN *DE NOVO* LIVER TRANSPLANT PATIENTS

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LCP-Tacro™ (tacrolimus, LifeCycle Pharma A/S) is an extended release tablet formulation of tacrolimus designed for once daily (q.d.) administration. In a previous Phase 2 conversion study in stable liver transplant patients, LCP-Tacro tablets showed 31% greater bioavailability, reduced Cmax/Cmin ratio and robust AUC to Cmin correlation (0.94) as compared to Prograf® capsules (tacrolimus, Astellas). The present Phase 2b study will evaluate tacrolimus exposure (AUC0-24, Cmax, C24) and safety in *de novo* adult liver transplant recipients randomized to LCP-Tacro tablets q.d. vs. Prograf capsules b.i.d. Eligible patients are male or female, $\geq$18 years old, with calculated MELD $\leq$30 at the time of transplantation and CIT $\leq$10 hrs, who received a whole liver allograft from a deceased donor. Patients are randomized (1:1) within 72 hrs after transplantation to LCP-Tacro tablets 0.07-0.11 mg/kg q.d. (0.09-0.13 mg/kg for African-Americans) or Prograf capsules 0.10-0.15 mg/kg/day in two divided doses (b.i.d.), with the first dose administered within 72 hrs after reperfusion of the graft. Subsequent doses of are adjusted to maintain whole blood tacrolimus trough levels of 5-20 ng/mL. 24-hour PK is obtained on D1, D7 and D14 with periodic trough level and efficacy/safety monitoring through M12 post-transplant. 24 of 60 eligible patients have been randomized to date (LCP-Tacro 13, Prograf 11). 7 SAEs have been reported; 3/7 were suspected to be related to the study medication (aphasia, D3 [LCP-Tacro]; hyperglycemia, D16 [Prograf]; elevated creatinine D44 [LCP-Tacro]). No deaths or graft losses have been reported. At presentation, the PK results including data on dosing and AUC vs. trough correlations for all patients for the first two weeks will be presented. (Sponsored by LifeCycle Pharma A/S. ClinicalTrials.gov NCT00772148).

P-87 A PHASE 2, OPEN-LABEL, MULTI-CENTER, PROSPECTIVE CONVERSION STUDY TO COMPARE THE PHARMACOKINETICS AND SAFETY OF LCP-Tacro™ TABLETS ONCE-A-DAY TO PROGRAF® CAPSULES TWICE-A-DAY IN STABLE LIVER TRANSPLANT PATIENTS: RESULTS AT 12 MONTHS

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LCP-Tacro™ tablets (tacrolimus, LifeCycle Pharma A/S) is an extended release formulation of tacrolimus designed for once-daily (q.d.) administration. This study assessed the pharmacokinetics (Cmax, C24, and AUC0-24), and safety of q.d. LCP-Tacro tablets vs. twice daily (b.i.d) Prograf® capsules (tacrolimus, Astellas) in stable liver transplant patients. Following one week of observation on a stable dose of b.i.d. Prograf capsules, baseline 24-hour tacrolimus PK assessment was performed on D7 followed by conversion to q.d. LCP-Tacro tablets on D8 and a 2-week period of observation with 24-hour PK assessments on study D14 and D21. Among 57 evaluable patients, LCP-Tacro showed $\sim$31% greater bioavailability, mean conversion ratio 0.71 (LCP-Tacro:Prograf; range 0.67-0.80) representing $\sim$30% reduction in daily tacrolimus dose, a lower Cmax/Cmin ratio than Prograf capsules with good tolerability and robust AUC to Cmin correlation (0.94). After completion of the PK evaluation on D22, patients were allowed to continue in a 50-week extension study (total 52 weeks on LCP-Tacro). 24-hour PK assessment was repeated at W26. At W6, 10, 18, 26, 39 and 52, vital signs, safety labs, urinalysis, tacrolimus trough levels, concomitant medications and adverse events were assessed. 49 patients enrolled in the extension study; 6 patients discontinued prematurely and 43 continue on q.d. maintenance with LCP-Tacro with good tolerability. 4 patients exhibited serious adverse events (anteroseptal infarct, D11; abdominal pain, D143; fever, D90; metastatic carcinoma of unknown origin, D232); none were suspected to be related to the study medication. One patient experienced a mild BPAR on D45. No deaths or graft losses have been reported. PK results at W26 and 12-month safety/efficacy will be presented. (Sponsored by LifeCycle Pharma A/S. ClinicalTrials.gov NCT00608244)

P-88 SOTRASTAURIN, A NOVEL PROTEIN KINASE C-INHIBITOR, IN COMBINATION WITH TACROLIMUS: PHARMACOKINETIC INTERACTION IN RENAL TRANSPLANT RECIPIENTS

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Preparing for studies combining sotrastaurin with tacrolimus, a drug-interaction study was conducted in healthy subjects and subsequently PK data was assessed in a multicenter phase 2 study.
Methods: *Healthy subject study:* 20 subjects received in a randomized order, 400mg sotrastaurin or 7mg tacrolimus or their combination. Sotrastaurin increased tacrolimus AUC from 322$\pm$117 to 594$\pm$142 ng.h/ml ($p<0.001$) without effecting the half-life.
Clinical study: 216 *de novo* renal transplant recipients, randomized into study CAEB071A2203, received [arm-1] standard-exposure tacrolimus with MPA (n=74); [arm-2] standard-exposure tacrolimus with sotrastaurin 200mg bid (n=76); or [arm-3] reduced-exposure tacrolimus with sotrastaurin 200mg bid (n=66). Initial tacrolimus C0-levels were targeted between 8-15 or 5-8 ng/mL for standard-exposure or reduced-exposure respectively, with down-tapering thereafter.
Results: In the entire study population tacrolimus C0-levels were similar for arm-1 and arm-2 (p=0.70), however, doses were lower in arm-2 (p=0.02). Dose normalized C0-levels in all three arms determined the extension of interaction on tacrolimus C0-levels as tacrolimus doses in arm-2 and arm-3 were 15% and 24% lower compared to arm-1 (p=0.07 and 0.003).
In a PK-substudy (n=85) of study CAEB071A2203, AUCs were similar in arm-1 and arm-2 (p=0.07) but with a corresponding lower tacrolimus dose in arm-2 (p=0.06). Consequently, dose-normalized AUCs were statistically different (p=0.01). Comparable AUC/dose-relationships between arm-2 and arm-3 (p=0.78) indicate similar interaction of sotrastaurin with tacrolimus regardless of the target tacrolimus exposure (Table).

	[Arm-1]	[Arm-2]	[Arm-3]
Dose (mg bid)	6.4$\pm$3.2	4.7$\pm$2.2	3.3$\pm$1.6
AUC (ng·h/mL)	143$\pm$56	161$\pm$69	107$\pm$45
AUC/dose (ng·h/mL/mg)	26$\pm$10	40$\pm$21	41$\pm$26

Conclusion: Firstly, we showed that sotrastaurin increases tacrolimus C0-levels by <2-fold. Secondly, lower tacrolimus doses are needed in combination with sotrastaurin versus with MPA to achieve tacrolimus target C0-levels Finally, this interaction could already be compensated for in the first week post-transplantation.

P-89 TOLERABILITY OF MYCOPHENOLATE MOFETIL IN MAINTENANCE LIVER TRANSPLANT RECIPIENTS: A 10-YEAR SINGLE CENTRE EXPERIENCE

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Introduction: Mycophenolate mofetil (MMF) is one of the cornerstone immunosuppressive drugs after liver transplantation (LT). Its major interest is related to a specific toxicity profile, different from that of calcineurine inhibitors (CNI). The aim of this retrospective study was to evaluate the tolerability of the addition of MMF in maintenance LT recipients.

Patients and methods: From January 1996 to January 2006, in our centre, MMF was introduced after LT in maintenance patients because of (1) histological features of rejection, i.e. insufficient immunosuppression, or (2) CNI toxicity, (renal impairement, diabetes, hyperlipemia, ...) in order to reduce CNI dosage.
Results: The study population included 208 patients, of median age 54±9, and the median delay between LT and MMF introduction was 54±43 months (ranging 2 to 181 months). The median dosage of MMF was 750 mg per day at initiation and 1170 mg at the end of follow-up.
After a median follow-up of 50±26 months, 26.4% of the patients under MMF did present at least one side-effect and MMF discontinuation rate was 13.8% (transient in 3.8%). The main side-effects were: digestive disorders (45%), pruritus ± rash ± mucitis (12,7%), or myelosuppression (16,4%). MMF withdrawal was due to: digestive disorders (17,2%), pruritus ± rash ± mucitis (17,2%), or myelosuppression (24,1%).
Biological data analysis disclosed no significant difference between initial and final values of WBC, Hb, platelets or GFR.
Conclusion: Our results from a large cohort with a long term follow-up suggest that the tolerability of MMF introduction in LT maintenance recipients is good. Approximately a quarter of the patients presented significant side-effets, from which digestive disorders were the most frequent. These side-effects led to treatment discontinuation in 10% of the patients.

P-90 PREOPERATIVE ANTILYMPHOCYTE THERAPY: EFFECT ON DAMP'S AND RENAL TRANSPLANT OUTCOME

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Initial immunosuppressive regimen may have a significant impact on long-term allograft function. Already in the donor existing dangerous molecules (DAMP's) are leading to activation of the innate immune response. We investigated the long-term follow up after renal transplantation using indoleamine 2,3 dioxygenase (IDO) and high motility group box-1 (HMGB-1) and the relationship of DAMP's to delayed graft function (DGF). The distinctive feature was the availability of donor sera.
Patients and methods: In a consecutive group of patients transplanted between 10/1989 and 06/1992 (n=194) treated either with quadruple drug induction (QDT, n= 142; ATG-F, CsA, AZA, MP) or triple drug (TDT, n=52; CsA, AZA, MP) as immunosuppressive therapy. Donor sera in 139 patients were available.
Results: There was a significant difference between HMGB-1 in PF vs. DGF. This was found even after 14 days after transplantation (2,23±1,28 ng/ml vs. 7,65±1,08ng/ml) and days till creatinine was below 200mmol/l (9,66+10 (PF) vs. 25,8+14 (DGF)). The correlation between HMGB-1 and DGF was r^2=0,718. With IDO we differentiated two groups of patients, all with no surgical failures, no delayed graft function, no rejection episode and no CMV-reactivation within the first 2 months: Gr. I (n=32) with IDO levels $<$4,0 μmol/L, Gr.II (n=29) $>$5,0 μmol/L at day 21 and thereafter at least for 3 times. There was no statistic difference in demographic data. Gr. I showed 1/5/10 year graft survival of 100/89/71% vs. Gr.II with 87/54/31% ($p<0,001$ at year 5 and 10, all data death censored).
Conclusion: Monitoring of IDO is a novel non-invasive tool of immune monitoring with the potency of discrimination concerning long-term function. Acute rejection is associated with an early increased serum concentration prior creatinine. HMGB-1, already existent in the donor, is supporting the idea of pretreatment to suppress immune reactions in the donor.

P-91 SAFETY OF RITUXIMAB THERAPY FOR PREVENTION OR TREATMENT OF ACUTE HUMORAL REJECTION AFTER RENAL TRANSPLANTATION

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Rituximab (RTX) is used in renal transplant recipients (RTR) for desensitization, induction therapy for positive crossmatch and to treat acute humoral rejection (AHR). Its safety is still controversial in this population.
We retrospectively analyzed 37 RTR treated with RTX between 2005 and 2007 for desensitization (5,4%), induction therapy (51,4%) or AHR (43,2%). The first RTX injection consisted in 375mg/m^2 with subsequent weekly injections until a CD19 count is $<$5/mm^3. Patients received antithymocyte globulins (62%) or basiliximab (38%), and mycophenolate mofetil, steroids and either tacrolimus (89%) or cyclosporine (11%). Plasmapheresis and Iv Immunoglobulins (IvIg) were associated.
Population (15 males and 22 females, with a mean age of 43.3 yrs) were followed for 820±327 days. The number of RTX injection was 1 (54%), 2 (37,8%), 3 (5,4%), or 4 (2, 8%). Initial safety was excellent. At the end of the follow-up, patient and graft survival was 92% and 88%. Surgical complications occurred in 11 patients (6 urological and 5 gastrointestinal including 1 fatal ulcer perforation). We observed 33 infectious complications in 22 patients. Bacterial infections were present in 23/33 (6 pneumonitis, 5 septicemia, 5 GI tract, 5 skin infections, and 2 pyelonephritis). Opportunistic infections were reported in 9 patients (2 PCP, 1 CMV disease, 5 BK virus replication with 4 nephropathy and 1 HCV recurrence (among 9 HCV+ and 2 AgHBs+). There was no correlation between infectious complications and the number of RTX injection and/or the CD19 counts.
In conclusion, even though the graft and patient survival remain within the usual range, RTX treatment of humoral complications is associated with a high incidence of infections including opportunistic infections. A specific follow-up and prophylaxis approach should be considered in this population.

P-92 EVEROLIMUS (EVL)-INDUCED PNEUMONITIS IN PATIENTS WITH A PAST HISTORY OF SIROLIMUS (SRL) PNEUMONITIS

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Introduction: Resolution of Sirolimus (SRL)-induced pneumonitis after conversion to everolimus (EVL) has been already reported. However, EVL may also be associated with pneumonitis. We report here EVL pneumonitis in 3 renal transplant recipients (2 male, 1 female).
Patients: Mean age at the time of diagnosis was 58.614.6 years. Among them, 2 patients already experienced SRL-induced pneumonitis. The indication for EVL introduction was cancer, chronic nephropathy and BK nephropathy with a mean delay of 4127 months after transplantation. Symptoms occurred 211147 days after EVL introduction. The initial clinical symptom was fever in all patients, associated with dyspnea and cough in one. Bilateral crepitus were found in 2 patients. Laboratory tests found high C-reactive protein levels (11519 mg/L) and anemia (10.71,1 g/dL). Mean EVL blood through level at diagnosis was 9.4 ng/ml ranging from 7.5 to 13.2 ng/ml. Two patients had bilateral alveolar or alveolo-interstitial pulmonary infiltrates on radiography and CT scan, predominantly in the lower lobes. The other patient had only small ground-glass opacities. BAL was performed in all cases and exhibits hypercellularity (0.336×10^9 cells/L) with predominance of macrophages. In all cases, no infectious agent was found whereas intrapulmonary hemorrhage was present in one patient. EVL therapy was discontinued in all 3 cases with clinical and biological improvement within 72 hours and one week.
Conclusion: EVL-induced pneumonitis should be considered as a possible complication of such treatment. Patients receiving EVL should be carefully selected and monitored including chest CT scan, especially when a past medical history of SRL-pneumonitis is present. In this setting, one should carefully assess the risk-benefit ratio of this maneuver.

P-93 HISTOLOGICAL RECURRENCE OF HENOCH-SCHONLEIN PURPURA AFTER RENAL TRANSPLANTATION IS FREQUENT BUT NOT ASSOCIATED WITH NEGATIVE CLINICAL OUTCOME

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Henoch-Schonlein purpura (HSP) recurrence after renal transplantation (RT) has been reported in 35% of patients with 11% graft loss at 5 years. The incidence of histological recurrence is currently unknown. We investigated this incidence using routine renal biopsy (RRB).
RTR with biopsy proven HSP as initial nephropathy were included. Histological recurrence was defined as either optical deposition or IgA deposits visualized by immunofluorescence (IF) within the mesangium and/or along the glomerular capillary walls.
We included 13 patients (11 males and 2 females) receiving 18 RT (5 patients had 2 RT) between 1988 and 2008 with a follow-up of 95 months (range 13-1294). RB of native were available in 10 patients exhibiting grade 2 (n=2), 3a (n=1), 3b (n=3), 4 (n=3) and 5 (n=1) nephropathy (Pillebout et al, JASN). Patient survival was 100% and no graft loss was related to recurrence (1 acute and 4 chronic rejections). RRB were performed at M3 and M12 and when clinically indicated. On 64 biopsies available, histological recurrence with mesangial deposition was diagnosed in 8/13 (62%) patients and 11/18 grafts (61%) with IgA deposition on IF in 10 grafts. 3 patients with recurrence on their first grafts present recurrence on the 2nd graft. There was no correlation between the histological characteristics on the native kidney and the recurrence. The mean delay for recurrence was 16.4 months (range 1-60 months). All the re-

currence but one were not associated with clinical or biological signs. At the last follow-up, serum creatinine in all patients was 152 μmoles/L.
When routine RB are performed, histological recurrence of HSP is frequent but usually not associated with clinical signs. Short term prognosis of recurrence is good but remains to be determined in the long term.

P-94 MANAGEMENT OF LATE RISING CREATININES IN KIDNEY TRANSPLANT RECIPIENTS: THE BENEFITS OF A PROACTIVE APPROACH

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The advent of calcineurin inhibitors (CNI) was associated with significant improvements in kidney transplant outcomes in the first year but also increasing chronic allograft nephropathy and late graft failure. A lot has been published about CNI minimisation/avoidance but many clinicains remain wary of late rejection.
We looked at the outcomes of two groups of long term renal transplant recipients with documented rising creatinine. Of 108 randomly selected patients transplanted between 1997 and 2007, two separate groups were identified: Those with rising creatinines that eventually stabilised or improved (Group I) and those that did not (Group N).
Methods: Case notes were retrospectively studied, extracting details of immunosuppression, creatinine and strategies employed to manage any rise and graft outcomes and compared with Student t test.
Results: 33 patients were identified. Of these, creatinine improved in 17 (Group I) and did not ion 16 (Group N). Both groups were similar in terms of graft age, initial creatinine and initial immunosuppression. Patients in the improved group (I) were more likely to have had a biopsy or their CNI changed. These patients also achieved a significantly lower mean tacrolimus level (p=0.028) than those that saw no improvement. 37.5% of the grafts in the Group N (not improved) failed within the follow up period compared to 11.8% in Group I. Most of the graft failure was due to CNI toxicity/CAN. Reassuringly, there was no episode of rejection in the improved group (I).

Baseline characteristics, CNI management and graft outcomes in the two groups

	Group N no improvement	Group I improvement	P (95% CI) Student T test χ^2
Total number (N)	16	17	
Mean Length of follow up (years	5.89 (0.5-10.8)	4.98 (1.2-7.9)	P=0.202
Mean Initial creatinine (mmmol/L	176.33	160.23	P=0.345
CNI eliminated	2 (12.5%)	5 (29.4%)	P=0.22
Mean initial trough tacrolimus (ng/ml)	14.04 (6.5-25.1)	12.2 (7-17.9)	P=0.63
Mean final trough tacrolimus (ng/ml)	9.82 (6.1-16)	5.36 (1.6-8.1)	P=0.028
Failed graft	6 (37.5%)	2 (11.8%)	P=0.07

Conclusion: This audit data in real time practice in a district general hospital supports the evidence for proactive measures in a "creeping creatinine" scenario. These measures include CNI minimisation to achieve much lower trough levels and biopsy to confirm diagnosis and consider CNI elimination. These measures do not seem to be associated with increased rates of late rejection.

P-95 OSELTAMIVIR PROPHYLAXIS REDUCES THE OCCURRENCE OF INFLUENZA INFECTION IN TRANSPLANT RECIPIENTS

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Purpose: Influenza causes considerable morbidity and mortality in transplant recipients, who are immunocompromised and may not derive full protection from vaccination. In this population, antiviral prophylaxis could be beneficial. We investigated the efficacy and safety of oseltamivir (Tamiflu) for the seasonal prophylaxis of influenza in transplant patients.
Methods/Materials: When influenza was circulating, solid organ (SOT; liver, kidney or both) or allogeneic haematopoetic stem cell transplant recipients aged ≥1 year who were rapid test-negative for influenza and without influenza-like symptoms at baseline were recruited. Subjects were randomised to receive either oseltamivir (75mg for those ≥13 years or recommended weight-based unit doses for children 1–12 years) or placebo, taken once daily for 12 weeks in capsule or suspension form. The primary endpoint was the incidence of laboratory-confirmed clinical influenza (LCCI). Clinical symptoms were defined as fever >37.2°C, cough and/or nasal congestion.
Results: Most of the 477 subjects enrolled were male (66%), adult (96%), unvaccinated (60%) and SOT recipients (81%). In the intent-to-treat population, there was a lower incidence of LCCI with oseltamivir (1.7% [4/237] vs 2.9% [7/238] with placebo; p=0.544). Significantly fewer oseltamivir recipients had laboratory-confirmed influenza by RT-PCR (2.1% vs 8.4% with placebo; 95% CI: 2.3%, 10.7%), equating to a protective efficacy of 75%. Rates of serious adverse events (oseltamivir 8%; placebo 10%) and adverse events [AEs] (oseltamivir 55%; placebo 58%) were comparable. Gastrointestinal disorders (oseltamivir 21%; placebo 22%) were the most commonly reported on-treatment AEs. More placebo than oseltamivir recipients withdrew due to AEs (6% vs 3%, respectively). There were four cases of transplant rejection (all SOT recipients on placebo). Two deaths occurred, both in the placebo arm. No oseltamivir-resistant virus was detected.
Conclusions: Oseltamivir prophylaxis reduces the incidence of seasonal influenza infection in transplant recipients, and is generally well tolerated.

P-96 THE SUCCESSFUL TREATMENT OF ASPERGILLOSIS BY MONITORING INTRACELLULAR CYCLOSPORINE CONCENTRATION IN RENAL TRANSPLANT

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Antifungal agents are essential drug in the treatment of fungal infection in renal transplant. They are inhibitors of CYP3A4 and *p*-glycoprotein and can affect pharmacokinetics of calcineurine inhibitor. It is, therefore, hard to decide the proper dosage of cyclosporine in treating the fungal infection in transplant. We experienced a patient who has cutaneous and pulmonary aspergillosis, even the trough level of cysporine was 5-10 ng/dl, showed good graft fuction with the use of voriconazole.
Purpose: To cope with the pharmacokinetic discrepancy between trough serum and intracellular cyclosporine concentrations, we directly monitored the intracellular concentration of cyclosporine in T cell as a reason of proper immune suppression.
Methods: We measured the patient's genotype of MDR1, CYP3A4, CYP3A5, and CYP2C19 which are drug transporter and metabolizing enzymes regulating the plasma and cellular concentration of cyclosporine and voriconazole. We also compared intracellular cyclosporine concentrations in the absence and presence of voriconazole.
Results: The patient was confirmed that there were no functionally defected alleles in MDR1, CYP3A4, CYP3A5, and CYP2C19 enzymes. The cellular accumulation of cyclosporine was 3.2-fold increased by the presence of voriconazole, compared to that in the absence of voriconazole. Since the IC_{50} value of voriconazole for the inhibition of cyclosporine uptake was 2.2 μM and the expected steady state concentration of voriconazole was 5.7 – 8.6 μM, the coadministration of voriconazole could increase the cellular concentration of cyclosporine through the inhibitory effect of voriconazole on the cyclosporine efflux via P-gp.
Conclusion: Taken together, the increased intracellular concentration of cyclosporine through the P-gp inhibition might be the plausible reason of the successful treatment of aspergllosis while maintaining good graft function of the patient in spite of minimum dose of cyclosporine.

P-97 THE EFFECT OF HIGH DOSE METHYLPREDNISOLONE THERAPY ON *IN VIVO* CYP3A4/5 ACTIVITY AND CALCINEURIN INHIBITOR PHARMACOKINETICS IN RENAL TRANSPLANT RECIPIENTS: A PILOT STUDY

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Introduction: The calcineurin inhibitors (CNI) tacrolimus (Tac) and cyclosporine (CsA) are metabolised by CYP3A4 and CYP3A5. Corticosteroids are known to induce these enzymes, but, at present, our understanding of the effect of high dose corticosteroid administration on *in vivo* CYP3A4/5 activity and the clinical impact of corticosteroid – CNI interactions in renal transplant recipients is limited.
Methods: In this ongoing pilot study *in vivo* CYP3A4/5 activity and CNI pharmacokinetics were studied before and one week after initiation of high dose methylprednisolone therapy in 2 Tac and 2 CsA treated renal allograft recipients experiencing a subclinical acute rejection. At both time-points *in vivo* CYP3A4/5 activity was measured using the erythromycine breath test (EBT,

reflecting hepatic CYP3A4 activity) and orally administered midazolam (MDZ) as a drug-probe (apparent oral MDZ clearance reflecting CYP3A4/5-mediated first-pass metabolism). When clinically feasible (1 Tac and 1 CsA patient) MDZ was administered intravenously as well (systemic MDZ clearance reflecting hepatic CYP3A4/5-activity). Finally, CNI exposure (dose-interval AUC) was determined in all patients at both time-points.

Results: During high dose methylprednisolone therapy systemic MDZ clearance (1.0-1.4 fold), apparent oral MDZ clearance (1.2-2.5 fold, figure 1), EBT (1.0-1.9 fold) and CNI steady state clearance (1.0-1.8 fold) increased, whereas dose-corrected CNI $AUC_{0\text{-}12}$ decreased (0.6-1.0 fold, figure 2) in all patients. Although in some patients changes were rather limited, a marked effect was observed in others.

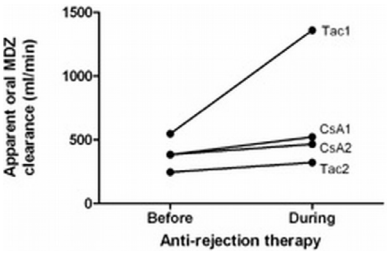

Figure 1. Apparent oral MDZ clearance.

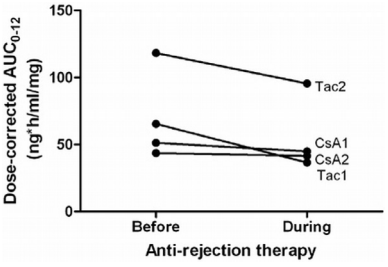

Figure 2. Dose-corrected Tac/Csa AUC_{0-12}.

Conclusion: These preliminary data indicate that in renal allograft recipients *in vivo* hepatic CYP3A4, hepatic CYP3A4/5 and first-pass CYP3A4/5 activity increase during anti-rejection therapy with high dose corticosteroids, resulting in increased CNI clearance. The extent of this induction differs substantially between patients. The implications of these findings for clinical response to anti-rejection treatment need to be assessed

P-98 *IN VIVO* CYP3A4/5 ACTIVITY IS SIGNIFICANTLY HIGHER IN TACROLIMUS TREATED VS. CYCLOSPORINE TREATED RENAL TRANSPLANT RECIPIENTS THREE MONTHS AFTER TRANSPLANTATION

Hylke de Jonge[1], Henriette de Loor[1], Kristin Verbeke[2], Yves Vanrenterghem[1], Dirk R. Kuypers[1]. *[1]Department of Nephrology and Renal Transplantation, [2]Laboratory of Digestion and Absorption and Leuven Food Science and Nutrition Research Centre (LFoRCe), University Hospitals Leuven, Leuven, Belgium*

Introduction/Aim: Both tacrolimus (Tac) and cyclosporine (CsA) inhibit the major drug metabolizing enzymes CYP3A4 and CYP3A5 *in vitro*. However, little is know about the extent of inhibition *in vivo*. Therefore we investigated whether Tac and CsA differentially affect *in vivo* hepatic and first-pass CYP3A4/5 activity in renal transplant recipients using midazolam (MDZ) as a drug probe (Streetman et al. Pharmacogenetics. 2000;10:187-216).

Methods: Two doses of MDZ (1 mg intravenously and 2 mg orally on 2 consecutive days) were administered to 14 male, age matched Tac (n=7) and CsA (n=7) treated renal allograft recipients 3 months after transplantation. Blood samples were collected during 8 hours after MDZ administration and MDZ plasma concentrations were determined by LC-MS/MS. Systemic MDZ clearance (reflecting hepatic CYP3A4/5 activity) and apparent oral MDZ clearance (reflecting CYP3A4/5 mediated first-pass metabolism) were calculated using WinNonlin version 5.2.

Results: Baseline characteristics, including age, weight, concomitant medication, hematocrit, serum albumin levels and renal function, did not differ between groups. All participating patients were homozygous *CYP3A5*3/*3* carriers (CYP3A5 non-expressers). Methylprednisolone doses were similar in all patients. No patient was taking any other drug or substance known to affect CYP3A4/5-activity. Systemic MDZ clearance (median Tac = 422 ml/min vs. CsA = 252 ml/min, p=0.04, figure 1) and apparent oral MDZ clearance (median Tac = 723 ml/min vs. Csa = 384 ml/min, p=0.03, figure 2) were significantly higher in tacrolimus treated renal transplant recipients.

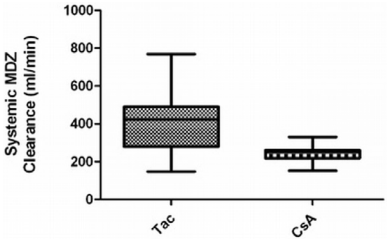

Figure 1

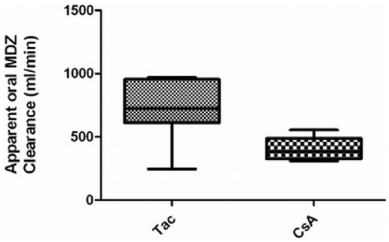

Figure 2

Conclusion: *In vivo* hepatic and first-pass CYP3A4/5 activity early after transplantation are significantly higher in tacrolimus treated as compared to cyclosporine treated renal transplant recipients, suggesting that *in vivo* cyclosporine is a stronger CYP3A4/5 inhibitor than tacrolimus. This finding could have important clinical implications for drug-drug interactions and possibly for calcineurin inhibitor related toxicity.

P-99 IMMEDIATE VERSUS DELAYED EVEROLIMUS TREATMENT IN *DE NOVO* RENAL TRANSPLANT RECIPIENTS AT RISK OF DELAYED GRAFT FUNCTION: 1-YEAR RESULTS OF THE CALLISTO STUDY

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Everolimus, a proliferation signal inhibitor (PSI) has been developed for use in combination with cyclosporine for prevention of allograft rejection after kidney transplantation. We compared effects of immediate (IE) versus delayed (DE) everolimus on a composite primary endpoint of BPAR, graft loss, death or loss to follow-up, delayed graft function (DGF) and wound healing complications (WHC).

Methods: 139 *de novo* deceased donor renal transplant recipients (RTxR) at risk of DGF were randomized to everolimus (1.5mg/day) either from day 1 (IE, n=65) or after 4 weeks of mycophenolic acid (DE, n=74) in combination with cyclosporine (C-2h monitoring). All patients received steroids and anti-IL-2R-antibodies.

Results: Risk factors for DGF in the IE and DE groups respectively were: donor age >55 years in 80% and 90.5%, cold-ischemic-time ≥24h in 30.8% and 33.8% and previous transplantations in 10.8% and 2.7%. The primary composite efficacy failure endpoint at 1 year occurred in 42 (64.6%) IE and 49 (66.2%) DE patients (Table).

Table 1. 1 year incidence of primary efficacy variables

	IE, n=65 (%)	DE, n=74 (%)	P-value
DGF	16 (24.6)	18 (24.3)	1.00
BPAR	13 (20.0)	15 (20.3)	1.00
Graft loss	6 (9.2)	5 (6.8)	0.75
Death	5 (7.7)	2 (2.7)	0.25
Loss to follow up	0 (0.0)	3 (4.1)	0.24
WHC (related to initial transplant)	26 (40)	28 (37.8)	0.86

The creatinine clearance (Cockcroft-Gault) was comparable between groups at 1 year (median; 39.9mL/min IE vs 43.1mL/min DE). Adverse Events/infections leading to study discontinuation occurred in 17 (26.2%) IE and 28 (37.8%) DE recipients.

Conclusion: In deceased-donor RTxR at risk of DGF immediate initiation of everolimus was as effective and safe as delayed everolimus with a similar low incidence of DGF and wound healing disorders.

P-100 THE CLEAR STUDY: A PROSPECTIVE, RANDOMIZED, CONTROLLED, OPEN-LABEL MULTICENTRE 6-MONTH STUDY COMPARING THE EFFICACY AND SAFETY OF A 5-DAY 3-G DAILY MMF LOADING DOSE VERSUS STANDARD 2-G MMF DAILY DOSING IN RENAL TRANSPLANT RECIPIENTS

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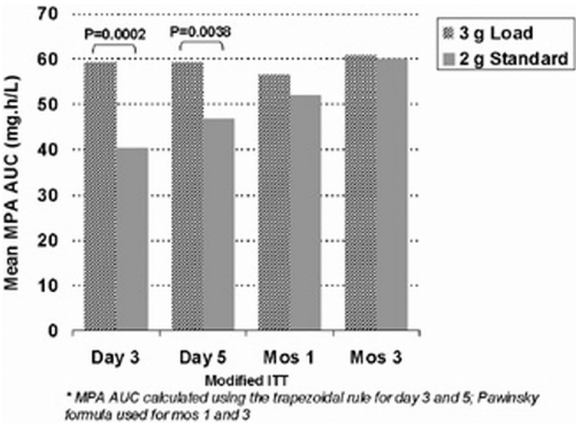
Adequate early mycophenolic acid (MPA) exposure may result in a decreased rate of acute rejection (AR) following renal transplantation.
Purpose: This study was performed to determine if a 5-day 3-g MMF (CellCept®) loading dose increases the proportion of renal transplant patients reaching MPA therapeutic levels (30–60 mg*h/L) by Day 5 versus standard 2-g daily dosing.
Methods: The loading-dose arm (n=68) received MMF 1.5 g BID Days 1–5, then 1.0 g BID; and the standard-dose arm (n=67) received MMF 1.0 g BID. Tacrolimus was adjusted to trough levels of 8–15 ng/mL. All patients received steroids and ~85% received an IL-2 receptor blocker. MPA AUCs were measured at Days 3 and 5 and Months 1 and 3.
Results: At Day 5, 47.5% of the MMF 3-g arm (n=65) achieved the MPA therapeutic window vs. 54.4% of the MMF 2-g arm (n=61, *p*=NS). At Day 3, MPA exposure was <30 mg*h/L in 14.1% of the 3-g arm vs. 33.3% of the 2-g arm (*p*=0.0113) and >60 mg*h/L in 45.3% of the 3-g arm vs. 16.7% of the 2-g arm (*p*=0.0006). Mean MPA AUC was significantly higher in the 3-g than the 2-g arm at Day 3 (*p*=0.0002) and Day 5 (*p*=0.0038), but similar at Months 1 and 3.



This resulted in a trend for fewer suspected and treated acute rejection episodes in the 3-g vs. the 2-g arm at 6 months (*p*=0.0546). No significant differences were seen in common adverse events or MMF discontinuations between groups.
Conclusions: A 3-g intensified dose of MMF increased early mean MPA exposure, decreased acute rejection and was tolerated.

P-101 CONVERSION TO EVEROLIMUS-BASED IMMUNOSUPPRESSION IN MAINTENANCE LIVER TRANSPLANT PATIENTS: RESULTS FROM 94 PATIENTS

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Introduction: The aim of this study was to evaluate the tolerance of the conversion from CNI to everolimus in maintenance liver transplant (LT) recipients.
Patients and methods: From January 2005 to March 2008, everolimus was introduced after LT because of (1) *de novo* or recurrent cancer after LT, (2) pre-existing liver carcinoma on the liver explant, associated with bad histological features or (3) CNI toxicity. CNI dosage was progressively reduced, until discontinuation.
Results: The study population included 94 patients (68 men and 26 women), of median age 57±10. The median delay between LT and everolimus introduction was 5±5 years (ranging 1 month to 17.8 years). The reason for everolimus introduction was adverse effects of CNI in 54% of patients (n=51), previous cancer on liver explant in 11% (n=10), or *de novo* or recurrent post-LT cancer in 35% (n=33). After a median follow-up of 12±7 months, 70% of the patients under everolimus did present at least one side-effect. The median dosage of everolimus was 2 mg per day at the beginning and 3 mg at the end of follow-up. The median trough level of everolimus was 6 μg/ml at the end of follow-up. The main side-effects were: hyperlipidemia (37%), dermatitis (19%), mucitis (15%), proteinuria > 300 mg/day (18%), edema (7%), hematotoxicity (4%, anemia (n=2), neutropenia (n=1), pancytopenia (n=1)) infection (3%), and lymphorrhea (3%). Global everolimus discontinuation rate was 21% (16% because of side-effects) after a median delay of 7±8 months.
Conclusion: Our results suggest that ERL introduction in LT maintenance therapy induces adverse effects in the vast majority of patients. These side-effects usually decreased or disappeared with ERL dosage adjustment, and/or symptomatic treatment, but led to treatment discontinuation in 16% of the patients.

P-102 GLUCOSE METABOLISM FOLLOWING CONVERSION FROM CNI TO SIROLIMUS BASED IMMUNOSUPRESSION IN STABLE RENAL TRANSPLANT RECIPIENTS

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Previous studies have suggested that the discontinuation of CNIs and their replacement with sirolimus is associated with a worsening of glycaemic regulation in renal transplant recipients. However other studies have not reported an increase in new onset diabetes after transplantation when sirolimus was added to CNIs and steroids. The aim of this study was to examine the impact of switching CNIs with sirolimus on renal function and glucose metabolism in patients with renal transplants in a single transplant centre.
Forty two patients underwent abrupt conversion from a CNI based immunosuppression regime to sirolimus based immunosuppressive regime. Sirolimus dose was adjusted to maintain trough levels between 8-12ng/ml. MDRD GFR and fasting glucose were collected on non diabetic renal transplant recipients for 24 months prior to conversion and subsequently for a further 48months. Results are presented as means and standard deviations. Differences between rates of change of quantitative variables were tested by means of linear mixed model tests Tacrolimus was used as primary therapy in 68% of patients.

Month	-24	-12	0	12	24	36	48
GFR (ml/min)	52±16	46±13	44±13	46±12	45±13	43±15	49±17
Glucose (mmol/l)	5.5±0.6	5.4±0.7	5.9±1.0	5.5±0.7	5.9±1.2	5.6±0.8	5.2±0.4

Steroids were used in 71% of patients prior to conversion and 68% of patients following conversion. Following conversion one patient developed NODAT. Fasting glucose levels in the remaining 41 patients showed no deterioration in glycaemic regulation following conversion to sirolimus. Conversion from CNI to sirolimus was associated with a statitically significant improvement in GFR of 2ml/min ($p<0.05$) immediately post conversion and then subsequently stabilised over the subsequent 48month period.
In conclusion the discontinuation of CNIs and their replacement with sirolimus was associated with an immediate improvement in graft function followed by stabilisation of graft function. This study did not observe any significant deterioration in glycaemic control with the switch of CNI s to a sirolimus based immunosuppressive regime.

P-103 RAPAMYCIN AS A THERAPY OF CHOICE AFTER RENAL TRANSPLANTATION IN A PATIENT WITH TUBEROUS SCLEROSIS COMPLEX

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We report the use of rapamycin in immunosuppressive treatment after renal transplantation as a therapy of choice in a patient with diagnosis of tuberous sclerosis complex (TSC). TSC is a genetical disorder, caused by mutations of TSC1 or TSC2 genes. Products of these genes, hamartin and tuberin, create a complex that inhibits mammalian target of rapamycin (mTOR), a key protein engaged in regulation of cell cycle. Mutations of TSC genes lead to constitutive activation of mTOR and result in uncontrolled proliferation, differentiation and migration of cells. In consequence malformations of many organs arise. We present a case of 47 – year – old female TSC patient with multisystem involvement (skin, brain, lungs and kidneys). She has developed end stage renal failure (ESRF) due to angiomyolipomas and subsequent bilateral nephrectomy. At

the age of 44 she started hemodialysis treatment and 10 months later underwent kidney transplantation. Immunosuppressive treatment consisted among others of rapamycin (mTOR inhibitor). Since the patient was discharged from hospital she has remained in a good clinical condition with stable graft function. Clinical evaluation after 2 years treatment with rapamycin revealed significant regression of skin lesions. Whereas brain, chest and abdominal cavity CT image remained stable. No complications of immunosuppressive treatment or TSC were observed. Experimental and clinical studies confirm that rapamycin exerts beneficial effect in TSC, providing new therapeutic option. Therefore immunosuppressive regimen with rapamycin after kidney transplantation should be considered as a treatment of choice in patients with TSC to avoid development or progression of the disease's complications.

P-104 THE IMPACT OF SIMULECT VERSUS LOW DOSE THYMOGLOBULIN INDUCTION ON BK VIRUS VIREMIA

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Introduction: BK virus nephropathy has become one of the most important early complications after kidney transplantation. At our center we have monitored BK virus viremia (BKVV) by PCR in renal transplant patients for years. Our induction therapy consisted of Thymoglobulin induction with MPA, Tacrolimus, and steroid maintenance. Because of concerns about the incidence of BKVV, after informed consent we treated patients with Simulect induction instead of Thymoglobulin and prospectively monitored the incidence of BKVV and acute rejection.
Methods: We enrolled 60 consecutively transplanted patients who were treated with Simulect induction and compared them to109 patients treated with Thymoglobulin transplanted immediately before. The average dosing of Thymoglobulin in the historical cohort was 6.8 mg/kg. The primary endpoint of our study was any positive BK virus PCR in blood.
Results: The six-month rates of acute rejection in the Simulect vs. Thymoglobulin arms were (11% vs 18%, p=0.20). Four patients experienced graft loss prior to six-months in the prospective Simulect patients. Six-month rates of BKVV between the study groups were not significantly different (29% Simulect and 25% Thymoglobulin, p=0.60). 6/56 patients (11%) in the Simulect arm and 16/109 (15%) in the Thymoglobulin arm had viremia rates >10000 units (p=0.48). The proportion of patients with positive BKVV was higher among patients with >5 doses of Thymoglobulin as compared to <5 doses (31.1% vs 20.3%) but not statistically significantly different (p=0.20). Acute rejection rates were similar (19% vs 18%) between high and low-dose Thymoglobulin groups.
Conclusions: Contrary to our expectations the switch from Thymoglobulin to Simulect induction did not impact the incidence of BKVV. Among Thymoglobulin treated patients a reduction in dose from 5 to 3 doses reduced the incidence of BKVV. From our study, there also was not a difference in acute rejection between low-dose Thymoglobulin and Simulect.

P-105 INCIDENCE OF DELAYED GRAFT FUNCTION (DGF) IN SIROLIMUS (SRL)–BASED REGIMENS COMPARED WITH CALCINEURIN INHIBITORS (CNIs) AND MYCOPHENOLATE MOFETIL (MMF) IN DE NOVO RENAL ALLOGRAFT RECIPIENTS

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Purpose: Several reports suggest that use of SRL may increase the incidence of DGF and prolong recovery of renal function. We present the incidence and duration of DGF from 2 large, multicenter trials in renal transplant patients receiving de novo SRL-based regimens versus CNIs and MMF.
Methods: DGF data were analyzed from 2 SRL-based studies that enrolled a total of 918 renal transplant recipients. The ORION trial compared 3 treatment groups: SRL+TAC elimination at week 13 (n=152); SRL+MMF (n=152); and TAC+MMF (n=139). The 318 trial compared SRL+MMF (n=314) and CsA+MMF (n=161). All patients received steroids and daclizumab (ORION trial) or basiliximib (study 318). Patients with donor organ cold ischemia time >30 hours or those from non-heart beating donors were excluded. DGF was defined as the need for dialysis within the first 7 days after transplantation and recovered graft function. Duration of DGF was defined as the number of days from transplantation to date of recovery or date of last dialysis. Because of higher than expected acute rejection rates in the SRL+MMF group, study 318 and the SRL+MMF group in the ORION trial were prematurely terminated.
Results: The incidence and duration of DGF were similar between treatment groups in each study (see Table). Mean recipient and donor age was similar among groups in each study. Mean cold ischemia time was approximately 12 hours in the ORION trial and 11 hours in study 318. Of note, approximately 60% of patients were recipients of deceased donors (DD) kidneys in each study.

	ORION Trial				318 Trial		
	SRL + TAC-Elim	SRL+MMF	TAC+MMF	p-Value	SRL+MMF	CsA+MMF	p-Value
	All Donors				All Donors		
DGF, % (n)	13.2 (20/152)	17.2 (26/152)*	15.1 (21/139)	0.736* 0.630†	18.5 (58/313)*	19.3 (31/161)	0.681
Mean duration of DGF, days +SD	13.8 ± 14.6	14.9 ± 16.1	9.0 ± 8.1		9.9 ± 9.1	8.5 ± 7.1	
Median duration of DGF, days (min-max)	10.0 (1.0-62.0)	9.0 (2.0-63.0)	7.0 (1.0-32.0)	0.615* 0.230†	7.5 (1.0-43.0)	7.0 (1.0-29.0)	0.564
	Deceased Donors				Deceased Donors		
DGF, % (n)	19.5 (17/62)	27.1 (26/96)	22.5 (23/99)	0.582* 0.580†	27.4 (51/186)	26.9 (29/92)	1.000
Mean duration of DGF, days +SD	13.9 ± 15.5	14.9 ± 16.1	8.9 ± 8.3		10.1 ± 9.5	7.6 ± 6.5	
Median duration of DGF, days (min-max)	11.0 (1.0-62.0)	9.0 (2.0-63.0)	7.0 (1.0-32.0)	0.482* 0.190†	7.0 (1.0-43.0)	6.0 (1.0-29.0)	0.378
	Living Donors				Living Donors		
DGF, % (n)	5.0 (3/60)	0 (0/56)	2.9 (1/62)	0.624* 0.470†	5.5 (7/127)	0.0 (0/69)	0.282
Mean duration of DGF, days +SD	7.3 ± 6.8	--	11.0		8.9 ± 5.7	12.5 ± 8.7	
Median duration of DGF, days (min-max)	5.0 (2.0-15.0)	--	11.0	1.000*	8.0 (1.0-17.0)	10.0 (3.0-28.0)	0.484

*Patient excluded from analysis because of withdrawal from study at day 7.
†Patient excluded because withdrawal from study at day 1.
*SRL+TAC-Elim vs. TAC+MMF; †SRL+MMF vs. TAC+MMF.

Conclusions: No significant differences in the incidence or duration of DGF were observed between treatment groups in the 2 randomized, multicenter studies when de novo SRL therapy was compared with CNI-based therapy.

P-106 EVALUATION OF MYCOPHENOLIC ACID EXPOSURE DURING MYCOPHENOLATE MOFETIL THERAPEUTIC DRUG MONITORING IN KIDNEY TRANSPLANTATION

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Purpose: We present the results of Mycophenolate mofetil (MMF) therapeutic drug monitoring (TDM) in kidney transplantation in Saint-Etienne University Hospital. After mycophenolic acid (MPA) quantification and AUC estimation, we proposed doses adjustments to physicians when required.
Method: We studied AUC estimations in kidney transplantation since December 2007. We used a limited sampling strategy for determination of AUC0-12h. Blood samples were drawn at 0.5, 1 and 3 hours post dose according to pharmacokinetic model predictions. MPA plasma levels were evaluated by validated LC MS/MS method.
AUC computation was performed in ADAPT II software (BMSR, CA, USA) with Bayesian estimator. A two compartments pharmacokinetic model with gamma distributed absorption time was used.
Results: Since December 2007, 296 MPA AUC were prescribed by physicians, 194 were evaluated during early post transplantation period or long term follow-up. MMF was associated with tacrolimus. MMF doses regimen were 250, 500 or 750 mg bid in most cases. Post transplantation delay ranged from 5 to 8395 days.
The mean AUC 0-12h was 40.5±19.4mg/L*h [8.4 -115.8]. A third of estimated AUC was below and 16% above the therapeutic range. We proposed 54 dose adjustments, only 5 were followed and successful. 48 dose adjustments were not followed or reevaluated. 1 dose adjustment was not pertinent. We found a significant correlation between AUC0-12h and dose per kg for 12h ($p<0.001$), suggesting that a dose below 4mg/kg/12h is associated with underexposure.
Conclusions: This first experience of MMF TDM in our hospital was judged successful by both Physicians and Pharmacologists. We observed that 51% of patients were out of therapeutic range and that some underexposure to MPA should be prevented by a minimum dose/kg/12h. Further improvements of our dose adjustment system are needed with more interactions with physicians to be fully efficient.

P-107 DE NOVO MALIGNANCIES OF KIDNEY TRANSPLANTED PATIENTS TREATED WITH THE PROLIFERATION SIGNAL INHIBITORS (PSI)

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This risk of de novo malignancies in kidney transplant recipients is increasing over time correlating with overall immunosuppressive exposure. The proliferation signal inhibitors have unique immunosuppressive properties; inhibit the proliferation of different cell lines, prohibit the apoptosis of the tumour cells,

have inhibitory effect on the malignant cells' growth. We investigated the effect and safety of proliferation signal inhibitors (PSI) in malignancies.
87 kidney transplanted patients were treated with PSI-Sirolimus (SRL). 9 patients had malignant tumour prior to transplantation, 78 patients developed de novo tumour. In anamnestic tumours time between diagnosis of tumour and transplantation was: 96,55±57,62 months, time since transplantation: 29,88±9,946 months. In de novo malignancies average time from transplantation to diagnosis of tumour was 56,8±47,2 months. Since diagnosis of tumour 33,03±29,46 months elapsed. Serum creatinine, eGFR, triglyceride, cholesterine before and after conversion to Sirolimus were compared.
Out of 14 kidney tumour patients 11 patients are still alive with a stable graft function, 2 patients died, 1 returned to dialysis. Out of 8 breast cancers 6 are alive with a good kidney function, 2 patients died. In the group of 8 pulmonary tumour patients 6 died. The time between diagnosis of tumour and death was 14,33±12,81 months. 2 patients are still alive 13 and 25 months after the tumour diagnosis. Altogether 34 patients died, time from the diagnosis of tumour was 24,82±27,14 months. Cause of death was propagation of the tumour (60%), cardiovascular, pulmonary embolism, pneumonia, tuberculosis, ileus etc. (40%).
Sirolimus therapy was safe; we did not have any acute rejection. No tumour recurrence was found. The combination of SRL- Mycophenolate mofetil or SRL-steroid was well tolerated and safe. We suggest the conversion to Sirolimus in kidney transplanted patients with malignant tumours.

Experimental immunosuppression

P-108 EVEROLIMUS-INDUCED DELAYED HEALING OF EXPERIMENTAL COLONIC ANASTOMOSES IS ASSOCIATED WITH PROLONGED INFLAMMATION

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Background: Delayed wound healing is one of serious side effects of mTOR-inhibitor based immunosuppression after organ transplantation. The aim of this study was to determine the effect of the mTOR-inhibitor everolimus on healing of colonic anastomoses and to investigate its underlying mechanism of action.
Materials and methods: Thirty male Sprague-Dawley-rats received a distal colonic anastomosis. Then, animals were randomized to three groups of daily treatment with either vehicle [V] or everolimus in two different dosages (1.0 mg/kg [E1]; 3.0 mg/kg [E2]). After 7 days, rats were sacrificed, the anastomoses were resected in toto and mechanical, histological and biochemical parameters for intestinal wound healing were assessed.
Results: Therapeutic levels of everolimus were obtained only with a dosage of 3.0 mg/kg (E1: 1.48±0.29; E2: 4.90±0.39 ng/ml). The anastomotic bursting pressure was significantly decreased by everolimus in both dosages (V: 143±17 [122-174]; E1: 117±25 [68-151]*; E2: 104±30 [45-146]* mmHg, *: $p<0.05$ vs. V) whereas hydroxyproline content was reduced only by the high everolimus dosage (V: 9.8±2.5 [5.5-13.7]; E1: 10.1±3.1 [6.5-13.9]; E2: 6.2±2.7 [3.1-10.8]* μg/mg dry weight; *: $p<0.05$ vs. V). Everolimus diminished cellular proliferation and new vessel growth and worsened the structure of the newly synthesized collagen fibers in the anastomotic granulation tissue. MPO-positive cells and IL-6 concentrations were increased as well as the activities of MMP-2 and MMP-9 in everolimus treated animals.
Conclusion: Everolimus impairs intestinal healing as shown by a reduction in anastomotic bursting pressure and collagen deposition. Prolonged inflammatory activity seems to be involved in the mechanism of how everolimus delays anastomotic healing in rats.

P-109 B-CELL DEPLETION DURING ALLOGENEIC SENSITIZATION LESSENS SECOND-SET REJECTION

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Background: The effects of B-cell depletion on allogeneic immune responses have not been well investigated.
Methods: A murine model of B-cell depletion was created using SCID/beige mice reconstituted with BALB/c splenocytes ex vivo depleted of B cells (B/c-SCID-B^-) or not (B/c-SCID). The B/c-SCID-B^- and B/c-SCID mice were then primed with C57BL/6 skin grafts and then sacrificed for immune assays 6 weeks after skin grafting.
Results: Before adoptive transfer, the BALB/c splenocytes with B-cell depletion were capable of comparable proliferation responses with those without depletion when stimulated with ConA. And, the skin graft survival in B/c-SCID-B^- and B/c-SCID mice were not significantly different (around 20 days). Six weeks after skin transplantation, flowcytometric analyses demonstrated that B-cell depletion reduced the percentage of central memory T cells (either $CD4^+CD44^+CD62L^+$ or $CD8^+CD44^+CD62L^+$) in the spleen of the B/c-SCID-B^- mice primed with skin grafts. Additionally, IFN-γ production of the splenocytes from the C57BL/6 skin graft-primed B/c-SCID-B^- mice was significantly reduced (p=0.0028 at 24h and p=0.0102 at 48h), as compared to the splenocytes from the B/c-SCID mice. The survival time of C57BL/6 heart grafts was significantly longer (p=0.0006) in SCID/beige reconstituted with B/c-SCID-B^- splenocytes (8.5±1.1 days) than that of the SCID/beige mice reconstituted with B/c-SCID splenocytes (6.0±1.1 days) primed with C57BL/6 skin 6 weeks before. Under cyclosporine immunosuppression (10g/kg/d), the difference in C57BL/6 heart survival was even significantly evident ($p<0.0001$) between the SCID/beige reconstituted with B/c-SCID-B^- splenocytes (17.5±6.4 days) and those reconstituted with B/c-SCID splenocytes (6.2±1.5 days).
Conclusion: B-cell depletion during allogeneic sensitization lessens second-set rejection.

P-110 IMMUNIZATION OF RECIPIENT WITH DONOR IMMOBILIZED NON-DIVIDING SPLENOCYTES SIGNIFICANTLY PROLONGS ALLOGENEIC HEART SURVIVAL

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Prior contact of recipient with donor transplantation antigens evokes humoral and cellular rejection reaction. Blood transfusions, pregnancy and previous grafts may cross-reactively immunize recipient against donor antigens. In all the listed cases donor antigen is mainly supplied in "passenger cells" These cells colonize recipient lymphoid tissues and produce progenies. This enhances immune response and subsequently rejection. The question arises whether metabolically immobilized non-dividing (mummified) donor cells administered to recipient prior to transplantation may mitigate rejection reaction, presumably by evoking formation of enhancing antibodies. Immobilization can be achieved by treatment of donor cells with pulverized NaCl. These cells retain their molecular structure but do not divide.
Aim: To immunize recipient with donor NaCl-treated splenocytes prior to heart transplantation.
Methods: BN rat spleen fragments were placed in pulverized NaCl and 7 d later implanted intraperitoneally into LEW rat on d 0 and 7. Seven days later heart tx from BN was performed. Non-immunized rats served as controls. No immunosuppression was given.
Results: The immunized LEW did not reject BN heart until d 20 (20±2), whereas control rats rejected the graft within 6±1 days ($p<0.001$). On histology, rejected hearts from immunized recipients revealed hypertrophied muscle with few infiltrates, in contrast to controls with dense infiltrates and necrotic areas. Deposition of IgG in graft vessels could be seen on immunohistochemical pictures
Conclusions: Immunization of recipient with mumified splenocytes retaining their molecular structure may be responsible for prolongation of allogeneic heart survival.

P-111 THE EXPRESSION OF INDOLEAMINE 2,3-DIOXYGENASE (IDO), HEME OXYGENASE-1 (HO-1), IL-7 mRNAs IN MESANGIAL CELLS WITH CYTOSKELETON DAMAGE AND IMPACT OF DIFFERENT IMMUNOSUPPRESSIVE AGENTS ON THEIR EXPRESSIONS

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Objective: To investigate the expression changes of indoleamine 2,3-dioxygenase (IDO), heme oxygenase-1 (HO-1) and IL-7 mRNAs in damaged mesangial cells and influence of different immunosuppressive agents on their expression.
Methods: The cytochalasin B was first cultured with mesangial cell line (HBZY-1) for 2hrs to reversally damage the cell framework (microbule and microfilament) and then HBZY-1 was divided into 5 groups: (1) Blank group, only received dissolvant; (2) CsA group, 3mg/ml; (3) FK506 group, 1mg/ml; (4) MMF group, 0.3mg/ml; (5) RAPA group,10ng/ml.Subsequently, IDO, HO-1 and IL-7mRNAs were detected by RT-PCR and real time-PCR at 6h, 12h, 24h respectively (expressed as CT values).
Results: (1) IDO:The expression of IDO mRNA in CsA and FK506 groups was significantly reduced in a time dependent manner; RAPA had no significant effect on it, in MMF group its expression was significantly higher than those in other groups ($p<0.05$).Moreover, the expression in FK506 group was significantly lower than those in other groups ($p<0.05$). (2) HO-1:The expression of HO-1mRNA in CsA, FK506 groups was reduced gradually.In RAPA group,it was slightly increased at 12h.In MMF group, the expression was signif-

icantly increased at 24h. (3) IL-7:The expression of IL-7mRNA in CsA, FK506 and RAPA groups was significantly reduced.In MMF group, it was first presented decreased tendency, and then obviously increased.The expression in CsA group was higher than those in RAPA and control groups at 6h, 12h ($p<0.05$).At 24h, the expression in CsA, FK506 and RAPA groups was significantly lower than those of MMF and control groups ($p<0.05$).
Conclusions: (1) CsA and FK506, especially FK506, have an inhibitory effect on expression of IDO, HO-1mRNAs in cultured mesangial cell. (2) RAPA has the same effect on HO-1mRNA, but has no effect on IDOmRNA. (3) MMF can significantly increase the expression of IDO and HO-1mRNAs. (4) MMF can increase IL-7mRNA expression, but CsA, FK506 and RAPA have significant inhibitory action on it.

P-112 THE MINIMAL DOSE OF FK506 IS SUFFICIENT TO INHIBIT REJECTION OF VENOUS ALLOGRAFT AFTER ITS TRANSPLANTATION TO ARTERIAL SYSTEM IN RATS

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Introduction: FK506 blood level of 5.0 ng/ml is sufficient to inhibit rejection in arterial wall. Because of different structure of the venous wall we hypotethise that the half-dose of FK 506 used in arterial transplantation could be sufficient to suppress rejection in venous wall.
Material and methods: Brown-Norway (BN) iliolumbar veins were transplanted into abdominal aorta of Lewis (LEW) rats. Low (0.2 mg/kg–group C) and minimal (0.1 mg/kg–group D) dose of FK 506 was given daily intramusculary. Isogeneic (group A) and allogeneic (group B) transplanted rats with no immunosuppression served as controls. Grafts were harvested and prepared for light microscopic evaluation on day 30 after transplantation. The presence of endothelial cells, the intensity of intimal proliferation, the presence of immunoglobulins and the degree of CD4+ and CD8+ cellular adventitial infiltration were determined.
Results: The thickness of intima in group D (15.0 ± 7.0 μm) did not differ from group C (15.0 ± 8.0 μm) and group A (13.0 ± 7.0 μm). Intimal proliferation in group B was statistically lower (2.0 ± 1.0 μm) compared to all previous groups. Immunohistological staining revealed no IgG deposition in the tunica media of any experimental group. The degree of CD4+ and CD8+ cellular adventitial infiltration in group D (7.7 ± 8.3; 2.6 ± 4.3) was comparable to group C (5.8 ± 4.6; 1.8 ± 2.6) as well as to isogeneic group A (12.5 ± 7.7; 0.8 ± 1.7). The degree of cellular infiltration in group B was significantly higher (42.7 ± 20.0; 24.1 ± 14.0) when compared to all previous groups. FK 506 blood levels differed significantly between group C (5.57 ± 0.96 ng/ml) and D (3.20 ± 0.66 ng/ml) on day 30.
Conclusion: The minimal dose of FK506 was sufficient to suppressed acute rejection of venous allograft transplanted to arterial system in rats.
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P-113 IN VITRO EVALUATION OF THE ROLE OF IMMUNOSUPPRESSIVE THERAPY ON LIVER FIBROGENESIS

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Hepatic fibrosis,an outcome of many chronic liver diseases, is characterized by an accumulation of extracellular matrix, mainly collagen, produced by activated intrahepatic fibroblasts. Hepatitis C-related cirrhosis is the main indication of liver transplantation, recurrence is universal, resulting in accelerated progression toward fibrosis. The role of immunosuppressive therapy in this context in unknown. In this study, we tested the hypothesis that some immunosuppressive drugs may inhibit activation and collagen production of intrahepatic fibroblasts.
Methods: Human intrahepatic fibroblasts were isolated from normal liver fragments obtained during liver resections. Fibroblasts were cultured and immunosuppressive agents were added: cyclosporine, tacrolimus, everolimus, sirolimus, mycophenolic acid, azathioprin, and hydrocortison. Then, type I, III, and IV collagen and alpha-SMA levels were measured by RT-PCR followed by real time PCR. Cell proliferation was evaluated using 3[H]Thymidin incorporation.
Results: Cyclosporine decreased mRNA expression of type I, III, and IV collagens and of alpha-SMA in fibroblasts ($p<0.05$, <0.001, 0.01 and <0.01, respectively, versus untreated cells). Tacrolimus enhanced the expression of type I collagen mRNA ($p<0.05$) but had no effect on alpha-SMA mRNA, and on collagen III and IV expressions. Mycophenolic acid decreased type I, III, IV collagen and alpha-SMA mRNA expressions ($p<0.05$, <0.01, <0.05, and <0.05, respectively). mTOR inhibitors reduced type III and IV collagen mRNA expressions ($p<0.01$ and $p<0.05$, respectively). Sirolimus significantly decreased alpha-SMA mRNA expression. mTOR inhibitors, and mycophenolic acid significantly inhibited fibroblasts proliferation ($p<0.05$), while cyclosporine and tacrolimus did not.
Conclusion: Immunosuppressive therapy could modify the liver fibrogenetic process by altering the activation and proliferation of intrahepatic fibroblasts, and the production of extracellular matrix. Cyclosporine, mTOR inhibitors and mycophenolic acid may decrease fibroblast activation and collagen accumulation and thus have beneficial effects on fibrosis progression in patients with recurrent hepatitis C.

P-114 A NOVEL APPROACH TO DEPLETE ANTIGEN-SPECIFIC T CELLS

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Purpose: CD137 is expressed on activated T cells and is believed to be a reliable surrogate marker for antigen-specific T cells. In this study, we want to examine the possibility to kill CD137-expressing T cells using toxin-conjugated anti-CD137 mAb.
Methods/Materials: Doxorubicin was conjugated to anti-CD137 mAb. The efficacy of doxorubicin-conjugated anti-CD137 mAb was examined.
Results: First, we observed that PE-conjugated anti-CD137 mAb was internalized into CTLR8, the cell line that constitutively expresses CD137, 24 hours after its treatment. We next treated primary T cells with doxorubicin-conjugated anti-CD137 mAb, following their activation with anti-CD3 mAb. Doxorubicin-conjugated anti-CD137 mAb induced a majority of both $CD4^+$ T cells and $CD8^+$ T cells within 48 hours after its treatment, compared with control anti-CD137 mAb without doxorubicin conjugation. We further confirmed the specificity of doxorubicin-conjugated anti-CD137 mAb by showing that only T cells that expressed CD137 underwent apoptosis by staining with doxorubicin-FITC-anti-CD137 conjugate. Finally, we found that doxorubicin-conjugated anti-CD137 mAb was able to delete alloreactive T cells in vivo.
Conclusion: Our results indicate that CD137-targeted delivery of toxin is a good strategy to delete alloreactive T cells. This approach may be used to block allograft rejection.

P-115 ANGIOTENSIN II BLOCKADE DECREASES AGING PROCESS BY UPREGULATING *KLOTHO*, AN ANTI-AGING GENE, IN EXPERIMENTAL MODEL OF CHRONIC CYCLOSPORINE NEPHROPATHY

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Background: Klotho gene plays an important role in suppressing aging process, and it is regulated by renin-angiotensin system (RAS). The present study evaluated the effect of angiotensin II blockade with losartan (LSRT) on expression of Klotho in experimental model of chronic cyclosporine (CsA) nephropathy in mice.
Methods: Three separate experiments were performed. In the first experiment, klotho gene expression was evaluated in mice kidney with normal salt diet (NSD) and low salt diet (LSD) for four weeks. In the second experiment, mice on NSD, or LSD were treated with vehicle (VH group, olive oil, 1 mg/kg per day) or CsA (CsA group, 30 mg/kg per day) for one or four weeks. In the third experiment, mice on a NSD or LSD were given vehicle or CsA with LSRT 100 mg/L per day) for 4 weeks.
Results: The LSD group revealed decreased expression of Klotho mRNA and protein compared to the NSD group, and concomitant administration of LSRT did not affect Klotho mRNA and protein in the NSD group but increased the expression of Klotho mRNA and protein in the LSD group. The CsA group on LSD significantly decreased expression of Klotho mRNA and protein compared to the CsA group on NSD. Concomitant administration of LSRT on LSD increased the expression of Klotho mRNA and protein and improved tubulointerstitial fibrosis compared to the CsA group on NSD.
Conclusion: *Klotho* gene is regulated by RAS in a setting of CsA-induced renal injury, and angiotensin II blockade may inhibit aging process by upregulating the expression of Klotho gene in chronic CsA nephropathy.

P-116 IMPDH-ACTIVITY MEASUREMENT AND ITS POSSIBLE CLINICAL BENEFIT

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Introduction: The interpatient variability, changes over time of pharmacokinetic parameters and the potential for drug interactions make the systemic exposure of mycophenolic acid (MPA) unpredictable at a fixed-dose regimen. Monitoring IMPDH activity could be a target to optimize MMF therapy. In this study we prospectively investigated the relationship between IMPDH-activity, MPA levels, immunosuppressive trough levels and clinical outcome (BPAR).
Patients and methods: 95 kidney transplanted patients were prospectively monitored for pharmacokinetics (MPA) and pharmakodynamics (IMPDH) of EC-MPS treatment. Patients received a triple drug immunosuppressive regimen using EC-MPS, CsA or TAC and MP. Blood samples were taken at four timepoints in week 1, 2 and 3 months after transplantation (n=68, gender 32 f/ 34m; mean age: 53 years). IMPDH activity in PBMCs was measured using a validated HPLC-method. Indoleamine 2,3 dioxygenase (IDO) estimation was evaluated prospectively and correlated with rejection and biopsies.
Results: Samples for IMPDH activity measurement according to the protocol were available from 46 patients. The cohort was divided in group I (rejection, n= 16) and group II (no rejection, n=30). There was no correlation between IMPDH and the MPA-levels (r2=0,1286). Gr.I showed a significant lower Inhibition of IMPDH starting in week 1 irrespective the used dosage of CNI. G II showed significant ($p<0.01$) higher inhibition rates but no differences in MPA values. These results are in contrast to the symphony study. IDO showed a significant correlation with rejection, earlier than creatinine.
Conclusion: IMPDH activity measured as AUCact0-4, is significantly correlated with biopsy proven rejection and clinical outcome. The results are supporting our earlier theory, that IMPDH activity is a promising marker to optimize treatment in renal patients. Fixed dose regimen for MPA should be individualized. IDO was an early marker for rejection (BPAR).

P-117 IN VIVO EXPANSION OF CD4+CD25+FOXP3+ T CELLS AFTER ATG INDUCTION THERAPY IS REFLECTED AT THE EPIGENETIC LEVEL

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Antithymocyte globulin (ATG) is used as an induction agent in solid organ transplantation. Beside depletion of circulating lymphocytes it has been recently shown that ATG (Thymoglobulin) leads to the expansion of $CD4^+CD25^+FOXP3^+$ T cells (Treg) in vitro (Lopez et al. 2006). Although this observation could not be confirmed in vivo (Louis et al. 2007) we evaluated the effects of Thymoglobulin on Treg induction in patients (n=15) who received either a combined kidney/pancreas or liver graft following Thymoglobulin induction therapy (1.5 mg/kg for 5 consecutive days) and patients who received a renal allograft treated with basiliximab (20 mg i.v. 2 hours before reperfusion and on day 4, n=15). Maintenance immunosuppression in both groups consisted of cyclosporine A or tacrolimus, mycophenolate mofetil and steroids. Thymoglobulin led to a rapid depletion of T and NK cells followed by a recovery of lymphocyte subsets within 5 ± 2.5 days after end of therapy whereas B cells were significantly induced within the observation period of 25 days. As induced CD4+CD25+FOXP3+ T cells after ATG treatment originate from CD4+CD25-Foxp3- T cells, we ascertained whether the conversion into CD4+CD25+FOXP3+ T cells is also reflected at the epigenetic level of the Foxp3 gene (Baron et al. 2007). Although we could not detect an augmentation of Foxp3 demethylation in these cells after co-incubation with ATG in vitro, we detected a significant increase of Foxp3 demethylation at day 20 posttransplantation compared to pretransplant levels within CD4+ enriched T cells of ATG treated patients. In summary, our in vivo data confirm recent observations that Thymoglobulin indcuces Treg in vitro. Although this seems to be a transient effect a potential relevance for transplant outcome in the long-term remains to be determined.

P-118 PHYTOHEMAGGLUTININ-INDUCED IL2 AND TNFSF2 mRNA AS A MARKER OF IMMUNOSUPPRESSIVE DRUGS

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Introduction: The efficacy and toxicity of immunosuppressive drugs vary among patients, however, no diagnostic test is available to personalize the use of each drug. This study was designed to develop such personalized medicine diagnostics.
Methods: Nine patients with kidney transplantation were recruited after the protocol was approved by the institutional review board. Blood was drawn periodically before and after transplantation and tacrolimus or cyclosporine treatment (CI). Blood was stored at 4°C overnight, then 50 mL each of whole blood was stimulated at 37°C for 2 hours with either solvent or phytohemagglutinin (PHA) in triplicate, then IL2 and other cytokine mRNA was quantified by the method we developed (Clin Chem 52:634, 2006).
Results: PHA-induced mRNA expression was compared before and after CI treatment in patients before transplantation. PHA-induced interleukin-2 (IL2) mRNA expression was significantly ($p<0.05$) reduced after CI treatment in 4 cares (GR: good respomders, Figure: tacrolimus cases). However, the other 5 cases (PR: poor responders) were not reduced with CI treatment although GR and PR group did not have any rejections. Tacrolimus reduced IL2 mRNA expression more than cyclosporine and cyclosporine have stronger reduction of TNFSF2 mRNA than tacrolimus.

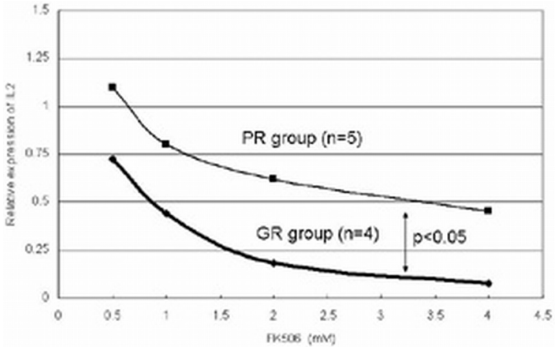

Figure 1. PHA-induced IL2 expression with tacrolimus.

Conclusion: Although the study was still in a preliminary stage, the quantification of PHA-induced IL2 mRNA will be a useful tool for the development of personalized medicine diagnostics for measuring the efficacy of immunosuppressive drugs.

P-119 TACROLIMUS INHIBITION OF CALCINEURIN ACTIVITY IN WHOLE BLOOD AND IN ISOLATED T-LYMPHOCYTES

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Tacrolimus (FK) is a potent immunosuppressive agent used in renal transplantation. It exerts its immunosuppressive action by inhibiting calcineurin phosphatase (CaN).
20 stable renal transplant patients (Rtx) receiving FK> 2 years and s-creatinin below 200 μmol/l, had blood drawn at trough level (T:0) and 2h post dose (T:2). Furthermore, 15 consecutively FK-treated Rtx had blood samples taken pre-transplant and 1 week post-transplant at (T:0) and (T:2).
T-lymphocytes were isolated using an E-rosette method and a fluorometric DNA assay was used to quantify T-lymphocytes. CaN activity was measured as the release of ^{32}P from a phosphorylated peptide in whole blood (WB) and T-lymphocytes. IFN-γ was determined in WB by an ELISA method after 5 hours of PHA stimulation.
The results are depicted in table 1 and table 2.
CaN activity in WB in both stable Rtx and recently Rtx revealed no differences between T:0 and T:2.
In T-lymphocytes we found significant inhibition in CaN activity at T:2 compared to T:0 in both stable Rtx (p=0,02) and recently Rtx (p=0,09).
The FK concentration was significantly increased at T:2 ($p<0,001$). The number of T-lymphocytes at T:2 were significantly decreased compared to T:0 (p=0,005/p=0,002).

Abstract P-119 – Table 1. Stable renal transplant patients

	T:0	T:2	P-value
CaN activity WB (U CaN)	0,45±0,04 (0,37-0,53)	0,44±0,04 (0,36-0,52)	P=0,83
CaN activity in T-lymphocytes (U CaN/10^9 T-lymphocytes)	7,58±1,48 (4,46-10,71)	3,40±0,98 (1,35-5,45)	P=0,02
Tacrolimus concentration (μg/l)	5,07±0,39 (4,24-5,92)	10,33±1,07 (8,09-12,57)	P<0,001
Number of T-lymphocytes (mill. cells/ml)	9,54±0,77 (7,9-11,2)	6,71±0,54 (5,6-7,8)	P=0,005

Mean ± SE (95%CI), n=20

Abstract P-119 – Table 2. Recently renal transplanted patients

	Before Tx	1 week post Tx T:0	1 week post Tx T:2
CaN activity in WB (U CaN)	0,39±0,03 (0,34-0,45)	0,31±0,03 (0,26-0,37)	0,28±0,02 (0,22-0,33)
CaN activity in T-lymphocytes (U CaN/10^9 T-lymphocytes)	3,87±0,56 (1,64-6,1)	4,54±1,40 (2,30-6,77)	2,51±1,18 (0,28-4,74)
Tacrolimus concentration (μg/l)	0	9,88±0,89 (6,77-12,98)	23,53±2,53 (20,42-26,63)
Number of T-lymphocytes (mill. cells/ml)	9,48±0,78 (7,46-11,50)	12,89±1,03 (10,79-14,99)	7,90±1,24 (5,80-10,00)

Mean ± SE (95%CI), n=18.

IFN-γ levels were significantly lower in the recently Rtx compared to stable Rtx (p<0,001).
CaN activity in WB and in T-lymphocytes display different profiles. This is in contrast to what has been demonstrated previously in cyclosporine treated patients. CaN activity measured in WB did not reveal the actual inhibition inside the T-lymphocytes.
Furthermore, the Inhibition of CaN activities in the T-lymphocytes are inversely proportional to blood tacrolimus levels which also could not be demonstrated in WB. Patients had a lower number of T-cells at T:2 compared to T:0. IFN-γ levels recently after transplantation decreased, but not in stable patients.

P-120 ALEMTUZUMAB (Campath-1H) FOR LYMPHOCYTE DEPLETION IN CYNOMOLGUS MONKEYS

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Purpose: Treating nonhuman primates (NHP) with alemtuzumab causes massive hemolysis, because the target CD52 molecule is expressed on erythrocytes. The identification of NHP with erythrocytes negative for CD52 (CD52-) would offer opportunities to investigate lymphocyte depletion/repopulation phenomena, as well as the use of alemtuzumab in preclinical transplantation models.
Methods/Materials: Using an agglutination screening assay, cynomolgus monkeys (Macaca fascicularis) with CD52- erythrocytes were identified. With flow cytometry, the affinity of alemtuzumab for monkey lymphocytes was 20x lower than for human lymphocytes. Six monkeys were treated with 20mg/kg alemtuzumab, followed by 1-4 weekly injections of 10-20mg/kg. Two of these monkeys received additional mycophenolate mofetil (MMF; 50-100mg/kg/day p.o.). Lymphocyte depletion of peripheral blood and lymph nodes was documented by flow cytometry.
Results: Complete depletion of T and B lymphocytes (>99.5%) was achieved with 20mg/kg. Repopulation occurred faster than in human patients, but could be suppressed by weekly injections. Without MMF, repopulation of CD20 B cells was complete within 3 months. CD8 T cells repopulated variably within 1-6 months, and repopulation of CD4 T cells was 67% after 1 year; repopulation was significantly delayed by MMF during the first 5 months (ongoing experiments) (figure 1). Among repopulating CD4 and CD8 T cells, a phenotypic shift was observed from CD45RA+CD62L+ naïve cells toward CD45RA-CD62L- effector memory cells (figure 2). In lymph nodes, the depletion of naïve cells was more profound than of memory cells, which may have initiated this homeostatic repopulation of memory cells.
Conclusions: This study proves the feasibility of alemtuzumab use in cynomolgus monkeys. A higher dose was required to obtain depletion comparable to human patients. The initial profound lymphocyte depletion was followed by memory T cell expansion, as has been observed in clinical transplantation. Its implications for graft rejection can be investigated using this NHP model.

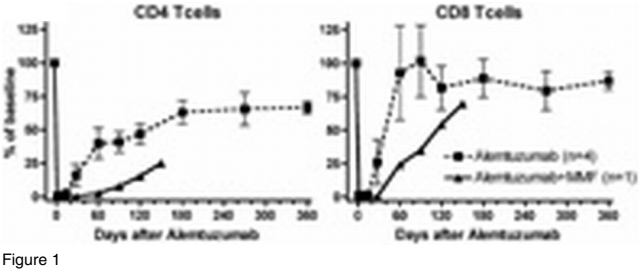

Figure 1

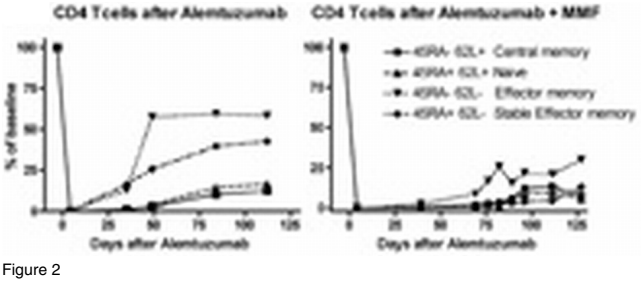

Figure 2

P-121 IMMUNOSUPPRESSIVE DRUGS INHIBIT RAT ISLET CELL PROLIFERATION *IN VITRO*

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Aim: Beta-cell replication is thought to play a significant role in maintaining pancreatic beta-cell mass. Whether immunosuppressive drugs affect replication of beta-cells in transplanted islets is not fully understood. The aim of this study was to determine the effects of immunosuppressive drugs, used in islet transplant recipients, on islet cell replication, in vitro.
Methods: Rat pancreatic islet cells were incubated with BrdU (10μM) in the presence or absence of different concentrations of cyclosporine A (CsA), tacrolimus, sirolimus or mycophenolate mofetil (MMF). Cell replication was determined by BrdU incorporation after 1 to 7 days of culture. Data are expressed as % of positive BrdU cells and as mean ± SEM for 3 or more independent experiments.
Results: Sirolimus (10 ng/ml) blocked almost completely islet cell proliferation from 24h (0.17±0.17 vs. 2.00±0.51; sirolimus vs. control, p<0.001) until 7 days of treatment (0.14±0.10 vs. 23.80±3.63; sirolimus vs. control, p<0.01). Additionally, the inhibitory effect of sirolimus was also observed at low concentrations from 0.1 ng/ml (2.75±0.97 vs. 13.43±0.76; sirolimus vs. control, p<0.001). After 2 days of treatment, MMF also inhibited cell proliferation in a dose-dependent manner (control: 9.48±2.79; MMF 1μg/ml: 5.54±1.89; MMF 5μg/ml: 1.75±0.70; MMF 25μg/ml: 0.98±0.07%). Treatment with CsA (200 ng/ml) and tacrolimus (10 ng/ml) during 5 days significantly reduced islet cell proliferation (control: 21.13±2.47; CsA: 2.52±0.94; tacrolimus: 3.68±1.06 (p<0.01)). None of the immunosuppressive drugs induced a significant increase of apoptosis. Furthermore, effect of immunosuppressive drugs on cell proliferation was reversible.
Conclusion: Our results indicate that immunosuppressive drugs, at therapeutic target concentrations, inhibit pancreatic islet cell proliferation in vitro. It is therefore suggested that progressive graft islet dysfunction may result, in part, from an impairment of beta cell replication induced by immunosuppressive drugs.

P-122 IMPAIRING EFFECTS OF CYCLOSPORINE AND TACROLIMUS ON TRANSCRIPTIONAL REGULATION AND SECRETION OF INSULIN IN RAT β-CELLS

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Introducing the calcineurin inhibitors cyclosporine (CsA) and tacrolimus (Tac)

into the field of transplantation has improved the outcome of organ transplants, but unfortunately complications such as post-transplantation diabetes mellitus (PTDM) cause morbidity and impairment of survival rates. The pathogenic mechanisms behind PTDM and the relative contribution of each calcineurin inhibitor remain controversial.
Consequently, we incubated INS-1E cells at low (3,3-6,6 mM) and high (16,7 mM) glucose concentrations and exposed them to various concentrations of CsA (0,1–10 μM), Tac (0,01-0,2 μM)and vehicle for 6 and 24 hours. Our aim was to measure insulin secretion and content together with calcineurin phosphatase activity and transcriptional markers involved in beta-cell function.
We found that both drugs primarily impaired insulin secretion while insulin content remained unaltered. Tac was able to inhibit basic ($p<0,01$) but not glucose stimulated insulin secretion as early as after 6 hours of exposure. After 24 hours both Tac ($p<0,05$) and CsA ($p<0,01$) inhibited stimulated insulin secretion while calcineurin activity was decreased by both drugs during all conditions. At very low concentrations CsA showed a paradoxical tendency towards increasing insulin secretion and content parallel to increasing gene expression levels of insulin, sterol regulatory element-binding protein (SREBP)-1c and nuclear factor of activated T-cells (NFAT)-c1. Expression levels of apoptosis associated genes BAX and BCL2 together with calcineurin A and NFAT-c4 were not affected by low concentration of either drug.
Our preliminary in vitro data suggest a slightly augmented acute diabetogenic effect of Tac in comparison to CsA. The impairing effects on insulin secretion are to some extent mirrored by decreased calcineurin activity, yet pending results are needed to elaborate on the molecular basis for diminished insulin output and whether one drug differs from the other.

P-123 CYCLOSPORIN A INHIBITS PROFIBROTIC EFFECTS OF INTERLEUKIN-4 AND TGF-β IN HUMAN INTRAHEPATIC FIBROBLASTS *IN VITRO*

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Hepatic fibrosis is characterized by an accumulation of collagen, produced by activated intrahepatic fibroblasts. TGF-β is an important inducer of liver fibrogenesis. We have shown that IL-4 is overexpressed in severe recurrent hepatitis C after liver transplantation, and that IL-4 exerts profibrotic effects by activating intrahepatic fibroblasts. In contrast, cyclosporin (CsA) was found to decrease fibroblast activation.
This study was designed to investigate the effects of CsA on TGF-β and IL-4 profibrotic activity in human intrahepatic fibroblasts *in vitro*.
Human intrahepatic fibroblasts were isolated from normal livers obtained from liver resections, and cultured without or with human TGF-β, human IL-4, CsA or combinations TGF-β+CsA or IL-4+CsA. RT-PCR followed by real time PCR for type I, III, and IV collagen and alpha-SMA (a marker of fibroblast activation) were performed. Collagen in supernatant was also measured using Sircol assay.
The incubation of human intrahepatic fibroblasts with TGF-β and IL-4 increased the mRNA expressions of alpha-SMA, and collagens ($p<0.05$ vs untreated cells) as well as the collagen levels in supernatants ($p<0.01$ vs untreated cells). CsA decreased the expression of alpha-SMA and collagens ($p<0.01$ vs untreated cells). mRNA expression of alpha-SMA was significantly lower under combined treatments TGF-β+CsA or IL-4+CsA ($p<0.01$ TGF-β vs TGF-β+CsA and $p<0.05$ IL-4 vs IL-4+CsA). Collagen levels in supernatants were decreased by combined treatments ($p<0.05$ TGF-β vs TGF-β+CsA, $p=0.05$ IL-4 vs IL-4+CsA). mRNA expression of collagens were also decreased in cells treated with combination when compared with cells treated by TGF-β or IL-4 alone ($p<0.01$ and $p=0.03$ respectively).
CsA inhibits the profibrotic effects of TGF-β and IL-4, by decreasing the activation of human intrahepatic fibroblasts and by inhibiting their collagen production. CsA may decrease fibroblast activation and collagen accumulation and thus exert beneficial effects on fibrosis progression.

P-124 SUNITINIB PREVENTS CHRONIC REJECTION IN EXPERIMENTAL KIDNEY TRANSPLANTATION

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Background: In clinical kidney transplantation chronic rejection remains the major reason for late allograft loss and accelerated atherosclerosis is one pathological manifestation of chronic allograft rejection. Both platelet derived growth factor (PDGF) and vascular endothelial growth factor (VEGF) induce atheroma proliferation alltough the role of VEGF remains somewhat contradictory. In addition, expression of both PDGF and VEGF is increased during the development of chronic rejection in experimental kidney transplantation. Sunitinib is a novel oral tyrosine kinase inhibitor with potent inhibitory effect on both VEGF and PDGF receptors. Therefore it could be a potential intervention for chronic allograft rejection. Here we investigated the effect of sunitinib on chronic rejection and growth factor expression.
Materials and methods: Kidney transplantations were performed from DA to WF rats and syngenic control transplantations were performed between DA rats. Allografts were immunosupressed either with CsA (1.5 mg/kg/d sc) or with CsA and sunitinib (2mg/kg/d p.o.). No immunosuppression was given to syngenic grafts. Grafts were harvested 90 days after transplantation for histology and immunohistochemistry (PDGF-A, PDGF-B, VEGF-A).
Results: In syngenic grafts, no histological signs of chronic rejection were seen whereas intense characteristics of chronic rejection were seen in CsA-treated allografts. Sunitinib was well tolerated and it almost completely prevented chronic rejection changes. Sunitinib also ameliorated renal PDGF-A and -B and VEGF-A expression.
Conclusions: Our results demonstrate that sunitinib is a potent inhibitor of both PGDF and VEGF and also that this combined inhibition prevents chronic rejection changes in experimental kidney transplantation in rats. Based on these findings sunitinib could be a potential intervention also in clinical kidney transplantation.

P-125 THE EFFECT OF INHIBITION OF INDIRECT T-CELL ACTIVATION ON CHRONIC REJECTION OF KIDNEY ALLOGRAFTS IN RATS

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Introduction: There is experimental and clinical evidence, that activation of T-cells throug the indirect pathway triggers chronic allograft rejection. The aim of this study was to establish a clinically applicable method to inhibit the indirect pathway of T-cell activation and to investigate whether this inhibition prevents chronic allograft rejection.
Methods: Lewis rats received 50×10e6 apoptotic (UVB-irradiated) F344 splenocytes intravenously or carrier (control). On day seven, all animals were immunized with F344 necrotic cells and three weeks later, delayed type hypersensitivity reaction against donor-type antigen was tested.
In the second part, Lewis rats received orthotopic F344 kidney transplants. Graft function was monitored by urnine creatinine and -proteine. At six months, grafts were investigated for vasculopathy using orceine stain. Reactivity of indirectly activated recipient T-cells was measured by CFSE-proliferation assays.
Results: As compared to controls (n=4), experimental animals (n=4) showed lower reactivity upon indirect activation on DTH: The difference of hind foot path diameter was 0,425±0,063 mm vs. 1,075±0,335mm. Following kidney transplantation, two experimentals and one control animal died from acute cellular rejection during follow up. Surviving animals in the experimental group (n=3) showed markedly better organ function than controls (n=4, urine proteine/creatinine 2089±1015 mg/g vs. 7637±2609 mg/g at 4 months post transplant). On histology 11,35±3,3% of vessels were affected by vasculopathy in the experimental group as compared to 17,2±3,14% in the control group. The proliferation assays revealed no measurable difference in indirect anti-donor reactivity of recipient spleen-T-cells following kidney transplantation.
Conclusion: Our results demonstrate that indirect T-cell reactivity is inhibited by pretreatment with UVB-irradiated donor cells. Inhibition of the indirect T-cell activation alone does not completely prevent chronic rejection of kidney transplants, suggesting that other factors may trigger the disease.

P-126 HUMAN MITOMYCIN C-TREATED DENDRITIC CELLS SUPPRESS ALLOGENEIC T-CELL RESPONSE IN-VITRO. AN EFFECT MEDIATED BY INDUCTION OF CD4+CD25+FOXP3+ TREGS

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In-vitro generated, suppressive dendritic cells (DCs) are considered to be a potential tool for tolerance induction in organ transplantation.We investigated the effect of Mitomycin-C (MMC) treated human DCs upon allogeneic T cells in-vitro and possible mechanisms responsible for their suppressive behaviour. The allostimulatory capacity of MMC-treated mature DCs (MMC-DC) upon T cells, was tested in-vitro. Briefly, human mature monocyte-derived DCs were cultured for 30 minutes with 75microg/ml MMC then washed and co-incubated

with allogeneic PBMCs. After 6 days, T-cell proliferation was measured. T cells were isolated from these cultures and restimulated using fresh untreated DCs under the same conditions. CD4+CD25+CD127dim/- Treg cells were isolated from the same cultures and FoxP3 expression as well as the suppressive capacity of these cells was tested, using flowcytometry and an in-vitro allogeneic T-cell stimulation assay, respectively. Briefly, CD4+CD25+CD127dim/- (Treg) cells, were co-incubated for 6 days (2:1, 4:1, 10:1 Treg/Tcell ratio) within cultures containing fresh mature DCs and allogeneic PBMCs. For all experiments, cell proliferation was measured using non-radioactive flowcytometric CFSE assay. Statistical analysis was performed using the non-parametric Mann-Whitney test ($p<0.05$ was considered satistically significant). Results from one out of three significant experiments are presented.
Human MMC-treated DCs actively suppress allogeneic T cell activation in-vitro (18.2% CFSE+TcellsMMC-DC vs. 95% CFSE+Tcellsuntreated controls, $p<0.001$). Once suppressed, T cells cannot be restimulated (11.5% CFSE+TcellsMMC-DC vs. 95% CFSE+Tcellsuntreated controls, $p<0.001$). Human MMC-treated DCs induce FoxP3+ Tregs (22% FoxP3+TregMMC-DC vs. 1.8% FoxP3+Treg untreated controls). Tregs induce lack of allogeneic T cell proliferation in-vitro in a concentration-independent manner (22.1%2:1Treg/Tcell ratio, 24%4:1Treg/Tcell ratio, 20.8%10:1Treg/Tcell ratio CFSE+Tcells vs. 92% CFSE+ Tcellsuntreated controls).
Our findings show that human MMC-DCs acquire suppressive activity in-vitro and induction of FoxP3+ Tregs could be one of the responsible mechanisms involved in this behavior.

P-127 HEPATITIS C VIRUS INFECTION INFLUENCE ON REGULATORY T CELLS (Tregs) LEVELS IN KIDNEY TRANSPLANTED PATIENTS

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It has been described that hepatitis C virus infection is related with the development of autoimmunity, so it would contribute to rise the levels of Tregs. This cell group characterized by presenting a CD4+CD25+FOXP3+ phenotype, play an important role in the maintenance of immunological self-tolerance as well as in controlling immune diseases such as infections by viruses that may impair the immune system.
However, there is no enough information concerning the role of Tregs in transplanted patients with hepatitis C virus infection.
The aim of the present study was to determine the influence of hepatitis C virus infection on Tregs levels.
To carry out the study, we selected three populations:
- First one composed of 16 healthy subjects (controls)
- Second one composed of 26 transplanted patients with hepatitis C virus infection
- Third one composed of 42 transplanted patients without hepatitis C virus infection.

The two transplanted populations had an average of time of transplant of 12 years.
Tregs populations were determined from peripheral blood by Flow Citometry by the use of monoclonal antibodies (anti-CD4, anti-CD25 and anti-human FOXP3).
We collected in addition interesting clinical data for the study concerning the immunosuppressive treatment and time of transplant.
Levels of Tregs for the three populations are shown in the table, where it can be observed that there are no differences in Tregs levels between transplanted patients with and without HCV infection (Table).

Levels of Tregs for studied populations

Study population	Tregs levels
Controls (n=16)	2,89±0,46
Transplanted patients HCV+ (n=26)	1,48±0,27
Transplanted patients HCV– (n=42)	1,56±0,24

These data suggest that HCV infection could not be important for the levels of Tregs in peripheral blood in transplanted patients.

P-128 EFFECT OF CALCINEURIN ANTAGONISTS ON HCV-ANTIGEN SPECIFIC PBMC RESPONSE IN LIVER TRANSPLANTED PATIENTS WITH VIRAL RECURRENCE

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Virus-specific PBMC responses were investigated in patients with HCV recurrence after liver transplantation. We enrolled 36 patients (pts) (22 Male – 14 Female; mean age 62 yrs)with HCV recurrence without episode of reject (histologically proven) on the following immunosuppressive regimen: Tacrolimus 3mg/daily (20 pts) with FK mean serum level of 6±1.2 ng/mL and Cyclosporin 400mg/daily (14 pts) with mean serum C2 level of 565±112 ng/mL. All sample were collect within 18 months from transplantation in mean. ELISpot assay was performed on PBMC after stimulation with a pool of HCV antigens (Core, NS3 and NS4 2mcg/mL) and PHL-A to evaluate IFN-gamma specific and non specific immune response, measured as spot forming colonies (SFC) (at least 200.000 cells per well). 10 Patients with chronic hepatitis C (CHC) were used as control group. Lymphocytes number was measured by Flow cytometry. Patients undergoing Tacrolimus treatment had higher IFN-γ SFCs than those underwent Cyclosporin therapy when stimulated with PHL-A (191±69 vs 122±56; $p<0.05$ U Mann Whitney) and HCV pool antigen (88±50 vs 63±21, $p<0.05$ U Mann Whitney). No differences where found in IFN-g SFCs among patients with CHC and those undergoing Cyclopsorin therapy. Patients under tacrolimus treatment had higher SFCs ($p<0.05$).No differences in Lymphocytes number among the two groups (900±26 vs 846±38) Patients with HCV recurrence on Tacrolimus therapy, without episodes of reject, seem to have a stronger specific and non specific Th1 immune network than those on cyclosporine treatment, however further studies are required to have a full understanding of involved mechanisms.

P-129 TACROLIMUS AND DIABETES MELLITUS: ONLY OVERDOSEAGE LEADS TO AN IMPAIRED INSULIN PRODUCTION IN THE RAT PANKREAS

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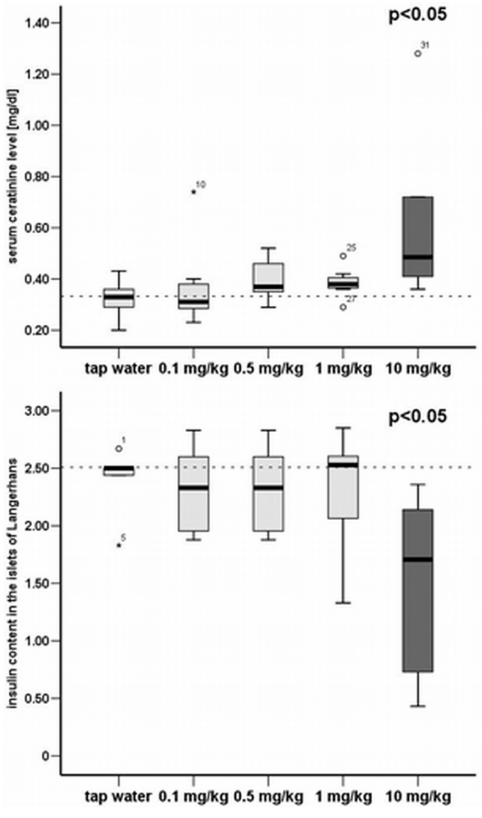
Introduction: Tacrolimus is an immunosuppressive agent which has been suspected to increase PTDM incidence. Complex clinical situation in the patients which undergone transplantation makes it difficult to elucidate the pathomechanism and the real impact of tacrolimus on glucose metabolism. In the present experimental study we analyzed exclusively the influence of the tacrolimus therapy on the pancreas beta-cell function.
Methods: Male Wistar Rats were fed with tacrolimus or tap water (control group) for two weeks. Following concentrations of tacrolimus were used: 0.1, 0.5, 1, and 10 (toxic) mg/kg b.w. (n=7). On the day 14-th after being fastened overnight rats were anesthetized, than serum probe and pancreas were taken and animals euthanized. Serum glucose, insulin and creatinine level were measured afterwards. Pancreas were stained with anti-insulin antibody used ABC immunohistology, afterwards staining intensity was measured (blinded) and all parameters compared.



Results: There were no differences in serum glucose and insulin serum levels between the study groups. Tacrolimus in the toxic group decreased insulin amount in the pancreas beta cells ($p<0.05$ vs. control) and at the same time increased serum creatinine concentration ($p<0.05$ vs. control). Rats in the toxic tacrolimus group were in a subjectively worse condition and one of them died at the 10-th day. There were no other significant differences between the groups.
Conclusions: Tacrolimus has no influence on the pancreas insulin production by the rat when given in a therapeutic dose over 14 days. Only toxic tacrolimus dose leads to an impaired pancreas insulin production, however does not cause hypoinsulinemia after two weeks treatment. Avoidance of high tacrolimus serum levels might reduce alterations of glucose tolerance in patients after transplantation.

P-130 HUMAN MACROPHAGES DRIVEN TO A NOVEL STATE OF ACTIVATION HAVE TOLEROGENIC PROPERTIES IN RENAL TRANSPLANT RECIPIENTS

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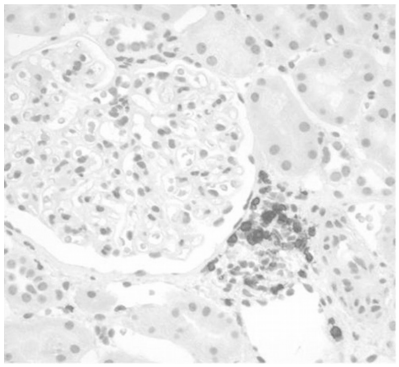
Background: Earlier studies have shown that human macrophage preparations can promote a state of alloantigen-specific unresponsiveness in recipients of renal transplants and may facilitate the safe, early minimisation of immunosuppression. A refined cellular product with a more homogeneous phenotype has now been developed: these cells have been called *regulatory macrophages* (M-*regs*). Here, we describe the production and preoperative administration of donor-derived M-*regs* to two recipients of living-donor kidney transplants.
Methods: Both patients received an infusion of $>7 \times 10^6$ viable M-*regs*/ kg bodyweight 7 days prior to transplantation under cover of 1 mg/kg/day azathioprine. After transplantation, the patients received reducing doses of prednisolone and tacrolimus. Immunomonitoring was undertaken within RISET.
Results: Infusion of M-*regs* was without complications and both patients were successfully minimised to low-dose tacrolimus monotherapy. Protocol biopsies revealed no signs of rejection in either patient, although patient CA was notable for the clusters of quiescent B cells present in his graft.



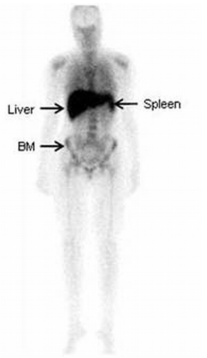


Figure 1 (left). A CD20$^+$ cell cluster in the graft of patient CA.
Figure 2 (right). In a single patient, ^{111}In-labelled M-*regs* migrated via the blood to the liver, spleen and bone marrow, but not to the lymph nodes.

Serial analyses of the immunological status of the patients by flow cytometry and gene expression profiling illustrated the dynamic nature of responses to solid organ transplants: after an initial phase of immunological activation, Foxp3 and TOAG1 expression in peripheral blood of both patients was markedly increased. Short-term tracking of ^{111}Indium -labelled M-*regs* in patient MM revealed that the cells traffic from the lungs to spleen, liver and haematopoietically-active bone marrow via the blood, but do not migrate to lymph nodes.
Ventilation and perfusion scintigraphy in patient CA demonstrated that M-*reg* infusion did not measurably impair pulmonary perfusion.
Conclusions: Administration of M-*regs* has been shown to be feasible and was without adverse consequence in two patients. Both patients underwent successful immunosuppressant minimisation and were found to express biomarkers of tolerance.

P-131 DOES TACROLIMUS INFLUENCE THE ABILITY OF POSTOPERATIVE WOUND HEALING IN A RODENT MODEL?

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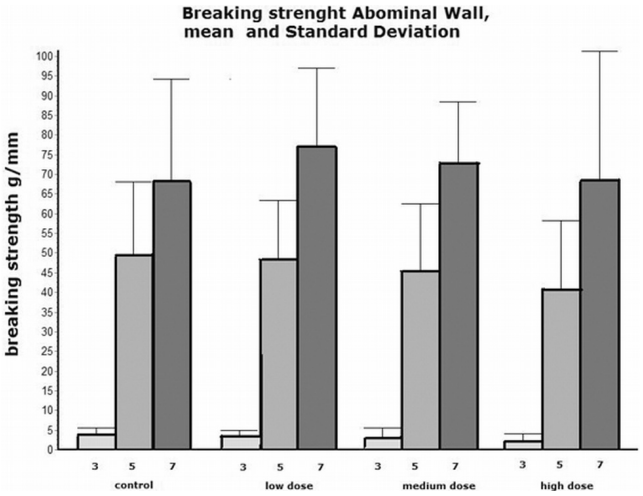
Introduction: Use of immunosuppressant drugs in organ transplantation is obligatory but also associated with wound healing disturbances. Tacrolimus is supposed to have a relatively low complication rate. Because clinical regimens are carried out with combinations of medication, this presumption can only be tested in animal models. It is of clinical importance to determine the side effects of individual drugs, to establish the optimum regime for solid organ recipients.
Methods: Three groups of 33 male Wistar rats started a daily subcutaneous dose of 0,5 mg/kg, 2 and 5 mg/kg Tacrolimus. The control group received saline. On day 0 a resection of 1 cm ileum and 1 cm colon was performed, and end-to-end anastomoses were constructed using 8 interrupted sutures. Ten rats of each group were killed and analyzed on respectively day 3, 5 and 7 postoperatively. For analysis mechanical tests (bursting pressure BP, breaking strength BS), biochemical tests (collagen content and gelatinase activity) and histological parameters were investigated.
Results: Mean BS of the abdominal wall of the control group was 3.9 ± 1.6 g/mm at 3 days, increasing to 49.7 ± 18.3 and 68.3 ± 25.9 g/mm at 5 and 7 days postoperatively.



In the experimental groups the same, very significant, increase in strength is seen ($p<0.0001$). Breaking strength of the ileum and colon anastomoses, as well as bursting pressures, follow the same pattern of incremental wound strength. Altogheter, **no** significant difference is found when control groups are compared with their corresponding experimental groups. The findings were supported by absence of a difference in hydroxyproline content. Mean trough levels of the experimental groups measured 4,9 (0,5 mg/kg/day) to 12,3 (5 mg/kg/day) ng/ml.
Conclusion: Tacrolimus, as a single drug, does not impair wound healing.

P-132 ROUTINE USE OF EARLY INTRAVENOUS TACROLIMUS IN INTESTINAL TRANSPLANTATION MAINTAINS MORE CONSISTENT BLOOD LEVELS WITHOUT NEGATIVELY IMPACTING RENAL FUNCTION

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Background: Intravenous tacrolimus (IV tac) has been utilized in a limited fashion in certain experimental protocols in transplant patients. Continuous IV tac offers the advantage of a consistent infusion of tacrolimus which results in less variability in blood levels and less dependence upon enteral absorption. This study evaluates the post-transplant serum creatinine in intestinal transplant patients receiving IV tac compared to those receiving enteral tacrolimus only (Ent tac).
Methods: All patients undergoing intestinal transplantation at our center over a 5 year period received either early IV tac or Ent tac. For patients receiving IV tac, blood levels were measured twice daily with the continuous infusion changed to maintain a level of 12-15ng/mL. Patients receiving Ent tac were managed based upon a once daily blood trough level drawn 11 hours post-dosage with a goal of 12-15ng/mL. Serum creatinine was measured once daily. Transplanted organs included isolated small intestine, modified multivisceral and multivisceral transplants (total n=80). Patients receiving simultaneous kid-

ney transplant were excluded from the analysis (n=13). All patients received rabbit anti-thymocyte based induction therapy with pulse steroids.
Results: There were 14 Ent tac and 53 IV tac patients. There were no differences between the two groups in early graft function or episodes of rejection. There was less day-to-day variability in serum tacrolimus levels for the IV tac group. Serum creatinine did not differ in the first 30-days for the two groups and is shown in the figure below.

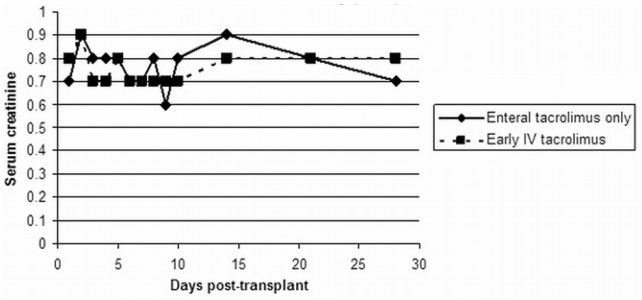

Figure 1. Comparison of serum creatinine levels post-transplant for intestinal transplant recipients receiving early IV tacrolimus (n=53) or enteral tacrolimus only (n=14).

Conclusions: IV tac is safe and effective in the early post-transplant period in achieving and maintaining therapeutic serum tacrolimus levels. Our center routinely uses IV tac in intestinal transplantation in the early post-transplant period and in patients with severe rejection in which absorption of tacrolimus is unpredictable.

P-133 RABBIT ANTITHYMOCYTE GLOBULIN (rATG) IMMUNOSUPPRESSION INDUCTION IN 1000 CONSECUTIVE ADULT, DECEASED DONOR LIVER TRANSPLANTS

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Background: Immunosuppression induction therapy may be associated with immunosuppression-related complications such as an increased risk of infection, neoplasm, and hepatitis-C recurrence. Our center has utilized 3 distinct induction immunosuppression protocols over the last 7 years. This study reports a comparison of these three protocols for transplant outcomes and complications.
Methods: Data were obtained from the transplant database and all medical records for liver transplant patients between 2001 and 2008. Induction immunosuppression consisted of (1) rabbit antithymocyte globulin (rATG) induction given as three doses (6mg/kg total) with first dose intraoperatively (OR ATG), (2) rATG as in #1 but first dose started 48-hours post-transplant (Delayed ATG), and (3) delayed rATG as in #2 but with addition of single dose of rituximab 72-hours post-transplant (Delayed ATG+Ritux). All rATG was given with a rapid steroid taper of 3 doses. Maintenance immunosuppression was with tacrolimus monotherapy (goal level 7-10ng/mL). Outcomes included graft/patient survival and immunosuppression related complications.
Results: Groups consisted of (OR-ATG) n=166 (16%), (Delayed ATG) n=259 (26%), and (Delayed ATG+Ritux) n=588 (58%)(total n=1013). There was no difference among the groups in patient survival up to 5-years post-transplant. The subgroup of patients with hepatitis C did not differ in survival. There was no difference in the incidence of infectious complications or the incidence of de novo tumors. The overall survival and survival among patients with hepatitis C and hepatocellular carcinoma is similar to that reported in the literature for all LT recipients. The incidence of post-transplant complications is similar to that reported in the literature. The incidence of post-transplant lymphoproliferative disorder was less than 1%. Episodes of rejection within 1-year of transplant was less than 5%.
Conclusions: Induction immunosuppression can be safely used in all adult liver transplant recipients with good efficacy and minimal immunosuppression-related side effects.

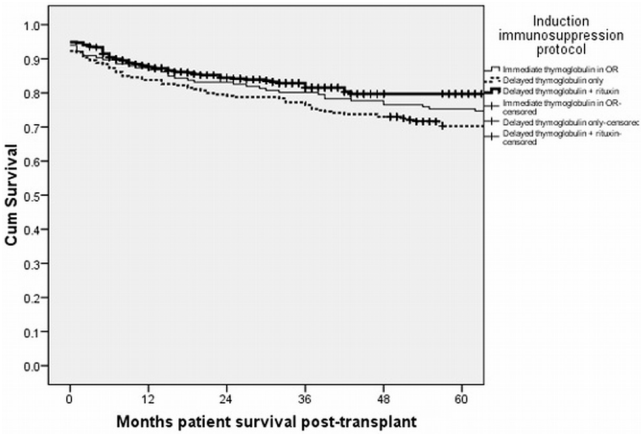

Figure 1. Kaplan-Meier patient survival post-liver transplant for 3 rabbit antithymocyte globulin (rATG) immunosuppression induction therapies (total n=1013).

P-134 PATHOPHYSIOLOGICAL MECHANISMS UNDERLYING THE CARDIOVASCULAR SIDE-EFFECTS OF SIROLIMUS VERSUS CYCLOSPORIN

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The mechanisms underlying the cardiovascular side-effects of the immunosuppressive drugs Cyclosporin A (CyA), a calcineurin-inhibitor, and Sirolimus (Sir), a rapamycin, remain to be elucidated. This study intended to compare the effects of CyA and Sir on blood pressure (BP) and on other cardiovascular indexes.
Three groups of male Wistar rats (n=8) were tested during 7 weeks with the following diets: control (vehicle), CyA (5 mg/kg/day Sandimmune Neoralâ) and Sir (1 mg/kg/day Rapamune®). BPs and HR were evaluated by the "tail cuff" method, while the following parameters were assessed in serum: haematology, biochemistry, plasma and platelet catecholamines (CAs) and 5-HT measures (HPLC-ECD), lipid peroxidation via malonaldehyde (MDA) content and total antioxidant status (TAS). Results are means $\pm$ sem (ANOVA/Fisher's *PLSD*).
While BP was higher in both the CyA and Sir groups, versus the control, the HR was elevated in the former but unchanged in the last. The dyslipidaemic pattern of the CyA group was even more evident in the Sir group, being LDL-c and TGs significantly higher ($p<0.05$) versus CyA. RBC, HCT, Hb, MPV and PDW were also higher in the Sir group vs CyA ($p<0.05$). While plasma and platelet 5-HT contents were augmented in the Sir rats, CAs levels were unchanged. The increased oxidative profile (MDA vs TAS content) in the CyA group was not confirmed in the Sir treatment.
This study has demonstrated that the cardiovascular disturbances underlying HT development might be associated with distinct molecular/cellular mechanisms probably explained by the differences on mechanism of action for immunosuppression.

P-136 INHIBITION OF BLADDER TUMOR GROWTH BY IMMUNOSUPPRESSION AGENTS: EXPERIMENTAL STUDY

Belmiro Parada[2], Flávio Reis[1], Arnaldo Figueiredo[2], José Sereno[1], Edite Teixeira-Lemos[1], Pedro Nunes[2], Alfredo Mota[2], Frederico Teixeira[1]. *[1]1Institute of Pharmacology & Experimental Therapeutics, Medicine Faculty, Coimbra University, Coimbra, Portugal; [2]2Department of Urology & Renal Transplantation, University Hospital, Coimbra, Portugal*

Introduction and aims: Identification of drugs with tumoral preventive properties could be an effective way to decrease the morbidity and mortality associated to bladder cancer. We investigated the anti-carcinogenic effects of Sirolimus and Cyclosporine on a rat bladder carcinogenesis model with N-butyl-N(4-hydroxibutil)nitrosamine (BBN).
Materials and methods: Male Wistar rats (six week old) were divided in several groups:
A) Carcinogenic model: BBN 0.05% in drinking water (n=20), week 1 to week 8.
B) Sirolimus 1 Group: BBN 0.05% + Sirolimus 1 mg/kg/day (n=12);
C) Sirolimus 2 Group: BBN 0.05% + Sirolimus 2 mg/kg/day (n=8);
D) Cyclosporine A Group: BBN 0.05% + Cyclosporine 5 mg/kg/day (n=16);
E) Control groups: Sirolimus 1-2 mg/kg/day (n=6), Cyclosporine 5 mg/kg/day (n=4),
At week twenty, the rats were killed. The number and size of tumors were recorded. The bladders were stained for histological evaluation. Blood was sent for determination of several tumoral and inflammatory factors (TGF-β, TNF-a, PCR, IL-1β, IL-6, IL-10). Lipid peroxidation, through serum malonaldehyde (MDA) content, and total antioxidant status (TAS) were also evaluated.
Results: In our study, there was a statistically significant reduction in the incidence of bladder tumors in rats treated with Sirolimus 2 mg/kg/day (table 1), with less aggressive histological changes. Rats in this group had lower levels of TGF-β and a higher anti-oxidant status (MDA/TAS). Sirolimus 1 mg/kg/day induced a higher number of tumors. Cyclosporine showed no significant inductive or preventive effect on bladder carcinogenesis.

Table 1. Macroscopic results

Group	% Rats with Gross Tumor	Mean Number Tumor/rat	Mean Tumor Volume/rat (mm^3)
BBN	65	0,75	89,96
Sir 1mg	91,7*	2,5*	35,02
Sir 2mg	37,5*	0,38*	0,11*
CsA	56,3	0,87	20,26
Controls	0*	0*	0*

*P<0,05 vs BBN group.

Conclusions: In our study, both Sirolimus 2mg/kg/day had chemopreventive properties of urothelial bladder tumors in rats.

Histocompatibility

P-137 LATE ACUTE ANTIBODY MEDIATED REJECTION ON TOP OF DENOVO MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS AFTER 9 YEARS OF RENAL TRANSPLANTATION

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Background: Acute antibody mediated rejection (AMR) is rarely reported as a long term complication of renal transplantation which can present on top of another chronic pathology affecting the graft.
Case summary: A 45 years old gentleman with chronic kidney disease due to unknown etiology. He had history of hypertension and hepatitis B infection with mild non-specific reactive hepatitis before transplantation. He received renal transplantation from his sister with 4 HLA mismatches. He received antithymocte globulin induction therapy and was maintained on steroids, azathioprine (AZA) and cyclosporine A (CsA). Up to eight years post-transplantation he was clinically and biochemically stable. He lost follow up for about one year, and then presented with nephritic nephrotic state and rise of serum creatinine to 210umol/l. He had no evidence of active hepatitis, cryoglobulinemia or significant radiological or serological abnormality. Graft biopsy revealed picture suggestive of acute AMR on top of denovo membranoprolipherative glomerulonephritis (MPGN) with focal crescent formation, diffuse immune complex deposition and peri-tubular capillaries (PTC) C4d positivity. Anti-HLA donor specific antibodies (DSA) were highly positive for B and T cells class I and class II. He was treated with intravenous immunoglobulin, plasma exchange, and anti-CD20 (rituximab). AZA was changed to mycophenolate mofetil and CsA to tacrolimus. He had partial response and s.creatinine continued at 220 umol/l.
Conclusion: This patient developed late acute AMR on top of denovo MPGN 9 years post-renal transplant which is a rare complication. Acute AMR was diagnosed by highly positive anti-HLA DSA, histopathological features and C4d deposition in PTC. He received aggressive anti-rejection treatment and his condition could be stabilized.

P-138 ANALYSIS OF DONOR SPECIFIC ANTIBODIES THE DAY OF THE GRAFT TO AVOID ACUTE REJECTION IN KIDNEY TRANSPLANTATIONS PERFORMED ACROSS A POSITIVE FLOW CYTOMETRIC CROSS MATCH

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Rationale: The prognosis of renal transplantations performed across a positive flow cytometric crossmatch (FCXM) remains controversial. The goal of this study was to analyze the graft outcome of these patients, according to the presence or not of donor specific antibodies (DSA).
Method: Between 2004 and 2007, 45 patients were transplanted in our centre, across a positive historical FCXM. The serum of the day of the graft (D0) and the historical serum the strongest at the FCXM, were analyzed using the most up-to-date flow beads single antigen assays in class I and in class II (Labscreen, One Lambda).
Results: 32 patients were transplanted across a positive D0 FCXM. Historical DSA were found positive in 34 recipients. D0 DSA were found positive in only 28 patients. There were 8 acute T cell-mediated acute rejections and 7 acute antibody-mediated rejection episodes. Occurrence of acute T cell-mediated or antibody-mediated acute rejection was associated with a lower GFR at 18 months post-transplantation (p=0.06 and 0.04 respectively), when compared with the GFR of patients who did not experience any acute rejections. Two factors emerged as independently associated with the occurrence of acute rejection, which were the presence of a D0 DSA (OR=10.90, p=0.009) and a D0 positive FCXM on B cells (OR=12.06, p=0.007). The sensitivity, specificity, positive and negative predictive value of a concomitant positivity of D0 FCXM and D0 DSA for predicting the occurrence of an acute rejection, were 87%, 73%, 62% and 92%, respectively,.
Conclusion: The identification of DSA in the D0 serum appears as a very sensitive test to predict the occurrence of acute rejection in patients transplanted across a D0 positive FCXM.

P-139 REJECTION AFTER HLA ANTIBODY INCOMPATIBLE KIDNEY TRANSPLANTATION; ASSOCIATION WITH ANTIBODY LEVELS AND SPECIFICITIES

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Transplantation of kidneys across a donor specific HLA antibody barrier may be successful, but there is a significant risk of acute antibody mediated rejection. It is important to try and identify the risk of rejection in advance of the transplant.
Sixty seven patients received HLA antibody incompatible transplants between 2003 and 2008. Donor-specific antibodies were assessed by microbead testing and conventional crossmatching.
Thirty six patients (54%) had rejection episodes in the first 12 months. In all but one case the histological and serological features were compatible with an antibody-mediated event. The risk of rejection was not related to age, gender or first graft/regraft status. The risk of rejection was associated with pretreatment level and their HLA specificity/ies, as shown in the Table.

Rejection risk							
HLA Class 1	×			×	×		×
HLA DR		×		×		×	×
HLA DP/DQ/BRB3-4			×		×	×	×
CDC +ve	1/1	0	1/3	1/3	1/2	0	6/8
FC +ve	5/12	0/1	1/4	2/2	1.3	3/4	5/5
FC –ve/bead +ve	5/12	1/1	0/3	1/1	0/2	0	0

The majority of patients fell into one of three groups. First, 24/25 patient with HLA Class 1 DSA only were cytotoxic (CDC) crossmatch (XM) –ve, and the rejection rate was 10/24 (42%), the same in both flow cytometric (FC) XM +ve and FC XM –ve groups. Second, 10 patients had DSA directed only against HLA DP or DQ or DRB3-4, and 2 (20%) had a rejection episode. Third, 13 cases had DSA against Class 1 +DR +DP or DQ or DRB3-4, 13/13 were CDC XM +ve or FC XM +ve, and 11/13 (85%) experienced rejection.
In summary, patients with HLA Class 1 DSA tended to have lower DSA levels, and a risk of rejection that did not depend on whether the FC XM was +ve or -ve. Those with DSA against only HLA DP, DQ or DRB3-4 had a low risk of rejection, but when there were also DSA against HLA Class 1 and DR, the crossmatch was positive and the rejection risk was high.

P-140 KIR AND CYTOKINE GENE POLYMORPHISMS IN HEART TRANSPLANT RECIPIENTS

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KIR (Killer Immunoglobulin-like receptors) and cytokines play a central role in NK cell and T-cell activation. However, the role of cytokine gene polymorphisms and recipient/donor KIR repertoire in solid organ transplantation is still unclear. We analyzed the incidence, grade of rejection and survival during the first year after heart transplantation with respect to patient cytokine gene polymorphisms and KIR genotypes. One hundred and fifty patients who received heart transplant in our center in the period 2000-2008 were studied. For all patients, SSO KIR genotyping on the Luminex platform and SSP-PCR typing of IL-12, IL-18 and IFN-gamma gene polymorphisms was performed.
While there was no significant correlation between AA and AB/BB KIR genotypes and survival, patients having the KIR 2DS5 gene in the KIR genotype appeared to be predisposed to heart transplant failure due to severe cellular rejection (R3) (p=0.036). The presence or absence of other non-framework KIR genes in recipients' genotype was not significantly associated with graft rejection.
Concerning cytokine gene polymorphisms, surprisingly, patients with the high-production genotype for IFN gamma (SNP +874 TT and 3'UTR5644 GG) had lower probability for development of rejection grade 2R within the first post-transplant year (p=0.02, OR=8.1 and p=0.01, OR=8.8 respectively).

Conclusion: Our study suggests that the presence of the KIR 2DS5 gene in the KIR genotype might be associated with a higher risk of heart transplant failure (due to rejection) while the high-producing IFN gamma genotype may be associated with lower risk for development of severe heart transplant rejection.

P-141 HOW USEFUL IS THE SCREENING ON THE CDC VERSUS FLOW CYTOMETRY CROSSMATCH (FCXM)?

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Prior sensitization in the context of blood transfusion, pregnancy or organ transplantation has a significantly negative impact on the outcome of solid organ transplantation. Hence regular alloantibody screening and crossmatching (XM) protocols have been implemented in all transplant programmes. At our laboratory the standard crossmatch is the complement-dependent cytotoxicity (CDC) crossmatch before transplantation. However with the development of more sensitive techniques we started to perform retrospectively FCXM on sera from kidney transplant (KTx) patients. We are now analyzing the CDCXM and FCXM results to determine the importance of a FCXM before KTx.
867 sera from KTx patients grafted between 1998 and 2008, 778 KTx and 39 re-KTx, were studied by CDCXM and FCXM. $2{,}5\times10^6$ enriched T and B lymphocytes were used for CDCXM and a two and/or three colour and IgG antibody binding were used for FCXM. All patients were screened by CDC and Luminex (Lx) and/or ELISA (Lat) and all samples (n=867) were CDCXM negative for T and B cells.
The FCXM results showed that 31 sera (3,6%) were positive. All those sera belong to the group (n=530) screened positive by CDC and Lx and/or Lat (CDC neg/Lx-Lat pos=30 (FCXM pos=2); CDC pos/Lx-Lat neg=366 (FCXM pos=14); CDC pos/Lx-Lat pos=134 (FCXM pos=15)). No FCXM positive among the 337 screened negative patients.
Since the Lx and Lat screening have a similar sensitivity and specificity to FCXM, we believe that organ allocation may be safely done without CDCXM in patients that always showed to be negative by CDC and Lx or Lat screening. However a FCXM is the most apropriate test for the population that are screening reactive. This policy will save time and money.

P-142 Hla CLASS I ANTIBODY FREQUENCIES IN THE SOUTHERN PORTUGAL KIDNEY CANDIDATE IN WAITING LIST

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Standard complement-dependent cytotoxicity (CDC) is considered the reference technique in anti-HLA antibody (HLAab) detection/identification. Over the last years the implementation of new technologies have increased the laboratory ability of identification and lowered the limit detection of these antibodies. The aim of this study was to investigate the frequencies of HLAab Class I in the sensitised candidates of our waiting list.
Material/Methods: 295 sensitised candidates waiting for kidney transplant, with a positive HLAab class I history (by CDC-PRA>5% and/or luminex technology (Lxtec)) were included. The historic existing sera of these candidates were studied by Lxtec, Single Antigen Bead assay (LABScreen® Single Antigen HLA Class I, Onelambda).
Positivity was defined when MFI was higher them 1000, HLAab against HLA-A,B,Cw was evaluated.
Results/Conclusions: By Lxtec we found antibodies against all HLA antigens. The most frequent antibodies were against HLA-B76, B57, A24, A23, B27, B82, B58, A66, B38, A25 percentage ranging from 34% to 27%. The less frequent was mainly anti-HLA-Cw. Our results were: anti-HLA-A n=33 (11%), anti-HLA-B n=30 (10%), anti-HLA-Cw n=8 (3%), anti-HLA-A+B n=69 (23%), anti-HLA-A+B+Cw n=81 (27%), anti-HLA-A+Cw n=6 (2%), anti-HLA-B+Cw n=16 (5%), 52 candidates were negative.
When comparing CDC and Lxtec, 250 candidates were studied by both technologies. From these 250: 129 had no specific antibody identified by CDC, in 57 the CDC and Lxtec identification did not correlate and 64 were identified by both technologies.
Despite the fact the study only evaluates anti-HLAab (IgG), possible explanation for the number of negative candidates, a high number of antibodies were found.
This technology allowed the detection: of antibodies directed against rare HLA antigens; of lower titter antibodies, not detected by CDC and a more precise identification of these antibodies.

P-143 DETECTION AND IDENTIFICATION OF HLA ANTIBODIES. COMPARISON OF COMPLEMENT DEPENDENT CITOTOXICITY (CDC) AND ENZYME LINKED IMMUNOSORBENT ASSAY (ELISA)

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Because of the characteristics of the CDC test the results obtained often differ intra and interlaboratory.We have performed ELISA antibodies screening and identification.Our aim was to compare panel reactive antibodies (PRA) results obtained with CDC and ELISA, to find out the distribution of anti class I and class II antibodies and to identify donor specific anti HLA antibodies (DSA) and not donor specific antibodies (NDSA) in sera from 16 first transplant patients and 6 regrafted patients.
In CDC tests, a panel of 30 lymphocytes was used.Sera were tested with and without DTT treatment. PRA was considered positive if over 3% and didn't become negative after DTT incubation,thus indicating IgG isotype.
ELISA tests to detect and identify anti HLA-IgG class I and class II antibodies were performed according to the manufacturer's instructions.(One Lambda LATM,LAT1288,LAT 1288 antigen trays).
776 sera from patients on the kidney and pancreas transplant waiting list and from 22 immunized kidney transplanted patients were tested being 113 (15%) CDC positive and 182 (23%) ELISA positive.

Table 1. Anti HLA IgG detection and distribution according to molecular class I and class II target

			Class I	Class II	Class I and II
CDC (–)	ELISA (+)	73	27(37%)	26(36%)	20(27%)
	ELISA (–)	553			
CDC (+)	ELISA (+)	105	31(30%)	9(9%)	65(62%)
	ELISA (–)	8			
CDC (+) negative post-DTT	ELISA (+)	4	2(50%)	0(0%)	2(50%)
	ELISA (–)	33			

Table 2. DSA and NDSA in first and second kidney transplants

				Class I	Class II	Class I and II
First Transplant	16 (73%)	DSA	13 (81%)	2 (15%)	3 (23%)	8 (62%)
		NDSA	3 (19%)	1(33%)	0 (0%)	2 (67%)
Second Transplant	6 (27%)	DSA	5 (83%)	2 (40%)	1 (20%)	2 (40%)
		NDSA	1 (17%)	0 (0%)	1 (100%)	0 (0%)

Though it's a small number it's interesting to note that in 6 regrafted patients, 4 had DSA against the first transplant donor and one against the first and second transplant.
Comparing CDC and ELISA we conclude that ELISA added sensitivity (93%),and identified 73 (10%) patients who had been CDC negative but turned out to have anti HLA IgG. On the other hand, the finding of 41 (5%) patients CDC(+) and ELISA(–) pointed out antibodies other than HLA, showing that there is still a gap in antibody identification.
Our conclusion is that to confirm or exclude the presence of antibodies more than one test is necessary. In our laboratory CDC and ELISA behaved as complementary methods for antibody screening.

P-144 CLINICAL RELEVANCE OF LUMINEX DONOR-SPECIFIC CROSSMATCHES: DATA FROM 165 RENAL TRANSPLANTS

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The clinical significance of the presence of donor-specific anti-HLA antibodies prior to renal transplantation detected solely by solid-phase techniques remains unclear.
This study was designed to determine the clinical relevance (acute rejection <6 months, graft survival) of the recently introduced bead-based Luminex donor-specific crossmatch (LumXm). A group of 165 patients, transplanted with a negative CDCXm between 1997 and 2001, was tested with a median follow-up of 8 years.
32 of 165 recipients had a positive LumXm: 16 were positive for class I, 15 for class II, 1 for both class I and II.133 recipients were negative.
Acute rejection-free survival (Kaplan-Meier) for all recipients was 77%, there was no difference between LumXm positive and negative recipients. Overall graft survival after a median follow-up time of 10 years was 56%. Recipients with a positive class I LumXm had worse 10-year graft survival: 27% vs 56% (p=0.006, cox-regression odds ratio=2.47). On the contrary, positivity for class II LumXm was not a significant risk factor for graft failure (p=0.7).
In conclusion, pre-transplant donor-specific anti-HLA antibodies detected by LumXm, had no correlation with acute rejection episodes. A positive class I LumXm resulted in worse long-term graft survival compared to a negative one.

P-145 *DE NOVO* PRODUCTION OF ANTI-HLA DONOR-SPECIFIC ANTIBODIES IN KIDNEY ALLOGRAFT RECIPIENTS: CLINICAL SIGNIFICANCE

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It has been suggested that post-transplant development of donor-specific antibodies (DSA) is predictive of adverse outcome in kidney transplantation.
In 466 kidney transplanted patients we analyzed the clinical impact of post-transplant HLA-DSA by FlowPRA Screening Beads/Luminex-Single Antigen Beads.
Seventy-three (15.7%) patients developed HLA-DSA and, as expected, graft failure (GF) was significantly higher in DSA-positive than in the DSA-negative patients ($P<0.0001$). Only 29 out of 73 (39.7%) patients with *de novo* HLA-DSA production lost their graft while 34 (46.6%) had functioning graft (FG). The remaining 10 patients (13.7%) suffered chronic allograft dysfunction (CAD).
Searching for causes of these different graft outcomes we compared graft course and DSA specificity/strength of DSA positive patients belonging to GF and FG groups.
GF-DSA-positive patients showed a higher incidence of acute rejection than FG-DSA-positive patients (37.9% vs. 14.7%, P=0.04). Graft failure occurrence had a mean value of 15.5±10.8 months, while FG-DSA-positive patients had a long period (58.4±41.2 months) of good function from DSA appearance ($P<0.0001$).
As for DSA characteristics, 8 out of 34 (24%) FG-DSA-positive patients showed production of antibodies specific for mismatched DQA1 molecule/s. The GF-DSA-positive patients had a higher incidence of wide antibody patterns specific for "public epitopes" of HLA mismatched donor molecules than FG-DSA-positive ones (65.5% vs. 32%, P=0.01).
Considering the strength of DSA (MESF values), 35% of FG-DSA-positive patients had low values (<100.000) vs. 3.5% of GF-DSA-positive ones (P=0.002).
Our data demonstrate that *de novo* production of HLA-DSA is associated with poor graft survival but may also occur in patients with good graft course. Characterization of antibody specificity, identification of antibody epitope and evaluation of DSA strength may be helpful in identifying patients who need implementation of therapeutic measures.

P-146 QUANTIFICATION BY QUANTIPLEX OF HLA DONOR SPECIFIC ANTIBODIES: CASE REPORT

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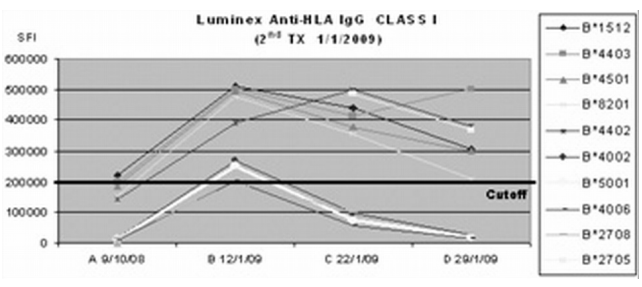
Introduction: Numerous reports have demonstrated the importance of monitoring HLA Antibodies (Ab). Actually we can quantify and monitoring Donor Specific Antibodies (DSA) by Quantiplex.
Materials and methods: We used Labscreen Single Antigen class I and Quantiplex (OneLambda) to study a female patient aged 51, who undergone 2nd Kidney Transplant (Tx).
1st Tx -2001/02, Donor HLA-A2; B51, *B44*; DR7.
Renal artery thrombosis occurs in surgery and the graft was removed.
HLA Ab (2008/01) – B76, *B44*, B45, B82.
2nd Tx 2009/01, Donor HLA -A2, 33; *B50*, 65; DR1.
Crossmatch was negative by CDC and Flow Cytometry.
Immunosuppressive induction: Prednisolone, Tacrolimus, MMF, rabbit antithymoglobulin.
Results: Immediate graft function, reaching normal serum creatinine in day 5. Acute deterioration of graft function (oliguria) detected in day 7 (serum creatinine 3,4 mg/dl). Suspecting a kidney rejection an empiric course of methilprednisolone was administered and graft biopsy made (humoral rejection Banff II).



DSA were detected (B61, *B50*, B27) with significant level of anti-*B50* Standard Fluorescent Intensity (SFI)=250853 U, (Cutoff 200000 U).
Promptly plasmapheresis (10), associated human low-dose immunoglobulin (0,5 mg/kg, 4×) was initiated on day 12. Graft function improves initially (creatinine 1,4 mg/dl). A second declining in graft function and the rise of DSA made suspicion of refractory humoral rejection, confirmed by a second biopsy. As a rescue therapy Rituximab (325 mg/m^2) was administered. The patient recovery graft function gradually (creatinine 1,4mg/dl) with concomitant reduction of DSA.
DSA anti-*B50* reach a significant value in day 12 after Tx and decline after plasmapheresis and IVIG and to insignificant value with Rituximab (SFI=18791U).
Conclusion: This new technology of DSA quantification may be a useful tool in management of kidney graft. This will allow a prompt and efficacious therapeutic approach in acute treating and follow-up of acute rejection.

P-147 RESULTS OF PREEMPTIVE KIDNEY RETRANSPLANTATION VERSUS RETURN TO DIALYSIS PROGRAM AFTER GRAFT LOST. IMPACT OF IMMUNOLOGICAL SENSITIZATION IN KIDNEY GRAFT LOST

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Introduction: Graft lost is considered one of the great problems in solid organ transplantation. Return to dialysis makes easier immunological sensitization with the difficult to find an optimal donor. Our aim lie in compare preemptive retransplant (group A) with return to dialysis (group B) in term of alloreactivity and immunological sensitization and results in future retransplants.
Material and methods: Retrospecive study of 11 preemptive retransplants in our center (Jan/01- Dec/08) versus 121 with graft lost and return to dialysis (67 retransplant). Anthropometrics, nephrological parameters, historical and current immunological data (HLA Typing, CDC HLA antibodies and CDC/FCXM) were evaluated. Statistical analysis by *SPSS* (*vs* 14.0; $p< 0,05$)
Results: Group A were younger (47,19 yrs vs 48,88) and at first transplant younger too (31,38 vs 35,74). Female sex in group A (62.5%) and males in group B (55.4%). Glomerulopathy first ESRD (37.5%/19%); secondly unknown in group A and diabetic nephropathy in group B. Previous transplant: Group A:1.25±0.25; Group B: 1,18±0,39. Not sensitized at retransplant: Group A:90%; Group:46.3%(hipersensitized: 27.3%). Positive historical FCXM:Group B: 18.8%;Group A:none. Time Prior transplant-graft lost: 98,06±70,00 months; 36,95±30,61 on dialysis (23,77±18,59 on waiting list). Graft lost-maximum peak PRA: 30,01±17,29 months (higher title of PRA: 30.07, and current title at retransplant in group B 12.09 (0.56 in group A). Immunosuppressant protocol in group A: Basiliximab, tacrolimus, micofenolate and prednisolone. 62,5% none acute rejection; 93,8% patient and graft survival. GFR/proteinuria in group A (Pre retransplant, 1m, 12m, 5y): 12.38 ml/min/163, 1 mg/24U; 69/43, 7; 66.8/36, 2; 68.6/29.4
Conclusions: Preemptive retransplant is an excellent option face with graft lost, avoiding immunological sensitization and guarantying good results in renal graft function, patient and graft survival rates. PRA appear frenquently and later than expected after graft lost.

Heart

P-148 ASSOCIATION OF NT-PRO BRAIN NATRIURETIC PEPTIDE LEVELS AND ECHOCARDIOGRAPHIC VARIABLES IN LONGTERM HEART TRANSPLANT RECIPIENTS

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The diagnostic value of N-terminal pro-brain natriuretic peptide (NT-proBNP) after heart transplantation (HTx) is still incompletely understood. We investigated the relationship between NT-proBNP levels and echocardiographic variables in HTx patients with preserved systolic graft function.
Patients and methods: 176 asymptomatic pts (28f/148m), aged 60±11yrs, 105±58 mo postHTx, donor age 34±12yrs were studied. Echocardiography and NT-proBNP (sandwich immunoassay by Roche Diagnostics) sampling was performed at the same follow-up visit.
Results: Median resting NT-proBNP level was 394 pg/ml (25th –75th percentile 165-758; range 17 – 7792 pg/ml). In multivariate analysis, log-

transformed NT-proBNP levels correlated significantly with left and right atrial dimensions (r=0.45 and r=0.40, both $p<0.0001$), left ventricular end-diast.diameter (r=0.18, $p<0.05$), left ventricular hypertrophy grade (r=0.19, $p<0.05$), left ventricular diast.dysfunction stage (r=0.17, $p<0.05$) and time after HTx (r=0.32, $p<0.0001$).
Conclusion: Our data – confirming earlier results of a time dependent rise in NT-proBNP levels late after HTx–demonstrate that increased endocrine activity of the nonfailing transplanted heart is associated with left ventricular size, mass and a restrictive filling pattern.

P-149 PSYCHOSOCIAL PARAMETERS OF COMPLIANCE AND SURVIVAL OF PATIENTS WITH ADVANCED HEART FAILURE

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Purpose: Compliance is critical for care of chronic heart failure (HF) patients, heart transplant candidates. Several psychosocial factors are considered risk factors of noncompliance. They include persistent anxiety and depressive symptoms, alcohol and nicotine abuse, lack of social support, low socio-economic status, presence of the organic psychosyndrome, and maladaptation. To evaluate psychosocial parameters and survival related to compliance in patients (pts) pts with advanced HF.
Methods: 412 pts (360 males) admitted to HF centre, mean age 50.0±10.7 years, were included. In 60%, primary cause of HF was cardiomyopathy. 52% of pts were in functional class NYHA III, 15% in NYHA IV. Mean left ventricular ejection fraction was 21.0±4.5%. Median survival of all pts was 48.0±5.4 months (CI=37.4-58.6). We used Beck Depression Inventory (BDI) to assess depression, Spielberger Questionnaire of Anxiety (STAI) anxiety, Visual Analogue Scale (VAS) for socio-economic status, and GTO and TMBM scores for organicity. Survival was evaluated using LogRank test.
Result: Mean BDI score of the whole group was 10.6±6.3. Depression was present in 214 (52%) of pts. Mean STAI score was 33.2. Anxiety was present in 53% of pts. 13% of pts had a lack of social support and 14% had low socio-economic status. 20% of pts were smokers and/or alcohol drinkers. Organic psychosyndrome was present in 14% of pts.
Any degree of depression was significantly associated with worsened survival (LogRank=7.2, p=0.007). Although pts with high anxiety (LogRank=0.11, p=0.74), low socio-economic status (LogRank=2.02, p=0.16), lack of social support (LogRank=0.53, p=0.47), alcohol and nicotine abuses (LogRank=0.05, p=0.83), presence of organicity (LogRank=0.05, p=0.82) had shorter survival, differences were not significant.
Conclusion: Prevalence of depression and anxiety among HF patients is high. Depression is the only psychosocial parameter of compliance that significantly predicts shorter survival of heart failure patients.

P-150 HYPOMAGNESEMIA AFTER HEART TRANSPLANTATION: SURPRISINGLY REMAINS A PROBLEM

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Purpose: Magnesium (Mg) plays a major role in the control of cardiovascular functions. Low serum Mg usually reflects a profound deficiency of total body Mg. Purpose of this study was to examine Mg levels after heart transplant (HTx) in context of selected aspects of its metabolism, possible causes, and consequences.
Methods: Data from 113 patients (99 males), average age 52.4 (20-73) yrs, at regular follow-ups 77.2 (1-224) months after HTx were analyzed retrospectively. 86 pts received ciclosporin (CSA), 20 tacrolimus, 6 sirolimus, 1 patient everolimus, and 62 were taking prednisone. Occurence of hypomagnesemia according to the local laboratory range (less than 0.7 mmol/L) was recorded. The cohort was divided in two groups (with and without hypomagnesemia, resp.). Age, time since HTx, systolic (sBP) and diastolic (dBP) blood pressures, heart rate (HR), serum creatinine and potassium, prednisone dose, and blood CSA concentration where appropriate were assessed and compared between the groups. Differences were evaluated using Student's t-test.
Results: Average serum Mg was 0.72±0.13 mmol/L. Mg was low in 48 (42.5%) pts. There were no differences between the two groups in age, time since Tx, sBP, dBP, and creatinine level (p=n.s.). In comparison with the non-low Mg group, the low-Mg group exhibited higher HR (85.4±11.4 vs. 92.4±10.5 beats/min, $p<0.01$) and lower potassium (4.50±0.57 vs. 4.14±0.61 mmol/L, $p<0.01$). Low-Mg pts received higher prednisone doses than pts without (5.88±6.9 vs. 3.03±4.13 mg/day, $p<0.05$). Low Mg level was associated with higher CSA (199.4±93.7 vs. 150.7±47.3 ng/mL, p=0.01).
Conclusions: Prevalence of low Mg level after HTx is strikingly high. Higher HR among patients with low Mg level can indicate its possible role in HR control after heart Tx. Mg level was not associated with age or renal function but CSA level and prednisone dose. Low Mg also reflected low serum potassium.

P-151 IMMUNOSUPPRESSION WITH TACROLIMUS MONOTHERAPY IN RENAL TRANSPLANTATION: A 6 YEARS ANALYSIS

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Background: Long term outcome of kidney recipients on monotherapy with calcineurin inhibitors is poorly reported in literature. While some authors have reported their experience with cyclosporine, data with tacrolimus (Tac) monotherapy are lacking. This study aimed to evaluate the long term outcome of patients on Tac monotherapy in our institution.
Methods: This retrospective monocentric cohort study was conducted in 91 first kidney recipients transplanted between 1998 and 2003. After an initial triple regimen, patients were treated with Tac monotherapy at month 6. At the end of the follow-up, two groups were distinguished: successful Tac monotherapy group (sTac) and unsuccessful Tac monotherapy group (unTac) in witch additional immunosuppressive agents or Tac withdrawal was required. Cohort and individualized subgroups were analysed.
Results: Median cohort follow-up was 7.1 year. Overall patient and graft survival in the ITT population was 93.7 and 89% respectively at 6 years follow-up. Tac monotherapy was achieved in 93.3% of patients at the 6th month post-transplantation and was maintained in 57.8% of ITT patients at the end of the follow-up. Incidence of acute rejection and chronic allograft nephropathy was 13.2%. Median serum creatinine was 132 and 117μmol/L at year 4 and 6 respectively, 112μmol/L in sTAC group at year 6. Incidence of new-onset diabetes mellitus, cancer and CMV disease were 21.7, 13.2 and 14.3% respectively. Only one non fatal cardiovascular event occurred.
Conclusion: Tacrolimus monotherapy can be achieved in a majority of low immunological risk patients and was associated with excellent long term kidney function and patient/graft survival.

P-152 POST-TRANSPLANT OUTCOME OF DILATED CARDIOMYOPATHY CAUSED BY DYSTROPHIN GENE DEFECTS

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Patients with dystrophin (DYS) gene defects may develop dilated cardiomyopathy (DCM) and congestive heart failure (CHF). Heart transplantation (HTx) is established as an effective therapy.
Purpose: To describe the follow-up and to evaluate the outcome of DCM patients with DYS gene defects who underwent HTx.
Methods: DCM was diagnosed according to WHO criteria. DYS gene screening was performed in male patients with both normal and increased sCPK and in the presence of DYS defects immunostaining in endomyocardial biopsy. The genetic testing consisted of multiplex test for deletion defects and direct automated sequencing of the 75 exons and flanking regions of the gene.
Results: We identified DYS gene defects in 44 of 424 male probands with DCM (10.3%); the defects were multiple deletions in 42 and point mutations in 2 cases. Seven young (2±0.7 years) patients with Duchenne muscular dystrophy were excluded from the study. Of the 37 young-adult patients, 31 had DCM plus Becker Muscular Dystrophy (BMD) while the remaining 6 only had DCM. The mean age at clinical presentation was 34±15 years. Thirty-two of the 37 patients had increased sCPK (86%). During 80±41 months of follow-up, the following events were recorded: HTx (n=8, 22%), CHF death (n=9, 24%). No patient died suddenly or developed life-threatening ventricular arrhythmias. Among the HTx patients, 7/8 (87.5%) are alive and in good clinical conditions after a mean follow-up time of 7±4 years.
Conclusions: In our experience, the outcome after HTx for DYS patients with DCM is characterised by good clinical conditions during a long-term follow-up without any myological functional deterioration.

P-153 RELATIONSHIP BETWEEN BNP LEVEL DYNAMICS AND MYOCARDIAL REVERSE REMODELING IN PATIENTS REFERRED AS HEART TRANSPLANT CANDIDATES WITH SHORT HISTORY OF NON-ISCHEMIC HEART FAILURE

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Patients suffered from the first episode of severe heart failure are often referred to our heart failure clinic as potential heart transplant candidates. Aim of this study was to assess the efficacy of proper led farmacotherapy and value of BNP monitoring.
Methods: 18 patients with short history of non-ischemic heart failure with LVEF 20-30% were consecutively examined. The follow-up took from 6 upto 24 months. The patients with toxic aetiology or postpartum cardiomyopathy were excluded. Complete farmacotherapy was titrated to maximal tolerated doses. Echocardiography, spiroergometry and BNP levels (chemiluminiscent method) were performed four times a year.
Results: Mean BNP level decreased from 312,7 ng/l to 107,1 ng/l, p=0,0025. Mean LVEF increased from 25 to 38%, p<0,001. The clinical improvement was observed in all patients. Nobody died, nobody was indicated to heart transplantation.
LVEF was normalized in 6 patients in the period from 4 upto 12 months from the beginning of the disease. BNP levels were normalized 4-11 months before complete LV reverse remodeling. Improvement of LVEF at least of 10% was observed in 8 pts, in all of them BNP levels were in the period of 1-4 months normalized. BNP levels decreased in all patients. In four of them BNP levels remainded in pathological range with no trend of reverse remodeling.
Summary: Patients who survived first manifestation of non-ischemic heart failure and were released from hospital to an ambulatory care have a relatively good prognosis under the condition of proper led farmacotherapy. We observed significant myocardial reverse remodeling in 67% patients. This phenomenon was preceded by the normalization of BNP level. There was no trend of reverse remodeling in patients with persisting pathological BNP levels.
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P-154 SEEKING TRANSLATIONAL EVIDENCE FOR A NEW INDICATION OF INTRAVENOUS IMMUNOGLOBULIN IN SOLID ORGAN TRANSPLANTATION

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Purpose: Infections remain the first cummulative cause of death in heart transplantation (HT). We assessed IgG hypogammaglobulinemia (HGG) as risk factor (RF) of infection in HT, and utility of intravenous immunoglobulin (IVIG) in HT recipients with HGG and infections.
Methods/Materials/Results: 1. Time course and RF of HGG after HT
Prospective study (n=75). Induction: 2-doses daclizumab; maintenance: tacrolimus or cyclosporine, mycophenolate mofetil and prednisone. Definition of HGG: IgG level <600 mg/dl post-HT (nephelometry, cost per determination: 10 euro). Surgical controls (SC): 17 patients undergoing heart surgery without immunesuppression. Baseline and 7d IgG levels were similar in HT and SC. Decreased levels of IgG were observed in HT at 1m, 3m and 6m. 54.6% patients had post-HT HGG. RF for HGG: Lower baseline IgG level (Cox RH 2.60; p=0.004); time of post-HT hospitalization (RH 1.03; p=0.0002) and pre-HT renal insuficiency (RH 5.37; p=0.004).
2. HGG as a risk factor of infection in HT.
Retrospective study (n=41). Induction: ATGAM. 46% had severe infections. Lower post-HT IgG (<589 mg/dL; RH 3.38; P = 0.019) was a RF of infection.
Prospective study (n=84). Induction: Daclizumab. 32.1% had severe infections. Lower post-HT IgG (<676 mg/dL; RH 4.03; P=0.02) was a RF of infection.
3. Tolerance and safety of IVIG in HT with HGG and infections.
Prospective follow-up study (n=104). 31 HT patients with post-HT HGG and severe infections were treated with IVIG [300-400 mg/kg with the goal to reach normal serum IgG levels (>700 mg/dL)]. IVIG was well tolerated. No moderate or severe adverse reactions were observed during follow-up. Post-IVIG number of infectious episodes was significantly lower as compared with pre-IVIG incidence in these patients.
Conclusion: HGG is a risk factor of infection in HT. IVIG is well tolerated and reduces post treatment incidence of infections.

P-155 MONITORING OF LYMPHOPROLIFERATIVE RESPONSES USING CFSE AND CLINICAL FINDINGS AFTER HEART TRANSPLANTATION

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Purpose: The flow cytometric analysis of lymphoproliferative responses (LPR) by serial halving of the fluorescence intensity of the vital dye carboxyfluorescein diacetate succinimidyl ester (CFSE) has become widely used around the world. CFSE-derived indices of LPR are equivalent to 3H-thymidine-based assays and allows the definition of proliferating cell subsets. We aimed to evaluate LPR using CFSE in heart transplant recipients and its association with development of rejection and infectious complications.
Material and methods: In a prospective follow-up study, 12 heart transplant recipients were evaluated. Induction therapy: 2-doses daclizumab, maintenance: tacrolimus or cyclosporine, mycophenolate mofetil and prednisone. Universal prophylaxis with gancyclovir. Immunological studies: Specific LPR were determined by CFSE assays using the mitogen PHA (positive control) and specific stimuli such as hepatitis B (HBs), Flu, pneumococcus polysscharide (PPS), tetanus toxoid vaccines and PPD (specific controls), after 6 days of culture. CD3, CD4 and CD8 T cell subsets were evaluated by flow cytometry. Time of studies: pre-heart transplantation (HT) and 3 months after HT.
Results: A significant decrease in LPR against specific stimuli was observed in the post-transplant evaluation as compared with baseline (pre-transplant) values: CD8+CFSE-HBs (0.05 vs 0.21%, p=0.04), CD8+CFSE-PPS (0.11 vs 0.41%, p=0.04). Higher mean CD3+CFSE PHA LPR were observed at 3 months after HT in patients who developed rejection (n=6) in comparison with patients without rejection (n=6, 55 vs 28%, p=0.04, respectively). On the other hand, patients who developed infections (n=5) disclosed significantly lower CD3+CFSE PHA LPR that those without infections (n=7, 27% vs 53%, p=0.04, respectively).
Conclusion: Although the study was performed in a small cohort of patients, the differences observed between patients with and without the analysed complications, suggest that LPR measurement using CFSE, might be useful to identify patients at higher risk of developing rejection or infectious complications.

P-156 PLASMAPHERESIS AND IMMUNE GLOBULIN: TOGETHER THEY ARE STRONG AGAINST HUMORAL REJECTION IN CARDIAC TRANSPLANTATION

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Acute cellular rejection during the first year after cardiac transplantation is a common problem. Antibody mediated (non-cellular) rejection (AMR), however, is rare and associated with a worse prognosis. Optimal therapy for AMR has not been defined and literature provides information on single case-reports and small series only. Here, we describe a successful treatment of AMR after cardiac transplantation.
Methods and materials: A 50-year old female underwent cardiac transplantation for non-compaction cardiomyopathy. Three weeks after transplantation, this patient evolved to chronic haemodialysis, because of tacrolimus toxicity and a history of renal failure pre-transplantation. Fifty-four days post transplantation she developed acute cellular rejection grade II, according to the ISHLT 2004 grading system. She was successfully treated with corticosteroids (1000 mg/day during three days). Unfortunately, she developed AMR at day sixty-three, refractory to pulse dose with steroids. The diagnosis was based upon histological features on light microscopy and a positive immunofluorescence (C3++, fibrinogen+++, C1q+ and IgM deposits in the vascular wall) on an endomyocardial biopsy. Graft dysfunction was associated with symptomatic heart failure, as well as echocardiographic signs (sm. med. annulus <5cm/s). Right heart catheterisation showed hemodynamic detioration, and inotropics had to be started. Plasmaphereris during five subsequent days, followed by plasmapheresis alternated by the administration of immune globulin during non-dialysis days (100 mg/kg, during 5 days) was started.
Results: A biopsy just after the last plasmapheresis session showed less C1q and C3 deposits in the vascular wall. A biopsy one, two and three months after combination therapy with plasmapheresis and immune globulin excluded any sign of AMR. There was also no feature of heart failure (sm. med. annulus >6cm/s, ejectionfraction 45%).
Conclusion: Plasmapheresis in combination with intravenous immune globulin seems to be an interesting treatment option against humoral rejection post-cardiac transplantation.

P-157 PRETRANSPLANT PREGNANCY- ASSOCIATED PLASMA PROTEIN A (PAPP-A) AS A PREDICTOR OF CHRONIC GRAFT VASCULOPHATY AND POSTTRANSPLANT CARDIOVASCULAR EVENTS

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Chronic allograft vasculophaty (CAV) remains to be one of the most serious complications after heart transplantation (HTx) and a main cause in death of patients survived the first year after HTx. Circulating levels of pregnancy- associated plasma protein A (PAPP-A), a zinc binding metalloproteinase, have been shown to be elevated in patients with chronic stable angina and acute coronary syndromes. We have studied the relationship between pretransplant PAPP-A plasma level and posttransplant cardiovascular events.
Methods: The study included 24 adult recipients with heart transplant (between 18 to 65 years old, 20 men and 4 women). 15 recipients were recruited before to 96 months post-transplant. Immunosuppression was achieved using a combination of mycophenolate mofetil, steroids and either cyclosporin. Plasma concentrations of PAPP-A (56 blood samples) were measured by ELISA ("Active PAPP-A ELISA DSLABS", USA).
Results: PAPP-A level in patients awaiting HTx was 11.5±3.7 mU/l, in recipients at the first year after HTx – 11.1±3.2 mU/l, in 1-16 years after HTx – 12.9±2.4 mU/l. PAPP-A median value was 11 mU/l.
Cardiovascular complications after HTx (end points: CAV, acute graft rejection 3A grade, acute graft rejection with hemodynamic compromise) developed in 75% recipients with pretransplant PAPP-A levels >11 mU/l and none of recipients with pretransplant PAPP-A levels <11 mU/l. During the first year after HTx end points have been revealed in 76,9% recipients with PAPP-A levels >11 mU/l and in 25% recipients with PAPP-A levels <11 mU/l.
In 1-16 years after HTx PAPP-A level was >11 mU/l in all recipients with CAV (14.4±1.8 mU/l) and was higher than in recipients without CAV (10.6±1.7 mU/l, $p<0.05$).
Conclusion: High level of pretransplant PAPP-A might be a prognostic marker for the development cardiovascular complications after HTx.

P-158 PLASMA LEVELS OF SOLUBLE CD40 LIGAND IN HEART TRANSPLANT RECIPIENTS

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Transplant coronary artery disease (TxCAD) is the main cause of late morbidity and mortality in patients (pts) after heart transplantation (HTx), but its pathogenic mechanisms are still unclear. CD40 ligand (CD154) is a transmembrane protein which is structurally related to TNF-a. Soluble CD40 ligand (sCD40L) has been suggested as a link mediator between inflammation and thrombosis. We investigated clinical and prognostic significance of sCD40L in heart transplant recipients.
Methods: 24 patients (pts) underwent HTx and were examined before and after HTx (42.5±7.5 years, 20 men and 4 women). Immunosuppressive therapy included steroids, cyclosporin, and mycophenolate mofetil. Plasma concentrations of sCD40L (84 blood samples) were measured by ELISA ("Bender MedSystems", Austria).
Results: sCD40L median value was 0.32 ng/ml. sCD40L levels in pts underwent HTx 1-5 years ago were significantly higher when compared to pts awaiting HTx and pts at the first year after HTx (0.97±0.5 vs. 0.5±0.3, and 0.77±0.5 ng/ml respectively, $p<0.01$, $p<0.05$). sCD40L levels in pts underwent HTx 5-16 years ago were significantly lower (0.2±0.2 ng/ml, $p<0.01$). Cardiovascular complications after HTx (TxCAD, and also an acute graft rejection with hemodynamic compromise) developed in 83,3% pts with pretransplant sCD40L levels >0.32 ng/ml and only in 10% pts with pretransplant sCD40L levels <0.32 ng/ml. Kaplan-Meier survival estimates showed better survival in pts with sCD40L levels <0.32 ng/ml (90% vs 16.7%, at 96 months of follow-up, p=0.0018). In pts underwent HTx 5-16 years ago sCD40L levels were significantly higher in recipients with TxCAD (0.3±0.1 ng/ml) than in recipients without TxCAD (0.12±0.14 ng/ml).
Conclusion: sCD40L levels obtained before HTx predict development of TxCAD and cardiovascular events during the first three years after HTx.

P-159 EFFICACY AND SAFETY OF COMBINED THERAPY OF TACROLIMUS AND ATORVASTATIN IN HEART TRANSPLANT RECIPIENTS

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Background: Lipid lowering therapy with statins has been associated with decreased mortality and morbidity in heart transplant recipients. Among available drugs, pravastatin, fluvastatin or low-dose simvastatin have been recommended due to low risk of pharmacokinetic interaction. However, these first-line statins possess rather modest lipid lowering effect and selection of alternative statins is limited due to interactions with cyclosporine A (CsA).
Aim: The aim of this prospective study was to evaluate safety and efficacy of conversion to tacrolimus and atorvastatin in CsA-treated heart transplant recipients and dyslipidaemia refractory to fluvastatin.
Methods: Thirty heart transplant recipients taking CsA and 40-80 mg of fluvastatin daily with total cholesterol levels >211 mg/dl (5.5 mmol/l) were recruited. After baseline assessment, they were converted to tacrolimus and atorvastatin at a starting dose of 20 mg/day and underwent clinical and laboratory follow-up at 1, 4, 7, 10 and 13 months.
Results: During 13 months of follow-up, treatment with tacrolimus and atorvastatin was tolerated in 24 patients (80%). No cases of myotoxicity or liver toxicity were observed. After conversion, the mean cholesterol level (as averaged from levels at 1, 4, 7, 10 and 13 months) was lower than before conversion (183±24 vs. 231±33 mg/dl, $p<0.0001$; relative reduction by 20.5±10.6%). As compared with baseline values, conversion resulted also in lower mean LDL-cholesterol levels (92±25 vs. 130±38 mg/dl, $p<0.0001$; relative reduction by 28.2±14.6%) and lower mean triglyceride levels (166±60 vs. 220±101 mg/dl, $p<0.0001$; relative reduction by 19.7±26.6%).
Conclusions: Conversion to tacrolimus and atorvastatin appears to be safe and effective lipid lowering therapy in CsA-treated heart transplant recipients with dyslipidaemia refractory to fluvastatin.

P-160 THE ROLE OF THE LEVITRONIX CENTRIMAG DEVICE IN THE THERAPY OF POSTTRANSPLANT HEART FAILURE

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Frequently the only therapy for primary graft- and right heart failure, as well as low output syndrome from acute rejection, is implantation of a mechanical circulatory support system, until recompensation or retransplantation. The Levitronix Centrimag device, which is a centrifugal pump designed for extracorporeal support and that operates without mechanical bearings or seals, might be an ideal device for this purpose.
At our institution, the Levitronix Centrimag was implanted in twelve heart recipients (mean age 53 years) for acute rejection (n=7), primary graft failure (n=1) and acute right heart failure (n=4). 8 pts have had VAD support before transplantation (CardioWest n=5, DuraHeart n=1, CorAide n=1, Thoratec LVAD n=1). In 7 cases the Centrimag device was implanted as femoro-femoral bypass, in 4 pts as a RVAD and in 1 pt as BVAD. The mean support time was 9 days. At least 9 pts could be weaned, 1 pt underwent retransplantation. 5 pts are long-term survivors.
In our experience, the Levitronix Centrimag seems to be safe and effective in the treatment of posttransplant heart failure, achieving effective circulatory support and ventricular off-loading. We propose its use in isolated right or biventricular graft failure either as a bridge to recovery or as bridge to re-transplant. Nevertheless, heart failure after cardiac transplantation severe enough to require mechanical circulatory support is currently associated with major complications and high mortality.

P-161 FP15 A NOVEL PEROXYNITRITE DECOMPOSITION CATALYST PROTECTS AGAINST MYOCARDIAL AND ENDOTHELIAL REPERFUSION INJURY AFTER ORTHOTOPIC HEART TRANSPLANTATION

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Purpose: Peroxynitrite is highly active free radical species which plays a central role in ischemia/reperfusion injury. In the present study, we investigated the effects of FP15, a novel peroxynitrite decomposition catalyst on postischemic myocardial and endothelial function in a canine heart transplantation model.
Methods: After 4 hours of ischemic preservation, 12 orthotopic heart transplantations were performed. At the beginning of reperfusion either saline vehicle (control, n = 6), or FP-15 (0.3 mg/kg, n=6) was applied. Left ventricular pressure-volume relationships were measured by a combined conductance

catheter and the slope of the end-systolic pressure volume relationship (Ees) was calculated before explantation and after 120 minutes of reperfusion. Coronary blood flow (CBF), endothelium-dependent vasodilatation to acetylcholine (ACH) and endothelium-independent vasodilatation to sodium nitroprusside (SNP) were also determined. Myocardial tissue samples were taken to determine ATP.
Results: Admimistration of FP15 led to significantly better recovery (given as percent of baseline) of Ees (89±4 vs. 46±7%, $p<0.05$). CBF was significantly higher in the FP15 group (49±8 vs. 22±5, ml/min, $p<0.05$). While the vasodilatatory response to SNP was similar in both groups, ACH resulted in a significantly higher increase in CBF in the FP15 group (70±10% vs. 28±8%, $p<0.05$). ATP content was significantly higher in the FP15 group (12.0±1.9 vs. 4.7±1.3 μmol/g drw).
Conclusions: The peroxynitrite decomposition catalyst reduces myocardial and endothelial reperfusion injury after orthotopic heart transplantation.

P-162 MECHANICAL CIRCULATORY SUPPORT IN END-STAGE HEART FAILURE AS BRIDGE TO HEART TRANSPLANTATION

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Background: Shortage of organs for cardiac transplantation (Htx) is an important limitation for an effective treatment of patients (pts) with end-stage heart failure.Currently,in unstable pts,mechanical circulatory support (MCS) and particoularly ventricular assist devices (VAD) offer a successful bridge to Htx.We report our experience with long-term pulsatile and continuous flow blood pumps.
Methods: Between March 2002 and February 2009, 36 transplantable adult pts were supported on long-term MCS at our institution. LVAD support (Group A) was established in 25 pts (19 HeartMate II LVAS: 15 men, age 50±9.6 (range 31-64) years; 6 HeartMate I XVE LVAS: 5 men, age 52.5±9.1 (range: 38-61) years). BVAD support(Group B) was established in 11 pts (9 Thoratec paracorporeal: 7 men, age 46.5±11.9 (range: 23-63)years; 1 Thoratec implantable: man, 42 years; 1 CardioWest Syncardia Total Artificial Heart: man, 38 years).Indication at implantation were: ischemic cardiomyopathy(CMP) in 18 pts, idiopathic CMP in 16, restrictive CMP in 1,and post-myocarditis CMP in 1.
Results: Mean support time was 220±210.5 days in Group A (range: 1-665 days) and 87±71.6 days in Group B (range: 8-235 days). Early (30-days) mortality on VAD support was 27.7% (10 pts), 5 pts were in Group A and 5 pts in Group B, with multiple organ failure as main cause of death. Bleeding requiring re-operation occurred in 11 (30.5%) pts (7 Group A, 4 Group B) and cerebral haemorrhage in 3 (8.3%) pts (1 Group A, 2 Group B). There were 3 drive line infection (Group A) and 1 device failure (HeartMate I LVAS). Nineteen pts (52.7%) were transplanted (14 Group A, 5 Group B) and 4 pts (11.1%) are at home on the waiting list for transplantation. At follow-up survival rate after Htx is 63.1% (8 pts Group A, 4 pts Group B).
Conclusions: According to our experience, long-term MCS still proves to be successfull as bridge to Htx. End-stage heart failure pts benefited well from either pulsatile and non-pulsatile devices. Good mid-, long-term results achieved may support the use of these blood pumps even for permanent solution in no-transplantable pts.

P-163 CMV INFECTION IN THE NEW MILLENIUM

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Background: Cytomegalovirus (CMV) is a significant cause of morbidity in heart transplantation. However new diagnostic tools (CMV-PCR) as well as new treatment options (ganciclovir GCV) have been adopted in clinical practice. The aim of this analysis was to evaluate the incidence of CMV infection (Inf)/disease (Dis) between 2002-2008 in comparison with earlier eras.
Methods: We studied 823 heart transplant recipients (1984-2008) who received quadruple-immunosuppressive therapy. The study population was categorized into 4 groups according to donor and recipient CMV serology (D–/R–, D–/R+, D+/R–, D+/R+) and 4 eras (1984-91, 92-96, 97-02, 02-08). CMV Inf was defined as positive IgM serology (≤1990), positive EA (91-02) or increase of CMV-PCR ≥600 cps/ml (≥2002). Dis was defined as Inf with clinical symptoms. All patients received CMVIG and CMV-high risk patients (D+/R–) received prophylaxis with GCV for 3 weeks (97-01) and val-GCV for 3 months (≥02). The incidence of CMV Inf and CMV Dis was analysed between eras and groups.
Results: Overall Inf remained similar during the different eras (12 months: 35% vs. 34 vs. 30 vs. 34%, p=ns). Dis decreased significantly (12 months: 16% vs. 21 vs. 10 vs. 4%, $p<0.0001$). Since 1997 here was no death due to CMV. Inf and Dis decreased in the high risk (D+/R–) group during the eras (Inf: 12 months: 53% vs. 49 vs. 39 vs. 29%, p:0.09; Dis: 12 months: 24% vs. 31 vs. 22 vs. 0%, p:0.002). Between 02-08, Inf was highest in D+/R+ patients (12 months: 55% vs. 3 (–/–), 30 (–/+) and 29 (+/–)%, $p<0.0001$), however there was no difference in Dis (12 months: 8 (+/+) vs. 0 (–/–), 3 (–/+) and 0 (+/–)%)
Conclusion: In the era of new CMV diagnostics & therapeutics, CMV Inf is diagnosed earlier and therapy can be started before CMV Dis occurs. This approach can reduce morbidity and mortality. However, CMV +/+ patients might benefit from CMV prophylaxis with GCV

P-164 ROLE OF MARGINAL DONORS IN HEART TRANSPLANTATION

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Purpose: Over the last years (y.) changes in both donor and recipient profiles occurred in heart transplantation (HTX). Encouraging clinical outcome of marginal donors (d.) in candidates older than 60 y. of age lead us to consider suboptimal d. in younger recipients. Therefore our experience was retrospectively reviewed.
Methods: Among 172 pts undergone to HTX January 2000 to December 2008 undergone to HTX there were 69 (40%) aged over 61 y., Group 1, G1. Remaining 103 (60%), were ranging from 18 to 60 y. Organs retrieved from marginal donors were implanted in 59 G1 pts (85%) vs. 47 (46%) younger candidates, Group 2A, G2A. On the other hand 56 G2 pts had optimal organs and were enrolled in G2B group. Sex distribution, cause of end stage heart failure pre operative pulmonary hypertension occurrence, pre HTX clinical status, follow up mean length did not show any statistically significant difference
Results: Results are summarised on Table 1

Table 1. Results

Variable	G1A (59 pts, marginal donors)	G1B (10 pts, marginal donors)	p.v.	G2A (47 pts, marginal donors)	G2B (56 pts, optimal donors)	p.v.
Periop. mortality	3	2	n.s.	2	1	n.s.
60 mos. act. surv.	72%	77%	n.s.	81%	83%	n.s.
Permanent pace maker need	22%	2%	<0.005	15%	1%	<0.005
12 mos. ac. rejetion freedom	34%	31%	n.s.	25%	27%	n.s.
12 mos. infection freedom	28%	27%	n.s.	43%	42%	n.s.
60 mos. chronic rejection freedom	55%	57%	n.s.	70%	64%	n.s.
60 mos. neopasia freedom	76%	79%	n.s.	84%	81%	n.s.
60 mos. chronic renal failure freedom	73%	75%	n.s.	87%	88%	n.s.

Conclusion. Use of marginal donors may reduce mortality on waiting list. Further experience is therefore needed.

P-165 NON-INVASIVE ASSESSMENT OF MYOCARDIAL FUNCTION AND STRAIN RATE IMAGING BY DOPPLER MYOCARDIAL ULTRASONOGRAPHY IN KIDNEY TRANSPLANTED PATIENTS

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Aim: Aim of present study was to analyze left ventricular function using Doppler myocardial and strain rate imaging in patients with chronic renal failure 12 months after renal transplantation.
Methods: Thirty healthy subjects and 30 age and sex- comparable patients with chronic renal failure treated with renal transplantation underwent standard Doppler echocardiography and pulsed myocardial imaging (DMI) together with strain rate imaging from the basal segment (SRI) of left ventricle (LV) and intima-media thickness measurements (IMT) of carotid arteries.

Table 1. LV DMI analysis of LV

Variable	CRF – RT (n=30)	Controls (n=30)	p Value
LV mass index (g/m^2)	96,1±12.9	44,5±5,7	<0,01
LV ejection fraction (%)	56±15	58,7±6,3	NS
Mitral Peak E velocity (cm/s)	67±10,5	71±0,3	NS
Mitral peak A velocity (cm/s)	79,8±12,1	59±0,2	<0,05
Mitral peak E/A ratio	0,84±11,5	1,2±0,7	<0,05
Sm peak (cm/s)	110±35	180±34	<0,01
Em peak (cm/s)	96±15	160±24	<0,01
Am peak (cm/s)	115±18	88±11	<0,05
Em/Am	0,85±0,7	2,1±0,4	<0,001
Strain rate basal (1/s)	- 1,2±0,4	-1,8±0,3	<0,05
Intima-media thickness (mm)	0,089±0,011	0,057±0,008	<0,01

LV - left ventricular, E - early peak velocity, A - atrial peak velocity, Sm - myocardial systolic peak velocity, Am - myocardial atrial diastolic wave, Em - myocardial early diastolic wave.

Results: Left ventricular mass index was significantly higher in CRF patients, mitral inflow E/A was decreased as well as Em/Am from pulsed myocardial imaging. Srtain rate was reduced in renal transplant recipients and IMT was significantly higher.
Conclusions: Pulsed DMI and SRI are non-invasive, easy to repeat and valuable for detecting myocardial LV dysfunction in patient with chronic renal failure during follow-up after renal transplantation.

P-166 VALGANCICLOVIR UNIVERSAL PROPHYLAXIS OF CYTOMEGALOVIRUS INFECTION IN HEART TRANSPLANTATION

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Background: Cytomegalovirus (CMV) is a major cause of morbidity and mortality in heart transplant patients. The highest incidence of CMV can be observed during the period of most intense immunosuppressive regimen (first three post-transplantation months).
Purpose: To compare the incidence of CMV infection and its complications during universal prophylaxis and pre-emptive antiviral treatment.
Methods: We reported our first experience with 13 patients who underwent heart transplantation between November 2007 and July 2008. Prophylaxis was based on pretransplant donor (D) and recipient (R) CMV serology: R+/D-, R+/D+,R-/D+ received universal prophylaxis (oral valganciclovir for 100 days). The control group comprised of 25 patients, who underwent heart transplantation between November 2006 and July 2007 and received pre-emptive treatment.
Results: We didn't observe CMV infection in study group during first half-year after cardiac transplantation. In case of pre-emptive treatment 32% of patients had CMV infections during the same period. Also the lower incidence of acute cellular rejection grade Banff 2-4 was detected during universal prophylaxis.

The incidence of CMV infections and acute cellular rejection

Group	N	CMV infection	ACR Banff		
			0-1B	2	3A-4
Universal prophylaxis	13	0	12 (92%)	1 (8%)	0
Pre-emptive prophylaxis	25	8 (32%)	13 (52%)	11 (46%)	2 (8%)
p		0.061	0.034	0.055	0.778

ACR - acute cellular rejection.

Conclusions: Universal antiviral prophylaxis with valganciclovir in patients after heart transplantation seems to be an effective method to affect direct and indirect effects of cytomegalovirus.
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P-167 IODINE MANAGEMENT IN HEART TRANSPLANT RECIPIENTS

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Background: According to WHO iodine excreted with urine is a measure of its supplying. Due to International Council for Control of Iodine Deficiency Disorders (ICCIDD), the urinary iodine (UI) should be above 100 μg I per 1 L of urine. The moderate iodine deficiency (MID) occurs when UI is from 50 to 100 μg/L and the severe deficiency (SID) when UI is below 50 μg/L.
Material and methods: UI analysis in 32 heart transplant recipients (26 men and 6 women; mean age 50.4±12.6 yr) by modified PAMM method (the spectrophotometric measurement based on the Sandell-Kolthoff reaction). Results were evaluated and compared with thyroid stimulating hormone (TSH; μIU/mL), free triiodothyronine (FT3; pg/mL) and thyroxine (FT4; ng/dL). Hormones were measured using a Microparticle Enzyme Immunoassay (MEIA).
Results: The average UI in the whole group was 126.4±109.6. Unfortunately, SID in 12 patients (37.5%) and MID in 4 of them (12.5%) was noted (mean UI: 17.0±9.6 and 79.5±5.6, respectively). In the rest 16 patients (50%) average UI was high and amounted 220.1±72.1. TSH, FT3 and FT4 in the whole group was in the normal range. However, FT4 values significantly differed when SID and MID-patients were compared to those with recommended UI (0.8±0.2 and 0.9±0.1 vs. 1.1±0.2, $p<0.05$; respectively). Decreased values of TSH in 5 patients (15.6%) and FT3 or FT4 in 6 (18.8%) was noted.
Conclusion: Measurements of urinary iodine in heart transplant recipients together with thyroid gland hormones may be essential to monitoring and preventing thyroid gland disturbances.

P-168 EARLY ACTIVATION OF Wnt-PATHWAY IN HEART OF BRAIN DEATH RATS. A POSSIBLE LINK TO TRANSPLANT VASCULOPATHY (TVP)?

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Proteins of the wnt family have been implicated in cell-cell communication in a wide variety of developmental and physiolgical processes. Wnt signaling is required for different aspects of cardiac and vascular developemt, including myocardial specification, cardiac morphogenesis as well as endothelial and vascular smooth muscle cell proliferation. Defective Wnt signaling can result in vascular abnormalities.
The aim of our study was to evaluate the wnt pathway in hearts of brain death (BD) rats using RT^2 Profiler™ PCR Array (SABioscience, USA).
Methods: BD induction in DA rats was performed as described by Pratschke. 30,120,360 min after bd animals were sacrificed. RNA was isolated from hearts of sham operated and bd rats. cDNA synthesis was performed from 1μg RNA. Data were analysed using dddelta Ct method and are expressed as differences in fold up or down regulation. $p<0.05$ was considered to be significant.
Results: 30 min after bd we found a significant upregulation of Birc5 (3.09 fold), c-jun, (1,13 fold), Lef1 (1,59 fold), Pparg (1,53 fold) and Vegfa (1,55 fold). Tcf7 was significantly dowregulated (-1,43 fold) compared with sham animals. After 360 min bd Birc5 decreased to 1,8 fold upregulation, but Ccnd1 (Cyclin D) and Cdh1 (Cadherin) was 5,28 resp. 13.01 fold upregulated. Lef 1 and Tcf7 were 4.29 resp. 2.51 fold upregulated. Wnt 1 and Wnt 2 wer also upregulated (4 fold compared with sham) after 360 min. Ptch1, Foxa2, Hhip and Bmp2, genes related to the hedgehog pathway reached significant upregulation at 360 min of bd.
Conclusion: Cdh1 or E-cadherin are linked, independent from othe risk factors, with coronary atheriosclerosis. The activation of Wnt pathway in the heart of bd donors may be an explanation for TVP development after transplantation.

P-169 PROTEINURIA AND KIDNEY FUNCTION AFTER CONVERSION TO AN EVEROLIMUS BASED IMMUNOSUPPRESSIVE REGIME AFTER oHTX

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Background: Recent trials have proven that it is possible to minimize the dose of CNIs after oHTX when they are combined with mTOR inhibitors and therfore maybe minimize nephrotoxic side-effects of CNIs. New-onset proteinuria was reported for Rapamycin. In this study development of proteinuria and kidney function under immunosuppression with Everolimus in combination with CsA was tested.
Methods: 30 patients (26 male, 4 female) after oHTX were divided into group A (n=15) receiving Everolimus in combination with CsA and prednisolone and group B (n=15) receiving CsA, MMF and prednisolone.
Patients started 1.0 mg to 1.5 mg Everolimus per day and target Everolimus trough levels were between 3 – 8 ng/ml, CsA target trough levels for group A between 50 and 100ng/ml, for group B over 100ng/ml.
Proteinuria, Creatinine levels, development of hypertension as well as immunosuppressive levels were monitored over a follow-up period of 24 months retrospectively and statistically evaluated.
Results: Renal function was stable for both groups with a medium creatinine level of 1.79ng/dl in group A and 1.34 ng/dl for group B. Mean Everolimus trough levels were reached within one to three weeks. None of the groups showed a higher incidence of developing aterial hypertension.
In group A CsA through levels were reduced down to a medium of 68.5 ng/ml [$p<0.001$]. No higher incidences of acute rejection were seen.
In group A three patients [20%] had to discontinue Everolimus because of adverse side effects [vomiting, diarrhoea, edema].
Mortality was 0% in both groups and no differences were seen on infection or hospitalitation.
Conclusion: Everolimus in combination with CsA seems to have no influence on the development of proteinuria unlike to Rapamycin. Kidney function seems to be stable with the combination of Everolimus and low dose CsA.

P-170 WHAT ELSE DIFFERS CELLULAR REJECTION GRADE 1A FROM 0? ANNEXIN V AND BCL EXPRESSIONS IN ELECTIVE BIOPSIES RECEIVED FROM HEART TRANSPLANT RECIPIENTS

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Background: Despite of morphologic differences between non-rejection (0

due to ISHLT scale) and moderate focal cellular rejection (1a, ISHLT) i.e. lymphocytes aggregation, the genetic and clinical differences in CARGO studies were not shown.
Therefore the aim of the study was to compare the expression of selected antigens associated with apoptosis in heart transplant (HTx) recipients in the context of 0 and 1a cellular rejection. The expression of Annexin V, Bcl-2 (protective apoptotic activity), Bcl-xL (antiapoptotic activity) and Bcl-xS/L (other antiapoptotic mechanism) were assessed.
Material and methods: 17 heart transplant patients were retrospectively included into the trial (2 women and 15 men, mean age 46.2±13.9 yr, BMI 25.7±3.2). 10 biopsies presented rejection 0 and next 10 – 1a (due to ISHLT scale) – group A and B, respectively.
Endomiocardial biopsy specimens were processed using routine immunohistochemical method. The frozen sections were incubated with adequate antihuman antibodies from BioVision and Santa Cruz Biotechnology.
The expression was assessed according to IHC method i.e. 0- the lack of expression, 1- trace, 2- distinct and 3- strong. The correlation was analyzed between particular molecules expression.
Results: The significant increase of Bcl-2 expression together with rejection was observed. The expression of other antigens was also shown but without signs of any significant tendency. No correlation in group A was noted, on the contrary, in group B the significant strong and negative correlation between Bcl-2 and Bcl-xS/L was revealed.
Conclusion: Bcl-2 expression responds to the morphologic progression of graft rejection and is opposing to Bcl-xS/L activity.

P-171 FIRST DOCUMENTED CASE OF PARACOCCUS YEEI INFECTION IN A TRANSPLANTED HEART

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Introduction: Cardiac transplantation remains the only curative therapy apart of supportive mechanical support for end-stage heart disease due to inflammatory cardiomyopathy. Detection of pathogenic viruses and bacteria is crucial in order to avoid reinfection and may be challenging as described in this case report.
Case report: A 36 year old male patient with inflammatory cardiomyopathy underwent successful cardiac transplantation. First eight consecutive endomyocardial biopsies showed severe infiltrates comparable with bacterial myocarditis resulting clinically in dyspnea and NYHA stage II-III. PCR analysis of native myocardial samples revealed infection with Paracoccus yeei sp.nov and Parvovirus B-19. After administration of ciprofloxacin clinical conditions ameliorated and further biopsy showed a regression of infiltrates in the cardiac specimens. The patient finally was dismissed in a good state of health.
Discussion: Resumptive Paracoccus yeei, a gram-negative bacterial eugenic oxidizers should be included in diagnostically thoughts in remarkably cases of myocarditis. Treatment with quinolones resulted in clinical and histological improvement.

P-172 THE RESUSCITATED DECEASED DONOR HEART IS FUNCTIONALLY SUPERIOR TO THE BRAINSTEM DEAD DONOR HEART

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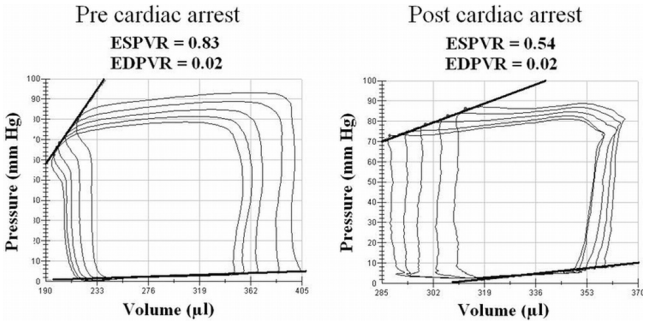
Background: Hearts from deceased donors are not currently utilized due to concerns that cardiac arrest would lead to irreversible myocardial injury. Using rodent models of organ donation we sought to compare cardiac function in the resuscitated post-ischemic deceased donor (DD) heart to that of the brainstem dead (BD) heart.
Methods: Sprague Dawley rats were subjected to hypoxic cardiac arrest (DD, n = 10) followed by 15 minutes of warm ischemia or brainstem death via subdural balloon inflation (BD, n = 10). In-vivo cardiac resuscitation in the DD group was achieved using extracorporeal membrane oxygenation. Load independent left ventricular (LV) contractility was assessed at baseline and following intervention via the end-systolic pressure volume relationship (ESPVR). LV myocytes isolated from each group were field stimulated with 50% suprathreshold voltage at 0.5 Hz for analysis of sarcomeric contractility (percentage of sarcomere shortening).
Results: Both groups of animals demonstrated a significant decline in contractile function (ESPVR) compared to baseline (DD pre 0.81±0.23 vs. post 0.53±0.1, $p<0.01$; BD pre 0.77±0.22 vs. post 0.32±0.16, $p<0.001$). The resuscitated DD heart demonstrated superior contractility to the BD heart (0.53±0.1 vs. 0.32±0.16), $p<0.01$. Sarcomere shortening was decreased in BD myocytes (n = 20, 7.4%±0.4) compared to DD (n = 17, 10.6%±0.6)and control myocytes (n = 18, 10.6%±0.5), $p<0.01$. Isoproterenol stimulation increased contractility in all myocyte groups, however sarcomere shortening was lower after isoproterenol in BD myocytes (12.3%±0.9) compared to DD (16.3%±0.7) and control (16.8%±0.4), $p<0.05$.



Conclusions: Contractility of the DD heart was superior to the BD heart, which is currently used for transplantation. The post-ischemic DD heart maintains viability and recovers satisfactory function following reperfusion. In the face of an ongoing shortage of donor organs the human deceased donor heart should be evaluated for use in clinical cardiac transplantation.

P-173 CMV THERAPY WITH IMMUNOGLOBULIN (Cytotect™) MONOTHERAPY IN NEUTROPENIC PATIENTS AFTER HEART TRANSPLANTATION -REPORT OF 4 CASES-

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Purpose: Recurrent infections with cytomegaly virus (CMV) negatively influence the long-term results of patients after heart transplantation (HTx). If detected late, initial neutropenia as a result of infection often is a contraindication for ganciclovir therapy. This study evaluates the safety and efficacy of a iv cytoglobulin monotherapy throughout the neutropenic period to allow ganciclovir therapy after improvement of WBC.
Methods/Materials: Retrospective review of electronic patient files and laboratory reports including CMV serology.
Results: From 11/2008 until 02/2009 4 pts. (1 male/3 female), 49 to 68 yrs. Old (m.: 50.8 yrs.), received monotherapy with iv-immunoglobulines (IVIG) (Cytotect™) (25-75 mg/kg). Time intervall after HTx was 3 – 40 months. Initial WBC was 0.8-1.1 10E9/l (m.: 2.4 10E9/l). In only 1 case CMV-virus was initially detected by PCR, initial CMV-IgM was 15 – 108 AU/ml (m.: 64,1 AU/ml).
Ganciclovir iv could be started after 1 to 5 days and 3 of 4 patients could be discharged in absence of CMV activity. 1 pt. who developed neutropenia in a very extended course of sepsis died from septic shock.
3 patients received oral valganciclovir prophylaxis prior to CMV infection episode and continued the therapy after discharge.
Throughout the course WBC improved to 2,4 – 8.5 10E9/l (m.: 4.8 10E9/l). Creatinine and bilirubine values remained stable as well as hemoglobine levels and RBC. Side effects of IVIG did not occur.
Conclusion:
A temporary treatment with iv immunoglobulines (Cytotect™) may be an option to bridge the time gap of neutropenia to allow for accurately dosed ganciclovir therapy after improvement of WBC.

P-174 THERE IS NO RELATION BETWEEN CYTOMEGALOVIRUS INFECTION AND MICROVASCULOPATHY DEVELOPMENT IN HEART TRANSPLANT RECIPIENTS

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Background: It was confirmed in clinical studies with intravascular ultrasound that even subclinical cytomegalovirus (CMV) infection may accelerate coronary vasculopathy (CAV).
Aim of the study: Was to compare occurrence of microvasulopathy in endomyocardial biopsies (EMBs) of heart transplant recipients with or without CMV infection.
Material and methods: We preformed a case-control retrospective study involving 58 pts. with CMV infection confirmed with pp65 antigen presence (49M/9F, 49±8y/o, ischemic c-pathy in 52%) and matched 58 control without

CMV disease. Microvasculopathy was assessed using 4 degrees grading system development by Hiemann et al. in elective EMBs performed 1 month and 12 months after transplantation.
Results: Significant acute rejection was observed in 22 vs. 21% of 1 month EMBs, and 3 vs. 5% of 12 month EMBs in CMV(+) and control group, respectively. Maximal microvasculopathy score was 2.05±0.93 vs. 1.88±0.94 in 1 month EMBs, and 2.29±1.12 vs. 2.28±1.20 in 12 month EMBs, respectively. Progression of microvasculopathy score between 1 month and 12 month EMB was observed in 40 vs. 41% of pts., and regression occurred in 22 vs. 21% of pts., respectively. None of differences was statistically significant.
Conclusion: Our data do not support the thesis that CMV infection promotes microvasculopathy development in heart transplant recipients.

Islets

P-175 IMPACTS OF TOLL-LIKE RECEPTORS (TLRs) IN ALLOGENEIC ISLET TRANSPLANTATION

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Purpose: Toll-like receptors on antigen presenting cells play important roles in bridging innate and adaptive immunity. Recently, their roles have also been demonstrated in epithelial cells as well as T cells. We investigated the roles of toll-like receptors on pancreatic islet cells in allogeneic islet transplantation together with roles of toll-like receptors on the recipient side.
Methods/Materials: Islet cells were isolated from C57BL6/J mice. Expression of toll-like receptors was measured using reverse transcriptase polymerase chain reaction (RT-PCR). After islet cells were stimulated by poly I:C and lipopolysaccharide, expression of cytokines and chemokines in islet cells were measured. To assess roles of toll-like receptors on the recipient side in allogeneic islet transplantation, islets from wild type Balb/C mice were transplanted to streptozotocin-induced diabetic wild type, MyD88 knockout or trif knockout C57BL6/J mice. Next, we transplanted islets from wild type, MyD88 knockout, trif knockout, or TLR-4 knockout C57BL6/J mice to streptozotocin-induced diabetic Balb/C mice in order to assess roles of toll-like receptors on the donor side. Blood glucose levels were monitored to assess islet graft survival.
Results: Murine islet cells expressed toll-like receptors (TLR1-TLR10) at basal status. Various proinflammatory cytokines and chemokines were upregulated in islets in response to TLR ligands. There was no significant difference in islet allograft survival between wild type and MyD88/trif knockout recipients. When islets from MyD88 knockout, trif knockout, or TLR-4 knockout C57BL6/J donor mice were transplanted to diabetic Balb/C mice, their islet allograft survivals were not better than the control group (islets from wild type C57BL6/J mice to Balb/C mice).
Conclusion: Toll-like receptors on islet cells may mediate immune activation in vitro. However, roles of toll-like receptors in allogeneic islet transplantation across major mismatch barriers were limited both in the recipient side and in the donor side.

P-176 GRAVES' HYPERTHYROIDISM AFTER STOPPING IMMUNE SUPPRESSIVE TREATMENT IN TYPE 1 DIABETIC ISLET CELL RECIPIENTS WITH PRETRANSPLANT TPO AUTOANTIBODIES

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Background: Islet cell transplantation has been shown to reproducibly achieve metabolic correction in non-uremic type 1 diabetic patients. However, with time several patients return to a C-peptide-negative state for which immune suppressive therapy is discontinued. These patients are further monitored to detect any consequences of the intervention protocol.
Methods: Between 1999 and 2002, we terminated immune suppressive treatment in 13 islet cell graft recipients in whom basal plasma C-peptide decreased under 0.2 ng/dl. These non-uremic type 1 diabetic patients had been enrolled in a protocol using one course of antithymocyte globulin (ATG-Fresenius®) and maintenance doses of a calcineurin inhibitor combined with mycophenolate mofetil.
Results: Clinical Graves' hyperthyroidism was observed in 4 out of the 13 patients in whom immune suppressive drugs were discontinued. The disease was diagnosed 30 to 71 months after start of the immune suppressive therapy, and 2 to 21 months after its discontinuation. These four patients exhibited a pretransplant positivity for thyroid peroxidase (TPO)-antibodies while the nine others were negative and remained so during a similar follow-up period.
Conclusions: Type 1 diabetic recipients of islet cell grafts with pretransplant TPO-autoantibody positivity exhibit a high risk for developing Graves' hyperthyroidism when immune suppressive treatment is discontinued for a failing graft. This observation should be taken into account when determining the risk-benefit ratio of islet cell transplantation in non-uremic TPO-autoantibody positive patients.

P-177 IMPROVED YIELD AND FUNCTIONAL PARAMETERS OF RAT PANCREAS ISLETS ISOLATED UNDER INTRAMUSCULAR ANESTHESIA

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Purpose: Intraperitoneal (IP) anesthesia is commonly used for laboratory experiment including islet isolation. However, the direct effects of anesthetics towards pancreatic islets have been neglected.
Methods: We compared the islet function and recovery yield from the rats that were anesthetized using IP and intramuscular (IM) injection. Lag time required to lose deep pain was measured according to the following anesthetics combinations. Lewis rats were anesthetized using ketamine and xylazine (K/X) or zoletil and xylazine (Z/X). Glucose challenging test was performed. To evaluate the effect of anesthetic agents (eg. ketamine, zoletil, xylazine alone and combination of K/X and Z/X) on cell lines (rat insulinoma; RIN-5F), we investigated cell viability, the amount of insulin and insulin mRNA expression levels of RIN-5F using methyltetrathiazolium (MTT) assay, Enzyme-Linked ImmunoSorbent Assay (ELISA), and real-time PCR.
Results: Compared with IP, the time needed for deep anesthesia in IM anesthesia was significantly shortened (K/X [IM: 313±66 sec, IP: 371±84 sec] and Z/X [IM: 206±76 sec, IP: 245±92 sec]). And the yield of isolated islets by IM anesthesia was significantly improved [K/X (IM: 1530±242 ea, IP: 1245±149 ea) and Z/X (IM: 1136±226 ea, IP: 511±154 ea)]. The functions of fresh islets, which were expressed by stimulation index, acquired under IM anesthesia was better preserved than that of IP. The viability and the insulin secretion of RIN-5F were decreased at 24 and 48 hours. Insulin gene expression levels were decreased at 24 hours as well.
Conclusion: Anesthetics may be absorbed through the pancreas surface to the islets and have a direct effect, resulting in islet exposure and deterioration during isolation. For rodent islet isolation, IM anesthesia is simpler and safer compared to IP anesthesia. It is suggested that IM anesthesia is versatile in laboratory animal experiments.

P-178 RESULTS OF ISLET AUTOTRANSPLANTATION AFTER EXTENDED PANCREATECTOMY FOR BENIGN DISEASE OF THE PANCREAS AND THEIR SIGNIFICANCE FOR LIVE DONATION

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Introduction: Islet autotransplantation is successful in the prevention of surgical diabetes after pancreas resection for chronic pancreatitis (CP), with insulin independence rates of 50% at 1 year. We report our experience with islet autotransplantation after extensive pancreatectomy for the resection of benign tumors of the pancreas and compare the results with those of autologous donors with CP and donors with brain death (DBD).
Methods: Between January 1992 and December 2008, 12 patients underwent extensive left pancreatectomy for benign lesions located at the neck of the pancreas. One patient had complete traumatic section of the pancreas. Eleven tumours were separated from the specimen and sent for extemporaneous pathological examination. After unequivocal diagnosis of benignity, the rest of the specimen was processed and unpurified pancreatic digest was infused into the portal vein. Isolation results were compared with those obtained from 10 CP patients or 307 DBD.
Results: Tumours were 8 cystadenomas and 3 insulinomas. Mean islet yields were 248'121 IEQ vs 110'290 in CP (p=0.03) and 345'201 in DBD (p=0.89). Normalized to weight of pancreatic tissue processed, we isolated 5'895 IEQ/gram vs 1'457 in CP (p=0.007) and 3'932 in DBD (p=0.005), and transplanted 3'839 IEQ/kg body weight vs 2'196 in CP (p=NS). Median follow-up for benign disease was 90 months, one patient died from unrelated causes after 12-years. After a 7.5-year follow-up, all patients have positive basal and

stimulated C-peptide levels and normal HbA1c, and 11/12 patients are insulin-free.
Conclusion: Islet autotransplantation after extensive pancreatic resection for benign disease is a successful procedure. Pancreatic surgical specimens (a situation near-identical to live donation) yield higher numbers of islets per gram of tissue and similar total islet numbers as whole organs from DBD.

P-179 INFLUENCE OF DONOR AGE ON ISLET ISOLATION AND TRANSPLANTATION OUTCOME

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Background: It has been suggested that the age of human organ donors might influence islet isolation and transplantation outcome in a negative way due to a decrease of in vivo function in islets isolated from older donors.
Methods: We retrospectively analyzed 332 islet isolations performed in our facilities and divided them into two groups depending on donor age (n=187 and n=145 for below and above 50 years, respectively). Pancreata were procured and processed according to established protocols. Isolation outcome was determined by islet yield, success rate (>250'000 IEQ) and transplantation rate. Beta cell function was assessed in vitro by stimulation indices in static incubation assays. Transplanted patients were divided into two groups depending on donor age of islet preparations (n=49 and n= 31 patients that received just islets from <50 and >50 year-old donors, respectively). In vivo function was assessed by the newly developed secretory units of islets in transplantation (SUIT) index and the C-peptide/glucose ratio 1 month after transplantation.
Results: There was no difference in islet yields between the two groups (249'200±11'400 and 245,900±9'800 IEQ for <50 and >50 year-old donors, respectively). Success rates were 45% for both groups, respectively. Overall, 85 (45%) islet preparations were transplanted from <50 year-old donors and 56 (39%) islet preparations were transplanted from >50 year-old donors. Stimulation indices were similar for both groups. SUIT indices and C-peptide/glucose ratios one month after transplantation were significantly higher in patients that received islets only from the younger donor population (41±4 vs. 26±4, p=0.008 and 1.38±0.12 vs. 0.87±0.1, p=0.003, respectively).
Conclusions: Our study shows that, in our donor population, donor age does not influence islet isolation outcome, in contrast to islet graft function.

P-180 ISLET AFTER KIDNEY TRANSPLANTATION FROM THE COLLABORATIVE ISLET TRANSPLANT REGISTRY: 1999-2008

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Background and purpose: We describe characteristics and glycemic outcomes of (islet-after-kidney or IAK) compared to islet alone (IA) from the Collaborative Islet Transplant Registry (CITR) 1999-2008.
Patients and methods: Detailed data are available on 53 IAK recipients and 343 IA recipients from the US, Canada and Europe.
Results: IAK vs. IA recipients had longer diabetes duration, lower weight and BMI, less severe hypoglycemia, lower bilirubin (p=0.02), and creatinine clearance, and higher ALT, AST, total cholesterol, triglycerides and serum creatinine (all p's<0.01). Insulin requirements, fasting glucose, fasting C-peptide and HbA_{1c} levels were similar. IAK vs. IA recipients received no mono T-cell depletion (vs. 7%, p=0.006), 76% vs. 91% sirolimus (p=0.003), 34% vs. 16% inosines (p=0.003) and 28% vs. 7% steroids (p<0.001). At 3-years post first infusion, 26% IAK were insulin independent vs. 28% IA (p=NS), nearly identical proportions (74%) in both groups retained graft function, 26% in both groups had HbA_{1c}<6.5%. Virtually all in both groups achieved freedom from severe hypoglycemia episodes. Post-transplant C-peptide and fasting blood glucose levels were similar. Those who returned to insulin took doses very similar to IA recipients. While serum creatinine started higher and calculated GFR started lower, both groups lost further function at gradual rates that are not statistically significant.
Conclusions: While IAK recipients attain and retain graft function, they do not maintain insulin independence at the same rates as IA (p=0.04), which in turn impacts the requirement for re-infusion, in this overall analysis unadjusted for baseline factors and immunosuppression. While they start out with lower kidney and liver function (p<0.01), post-transplant loss is no greater than IA. Accounting for differences in immunosuppression and other factors is warranted.

P-181 HUMAN ALLOGENIC BONE MARROW AND CORD BLOOD DERIVED MESENCHYMAL STEM CELL SECRETING TROPHIC FACTORS INFLUENCE ON ADP/ATP RATIO AND INSULIN SECRETARY FUNCTION OF ISOLATED HUMAN ISLETS FROM CADAVERIC DONOR

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Purpose: Successful islet transplantation (ITx) is not only dependants on number of islets for ITx, but also their quality; viability, metabolic activity and functions. Islet quality becomes to be worse during cultivation after isolation procedure. To overcome, the strategy of islet and mesenchymal stem cells (MSCs) coculture was established.
Methods/Materials: Human pancreatic islets were cocultured with MSCs, and the ADP/ATP ratio, glucose stimulated insulin release (GSIR) rate were evaluated to measure islet quality *in vitro*. Furthermore, to evaluate the released pattern of soluble factors in culture medium during human islet-MSCs coculture, we detected soluble molecules in islet culture medium (non-cocultured and cocultured with BM-MSCs and CB-MSCs) by ELISA (Enzyme-linked immunosorbent assays), respectively.
Results: In this coculture condition, ADP/ATP ratio and insulin secretory function were reduced and enhanced *in vitro*. It is imply that enhancement of islet quality in islet-MSCs coculture may be caused by MSCs-secreting active agents. In MSCs-cocultured medium, Interleukin-6 (IL-6), vascular endothelial growth factor-A (VEGF-A), hepatocyte growth factor (HGF), and transforming growth factor-β (TGF-β) were detected or increased in significant concentration by ELISA, which have been known to relate with signals of survival, function and angiogenesis/revascularization of islets. Additionally, known to be pro-inflammatory cytokines, the level of interferon-γ (IFN-γ) and tumor necrosis factors-α (TNF-α) were lower in cocultured medium than non-cocultured supernatants.
Conclusion: These results indicate that islet quality could be enhanced by MSCs secreted trophic molecules, and that is related with islet's intra-cellular ATP contents and insulin secretory function.

P-182 PORTAL VENOUS OXYGEN PERSUFFLATION FOR THE PRESERVATION OF NON HEART-BEATING-DONOR PANCREASES PRIOR TO ISLET ISOLATION

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Introduction: Pancreases from non-heart-beating-donors (NHBD) are not routinely used for islet transplantation due to low islet yield. We compare the severity of reperfusion injury, islet yield and islet in-vitro function after preservation with portal venous oxygen persufflation (PVOP) or static cold storage (SCS) in an NHBD rat pancreas model.
Methods: Pancreases were retrieved from male Wistar rats after 35 minutes of warm ischaemia. In one set of experiments, pancreases were preserved overnight at 4° C by SCS or PVOP with 100% oxygen (10-15 mmHg). The pancreases then underwent warm oxygenated reperfusion for one hour. Portal venous effluent was collected during reperfusion for measurement of amylase/lipase. Biopsies at end of reperfusion were homogenized for estimation of lipid peroxidation. In a second set of experiments NHBD pancreases preserved for 5 hours by either SCS or PVOP. All pancreases underwent islet isolation by standard technique. Islet yield and in-vitro function (static glucose stimulated insulin secretion test) were compared between the two preservation groups.
Results: Within the two preservation groups, the purified islet count and IEQ of PVOP (265 93,708 394) was better than SCS (175 73,322 140) (p<0.05). Islets from PVOP had better viability, lesser fragmentation and higher percentage of functioning islets i.e. stimulation index >1 (7/8 vs 4/8). There was no significant difference in lipid peroxidation, effluent amylase &lipase levels between the two preservation groups.
Conclusions: Preservation with PVOP improved the number and quality of islets when compared to SCS. Prolonged preservation with PVOP does not increase the extent of reperfusion injury in the pancreas.

P-183 COMPARATIVE IMPACT ON ISLET ISOLATION AND TRANSPLANTATION OUTCOME OF THE NEW PRESERVATION SOLUTION IGL-1 VERSUS UW AND CELSIOR

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Purpose: Institut Georges Lopez (IGL-1) is a new preservation solution similar to University of Wisconsin (UW) with reversed Na/K contents. In this study, we assessed the impact of IGL-1, UW and Celsior (CS) solutions on islet isolation and transplantation outcome.
Method: We retrospectively analyzed 302 islet isolations performed between January 2002 and September 2008. Pancreas were flushed and transported with IGL-1 (n=64), UW (n=181) or CS (n=57). Isolation outcomes were determined by islet yields, success rates (>250,000 IEQ) and transplantation rates. Beta cell function was assessed in vitro by stimulation indices in static incubation assays. Transplanted patients were divided into three groups depending on preservation solution of the donor pancreas and in vivo function was assessed 1 month after the patients first transplantation by the secretory unit of islet in transplantation (SUIT) index and the C-peptide/glucose ratio.
Results: IGL-1, UW and CS groups were similar according to donor age, body mass index and pancreas weight. Islet yields were 248,500±16,000, 252,800±9,300 and 249,300±18,200 IEQ for IGL-1, UW and CS groups, respectively. Success rates were 42, 49 and 46% in the IGL-1, UW and CS group, respectively. Altogether, 28 (44%) preparations in the IGL-1 group, 80 (44%) preparations in the UW group and 27 (47%) preparations in the CS group were suitable for transplantation. Stimulation indices were similar for all three groups. SUIT indices and C-peptide/glucose ratios 1 month after transplantation were slightly but not significantly higher in the IGL-1 compared to UW and CS groups (38±5.5 vs. 32.8±5.5 and 24.5±6.1; 1.25±0.17 vs. 1.09±0.15 and 0.87±0.25, respectively).
Conclusions: Our study shows that IGL-1 is equivalent to UW or CS solutions for pancreas perfusion and cold storage before islet isolation.

P-184 MECHANISMS OF RAPAMYCIN TOXICITY IN PANCREATIC BETA CELLS

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Purpose: Since the publication of the Edmonton protocol, rapamycin has been the primary immunosuppressant used in islet transplantation. However, there is growing evidence that rapamycin has deleterious effects on islet viability and function. The aim of this study was to elucidate some of the mechanisms of this toxicity. PKB activation has been shown to be important for islet viability and this was therefore the focus for our investigation. Phosphorylation of PKB at serine 473 (S473) is dependent on a functional mTOR complex 2 (mTORC2), comprising mTOR, rictor, mLST8 and mSin1. Rapamycin has previously been shown in other cell lines to affect mTOR/rictor binding, but this has not previously been shown in beta cells.
Methods: The mouse insulinoma cell line MIN-6 was used as an in vitro pancreatic beta cell model. Cells were treated with rapamycin 200nm for up to 96 hours. Viability was assessed by MTT assay and annexin V analysis using flow cytometry. Expression of total and phosphorylated PKB was determined by SDS-page electrophoresis and Western blotting. Immunoprecipitation was used to investigate mTOR complex formation.
Results: 200nM rapamycin treatment resulted in significant increases in beta cell apoptosis after 24hrs and a significant reduction in viability after 72 hours (figure 1). A significant decrease in PKB phosphorylation at S473 was also seen after 24hrs rapamycin treatment (figure 2a). Immunoprecipation of mTOR and rictor demonstrated loss of mTOR/rictor association after 72 hours rapamycin treatment (figure 2b).
Conclusion: This study shows reduced MIN-6 cell viability with rapamycin treatment. This was associated with reduced phosphorylation of PKB at serine 473. We presume this is due to rapamycin-induced dissociation of the mTORC2, which is necessary for phosphorylation of PKB at this residue. Rapamycin toxicity may be partially responsible for the poor long-term survival of islet allografts.

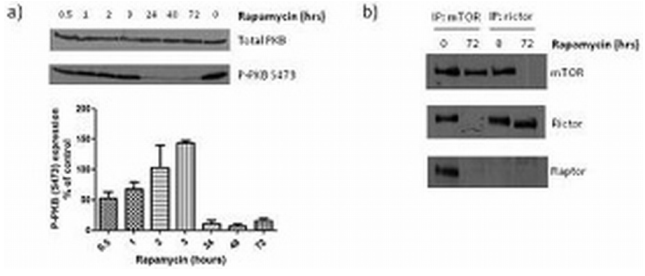

Figure 1. (a) Western blot of total PKB and PKB phospho-S473 with 200nM rapamycin. (b) Western blot of immunoprecipitation of mTOR and rictor with 200nM rapamycin.

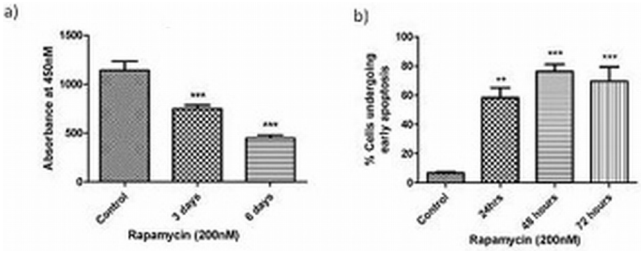

Figure 2. (a) MTT viability assay. (b) Annexin V apoptosis assay (***P<0.001, **P=0.001-0.1).

Kidney I

P-185 RESCUE IMMUNOSUPPRESSIVE THERAPIES IN LIVE RELATED RENAL ALLO-TRANSPLANTS: LONG TERM PROSPECTIVE RANDOMIZED EVALUATION

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Introduction: The majority of our patients were maintained on steroid, CsA and azathioprine as a primary immunosuppression; the policy -with the development of repeated acute rejection episodes -was to strengthen the maintenance immunosuppressive regimen by Tac or MMF. Up to our knowledge, there are no available data–among live related renal allotransplants- evaluating the long term efficacy and safety of these rescue immunosuppressive therapies.
Aim of the work: To evaluate the long term efficacy and safety of rescue immunosuppressive therapies among live related renal allotransplants.
Patients and methods: Based on long-term follow up data of 212 renal transplant recipients performed in Urology and Nephrology Center Mansoura University, and started their primary immunosuppressive protocol as steroid, cyclosporine and azathioprine. The cases were randomized at a ratio of 1 to 2 to receive more intensive maintenance immunosuppression by replacing TAC instead of CsA in 65 cases (group 1); and MMF instead of azathioprine in 147 cases (group 2).
Results: We found no significant difference between the two groups regarding rejection free cases or those who experienced one or more rejection episodes (p>0.5).Graft survival rates were 87.3% vs. 96.3% at 2-year and 78.7% vs. 80% at 5 years respectively (p=0.07). The corresponding patient survival rates were 98.4% vs. 98.5% at 1-years; 98.4% vs. 97.7% at 2-year and 94.4% vs. 94.4% at 5-year respectively (fig 2) (p=0.65%).Diabetic patients and those with serious bacterial infections were more prevalent among TAC rescue group compared to in the MMF rescue group (p= 0.001 and 0.04 respectively).
Conclusion: From this study we can conclude that conversion from CsA to TAC or from AZA to MMF is safe equipotent rescue especially with repeated acute rejections. However, MMF rescue therapy was more beneficial regarding graft survival.

P-186 A NEW TECHNIQUE FOR URETERIC STENTING DURING KIDNEY TRANSPLANTATION

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Purpose: Urological complications like ureteric leak or stenosis are a common problem after kidney transplantation (incidence up to 17.3%). A recent Cochrane review exhibited a significant reduction in urological complications by routine intraoperative stenting of the ureterocystoneostomy (UCNS). In most cases a double J stent is inserted, commonly removed after 3-6 weeks. Ureteric stenting increases the risk of urinary tract infections and includes the disadvantage of invasive removal and rarely other stent-related complications. We present a new technique of ureteric stenting with a percutaneous catheter combining the advantage of reduced urological complications with minimized stent-related complications.

Methods: Analysis of 80 patients undergoing kidney transplantation between September 2005 and March 2007. In all cases a new technique of intraoperative ureteric stenting by a so called "Pflaumer-catheter" was applied. This catheter is placed suprapubical through the abdominal wall into the urinary bladder, through the vesico-ureteric anastomosis up to the renal pelvis of the graft. The catheter is routinely removed on postoperative day 5-6 by easy pulling. Antibiotic prophylaxis was used in every patient during stenting.
Results: No ureteric leaks or stenosis in all 80 patients were observed after a follow-up of median 18 months (range 9 -27 months). In contrast, before ureteric stenting, the rate for ureteric leaks was 3.0% (5/156 patients) and the rate for ureteric stenosis 1.3% (2/156 patients) at our hospital over a five year period (2000 – 2004). No patient developed pyelonephritis or transplant loss due to urinary tract infection. No other specific stent-related complications occurred.
Conclusion: Intraoperative stenting with a Pflaumer-catheter proved to be a safe technique preventing urological complications in our patients. Benefits of our technique are the unproblematic catheter removal and the minimal risk of urinary tract infections because of the short duration of stent placement.

P-187 KIDNEY GRAFTS WITH MULTIPLE ARTERIES AND ARTERIAL RECONSTRUCTION – ANALYSIS OF A 10 YEAR PERIOD

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Purpose: Kidney transplantation is the treatment of choice for patients with end stage renal disease. Increasing numbers of recipients demand an expansion of the donor pool. The aim of our study is to analyse the outcome of grafts with multiple arteries and arterial reconstruction.
Methods: We prospectively collected and retrospectively analysed all patients undergoing kidney transplantation from 1997 to 2006. Patients were divided into three groups: group I: one artery (n=312), group II: multiple arteries and one arterial anastomosis to the recipient (n=85), group III: multiple arteries and multiple anastomosis (n=9). All groups were analysed with regard to graft and patient survival, creatinine level 1 and 5 years after transplantation, cold and warm ischemic time, operation time and postoperative complication rates.
Results: There were no significant differences between the three groups in graft and patient survival analysed by Kaplan Meier survival curves/log rank test. We found comparable creatinine levels 1 and 5 years after transplantation (p= 0.86 respective p= 0.31). There was a significant longer operation time in group 3 (mean 180min) compared with group 1 (mean 145min, $p<0.05$) and a trend to a longer operation time compared with group 2 (mean 149min, p= 0.06). Warm ischemic time did not differ significantly (mean group 1: 31min, group 2: 34min, group 3: 38min). Postoperative complications rates for vascular and urological complications, acute tubular necrosis/delayed graft function, rejection, lymphocele and wound infection were comparable in all three groups.
Conclusion: Our data suggest that kidney grafts with multiple arteries and multiples anastomosis can be used safely with comparable outcomes and complication rates.

P-188 PREDICTION OF GRAFT SURVIVAL OF LIVING DONOR KIDNEY TRANSPLANTATION: NOMOGRAMS OR ARTIFICIAL NEURAL NETWORKS?

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Purpose: An artificial neural networks model (ANNs) was developed to predict 5-year graft survival of living donor kidney transplants. Predictions from the validated ANNs were compared with Cox regression-based nomogram.
Methods: Out of 1900 living-donor kidney transplant patients; 1581 patients were utilized for training of the ANNs (training group), the remainder 319 patients were utilized for its validation (testing group). Many variables were correlated to the graft survival by univariate analysis. Significant ones were utilized for ANNs construction of a predictive model. The same variables were subjected to a multivariate statistics using Cox-regression model; their result was the basis of a nomogram construction. The ANNs predictive model and the nomogram were utilized to predict the graft survival of the testing group. The predicted probability(s) was compared with the actual survival estimates.
Results: The ANNs sensitivity was 88.43 (95% CI 86.4-90.3) %, specificity 73.26 (95% CI 70-76.3) % and predictive accuracy was 88 (95% CI 87-90)% in the testing group. While nomogram sensitivity was 61.84 (95% CI 50-72.8)% with 74.9 (95% CI 69-80.2) specificity and predictive accuracy was 72 (95% CI 67-77) %. The positive predictive value (PV) of graft survival was 82.1% and 43.5% for the ANNs and Cox regression-based nomogram respectively and the negative PV was 82% and 86.3% for the ANNs and Cox regression-based nomogram respectively. Predictions by both models fitted well with the observed findings.
Conclusion: These results suggest that ANNs was more accurate and sensitive than Cox-regression-based nomogram in predicting 5-year graft survival.

P-189 KIDNEY TRANSPLANTATION IN PATIENTS WITH AUGMENTATION CYSTOPLASTY: EARLY AND LONG TERM RESULTS

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Purpose: Low compliance, high pressure bladder is unsuitable for renal transplantation (RTX). Thus augmentation cystoplasty recommended for these cases before or after renal transplantation. In this study we assessed the early and long term results of kidney transplantation in recipients with augmentation cystoplasty.
Materials & methods: During 18 years (1989–2007) 1350 renal transplantation were preformed in our center. 21 cases of these recipients due to low compliance, high pressure bladder with median age 14 years (range 6–35) undergone augmentation cystoplasty, 3 to 6 months before renal transplantation. The etiology of bladder dysfunction included: Neurogenic bladder (15cases), posterior uretheral value (4cases) contracted bladder due to tuberculosis (2cases). For augmentation, detubularized ileal segment was used in 14 cases (In 5 of boys we transfer appendix as metrifanoff procedure) and detubularized one or both ureters were used in 7 cases. We evaluated early and late complications after Rtx and graft and patients survival in these cases who undergone augmentation cystoplasty.
Results: Mean follow up is 108 months (12–216), all patients is continent and 9 cases (40%) readmitted in the first year after RTX due to urosepsis. Rupture of augmented bladder in one case and bladder stone in another case recorded, One paraplegic cases with functioning graft died due to urosepsis and chronic rejection was the causes of graft loss in 4 case. Thus the patient and graft survival in 1,3,5 years after RTX is 100, 93%- 95%, 89%–95%,82% respectively.
Conclusion: Augmentation cystoplasty before renal transplantation is a safe and effective procedure of restoring lower urinary tract in recipients. Although the patient and graft survival is acceptable but there is high incidence of urosepsis, thus meticulous observation is needed.

P-190 PREOPERATIVE EVALUATION OF LIVING DONORS USING COMPUTED TOMOGRAPHY ANGIOGRAPHY (CTA) AND FORMAL ANGIOGRAPHY: COMPARISON WITH INTRAOPERATIVE FINDINGS

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Introduction: CTA is a minimally invasive modality to image the vasculature without the morbidity of direct large vessel vasculature access and its major indications in urology are assessment of the renal vasculature in preparation for donor nephrectomy, indentification of extravessel in evaluation of ureteropelvic junction obstruction and for diagnosis of renal artery stenosion.
Objectives: To assess the accuracy of CTA for the evaluation of renal vascular anatomy for preoperative donor assessment in living kidney transplantation.
Material & methods: CTA of 70 living donor kidney donors were analysed by two blinded observers and compared with intraoperative findings. Similary findings of formal angiography of 30 living donor kidney donors compared with intraoperative observations.
Results: In CTA group there were two patients each with two main renal veins on surgery that hadn't been seen on CTA. In the second group there was one patient with unrevealed two main renal veins before surgery. In both groups, all patients were diagnosed accessory renal arteries, if existed.
Discussion: Overall, the accuracy for renal main artery anatomy was 100% for both CTA and formal angiography. Accuracy for renal main vein anatomy was 97.1% and 96.6% for CTA and formal angiography, respectively. Hence, these two modalities had comparable results for renal main vasculature anatomy detection.

P-191 INCISIONAL HERNIA OF SURGICAL SITE AFTER KIDNEY TRANSPLANTATION AND ITS REPAIR WITH PROPYLENE MESH

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Purpose: Incisional hernia of surgical site remain an important problem after kidney transplantation (RTX). The purpose of this study was to determine the

incidence, timing and predisposing factors for incisitional hernia after RTX and the results of its repair with propylene mesh.
Methods: During 19 years (1989 – 2007) 1500 renal transplantation was performed in our center.
Of these patients who developed incisional hernia were evaluated in this study. The following data were collected from their records: age, weight at time of transplantation, history of diabetic disease, orrence of acute rejection, surgical complication, treatment method and result of treatment with propylene mesh.
Results: Of 1500 recipients 37 (2.5%) developed incisional hernia in surgical site. The median interval between RTX and developing of incisional hernia was 68 days (range 35 – 385). Predisposing factor were age over fifty years, female gender, diabetic disease ($P<0.005$). In 14 patients size of hernia was small and the repair was performed without using mesh but 3 of them developed recurrence of hernia 3 to 6 months after its repair and in 26 patients due to large size or recurrence of hernia, repair was done with using propylene mesh. In 3 cases after with using propylene mesh serous collection were developed which managed successfully with multiple puncture but recurrence of hernia or infection was not noted in this patients during follow- up period.
Conclusion: Predisposing factor such as age over 50 years, overweight and female gender and diabetic disease have a role in development of incisional hernia after RTX. Managing this complication with propylene mesh is a safe and effective method.

P-192 CLINICAL SIGNIFICANCE OF 25-HYDROXYVITAMIN D (25-OHD) INSUFFICIENCY IN RENAL TRANSPLANT RECIPIENTS

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Background: Vitamin D deficiency has been reported to be associated with the risk of insulin resistance, diabetes, albuminuria and cardiovascular disease, which is the major cause of mortality in CKD patients. Renal transplant recipients may also be susceptible to vitamin D deficiency.
Purpose: To investigate the prevalence of 25-OHD insufficiency and its association with insulin resistance, proteinuria, and other indicators of cardiovascular disease, such as PWV, ABI, FMD and Carotid IMT in renal transplant recipients.
Patient and method: Cross-section of 95 our renal transplant patients with mean age of 48 ± 10 (25-70) years, and mean post-transplantation months of 103 ± 53 was performed. We compared Insulin resistance (HOMA-IR) and the prevalence of proteinuria (random urine protein-creatinine ratio $\geq$ 0.2mg/mg) between 25-OHD insufficiency ($\leq$30ng/ml, N=19) and normal control group ($>$30ng/ml, N=76).
Results: Mean 25-OHD (ng/ml) was 40.2 ± 12.6, Of 95 transplant recipients, 19 (20%) have 25-OHD insufficiency. Mean posttransplant month was significantly longer 126 ± 49 in 25-OHD insufficiency than 97 ± 53 in normal 25-OHD (P=0.049). The prevalence of proteinuria was significantly higher 47.4% (9/19) in 25-OHD insufficiency than 19.7%(15/76) in normal 25-OHD (P=0.019). Vitamin D insufficiency is a significant risk factor of proteinuria, independent of age, posttransplant month, gender, and BMI (OR= 3.93, P=0.03). No association of vitamin D insufficiency with Insulin resistance and cardiovascular (CV) parameters was observed.
Conclusion: We concluded that 25-OHD insufficiency is not uncommon and is significantly associated with an increased prevalence of proteinuria in renal transplant recipients. However, we failed to revealed that 25-OHD insufficiency is associated with insulin resistance and CV parameters in kidney transplant recipients. Additional studies are needed to clarify the causal relationship of vitamin D with proteinuria and determine whether vitamin D therapy prevents or improves proteinuria, or markers of kidney and cardiovascular risk.

P-193 PREVALENCE AND CORRELATES OF INFLUENZA VACCINATION AMONG RENAL TRANSPLANT PATIENTS

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Background: Immunosuppressive regimens increase kidney transplant patients' risk of contracting life-threatening influenza. However, little information exists about the prevalence and correlates of influenza vaccinations in this population.
Purpose: The purpose of this study was to determine the prevalence and explore correlates of influenza vaccination in RTx recipients.
Methods: This cross-sectional study used data of the Supporting Medication Adherence in Renal Transplantation (SMART) study. The convenience sample consisted of 356 adult RTx recipients (58.1% male; mean age 52.9 years (SD 13.53)) recruited from two Swiss transplant outpatient clinics. Influenza vaccination status was assessed by self-report (yes/no). Known correlates of vaccination in chronically ill patients (older age, cohabitation, higher education, higher socio-economic status, financial stability, more co-morbidities, negative smoking status, and follow-up center attendance) were entered into a multiple logistic regression.
Results: Of the 356 patients, only 83 (23.3%) reported having been vaccinated against influenza in the previous year. Positive vaccination status was significantly related to older age (OR: 1.04; 95% CI: 1.02-1.06).
Conclusion: Despite national and international guidelines recommending influenza vaccination in RTx patients, influenza vaccination prevalence was low in this sample. This study's results suggest that transplant centers need to implement policies to maximize influenza vaccination of their patients.

P-194 MONITORING OF POLYOMA VIRUS BK AND JC VIRURIA AND VIREMIA IN KIDNEY TRANSPLANT PATIENTS: TWO YEARS PROSPECTIVE STUDY

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Introduction: Nephropathy due to polyomavirus (PVAN) is usually diagnosed by renal biopsy after worsening of renal function. This is normally at an advanced stage of the disease and involves a four-fold increase in the risk of graft loss.
Aim: To study the prevalence of active BKV and JCV infection and determined risk factors for reactivation and interstitial nephropathy.
Material and methods: The study included 76 kidney transplant recipients from cadaveric donors transplanted between August 2005 and July 2006 with a follow-up of two years. If the PCR in urine was positive, PCR was performed in blood. If this was positive or renal dysfunction was present, renal biopsy was performed.
Results: Viruria was positive in 33 patients (43%) and viremia in 8 (10%), 3 of whom (4%) developed nephropathy. No correlation was found between active infection and age or sex, either of the donor or the recipient, number of HLA mismatches or immunosuppressive therapy. The viral load in urine was significantly greater in the patients with viremia and PVAN. The patients with PVAN also had a higher number of copies in blood compared to the patients with viremia. Immunosuppression was reduced in the patients with viral replication in urine and blood with PCR becoming negative in urine in 39% and in blood in 87%. Renal function (creatinine clearance, aMDRD) at two years was 48 ml/min/1.73 m^2 in the patients with nephropathy and 65 ml/min/1.73 m^2 in the others. No patient lost the graft due to nephropathy.
Conclusions: The detection of BK and JC polyomavirus by protocolized PCR enables early diagnosis of nephropathy and prevents associated graft loss, with good renal function two years later.

P-195 CINACALCET FOR THE TREATMENT OF HYPERCALCEMIA IN 29 RENAL TRANSPLANTED PATIENTS WITH PERSISTENT HYPERPARATHIROIDISM

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Introduction: Persistent hyperparathyroidism (HPT) with hypercalcemia and hypophosphoremia is common after renal transplantation, and results in the need for parathyroidectomy. Cinacalcet may be a therapeutic option for these patients.
Aim: To analyze the efficacy of treatment with cinacalcet in patients with hypercalcemia (Ca $>$10.5 mg/dL) secondary to HPT.
Material and methods: We undertook a prospective study of 29 kidney transplant recipients with hyperparathyroidism who started treatment with 30 mg of cinacalcet. The mean follow-up was 13 months (Range: 3-29).
Results: Treatment with cinacalcet effectively reduced levels of calcium (baseline, 11.1 ± 0.8 vs. 9.7 ± 0.6 mg/dL at 12 months, $P<.05$) and intact PTH (iPTH) (baseline, 288 ± 155 vs. 236 ± 118 pg/mL, P:NS). Phosphorus levels increased from 2.5 ± 0.6 to 3.2 ± 0.8 mg/dL ($P<.05$). The mean dose of cinacalcet was 60 mg (Range: 30-120). Two patients required parathyroidectomy. Cinacalcet was well tolerated, except in two patients who had nausea and epigastralgia.
Conclusions: Cinacalcet is safe and effective in kidney transplant patients with hypercalcemia secondary to HPT. Of note was the low incidence of adverse side effects despite the high doses used in these patients.

P-196 THE EFFECTIVENESS OF A 5-DAY EXTERNAL STENTING PROTOCOL ON UROLOGICAL COMPLICATIONS AFTER RENAL TRANSPLANTATION

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Introduction: Ureteral stents are successful in reducing urological complications after renal transplantation. However, the optimal duration and method of stenting has not yet been clarified. The objective of this study is to investigate the frequency of urological complications using a 5-day external stented ureterocystostomy protocol.
Patients and methods: Between July 2005 and June 2007 all 196 consecutive renal transplant recipients were prospectively included in the study. A urological complication was defined as any cause leading to the placement of a percutaneous nephrostomy catheter and/or surgical revision of the ureterocystostomy.
Results: A urological complication occurred in 13/196 (6.6%) patients. In 2/66 (3.0%) of the patients who underwent living donor transplantation and in 11/130 (8.5%) of those who underwent deceased donor transplantation. In 8/13 patients the complication was managed using a temporary percutaneous nephrostomy catheter only. In the remaining 5 patients a surgical revision was necessary. Of all urological complications 39% occurred in the first two post-operative weeks and 70% within the first post-operative month. Acute rejection was a significant risk factor for the occurrence of a urological complication (odds ratio 3.48, 95% confidence interval [CI]: 1.11-10.87).
Conclusion: Acute rejection is the only significant factor associated with the occurrence of a urological complication. A 5-day routine external stent protocol is efficacious in living donor renal transplantation in preventing early postoperative ureter obstruction, but this stenting period seems inadequate for deceased donor renal transplantation.

P-197 RISK FACTORS FOR DELAYED GRAFT FUNCTION AFTER HAND ASSISTED LAPAROSCOPIC DONOR NEPHRECTOMY

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Introduction: Occurrence of delayed graft function (DGF) has a negative impact on the results of living kidney transplantation. The objective of this study was to investigate potential risk factors for DGF.
Methods: All 200 consecutive living donors and recipients between January 2002 and July 2007 were prospectively studied. DGF defined as the need for dialysis within the first postoperative week, was assessed and the associate risk factors were analysed.
Results: DGF was diagnosed in 12 patients (6%). Intraoperative and post-operative complications occurred in 10 donors (5%) and 24 donors (13.5%). One-year graft survival of kidney with and without DGF were respectively 52% and 98% ($p<0.0001$). Two donor risk factors for DGF were identified: lower counts per second on time to peak activity during renal donor scintigraphy (odds ratio (OR) 6.04, 95% confidence interval (CI): 1.24-29.45) and multiple renal veins (OR 15.33, 95%CI: 2.96-79.02). For the recipient only the second or more kidney transplantation (OR 4.45, 95%CI: 1.22-16.20) and acute rejection (OR 22.65, 95%CI: 4.75-108.1) were significant factors.
Conclusion: HALDN is a safe procedure. Peak activity during renal donor scintigraphy as an index of functional renal mass, multiple renal veins, second or more renal transplantation and acute rejection showed to be risk factors for DGF.

P-198 KIDNEY TRANSPLANTATION FROM SPOUSAL DONORS: A REPORT OF 11 CASES

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Objective: To summarize the clinical experience of kidney transplantation from spousal donors.
Methods: From April 2006 to December 2008, 11 recipients had been accepted renal transplantation from spousal donors. Potential donors underwent fully medical evaluation before operation, including donor-recipient HLA matching and a cross match test. The donor's operation performed the incision either underneath the 12th rib approaching the dorsal lumbar and the transplantation operation adopted the extraperitoneal approach in the contralateral fossa iliac. All recipients received mycophenolate mofetil and corticosteroids in combination with low-dose cyclosporine or low-dose tacrolimus. All recipients and donors accepted follow-up after operation.
Results: All spousal donors were discharged within 7 days without any complication. Serum creatinine levels of 10 recipients recovered normal within three days post-operation, one of them occurred acute allograft rejection at the eighth day postoperative and returned normal after given intravenous methylprednisolone. One recipient recovered normal within two weeks. After follow-up from 2 months to 20 months with the median time of 8.2 months, all recipients and donors kept normal kidney function.

Clincal data

Case No.		ABO/Rh	Gender/ age	Duration of dialysis	Primary disease	HLA
1	donor	O/Rh(+)	F / 44			
	recipient	B/Rh(+)	M / 57	0	chronic glomerulonephritis	3-coli mismatch
2	donor	B/Rh(+)	M / 50			
	recipient	B/Rh(+)	F / 45	0	polycystic kidney	4-coli mismatch
3	donor	B/Rh(+)	M / 45			
	recipient	B/Rh(+)	F / 40	0	chronic glomerulonephritis	5-coli mismatch
4	donor	O/Rh(+)	F / 31			
	recipient	O/Rh(+)	M / 47	8 months	chronic glomerulonephritis	4-coli mismatch
5	donor	O/Rh(+)	F / 43			
	recipient	O/Rh(+)	M / 40	4 months	polycystic kidney	4-coli mismatch
6	donor	A/Rh(+)	F / 44			
	recipient	A/Rh(+)	M / 46	0	chronic glomerulonephritis	3-coli mismatch
7	donor	O/Rh(+)	F / 28			
	recipient	A/Rh(+)	M / 28	5 months	chronic glomerulonephritis	1-coli mismatch
8	donor	B/Rh(+)	F / 36			
	recipient	B/Rh(+)	M / 37	0	chronic glomerulonephritis	4-coli mismatch
9	donor	B/Rh(+)	F / 36			
	recipient	B/Rh(+)	M / 40	0	chronic glomerulonephritis	5-coli mismatch
10	donor	A/Rh(+)	F / 40			
	recipient	A/Rh(+)	M / 48	1.5 months	chronic glomerulonephritis	6-coli mismatch
11	donor	A/Rh(+)	M / 53			
	recipient	A/Rh(+)	F / 36	0	chronic glomerulonephritis	4-coli mismatch

F, female; M, male.

Conclusion: Kidney transplantation from spousal donors is safe and effective procedure. Spousal kidney donation has become an important source of donor kidneys to combat the problem of organ shortage.

P-199 POSTURAL EPIGASTRIC PAIN AS A SIGN OF CMV GASTRITIS IN RENAL TRANSPLANT RECIPIENTS: A CASE-BASED REVIEW

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Background: Cytomegalovirus (CMV) infection is a common cause of morbidity and mortality among patients receiving chronic maintenance immunosuppression and is often considered the most important infection in renal transplantation. CMV gastritis has been reported in transplant patients. Symptoms are usualy considered nonspecific, and gastroscopy with biopsy is usually performed to establish the diagnosis.
Methods: We report a case of primary CMV gastritis in a renal transplant recipient. A 34-year-old man presented 3 months after renal transplantation with a 1-week history of epigastric pain that decreased in supine position, increased while sitting, and further increased when standing or walking. The immunosuppressive regimen consisted of tacrolimus, mycophenolate mofetil, and prednisone. Evaluation revealed CMV viremia with a high viral load and CMV gastritis was confirmed by gastroscopy, histopathologic examination and cultures. Intravenous ganciclovir was started and continued 3 weeks. The epigastric pain completely resolved after treatment with ganciclovir.
Conclusions: Postural epigastric pain as a sign of CMV gastritis is fairly rare in renal transplant recipients. To our knowledge this is the third article presented to the literature so far.

P-200 NONINVASIVE PRE-TRANSPLANT CARDIAC RISK ASSESSMENT WITH CALCIUM SCORING AND ANGIOGRAPHY BY HIGH RESOLUTION COMPUTED TOMOGRAPHY

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Purpose: Calcium scoring by computed tomography is a noninvasive diagnostic modality to screen for coronary arteriosclerosis. Herein a description of the use of this technology is presented for the assessment of coronary artery disease in pre-transplant end stage kidney disease (ESKD) patients.
Methods: Retrospective and descriptive analysis done: Dec 2006–Aug 2008.

Record the results of coronary artery computed tomography calcium scoring in addition to traditional nuclear stress cardiac testing. Patients considered to be at higher risk for arteriosclerosis were: age greater than 45 years, greater than 5 years on dialysis, diabetes, past history of cardiac disease.

Table 1. Clinical characteristics

Description	Results
n	128
Patients that got a nuclear stress test	128 (100%)
Patients that got a cardiac cath	25 (20%)
Age, yr	54±11
BMI, kg/m^2	28±5
Mean age of ESKD onset	46±14
Median time on dialysis	30 (6–214)
Race	
Caucasian	66 (52%)
African American	50 (39%)
Other races	12 (9%)
Cause of ESKD	
Hypertension	34 (27%)
Diabetes	31 (24%)
Hypertension & Diabetes	19 (15%)
Unknown etiology	12 (9%)
Other causes	32 (25%)

Mean ± standard deviation; mean (range).

Table 2. Coronary artery calcium scoring (CACS)

Description	Calcium Score
Median calcium score for all patients	130 (0–10,764)
Mean CACS score by risk factor:	
Ischemia on nuclear stress test	1715±2869
History of cardiac disease	1289±2548
Diabetes > 5 yr	994±1591
On dialysis > 5 yr	787±1704
Hypertension > 10 yr	641±1685
Age > 50 yr	630±1337

Mean ± standard deviation; mean (range).

Conclusion: Coronary artery calcium scoring has a high negative predictive value in ESKD patients undergoing pre-transplant cardiac risk assessment.

P-201 RENAL TRANSPLANTATION IN MALAYSIA: INFLUENCE ON LONG-TERM SURVIVAL OF NON IMMUNOLOGICAL FACTORS

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Introduction: Since the introduction of CsA into clinical practice in the late 1970's and early 1980's, many transplant centres around the world have reported at least >80-85% one-year renal allograft survival. However, despite the short-term success, the Eurotransplant data demonstrated that there was not much change in the half-life of primary cadaver renal allograft in pre-CsA and post-CsA era (9.7 vs 11.6 years respectively). Thus, while CsA has clearly improved the survival of renal allograft in the short-term, the long-term outcome is less certain. There are increasing data to suggest that the non-immunologic factors may play a significant contribution to chronic renal allograft dysfunction.
Methods: We analyzed data from Malaysian Dialysis & Transplant Registry from year 1993-2002. The overall unadjusted patient and graft survival rates appeared to improve in year 1998-2002 compared with year 1992-1997 results. We decided to evaluate potential patient and transplant characteristics (non-immunological factors) as predictors of long-term graft survival.
Results: There was a total of 1400 renal transplantation reported to MDTR between 1993-2002. After adjustment (Cox proportional hazards models) for multiple risk factors, the risk of graft failure in all transplants has decreased by 25%, while the risk of patient death has fallen by 39% (p=0.024) for the 1998-2002 cohorts comparing with the 1993-1997 cohorts. The higher relative risks of graft failure are associated with recipient ages 55 and older (RR=1.63, p=0.011), with diabetes mellitus (RR=1.44, p=0.049), receives cadaver donor graft (RR=2.26, p=0.000) or unrelated live donor graft (RR=1.43, p=0.014), with HBsAg seropositivity (RR=1.6, p=0.005), and with anti-HCV seropositivity (RR=2.10, p=0.000). Preliminary analysis which was unadjusted for other covariates that might influence graft survival outcome suggests that there may be slight graft survival advantage associated with the use of tacrolimus and mycophenolate mofetil.

P-202 CYTOMETRIC ANALYSIS OF TH1/TH2 CYTOKINES IN THE URINE OF PATIENTS PRIOR TO THE KIDENY TRANSPLANTATION

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Introduction: Acute allograft rejection (AR) remains a major problem after kidney transplantation and crucial determinant of long-term graft function. Potential mediators of alloimmune response leading to AR are cytokines. To further explore the relation between cytokine pattern and frequency of AR episodes we analyzed Th1/Th2 cytokine concentrations in the urine of patients prior to the kideny transplantation.
Materials and methods: The project included 44 patients undergoing kidney transplantation during 2007-2008. During the six-month period following the transplantation AR was diagnosed in 11 patients. Urine samples were collected 1 day before the transplantation. Each sample was tested for concentrations of IL-2, IL-4, IL-5, IL-10, IFN-γ and TNF-α using the Human Th1/Th2 Cytometric Bead Array method.
Results: Non-rejection (NONAR) and rejection (AR) groups of patients did not show significant differences in pretransplantation epidemiological and clinical characteristics. Cytometric analysis showed significantly higher pretransplant concentrations of IFN-γ ($p<.00005$), TNF-α ($p<.004$) and IL-10 ($p<.000001$) in the urine of patients with diagnosed AR. No significant differences in urine concentrations of IL-2, IL-4, IL-5 between the two groups were observed ($p>.05$).

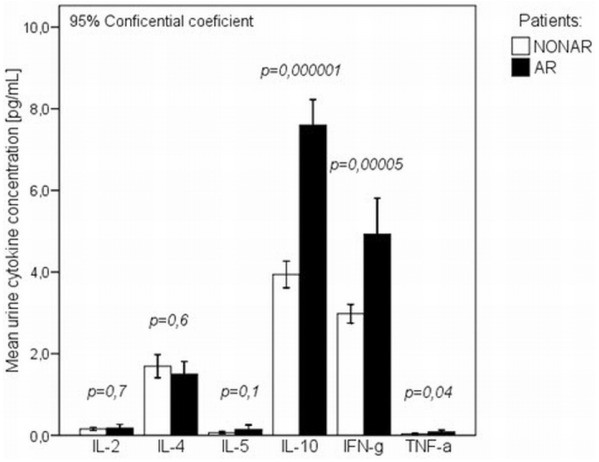

Figure 1. Mean urine cytokine concentrations [pg/mL] in non-rejection (NONAR) and rejection (AR) patients prior to the kidney transplantation.

Discussion: Elevated pretransplant concentrations of urine IFN-γ and TNF-α in AR patients, not accompanied by higher concentrations of IL-2, may suggest an ongoing undetected nonspecific and local Th1 immune response, capable of amplifying the alloimmune response in the early phase postsurgery, leading to AR. Higher concentrations of IL-10 found in the urine of AR patients, in turn, can partially result from peripheral regulatory mechanisms controlling the ongoing immune reaction, and partially from activation of monocytes/macrophages. These results suggest that higher concentrations of IFN-γ, TNF-α and IL-10 in the urine of patients prior to the kidney transplantation can be considered as risk factors increasing the probability of AR episodes.

P-203 IMMUNOLOGIC INTOLERANCE TO THE RENAL ALLOGRAFTS. ANALYSIS OF THE THERAPEUTIC ATTITUDE AND MAGNITUDE OF THE INFLAMMATORY STATE IN A SERIES OF 199 PATIENTS

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Introduction: Immunologic intolerance syndrome to a failed renal allograft (IIS) can to complicate the patients evolution that restarts dialysis associating to a chronic inflammatory state.
Objective: Retrospective revision about renal transplanted patients that restarted dialysis among 1995-2007. Identification of patients with IIS, therapeutic attitude and evaluation of inflammatory state.
Material and methods: It is analized: age, sex, renal allograft loss causes, it's time half survival, half time descent of steroids after beginning dialysis, time begins IIS after suspending inmunosupresion treatment. Hb,PCR, Fer-

ritina, Albumin and other biological parameters, before and after the treatment (medical, vascular embolization or Transplantectomy).
Results: 199 patients restarted dialysis in 12 years (1995-2007). The survival of the renal allograft was 7,7±5,54 years. 45 patients presented IIS (22,6%). 29 male and 16 female, half age 47,4 years (71-23 years). 15 patients (7,5%) they were retrasplanted, 8 of these (53,3%) IIS presents. To the restart of the dialysis all they were in descending steroids treatment. Half time of suspension them 10,43±4,85 weeks.
Half time of beginning of the symptoms after inmunosupresor treatment was 25,1 weeks.
Treatment: 3 patients (6,6%) steroids were restarted (1 patient transpantectomy required because symptons continued). 31 patients were embolitationed (68,8%): 9 patients presented therapeutic failure (20%): 2 were embolized again and 7 were transplantectomiced.
Complications: 2 patients had septic renal allograft and transplantectomy neded. 11 patients initially were trasplantectomy without problems (24,4%). Total trasplantectomy 21 (46%).

Table 1. Parameters with significance

	Before treatment	After treatment	Significance
ALB	3,22±0,35	3,6±0,36	=0.005
PCR	8,7±10,07	2,1±2,9	NS
Hemoglobine	8,8±1,32	11, 63±2,37	<0,0005
Ferritine	377,8±306,05	489,77±424,18	NS

Conclusions: The IIS has a high prevalence. The immunologic factor are implicated to the inflammatory state. The Embolitation and the Trasplantectomy are the ellection treatment and solution the inflamatory problem.

P-204 TWENTY YEAR EXPERIENCE IN A TRANSPLANT CENTRE. ANALYSIS OF FIRST KIDNEY TRANSPLANTATION RESULTS

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Aim: To compare the results of first kidney transplantation of the periods 1987 – 1996 (FP) and 1997 – 2006 (SP) in one transplant unit.
Methods/Materials: Seven hundred and sixteen patients (716), entered the study. In the first period (FP) 225 men and 124 women and in the second period (SP) 238 men and 129 women were transplanted. Cumulative patient (CPS) and graft (CGS) survival after removing the first trimester patient and graft losses was calculated. Systolic blood pressure (SBP), diastolic blood pressure (DBP) and serum creatinine (Scr) of the first five years were measured. Donor age, living (LD) and cadaveric (CD) donors and mean first hospitalization time, were recorded.
Results: There was statistically significant (ss) difference in the age between men (39.36±11.71 and 41.74±12.74, p=0.037) and women (37.50±12.09 and 41.38±13.90, p=0.019) of FP and SP respectively. CD were 125 and 178 in FP and SP respectively (p= 0.02). CD age was 37.53±18.04 and 47.46±18.35 years in the FP and SP respectively (p= 0.000). Removing the immediate post-transplant losses (first trimester) the LD CGS (including deaths) at 5 and 10 years was 74.77% and 53.67% in the FP and 83.81% and 67.07% in the SP respectively (p=0.014). The days of first hospitalization were 22.78±14.63 and 20.01±13.29 in he FP and the SP respectively (p= 0.009). Five year mean SBP and DBP of the SP were ss lower compared to mean SBP and DBP of the FP (p=0.021 and p=0.001 respectively).
Conclusion: In spite the ss increase of recipient and CD age and ss increase in the number of cadaveric transplants in the SP there was a ss decrease of first hospitalization days, decrease of SBP and DBP and a ss increase in ten year LD graft survival during this period.

P-205 STUDY OF RISK FACTORS AND LONG TERM PROGNOSIS OF POST KIDNEY TRANSPLANT DIABETES MELLITUS (PTDM): A SINGLE CENTER EXPERIENCE

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Purpose: Is to examine the diabetic risk profile of PTDM and its impact on patient and graft survival.
Methods: The analysis included 2019 renal allograft recipients, transplanted between 1976 and 2008 in a single institution, Mansoura Urology & Nephrology center, Egypt. Risk factors, patient and graft survival were analyzed by univariate & multivariate analyses, Cox regression consider PTDM as a time dependent variable.
Results: After a mean follow up period of 8.8±5.8 years, 450 (22.2%) recipients developed PTDM. They were compared with a control group of 455 patients without DM. Both groups were homogenous regarding the time of transplantation, the donor's age, sex, consanguinity & matching. Fifty% of cases discovered during the first 6 months post transplantation. 151 patient were controlled on insulin and the remaining were controlled on diet regimen or oral anti diabetics. The diabetic recipients were significantly older (35.2±9.9 Vs 28±9.6, P<0.01) and obese body mass index (BMI) 28.8±9.6 Vs 25.2±4.3, P<0.01). Family history of DM was significantly positive among the PTDM group (216 Vs 64, P<0.01). Hepatitis C virus (HCV) infection was predominating among the diabetic group. Medical complications (post-transplant hypertension, hypercholesterolemia, ischemic heart disease, proteinuria, retinopathy and neurological complications), were significant in the diabetic group. Patient survival was significantly lower in the diabetic group while the graft survival was comparable. Logistic multivariate regression analysis revealed that the age, positive family history of DM, BMI, HCV infection and hypercholesterolemia were of significant risk factor.
Conclusion: PTDM is a major problem endangers the patient life and must be minded to consider such patient as especially at higher risk for diabetic complications. The management of PTDM not differs from the treatment of type2 DM in the general population.

P-206 EVALUATION OF THE EFFICACY AND SAFETY OF CONVERSION TO SIROLIMUS IN 85 RENAL TRANSPLANT RECIPIENTS

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Introduction: Treatment with sirolimus (SRL) is a proven therapeutic option in renal transplant recipients, especially those who develop chronic graft nephropathy (CGN) or neoplasm.
Aim: To analyze the efficacy and safety of conversion to SRL in renal transplant recipients.
Material and methods: We undertook a retrospective study of 85 patients converted to SRL, 47% for tumors (T), 39% for CGN, and 14% for other causes. The follow-up period was 34 months (range: 1-93).
Results: Baseline creatine was 1.8±0.69 (1.6±0.59 T vs. 2.3±0.6 CGN). At one year, the creatinine was the same in both groups, 1.8; P=NS. Graft survival at 12 months was 89% (81% T, 81% CGN, 100% other causes). SRL was withdrawn in 34% of the patients (18% for side effects, 7% for patient death, 9% for graft loss). The creatinine and proteinuria were significantly greater in those who returned to dialysis because of CGN than those with conserved renal function. Patients who developed pneumonitis had a lower baseline MDRD, but no differences in SRL levels. Side effects occurred in 40% of the patients, with no differences in renal function, proteinuria or SRL levels. Renal function showed a significant improvement in the patients who continued SRL (45.7 vs. 50.7 at 12 months; P<0.08), more marked in those who converted due to CGN. Increases were seen in levels of serum lipids, as well as the percentage of patients treated with statins. Proteinuria increased significantly, as did the percentage of patients treated with ACE inhibitors/ARA2.
Conclusions: Conversion to sirolimus in patients with CGN is safe when renal function has still not undergone marked worsening and there is no proteinuria. Patients who are converted experience a significant improvement in renal function.

P-207 THE IMPACT OF DONOR:RECIPIENT SIZE DISCREPANCY IN PAEDIATRIC RENAL TRANSPLANTATION ON SHORT AND LONG-TERM OUTCOMES

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Objectives: Outcomes of paediatric renal transplantation are unfavourable compared to adults. Small children are particularly disadvantaged from a lack of donors matched for size. Transplantation of adult kidneys into paediatric recipients is technically difficult and associated with complications such as longer warm ischaemic times, abdominal compartment syndrome and graft hypoperfusion. Hence we sought to study outcomes in small paediatric recipients of large and small grafts.
Methods: All paediatric transplants in low-weight recipients (<20kg) were included in this study. Recipients were stratified into two groups comprising 'high' and 'low' donor:recipient weight ratios based on the median value. Primary

outcomes were rates of primary non function (PNF), delayed graft function (DGF), acute rejection (AR) and 1 year graft survival. Secondary outcomes were serum creatinine and body weight. Statistical analysis comprised Student t test for comparison of ordinal data means, Chi squared for categorical data and a 5% level of statistical significance.
Results: Twenty three transplants were performed in recipients <20kg. 22 were implanted in extraperitoneal positions. 12 patients had 'low' donor:recipient weight ratios and 11 'high' ratios about the median value (4). There was no significant difference in rates of the primary outcomes; though 1 graft was lost at 2 months in the low ratio group. Secondary outcomes are shown in Table 1 and were comparable between groups.

Comparison of groups based on donor:recipient weight ratio

	Size:weight ratio < 4 (n=12)	Size:weight ratio > 4 (n=11)	P value
Creatinine 3 months (μmol/L)	63±14	68±21	0.63
Creatinine 6 months (μmol/L)	63±14	73±19	0.35
Creatinine 12 months (μmol/L)	65±17	76±13	0.58
Creatinine 24 months (μmol/L)	72±17	84±53	0.12
Body weight 3 months (kg)	20±5	17±3	0.13
Body weight 6 months (kg)	20±5	17±4	0.67
Body weight 12 months (kg)	22±6	18±4	0.54
Body weight 24 months (kg)	27±8	22±4	0.13

Figures are expressed as mean ± SD.

Conclusion: Donor:recipient weight ratio does not impact on rates of PNF, DGF, AR and 1 year graft survival. Size mismatched grafts from large donors have comparable outcomes to conventional size matched grafts in small (<20kg) paediatric recipients.

P-208 EFFECT OF TEMOCAPRIL AND CANDESARTAN ON PAI-1 AND TGF-BETA EXPRESSION IN CYCLOSPORINE-TREATED NEPHROTOXIC RATS

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Introduction and objective: To examine and compare the effect of temocapril and candesartan on PAI-1 and TGF-beta expression in cyclosporine (CyA)-treated nephrotoxic rats, we planned and carried out the following study.
Methods: Ten-week-old male Wistar rats were divided into six groups (ten animals each). Group 1 received a medium only. Group 2 received 30 mg/kg/day (i.e. experimentally nephrotoxic dose) of CyA only. Group 3 received both 30 mg/kg/day of CyA and 1 mg/kg/day of temocapril. Group 4 received both 30 mg/kg/day of CyA and 0.1 mg/kg/day of candesartan. Group 5 received 1 mg/kg/day of temocapril only. Group 6 received 0.1 mg/kg/day of candesartan only. All drugs were given orally once a day for fourteen days. On the fifteenth day, after blood pressure monitoring and blood sampling, kidneys were removed and processed for Western blotting, reverse transcriptional-polymerase chain reaction, and immunohistochemistry to examine PAI-1 and TGF-beta expression.
Results: PAI-1 and TGF-beta were up-regulated in group 2, and down-regulated in groups 3 and 4.
Conclusions: Inhibition of renin-angiotensin axis would have potential to prevent nephrotoxic side effect of CyA through diminishing PAI-1 and TGF-beta expression.

P-209 HEAD AND NECK MALIGNANCIES IN RENAL TRANSPLANT RECIPIENTS

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Renal transplantation is associated with increased incidence of cancer. We reviewed our database of renal transplant recipients to determine the incidence and outcome of patients with malignant changes located at the head and neck. A total of 1232 renal transplant recipients have been followed at Department of Dialysis University Hospital Centre Zagreb from 1972 to 2008. The mean length of follow-up was 9.4±4.8 years. Twenty one patients (1.7%) developed 27 head and neck malignancies. The average time from transplantation to development of cancer was 56.8 months. Eighteen malignancies were cutaneous in origin and 9 were noncutaneous. Of cutaneous malignancies, 88.9% were basal cell carcinoma; one patient had Merkell-cell carcinoma and one patient developed squamous cell carcinoma. Six cases of basocellular skin cancer were recorded in one fair-skin patient. Noncutaneous malignancies involved the oral cavity (2 cases of Kaposi's sarcoma and one pharyngeal cancer) and the thyroid gland in 3 patients each. Two patients had posttransplant lymphoproliferative disorder occurring at the head and neck. One patient had brain tumor (astrocytoma). Radical surgery, radiation, and/or chemotherapy were necessary in 33.3% of patients. Immunosuppression was reduced in all patients, and 12 patients were switched from the calcineurin-based immunosuppression to sirolimus. They all have stable graft function. None of the patients died from cancer. Immunosuppression was ceased in one patient with Kaposi's sarcoma who returned to dialysis and died 10 years later from heart failure
Conclusion: An increased incidence of cancer occurring in the head and neck was recorded. Patients should be educated to avoid sun exposure especially in the Mediterranean area. Careful skin and oral examination is mandatory for discovering cancer before dissemination. Sirolimus is safe alternative to calcineurin-based immunosuppression in patients who developed head and neck malignancies.

P-210 RENAL TRANSPLANTATION IN CROATIA AFTER JOINING EUROTRANSPLANT

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Background: Eurotransplant (ET) is responsible for the mediation and allocation of organ donation procedures in Austria, Belgium, Croatia, Germany, Luxemburg, the Netherlands and Slovenia. Croatia joined ET in August 2007. This report presents data on renal transplantation in the largest renal transplant centre in Croatia after joining ET. One-year allograft survival in our centre before joining ET was 92%.
Results: From August 2007 to December 2008, 122 patients received a renal allograft allocated by ET. There were 72 male and 50 female patients, age ranging between 9 and 73 (mean age 46,8±1,4) years. Patients were previously treated with dialysis for 1 to 22 (mean 9,7±0,5) years. Twenty-seven patients had been dialyzed for more than 15 years (22,1%), and 12 had previously been transplanted. Positive hepatitis C status was found in 17,2% of patients, while 3 patients had both chronic HCV and HBV infection. Delayed graft function was recorded in 40,1% of patients. Complications included acute rejection in 6 patients, herpes zoster reactivation in 4, CMV reactivation in 7, BK virus infection in 2 and posttransplant diabetes mellitus in 3 patients. Surgical complications included delayed wound healing in 10 patients, urinoma in 2, lymphocele in 4, and bleeding in 4 patients. Graftectomy was performed in 7 patients. Two patients died, one from cardiac decompensation and one from pulmonary aspergillosis.
Conclusion: Number of renal transplantations performed in our centre increased after joining ET. The most important change was different allocation policy based on waiting time, in comparison to the previous allocation based on HLA compatibility. Short time results are worse than those obtained in our centre before joining ET, what is the consequence of transplantations performed in patients who were treated with dialysis for more than 15 years.

P-211 THE IMPACT OF VERY PROLONGED COLD ISCHAEMIA TIME ON SHORT AND LONG-TERM OUTCOMES IN RENAL TRANSPLANTATION

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Aims: The increasing demand for renal transplantation, and reduced conventional donor pool, has increased use of marginal donors. Very prolonged cold ischaemic times (CIT) have hitherto precluded transplantation, and the outcomes in recipients of such grafts is not well established. Herein we describe the short and long term outcomes in recipients of renal transplants where CIT has exceeded 24 hours.
Methods: From January 1995 to September 2005, 101 renal transplants were performed using donors with CIT >24 hours. Duration of delayed graft function (DGF), graft and patient survival, and calculated estimates of GFR (abbreviated MDRD equation) were compared with recipients of grafts were CIT did not exceed 24 hours (n=942). Ordinal data were compared using student t test (SPSSv14). Data are expressed as means±SD using a 5% level of statistical significance.
Results: No statistical significance was seen between the two groups in DGF (p=0.52), graft survival (p-0.94) or days of recipient survival (p=0.28). eGFR was significant at 5 days (p<0.001), but became non-significant from 6 months onwards
Conclusions: Renal transplantation from donors with a very prolonged CIT (>24 hours) results in comparable durations of DGF, graft and recipient survival to conventional donors (CIT<24 hours). Though immediate eGFR is reduced where CIT is prolonged, eGR from 6 months to 5 years are comparable.

P-212 THE VALUE OF RESISTIVE INDICES AS A PREDICTOR OF SHORT AND LONG-TERM OUTCOMES IN NON-HEARTBEATING RENAL TRANSPLANT DONORS

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Aims: The increasing demand for renal transplantation, and reduction in cadaveric donor numbers, has prompted increased use of non-heartbeating donors (NHBD). Rates of delayed graft function (DGF) are 48-94% in NHBD and graft surveillance with Doppler ultrasound (USS) is used to monitor graft perfusion during periods of DGF. Ultrasonographic parameters such as the resistive index (RI) may usefully predict renal function and vascular complications. This study describes the role of early USS in monitoring grafts from NHBD with DGF.
Methods: From April 2002 to September 2005, 77 renal transplants were performed from NHBD. Four grafts had PNF and were excluded from further analysis; 44 grafts had DGF defined by a need for dialysis within the first week after transplantation (60%). All recipients had USS within 3 days of transplantation during which RI was measured. Multiple regression was used to correlate RI, donor parameters and graft outcomes.
Results: RI (mean 74%±8%) showed no correlation with early (Day 5) calculated glomerular filtration rate (eGFR) (β=-0.35;p=0.16) or eGFR 1 year after transplantation (β=0.61;p=0.92). RI showed no correlation with 1 year graft (β=0.33;p=0.16) or recipient survival (β=0.33;p=0.16). The only predictor of long-term graft function was donor age as increased donor age was negatively correlated with eGFR at 1 year (β=-0.78;p=0.04).
Conclusions: The use of early USS, and measurement of RI, does not reliably predict short or long term graft or recipient outcomes during DGF in recipients of NHBD renal transplants.

P-213 METABOLIC BONE DISEASE IN AFTER RENAL TRANSPLANTATION IN PATIENTS WITH BALKAN ENDEMIC NEPHROPATHY

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Metabolic bone disease is common in renal transplant recipients and frequently manifests with pain, fracture, osteonecrosis or avascular necrosis. These complications significantly impair quality of life and increase mortality and need for hospitalizations. In the present study we evaluated bone status of renal transplant recipients with Balkan endemic nephropathy (BEN).
There were 10 female and 9 male patients with BEN age at transplantation ranging from 47 to 68 years (mean 57 years), previously treated with hemodialysis for 1-14 (mean 5.5) years. Bone pain was present in 12 patients, 3 patients developed nephrolithiasis, and one patient had bone fracture. Intact PTH ranged from 3.52 to 17.8 (mean 7.47) pmol/L, mean BALP was 32.6 mg/L, mean vitamin D concentration was 55.6 mg/L. Mean octeocalcin value was 12.78 mg/L, and crosslaps 1.31 mg/L. Parathyroidectomy after transplantation was performed in 2 patients because of severe hypercalcemia, while three patients received pamindronate. Renal transplant recipients with other primary renal diseases and the mean age of 54 years had mean BALP 45.78 mg/L, iPTH 6.38 pmol/L, vit D 65.7 mg/L, crosslaps 1.18 mg/L and osteocalcin 15.65 mg/L.
On bone densitometry at 6 months after transplantation femoral T score was -2,11 (range 0.97 – 2,8), antecubital -3,7 (range 0,65 – 4,5) and vertebral -2,01 (range 0,87 – 4,3). No further significant bone loss was observed after the first year, and bone mineral density remained relatively stable but low.
Our results demonstrate that patients with BEN suffer from significant bone loss after renal transplantation. High serum calcium, relatively low PTH and low BAIP suggest adynamic bone disease. However, low osteocalcin and increased crosslaps indicate increased bone resorption, which is higher then in renal transplant recipients with other primary renal diseases.

P-214 EARLY POST-TRANSPLANT INFLAMMATORY RESPONSE PREDICTS LATER ANEMIA IN KIDNEY TRANSPLANT RECIPIENTS

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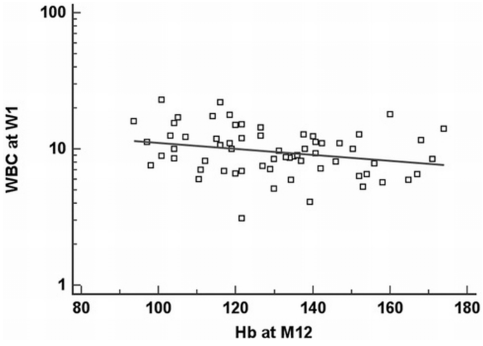
Purpose: Delayed graft function within one week post-transplant has a major adverse impact upon both short and long-term allograft survival and acute rejection in the early post-transplant period (1 to 12 weeks) affects kidney function adversely. Allograft rejection, as an ongoing inflammatory state, results in increased erythropoietin resistance, which leads to decreased hemoglobin (Hb) level. Therefore, we conducted this study to evaluate whether an inflammatory response in the early post-transplant period could predict later anemia.
Design: Retrospective cohort study based on the analysis of 64 existing clinical records.
Outcome: Anemia identified at 12 months (M12) post-transplant. *Predictor*: White blood cells (WBC) count obtained by the end of the first week post-transplant (W1). *Covariates*: Donor's age, recipient's age and sex. Kidney function and acute rejection episodes were not taken into account as covariates because they were intervening variables on a causal pathway between a predictor and an outcome and because of collinearity.
Results: The significant correlation was found between WBC at W1 and Hb at M12. Pearson correlation coefficient r was -0.26, and 95% confidence interval (CI) for r was -0,47 to -0,015 (p=0.03).



Univariate logistic regression analysis showed significant association between WBC at W1 and Hb at M12 (OR 1.20; 95% CI 1,04 to 1,39, p=0.01). After the adjustment for donor's and recipient's age by transplantation and recipient's sex, multiple regression model showed that WBC count at W1 remained predictive of anemia at M12 (OR 1.17; 95% CI 1,01 to 1,36, p=0.03). Since all patients received steroids at the same dose (7 mg/kg) in an induction protocol, dose variation as a possible cause of varying WBC count can be ruled out.
Conclusion: WBC count obtained at W1 was the predictor of post-transplant anemia at M12.

P-215 MAIN CHARACTERISTICS OF CADAVERIC KIDNEY TRANSPLANT AT 10 YEARS AFTER TRANSPLANTATION

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Aim of this study is to characterize the main features of kidney transplant patients with an actual graft survival of 10 years and to define the main differences of patients with a serum creatinine (sCr) of $\leq$1.5 mg/dl with patients with sCr $>$1.5.
121 out of 202 patients transplanted in 1991-1998 have an actual graft survival of 10 years (59.6%). All patients had a CNI based immunosuppression. We observed at 10 years main demographic, transplant related and clinical data.
Actual graft survival was 59.6%. 81 patients had excellent graft function, 40 patients had good or fair renal function. Patients with sCr $>$1.5mg/dl at multivariate analysis had the following characteristics: older donor age (43.5 vs 32.9 years; p$<$0.001), longer cold ischemia time (22.2 vs 19.7 hours;p$<$0.05), lower Hb levels (12.4 vs 13.2 g/dl;p$<$0.01), despite higher use of EPO (p=0.03). Higher PTH levels (12.5 vs 9.5 pmol/l;p$<$0.05).Blood pressure was similar,but the use of antihypertensive drugs was significantly different (1.97 vs 1.23 drug/patient; p$<$0.001).No differences were observed in HLA mismatches, serum lipid levels, Cya dose, use of statins.
With a CNI based immunosuppression we obtained an actual graft survival at 10 years of 59.6% with 2/3 patients with an excellent graft function. In our series older donor age and longer cold ischemia time were the main determinants of worse renal function. Main consequences of poorer renal function were lower Hb levels, higher PTH levels, similar blood pressure with higher use of antihypertensive drugs.Such results were obtained thank to strict medical control and early therapeutical intervention. Under this point of view the develop of the so called "remission clinic" is highly recommended.

P-216 KIDNEY GRAFT SURVIVAL RATES DO NOT IMPROVE BY ERA: THE IMPACT OF FACTOR AGE

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Donor and recipient age dramatically increased in our country. Aim of this study

was to verify the impact of this factor on graft survival rate (GSR). We compared both the 5-year actual GSR and the 5-year death censored GSR of 89 recipients transplanted in 1991-1995 (period A) with 221 recipients transplanted in 1996-2000 (period B). Due to the introduction of immunosuppressants such as MMF, Neoral and IL-2R inhibitors, we expected an improvement in period B GSR.
Period B 5-year GSR was lower with respect to period A (76.3% vs 82%). The death censored GSR was similar (87.1% vs 87.5%). The period B acute rejection incidence was 18% vs 40% of period A ($p<0.001$). Both overall donor and recipient age had the highest impact on 5-year GSR: for donor age 21-50 yrs 86.2% vs 65.7% for donor age >50 yrs ($p<0.0001$).Similar effect was observed for recipient age: 84.1% for age 21-50 vs 68% for age >50 yrs (p=0.0023). In period A donors >50 yrs were 23.6% vs 50.2% in period B ($p<0.001$). Similarly period A recipients >50 were 35.9% vs 42.9% in period B ($p<0.01$). Considering the death censored 5-year GSR for period B with respect to period A, we observed a significant improvement either for donor >50 yrs (82.5% vs 65.8%) and for recipients >50 yrs (90.2% vs 81.2%).
Kidney GSR of patients transplanted in 1991-1995 was higher with respect to 1996-2000. These data disagree with the GSR expected by the reduction of 1-year rejection rate due to new immunosuppressants. Expanded donor criteria can account for such discrepancy. Most of graft failure were due to death with function, but also a poorer quality of kidneys accounts for this phenomenon.

P-217 SUBCLINICAL ACUTE REJECTIONS IN PROTOCOL BIOPSIES PERFORMED AT 3 MONTHS AFTER KIDNEY TRANSPLANTATION

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Purpose: To detect subclinical acute rejection (SAR), borderline changes (BL) and possible clinical/laboratory associations including graft expression of several genes associated with B-cell and T-cell mediated inflammation and rejection.
Methods/Materials: The protocol biopsies were performed in 257 patients (pts) with stabilized graft function. Histomorphological changes were graded according to the Banff 2003 classification. The real-time (RT-PCR) was used to identify intragraft mRNA expression of cytokines and chemokines in 163 kidney graft recipients.
Results: SAR was found in 17 pts (6.6%), BL in 15 pts (5.8%). Pre-biopsy acute rejections were significantly more frequent (84%, $p<0.001$) in pts with SAR+ BL, when compared to pts with normal findings. In pts with SAR+BL, the mean serum creatinine (S-cr), and glomerular filtration rate calculated by MDRD were significantly different ($p<0.01$) from those in pts with normal finding. Using the ROC curve analysis, the cut-off point for S-cr 170 μmol/L was found to discriminate normal findings from SAR+BL (odds ratio 16,3 with CI 5,6-47.9). In pts with SAR+BL, intrarenal expression of RANTES, IP-10 ($p<0.001$), C3, CD3, IgJ ($p<0.01$) and CD20 ($p<0.05$) were higher when compared to pts with normal findings. C3 ($p<0.001$), TGF-β, RANTES, IP-10, CD3 ($p<0.01$), HMOX1 and CD20 ($p<0.05$) gene expressions correlated with proteinuria at the time of biopsy, and the expression of MCP-1, IP-10 and C3 correlated with s-Cr 12 months after transplantation ($p<0.05$).
Conclusion: The relationship between early posttransplant acute rejections and SAR+BL was confirmed. Pts with stabilized S-cr ≥170 μmol/L at 3 months posttransplant were found to be at risk for SAR+BL. Pts with SAR or BL are at risk for late acute rejection or graft loss. High RANTES and IP-10 gene expression increased the risk of graft loss.
Supported by Internal Grant Agency, Czech Ministry of Health NR8897-4.

P-218 LOW DOSE THYMOGLOBULIN THERAPY FAILS TO DEPLETE CD8 AND TOTAL B CELLS: A NEW APPROACH TO REDUCE SIDE EFFECTS WHILE MAINTAINING EFFICACY

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Thymoglobulin (rATG) is an induction immunosuppressive therapy that at standard doses results in persistent lymphocyte depletion which predisposes patients to an increased risk of infection and malignancy. We showed that low dose rATG (LD-rATG) induction therapy is efficacious and better tolerated. We now examine whether LD-rATG therapy leads to prolonged changes in peripheral lymphocyte subsets. Peripheral blood leukocytes (PBL) were isolated from 15 patients at three months following LD-rATG at 3 mg/kg together with tacrolimus, mycophenolic acid and prednisone. PBL were analyzed by flow cytometry and compared to 6 normal controls. Simultaneous protocol biopsies showed normal histology in 14 and 1 had borderline changes. Similar to full-dose rATG, LD-rATG treatment showed a marked decrease in the absolute number (cells/mcl) of total lymphocytes (1,760 vs 742 $p<0.01$), CD4 (850 vs. 307 $p<0.01$), both naive and memory CD4 (343 vs 72 $p<0.01$; 439 vs 183 p=0.02 respectively), NK (278 vs 103 $p<0.01$) and CD3+,4+,25+,127- Treg cells (42 vs 14 $p<0.01$). In contrast, CD8 (339 vs 254 p=0.43) and total CD19 B cells (212 vs 122 p=0.12) were not significantly reduced. Only CD4 cells were disproportionately affected by LD-rATG resulting in a lower than normal CD4/8 ratio (2.5 vs 1.2 $p<0.01$). In summary, LD-rATG results in prolonged reductions in the absolute number of many PBL subsets without any sparing or promoting effects on Treg cells. In contrast to full dose rATG therapy, lower doses did not lead to prolonged CD8 and total B cell depletion. These sparing effects of low dose rATG may be responsible for lower overall toxicity while maintaining equivalent efficacy.

P-219 LOW HDL LEVELS IN RENAL TRANSPLANT RECIPIENTS IS ASSOCIATED WITH A GREATER RISK OF ADVERSE CARDIOVASCULAR EVENTS

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Continued improvements in the management of renal transplant recipients have resulted in excellent early patient and renal allograft survival. Today, the major obstacle facing renal transplantation is late allograft failure. The major cause of late graft failure is patient death due to cardiovascular (CV) disease. Risk factors for CV disease such as diabetes, hypertension and elevated LDL levels are well documented, but the role of HDL is not studied. We examine the correlation between HDL levels and CV events post-renal transplantation. We retrospectively reviewed 324 charts of patients transplanted at our center from 2001 to 2007, and were followed for at least one year for demographics, laboratory data and clinical outcomes. CV events were defined as sudden death, myocardial infarction, new onset angina, stroke, TIA, CHF, new onset arrhythmia, amputation and new onset ischemic-related ulcers or infections. Our population had 92 CV events over 1,913 total patient years of follow up. CV events were equal between sexes (p=0.80) and those taking or not taking statins (p=0.32). Risk factors predisposing to CV events included high LDL (p=0.01), diabetes ($p<0.001$), preexisting CV disease (p=0.01) and deceased donor transplants (p=0.01). Low HDL levels were defined as less than 45 mg/dl in women and 40 mg/dl in men. Patients with low HDL experienced more CV events (60% low vs. 26% normal HDL, $p<0.05$) and all cause mortality ($p<0.05$). Therefore, low HDL is associated with an increased risk of CV events post-transplantation. Our study shows that low HDL also plays a significant role in late graft loss due to increased CV mortality.

P-220 IS PERIOPERATIVE PROPHYLACTIC ANTIBIOTIC THERAPY NESESSARY IN THE NEW ERA OF KIDNEY TRANSPLANTATION?

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Continued advancement in renal transplant surgery and immunosuppression have significantly reduced post operative (op) complications and improved short term allograft survival rates. However, certain issues remain unresolved such as routine use of perioperative prophylactic antibiotic therapy (PPAT). Currently, most centers treat their kidney transplant (ktx) recipients with one or several doses of PPAT. We retrospectively evaluated clinical course of 349 ktx recipients in our center who did not receive any PPAT except PCP and CMV. All pts transplanted from 7/2001 to 2/2008 were reviewed. Of the 365 pts 13-80 years old, only 16 pts (4%) received PPAT.

Table I. Patients and donors demographics

Female	African American	Average R. age ± SD	Average D. age ± SD	Living donor	Average CIT (h)	DM	Average dialysis (day)
42%	28%	48±15	41±17	23%	17±7	30%	643±371

PPAT (2-5 days) were given only if the culture from donor kidney bath was positive (9) and if surgery lasted longer than 6 hours (7). The ureteral anastomoses were stented only in 13% of cases. All pts received Valgancyclovir or acyclovir and Bactrim for PCP and CMV prophylaxis starting POD2 until 3 months. 77% of pts received low dose Thymoglobulin (total 3-5mg/kg) induction while the rest received Simulect. Steroids were given 250mg i.v. pre-op and 125mg i.v. POD1 and 30mg po POD2 and reduced to 5mg by day 30. All pts received triple immunosup. therapy: tacrolimus, mycophenolic acid, and prednisone. Only 7 (1.9%) developed wound infection and 5 (1.3%)experience urinary infection (UTI) within first post-op month. UTI was more common in stented pts ($p<0.01$). No other infection was observed in the first post tx month. No pt or graft was lost due to infection.

Our study shows that despite presence of many risk factors for wound and other infections in the ktx pts, infections were rare in the absence of PPAT,occurring in only 4%. We suggest that PPAT be used only in selected cases to avoid cost and side effects.

P-221 MAINTENANCE OF LARGE TRIPTERYGIUM WILFORDII HOOK F FOR RECURRENT FOCAL SEGMENTAL GLOMERULOSCLEROSIS AFTER RENAL TRANSPLANTATION: TWO CASES CLINICAL OBSERVATION AND IN VITRO EXPERIENCE

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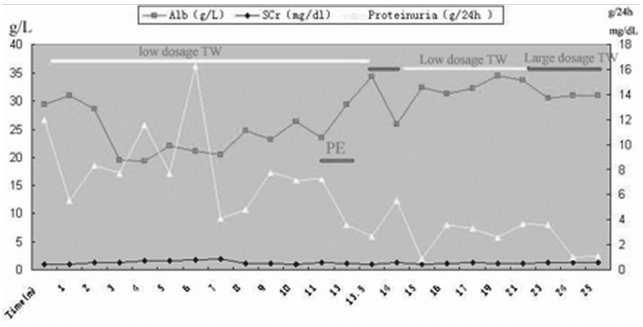
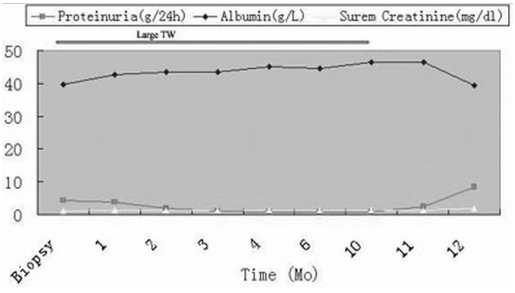
Recurrent FSGS after renal transplantation was a high risk for the renal allograft survival. We observe the effect of Tripterygium wilfordii Hook FT II (T II) on the recurrent FSGS after transplantation, and try to explore the mechanism of this effect through vitro experience. One cadaveric renal transplantation receipt had recurrent FSGS in two weeks after trasnplantation. The patient received the routine dosage of T II and plasmapheresis and the proteinuria decreased (2~3g/24h)and increased to 5g/24h one month later, after the large dosage of T II, the proteinuria decreased (<1.0g/24h) with the recovery of hypoproteinemia.



His proteinuria increased to 8.4g/24h once again because of cessation of TII for herpes zoster infection. Another living donor renal transplantation receipt had recurrent FSGS one month after transplantation. This case had heavy proteinuria (4.25g/24h) and renal dysfunction (1.42mg/dl). He received the large dosage of T II (120mg/day), the the proteinuria was greatly decreased to 0.78 g/24h, with the plasma-albumin increasing.he stopped the T II because of noncompliance, the proteinuria increased to over 8g/day again with the deterioration of renal graft function.



Now they repeated the large dosage of T II. In vitro experience, we used the Triptolide, one of the major active components of T II. In cultured mouse podocytes triptolide pretreatment prevented the puromycin-induced disruption of the actin cytoskeleton and microfilament-associated synaptopodin while protecting nephrin and podocin expression, this effect is also in a dose-dependent manner. The Triptolide also can reverse PAN-induced podocytes actin cytoskeleton disruption and podocyte synaptopodin distribution in PAN-induced injury. Therefore, we conclude that the large dosage T II can release the proteinuria from recurrent FSGS after renal transplantation through repairing the podcoyte injury.

P-222 EVALUATION OF VASCULAR LESIONS USING CIRCULATING ENDOTHELIAL CELLS IN PATIENT WITH RENAL TRANSPLANTATION

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Objective: To investigate the correlation between circulating endothelial cells (CECs) and vascular lesions in renal allograft.
Methodology: Total 62 renal transplant patients were divided into 4 groups approved by biopsy. These cases in AR group received C4d stain. The CECs were isolated from peripheral blood with anti-CD136-coated immunomagnetic Dynabead and were counted by microscopy during the biopsy time. CECs were compared in each group, and the correlation between CECs and C4d, vascular changes in different group.
Result: CECs count in each group was higher than healthy group. CECs count in acute rejection with endarteritis group was higher than that of normal group ($P<0.01$), ATN group ($P<0.01$) and CAN group ($P<0.01$), and there were no difference among ATN, normal and CAN group (P= 0.587); There were also no difference among normal group without hyaline arteriolar group, normal group with hyaline arteriolar and hyaline arteriolar thickening in chronic allograft nephropathy group (15.4±4.6 vs 13.2±4.0 vs 13.5±6.4). CECs count in C4d positive AR group was higher than C4d negative group (34.5±13.7 vs 20.0±9.3 $P<0.01$). The steroid resistant rate of CECs count increaseing (>24) AR was high (9/14 vs 3/11, $P< 0.05$).CECs count increasing was related to C4d positive (P=0.008, Kappa score 0.519) and inflammatory cells infiltrating in PTCs (P=0.002, Kappa score 0.573). The repeated CECs count decreased after intensive therapy in five severe AVR patients ($P<0.01$).
Conclusion: The elevation of CECs count in blood was related to the endarteritis and short poor outcome in acute rejection of renal allograft. CECs count wasn't related to the hyaline arteriolar and chronic hyaline arteriolar changes. Elevation of CECs was related to C4d deposition and inflammatory cells infiltrating in PTCs, suggest that it was related to the antibody mediate rejection.

P-223 OCCURRENCE OF LYMPHOCELE AFTER KIDNEY TRANSPLANTATION: IS THERE A ROLE OF HIGH MYCOPHENOLATE MOFETIL DOSING REGIMEN?

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Introduction: Lymphocele is a common surgical complication after renal transplantation. The incidence of lymphocele ranges from 0.6% to 16%.
Aim: To determine risk factor of complicated lymphocele in the era of modern immunosuppression.
Method: 311 renal transplants from January 2003 to September 2008 were retrospectively reviewed. We excluded patients who received sirolimus or underwent multiorgan transplantation. The complicated lymphocele was defined by the requirement for a surgical procedure related to cure the lymphocele.
Results: Of the 311 transplant recipients, 269 were included in the study.Among these 269 transplanted patients, 49 presented a lymphocele after transplantation (18,9%). Cold ischemia time, duration on the waiting list, gender, donor source, induction therapy (thymoglobulin vs basiliximab), dialysis modality were similar between the two groups. The univariate analyse is summarized in table 1.

Table 1

	Group with lymphocele (n=49)	Group without lymphocele (n=220)	p value
Recipient BMI >27kg/m^2	18 (36.7%)	48 (22.2%)	<0.05
Donor's age >60 yrs	20 (40%)	55 (25%)	<0.05
Recipient's age (yrs)	55.5±10.2	48.1±14.2	<0.001
Warm ischemiae (min)	42.8±12.3	37.8±10.1	<0.005
cyclosporine therapy	35 (71.4%)	114 (51.4%)	<0.05
MMF dosing regimen >2g/d	30 (61.2%)	63 (28.8%)	<0.0001

Mycophenolate mofetil (MMF) dosing regimen was higher in the lymphocele group compared with the non-lymphocele group (2,7±0.54 g/d vs 2,36±0.68 g/d, $p<0.05$). However the area under the concentration-time curves of mycophenolic acid was not significantly different between the two groups (43.7±15.3 h.mg/l vs 48±21 h.mg/l, p=0.33). Still in the multivariate analysis, lymphocele was associated with the higher MMF dosing regimen (OR 2.75, $p<0.01$), warm ischemia time (OR 1.035,$p<0.05$), recipient age (OR 1.04, $p<0.05$)
Conclusion: Even thought there is no clear explanation for this finding, our study suggest that high MMF dosing regimen may play a role in the lymphocele occurrence. Further studies are needed to confirm this finding.

P-224 THE ROLE OF SEX STEROIDS IN THE MAINTENANCE OF BONE DENSITY IN MALE KIDNEY RECIPIENTS

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The influence of sex steroids in the maintenance of bone density was investigated in 44 men with kidney transplant aged 24-69 years, with good and stable renal function (creatinine clearance ≥60 mL/min.over the study period). The following serum parameters were measured 1-194 months post-transplant: luteinizing hormone (LH), total testosterone, sex hormone binding protein (SHBG), iPTH, alkaline phosphatase (ALP), Ca, Pi. Bone mineral density (BMD) was measured in the lumbar spine, femoral neck and distal third of the radius using dual energy absorptiometry (DEXA) 1 -169 months after transplantation and 12-48 months later. The BMD change (delta BMD, ± %) was calculated per 12 months. LH was above the reference range in 7/44 patients, SHBG in 5/44 patients, and testosterone below the reference range in 3/44 patients. LH correlated significantly negatively with creatinine clearance. SHBG correlated significantly positively with calcium. Total serum testosterone correlated significantly positively with femoral neck BMD and T score. The patients were divided into 2 groups according to delta BMD for each localization: group 1: delta BMD <0, i.e. bone loss (lumbar spine N= 25, femoral neck N= 23, distal radius, N= 31), 2: delta BMD 0/>0, i.e. no bone loss or bone gain (lumbar spine, N=19, femoral neck, N= 21, distal radius, N= 11). Bone loss occurred in more than half of the kidney transplant recipients. Total serum testosteron levels were significantly lower in patients who lost the bone in the femoral neck than in those who did not.

Conclusion: Hypogonadism occurs in male kidney recipients with good and stable renal function. Low testosteron level has a detrimental effect on bone density in male kidney recipients.

P-225 DESENSITIZATION AND RENAL TRANSPLANT. PLASMAPHERESIS/IVIG STANDARD DOSES IN PATIENTS WITH HIGH IMMUNOLOGICAL RISK

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Objective: To report the experience of a transplant center in desensitization of patients with high immunological risk.

Material and methods: We included all the renal transplants from November of 1999 to January of 2008 in which we used plasmapheresis and standard dose of intravenous immunoglobulin (IVIG) as desensitization.

Results: 1.5% of the renal transplants had history of alloimmunity, 7 patients had positive crossmatch with their donor and 1 exclusively had high Panel-Reactive of Antibodies (PRA >30%); a patient with positive crossmatch and high PRA received 2 years before plasmapheresis and IVIG, whoever this was unsatisfactory. The schedule of the plasmapheresis was in alternating days with exchange of 1.5 plasmatic volume, subsequent to each session we administered a standard dose of Intravenous Immunoglubulin (IGIV 5gr/dose).

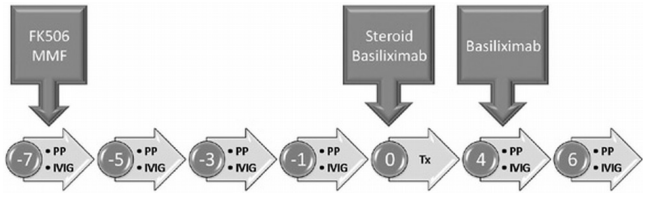

Figure 1

In 6 patients were made 4 pretransplant sessions, 1 of them required a posttransplant session; in a patient 2 sessions were made pretransplant and in another case one pretransplant and 2 posttransplant. The immunesuppression began equal than the first plasmapheresis with calcineurin inhibitor (Tacrolimus) plus, 6 patients with Mycophenolate Mofetil and 2 with Sirolimus. In 7 cases negative crossmatch were obtained before the transplantation. Two patients received humanized antibodies against CD25 (Basiliximab 20mg/dose) the day of transplantation and the fourth day.

A patient presented Delayed Graft Function (DGF) due to Acute Humoral Rejection (AHR). Just one patient needed a graft biopsy the 20th month which showed mild fibrosis. During their evolution all the patients have maintained a stable graft function.

Conclusions: The renal graft outcome in patients with high immunological risk after an adequate desensitization protocol is similar to that observed in non-sensitized patients at least during the first year of transplantation, according to our experience.

P-226 COMPARING AORTIC STIFFNESS IN KIDNEY TRANSPLANT RECIPIENTS AND PATIENTS WITH RESIDUAL RENAL FUNCTION

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Purpose: The poor cardiovascular survival of patients with renal insufficiency is ameliorated by transplantation. Carotid-femoral pulse wave velocity (PWV), a marker for aortic stiffness is able to independently predict total and cardiovascular mortality. PWV is high in dialysis patients and transplantation blunts PWV. However, information is missing whether the PWV adapts to the level of residual renal function.

Methods: In a cross-sectional setting PWV was determined in 44 renal transplant patients (RTx) and compared to the PWV of 44 age and sex matched patients with comparable residual renal function (CKD). Factors involved in the prediction of PWV were characterized in these patients. Pairs of patients were furthermore stratified according to duration of transplant follow-up, sex and median of age and median of blood pressure.

Results: Both groups revealed comparable estimated GFR (RTx: 42.9±18.4 versus CKD: 48.3±29.1 ml/min/1.73m^2) and protein-creatinine ratio (logPCR RTx: 2.33±0.45 versus CKD: 2.39±0.56 and PWV (RTx: 9.67±1.91 versus

Age	Medical history	Crossmatch title	PRA I PRA II	Plasmapheresis (weight)	Induction	Complication	Immunesuppression scheme changes	5th day creatinine (mg/dl)	Monitoring time (months)	Last creatinine (mg/dl)
57 fem	C Hepatitis 2 blood transfusions 7 pregnancies	1:8		4 pre (88 kg)	Tac, MMF			1.5	28	1.4
38 fem	SEL 2 blood transfusions 1996 Previus renal transplant 1 pregnancy	1:1	0% 54%	4 pre / 1post (56 kg)	Tac, MMF	Humoral rejection, C4d +		5.2	18	1.5
55 fem	4 blood transfusions 4 pregnacies	Negative	98% 97%	2 pre (58.5 kg)	Tac, MMF Basiliximab	Pancreatitis 3rd month	MMF→AZA	1.1	17	0.9
33 masc	7 blood tranfusions	1:8	30% 11%	4 pre (68.5kg)	Tac, Rapa		Rapa→MMF	1.2	12	1
19 masc	4 blood transfusions 2006 previus renal transplant	1:8	17% 0%	4 pre (62.8 kg)	Tac, Rapa		Rapa→MMF	1.6	12	1
50 masc	10 blood transfusions	1:4	0% 0%	4 pre (65 kg)	Tac, MMF		MMF→AZA	1.1	10	1
45 masc	Cistinosis C Hepatitis 10 blood transfusions 1977 and 1986 previus renal transplant 2004 PP+IVIG	1:1	73% 23%	1 pre / 2 post (43 kg)	Tac, MMF Basiliximab			0.9	9	0.9
37 masc	3 blood transfusions	1:1		4pre (68 kg)	Tac, MMF	Stroke 5th day	MMF→Myfortic	0.9	1	0.9

Abstract P-225 – Table 1

CKD: 9.72±3.21 m/s). The status of renal function (RTx versus CKD) did not predict PWV. Aortic stiffness did not differ between 3-12 months and >12 month of transplant function.
Discussion: Restoring kidney function by transplantation results in comparable aortic stiffness as compared to CKD patients with residual renal function. As dialysis patients have been reported to have higher PWV and this can be blunted by transplantation, our data suggest that stiffness can be reversed to the level of PWV present in CKD patients with residual renal function.

P-227 LIVING KIDNEY DONATION FOR RE-TRANSPLANTATION: OUTCOME AND RISK FACTORS

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Despite conclusive results after living kidney donation for graft function and graft survival the outcome after retransplantation in that transplantation category will be controversial discussed. Therefore, graft survival and risk factors for recipients after retransplantation by living kidney has been analyzed.
The data from 224 patients (m= 122, w=102) who underwent adult living related kidney transplantation between 1987 and 2008 were prospectively collected and relating to prognostic factors tested by multivariate analysis. Moreover, in addition to prognostic factors graft function and survival in 26 (11.5%) retransplanted patients after living kidney donation have been investigated. Half of the retransplanted recipients received induction therapy by thymoglobulin infusion and all patients in the course of the postoperative period a standardized immunosuppressive regimen containing calcineurin inhibitors, corticosteroids and mycophenolate mofetil.
During a median follow-up period of 57 months (5-256 months) the rejection rate and therefore graft function ($p<0.017$) and graft survival ($p<0.036$) in patients without induction therapy was significantly increased compared to patients with induction therapy. Differences between living related and living unrelated kidney transplantation have not been observed. In addition to retransplantation, number of HLA- mismatches and body mass index present further significant risk factors in living kidney donation.
In our opinion living kidney donation for retransplantation could be peformed under stringent indication with induction therapy and in case of rejection aggressive therapy for instance plasmapheresis or monoclonal antibody therapy should be recommended.

P-228 INDICATIONS AND RESULTS IN HIGH URGENCY KIDNEY TRANSPLANTATION

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Nearly 40 years kidney transplantation under high urgency (HU) request is implemented in Europe. Until now only few results regarding patient and graft survival compared to patients transplanted with standard priority on the waiting list are existent. Therefore we analyzed our patients transplanted for HU request and compared the outcome with patients transplanted with standard urgency during the same period.
Between 1996 and 2009 793 patients received a kidney transplantation at our department, whereas 23 patients were operated after HU priority request according to 2.6% of all patients. All patients were treated by a standardized operation and immunosuppressive regimen. We analyzed and compared parameters like serum creatinine levels, rejection events as well as patient and graft survival in both groups.
Within the median follow-up period of 72.1 months the median patient survival was 59.2 months and the graft survival 57.6 months. The 1-, 2-,and 3 year patient survival rate showed 87.5%, 87.1%, and 82.1% for HU transplanted patients in comparison to 95%, 92% and 90% of the patients transplanted without urgent request. The results for graft survival in both groups were similar with a little lower ranking.
In our opinion kidney transplantation based HU request is life-serving with even good results as in patients transplanted with standard priority and should be offered in all countries.

P-229 LONG-TERM FOLLOW-UP OF KIDNEY DONORS: QUALITY OF LIFE AFTER DONATION

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Purpose: The QoL concept is well-known in clinical medicine and is frequently applied for the assessment of surgical or other treatment modalities to determine their therapeutic success. There are several surveys and questionnaires that have been used for this purpose. The Short-Form 36 (SF-36), Giessen Subjective Complaints List-24 (GBB) and Zerssen's Mood-Scale (Bf-S) are internationally validated and frequently used questionnaires.
Methods/Materials: We evaluated the QoL of 45 kidney donors (Group I) and compared it to: 120 age and sex matched healthy individuals (Group II); and 40 patients who underwent nephrectomy due to renal tumor and hydronephrosis (Group III). The SF-36, GBB and Bf-S questionnaires have been mailed, e-mail-ed, or handed out to the donors and patients. The evaluation procedure was completely anonymous to ensure the maximal objectivity of the obtained results. All the respondents were free of any charges related to the filling or sending the questionnaires.
Results: In 5 out of 8 QoL items the donors scored better than the controls and patients. For 3 of them ("Social function", "Bodily pain" and "Vitality") the difference was statistically significant. The "Bodily pain" and "Vitality" indexes of the controls were higher as compared with the patients. The GBB scores of the donors were higher than that of the controls and patients however, these differences didn't reach significance. The mood analyses have shown significant differences between the groups in favour of the donors.
Conclusion: The donors have to be educated about the extent of psychosocial impairment that might occur in the postoperative period. They should be monitored for both, physical and psychosocial outcomes of the donation. Further prospective studies are needed to facilitate potential donors' understanding of the complex issues related to the organ donation.

P-230 A CASE OF DIFFUSE C4d DEPOSITION WITHOUT MORPHOLOIC ACTIVE HUMORAL REJECTION IN RENAL TRANSPLANTATION

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The immunohistochemical detection of the complement degradation product C4d in renal allograft biopsies has gained considerable clinical interest in recent years. The accumulation of C4d along peritubular capillaries is generally regarded as a marker for an antibody-mediated allo-response and is associated with poor graft survival. We present a case of patient whose diffuse C4d deposition was diagnosed after renal transplantation. A 54-year-old-woman with end-stage renal disease caused by IgA nephropathy received cadaveric kidney transplantation from 14-years-old-male. Pre-transplant donor-specific T- and B-cell cross-match was negative. Immunosuppressive treatment consisted of tacrolimus, mycophenolate mofetil, methylprednisolone and baxiliximab. The kidney functioned immediately after transplantation. On post-operative day 9, the level of serum creatinine rose from 1.1 to 3.5 mg/dL. The allograft biopsy specimen taken on the day revealed interstitial edema, neutrophilic infiltration in dilated peritubular capillaries (PTCs), mild interstitial lymphocytic infiltration, but no evidence of lymphocytic tubulitis. Immunofluorescent study of the allograft biopsy specimen showed a strong, diffusely distributed endothelial staining pattern in peritubular capillaries for the complement split product C4d. These findings suggested that C4d deposition without morphologic evidence of active rejection. So, we decided conservative treatment for the patient. On post-operative day 19, allograft function was recovered and the creatinine level was down to 0.9 mg/dL. Because our biopsy specimens showed C4d in PTC without active corresponding morphologic changes, we would interpret the present case rather as a subclinical episode of acute humoral rejection. The pathogenic role of C4d is not completely understood, further studies are warranted to uncover the true incidence of C4d deposition in all renal allografts, including those that are stable and those exhibiting dysfunction. Furthermore, more information on the mechanisms and consequences of PTC C4d deposition need to be elucidated in terms of guiding therapeutic decisions.

P-231 MINIMAL INCISION LIVING DONOR NEPHRECTOMY ASSISTED BY LAPAROSCOPIC INSTRUMENTS VIA THE RETROPERITONEAL APPROACH

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Objective: To explore a less-invasive and safe approach for clinical living donor nephrectomy (LDN).
Methods: From August 2007 to April 2008, 21 healthy donor were undergone LDN in our department. Laparoscopic instruments were applied in the procedure through a minimal incision via the retroperitoneal approach. In these procedures, deep small vessels, lymphatic ducts and connective tissues were separated and severed with a 23cm ultrasonic scalpel. The adrenal vein and the distal end of urinary tract were clipped with a Hem-o-lok clips before severed. The renal artery was clipped with two Hem-o-lok clips. The opening of the vena cava was sewed with 5/0 non-traumatic suture.
Results: The LDN was uneventful in all 21 cases. The amount of intraoperative blood oozing ranged from 60 to 200ml with a mean of 132±45ml; the length of incision ranged from 6 to 10cm with a mean of 7.6±1.0cm. The oper-

ation duration ranged from 150 to 270 min with a mean of 209±33 min. Warm ischemia time was ranged from 30 to 120 seconds with a mean of 70±30 seconds. On the 3rd day of operation the donors began eating food and getting out of bed and moving about. The kidney graft function well in all recipients and the creatinine on the 5th day of operation was 123±57umol/L.
Conclusions: This surgical modality has the following advantages:1) small incisions and minimal injury; 2)high surgical safety and 3) simplicity. It is worthy of considering to apply it to other open surgical approches in clinical practices for the benefit of patients.

P-232 A NATION-WIDE *PNEUMOCYSTIS JIROVECI* PNEUMONIA (PcP) EPIDEMIC IN GERMAN RENAL TRANSPLANT PATIENTS

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PcP is a potentially life-threatening complication in renal transplant recipients. While PcP was very rarely diagnosed in most German centres in the late 1990's, a dramatic increase of PcP was identified in several centres during the last years.
We retrospectively analyzed 60 cases of confirmed PcP-infection, diagnosed in 6 German transplant centres between 2004 and 2008. Affected patients had the following characteristics: male sex in 67%, deceased donor kidneys in 77%, median age at PcP-onset 58 years, median time after transplantation 142 days, 39% had a GFR <30 and 98% had a GFR <60. 82% were on a triple immunosuppression consisting of CNI, mycophenolate, and corticosteroids (97% received steroids, 92% mycophenolate, 45% Tac, 42% CyA, 10% sirolimus, 3% azathioprine); 33% had received IL2-RA and 28% ATG. Comorbidity revealed 32% with at least one biopsy-proven acute rejection episode, 42% with a CMV-infection and 17% with diabetes mellitus prior to the PcP-diagnosis. None of the patients had received a PcP-prophylaxis (TMP-SMX or pentamidine) after transplantation. There was no change in the prophylaxis regime in any of the 6 centers as compared to the 1990's. PcP occurred in local outbreaks with a local peak within few months. Of the 60 patients with PcP, 27% died in the course of the disease and 45% required treatment in an ICU.
In summary, following more than a decade of very rare PcP-infections, several German renal transplant centres experienced a sudden clustering of PcP-cases. Identification of identical strains in some centres led to the conclusion that patient-to-patient transmission did play a role in its pathogenesis. However, it remains unexplained why the outbreak occurred nationwide. We speculate that older age and more intensive immunosuppression might contribute to PcP-susceptibility. We are currently testing our hypothesis in a case-control study.

P-233 TRANSPLANTATION OF ORGANS FROM EXPANDED CRITERIA DONORS ABOVE 75 YEARS OF AGE – MADNESS OR NOT?

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Background: Is there an upper age limit for expanded criteria donors for transplantation? We address kidney transplant outcome of organs from deceased donors above 75 years of age.
Methods: From 1993 throughout 2007 a total of 2152 deceased donor kidney transplantations were performed at our center. Complete medical files of all deceased kidney donors above 75 years were the kidneys had been transplanted as single kidney were retrieved. Histological findings in graft biopsies at transplantation were evaluated to observe if this information could be helpful in predicting long term post-transplant outcome.
Results: Evaluation of 54 single kidney transplantations from donors >75 years (median 77.5, range 75.2-86.1) were assessed. Ninety three percent of the donors died of intracranial bleeding and 69% had a history of hypertension or cardiovascular event(s). Median recipient age was 70.1 (range 50.6-82.4). Thirty-three kidneys (61%) had primary graft function. Nineteen (35%) had delayed function from one to 38 days post transplantation. Two kidneys were never functioning and came from two separate donors with se-creatinine of 86 and 67 μmol/ l, respectively. Death censored graft survival at 1, 3 and 5 years were 87%, 83% and 83%, respectively. Patient survival was 81%, 75% and 59% at the same time points. At follow up at median 23 months (range 6 – 144 months), thirty-five recipients were alive with a median se-creatinine of 163 μmol/ l (range 103-348). Histological findings in graft biopsies did not help predict graft outcome.
Conclusion: Kidney transplants from deceased donors > 75 years perform acceptable as single transplants and should definitely be considered for use in older recipients.

P-234 IS ABO-INCOMPATIBLE RENAL TRANSPLANTATION A RISK FACTOR FOR BK VIRUS INFECTION OR NEPHROPATHY?

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Introduction: BK virus nephropathy (BKVN) is a troubling onset complication of renal transplantation, which may affect upwards of 8% of allografts in the current era of immunosuppression. Risk factors for the development of this condition appear to be a history of acute rejection, anti-rejection therapy and possibly increased donor/recipient HLA mismatching. However, no studies have demonstrated that ABO-incompatible renal transplantation (ABOiLDRT) is a risk foctor for BKvirus infection or BKVN due to over-immunosuppression.
Method: We have performed ABOiLDRT in 88 patients since 1993. We performed a splenectomy, eliminated anti-A and/or anti-B antibodies by DFPP, and administered a potent immunosuppressive regimen consisting of cyclophosphamide, anti-CD25 monoclonal antibody, calcineurin inhibitor and prednisolone. The calcineurin inhibitor dose was adjusted by monitoring $AUC_{0\text{-}4}$ target values.
We have performed BKvirus follow-up in all patients since 2005. BKvirus DNA detection in blood samples was performed using the quantitative real time PCR technique. The primers used for this assay are specific for BKvirus and have been designed to accommodate mutated strains. The range of detection is 1×10^3 copies/μL.
We investigated the incidence of BKvirus infection between ABOiLDRT and ABO-compatible renal transplantation group (n=120).
Results: The incidence of BKvirus infection after transplantation was 1.1% (1/88) in the ABOiLDRT group as compared with 5% (6/120) in the ABO-compatible group (p=0.127). The incidence of acute rejection during the first 3 months after transplantation was 18.2% in ABOiLDRT group, as compared with 20.8% (25/120) in the ABO-compatible group (p=0.634). Graft survival rates were similar in both groups (95.6% vs 96.3%) at 1 year (p=0.296). There are 4 patients with BKVN in ABO-compatible group, but no patient in ABOiLRT group.
Conclusion: Although total immunosuppression might be generally potent in ABOiLDRT, our center protocol of ABOiLDRT is not a risk factor for BK virus infection or BKVAN.

P-235 IMPACT OF POST-TRANSPLANTATION GLOMERULONEPHRITIS ON LONG-TERM OUTCOME IN CHINESE KIDNEY TRANSPLANT PATIENTS: A SINGLE-CENTER KIDNEY BIOPSY REPORT

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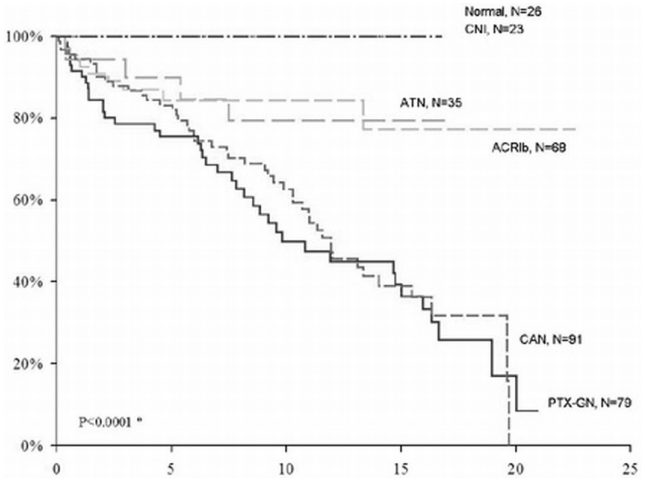
Background: Post-transplantation glomerulonephritis (*de novo* or recurrent GN) is a well known cause of renal allograft loss; however, the data in the Chinese population is lacking. We investigated the incidence, timing, and rates of renal graft loss caused by the PTx-GN in Chinese renal transplants.
Methods: A total of 322 kidney transplant patients with allograft biopsy-proved reports were retrospectively reviewed. Patients were subjected to surveillance allograft biopsy while daily proteinuria >500mg, increased plasma Cr> 0.5mg/dl compared to baseline level and active urine sediment (RBC>5 hpf). PTx-GN was diagnosed by graft biopsy analyzed by light, IF and EM microscopy. Patients with transplant-associated glomerular lesions, glomerulosclerosis associated to CAN or transplant glomerulitis were not considered. Primary endpoint was graft loss and survival censored by death.
Results: A total of 79 (25.0%) patients with a mean age of 39.28±11.26 years were diagnosed with PTx-GN. The mean time of disease onset in patients with PTx-GN was 5.48±5.24 years and was diagnosed by renal biopsy with a mean follow-up 8.13±5.81 years. The types of PTx-GN included IgA nephropathy 33 (41.77%) cases, focal segmental GN (FSGS) 24 (30.37%) cases, membranous GN (MGN) 8 cases, membranoproliferative GN (MPGN) 6 cases, and 8 cases in others. The cases of overall allograft loss in patients with PTx-GN were 45 (56.96%), of which 48.8% in IgAN, 24.4% in FSGS. The allograft survival rates in patients with PTx-GN was 91.50%, 75.60%, 49.93% at 1, 5, 10 years. Compared to the other pathological findings of allograft biopsy, inferior allograft survival rates was noted in patients with PTx-GN (P<0.0001).



Conclusions: In our study, post-transplantation GN imposes a strong negative impact on kidney graft suvival and an important cause of allograft loss in Chinese kidney transplant patients.

P-237 EFFECT OF DIFFERENT CALCINEURIN INHIBITORS ON OXIDATIVE STRESS 6 MONTHS AFTER KIDNEY TRANSPLANTATION

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Background: Oxidative stress (OS) is one of the leading causes of cardiovascular morbidity and mortality in chronic kidney disease. Restoration of renal function after transplantation is expected to improve the OS. However is still debated, whether cyclosporine and tacrolimus exert a different action on OS and antioxidant status.
Methods: This was a prospective cohort study evaluating changes in markers of OS and antioxidant kapacity in patiens on different calcineurin inhibitors. 41 kidney transplant patients were included into the study. Patients were randomly divided into two groups, based on the type of immunosuppressive calcineurin inhibitor. 19 patients (mean age 53,2±11 years) were treated with cyclosporin A (Group A), whereas 22 patients (mean age 48,1±9 years) with tacrolimus (Group B). Parameters of clinical biochemistry, advanced oxidation protein products (AOPP), total antioxidant status (TAS), hematology and glomerular filtration (MDRD) were measured in patiens before and 6 month after kidney transplantation.
Results: In Group A the mean levels of AOPP decresed from 175.1±88.8 μmol/l to 141.7±88 μmol/l and TAS from 1.869±0.295 mmol/l to 1.809±0.476 mmol/l. In Group B the mean levels of AOPP decrease from 193,7±140.6 μmol/l to 152.2±93.3 μmol/l and TAS from 1.934±0.273 mmol/l to 1.822±0.313 mmol/l. No differences in graft function, age, and others laboratory parameters were found between the two groups. Significant decrease of markers of OS was found 6 month after transplantation (p=0.035), but there was no statistically significant difference in the values of AOPP and TAS between patients treated with either cyclosporin or tacrolimus.
Conclusion: At 6 month after kidney transplantation study participants showed a decrease in OS markers compared to levels before transplantation. No diference in OS was found between treatment groups regarding the treatment regiment.
Acknowledgement: Supported by the grant NS/ 9964-4 of the IGA, Ministry of Health, Czech Republic

P-238 EXCHANGE DONOR PROGRAM IN KIDNEY TRANSPLANTATION AS A BETTER OPTION FOR EXPANDING DONOR POOL

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The limited number of living donors is the main problem in any living donor transplantation. Many attempts to expand donor pool are now introduced and performed in worldwide. We analyzed the exchange donor program by comparing with ABO incompatible and marginal donor transplantation as an effort of expanding donor pool. We retrospectively reviewed the records of the 128 exchange donor renal transplantations performed from August, 1991 to June, 2008 in our center. We analyzed graft survival rates, advantages and some other factors of the exchange donor kidney transplantation as a better option for expanding donor pool. The graft survival rate (1, 5, 10 year) of exchange donor transplantation were 92.8%, 81.1%, 76.1%, repectively. The acute rejection rate were 32.8%(42/128). The proportion of the exchange donor kidney transplantation was 15.9%. We suggest that exchange donor program definitely expands the donor pool in living donor kidney transplantation with many insurable advantages in comparison with ABO incompatible and marginal donor kidneys transplantations in practice.

P-239 HIGH IMMUNOLOGICAL RENAL TRANSPLANT RECIPIENTS HAVE GOOD EVOLUTION WITH POTENT IMMUNOSUPPRESSION

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Objective: The aim is to evaluate the incidence of acute rejection, oportunistic infections and malignacies, graft and recipient survival between a group of high immunological risk renal transplant recipients and a group of without immunological risk, who received grafts from the same cadaveric donors since 2001 to 2006.
Material and methods: This is a prospective and observational study. The risk group (n= 50) included patients with high rate of antibodies (> 50%), recipients who had lost their first graft due to early rejection, cross match positive, black race or important histoincompatibility. They received thymoglobulin to mantain T-cell around 10 cells/μl, FK 506 after five days, mycophenolate mofetyl and steroids, with ganciclovir prophylaxis for CMV. The normal risk group (n=50), cyclosporine, mycophenolate mofetil and steroids. Recipients who lost their graft due to technical failure were excluded. The mean follow-up was 42,7 months. Both groups were similar respect to donor and recipient gender and age, HLA incompability, but the percentage of patients with high rate of performed antibodies and second transplant recipients was higher in the high risk group.
Results: The incidence of acute rejection histologically diagnosed was higher in the normal risk group (28,6% against 6,15%, p=0.03). There was no difference in opportunistic infections,or malignancies, although 2 recipients of the normal risk group developed lymphoproliferative disorders. The recipients survival was 97,9% at 1 and 3 years in both groups, and the graft survival was 89,8% and 84,8% in the high risk group against 93,8% and 90,4% at 1 and 3 years in the normal group (p=ns).
Conclusion: The evolution of high risk renal transplant recipients is similar to normal risk patients if a potent enough immunossuppresion is used. The incidence of acute rejection was higher in the normal risk group.

P-240 THE ROLE OF FOXP3+ REGULATORY T CELLS IN KIDNEY TRANSPLANTATION

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Purpose: One of the key mechanisms responsible for maintaining immunologic tolerance and for controlling T cell homeostasis is cell-mediated immunoregulation/ immunosuppression. Our project was aimed to investigate the relation between the level of pretransplant and posttransplant peripheral CD4+CD25+Foxp3+ Tregs and the development of acute rejection (AR) episodes in patients after kidney transplantation.
Methods and materials: The project included 44 patients undergoing kidney transplantation. During the six-month period following the transplantation AR was diagnosed in 11 patients. Peripheral blood samples were collected 1 day before and 10 days after the transplantation and tested for concentrations of CD4+CD25+Foxp3+ cells by means of flow cytometry.
Results: NONAR and AR patients did not show significant differences in baseline characteristics ($p>0.05$). The pretransplant analysis showed significantly lower mean levels of peripheral Tregs in rejection (AR) patients vs. control group ($p<0.05$). A lower level of Tregs was also observed in non-rejection (NONAR) patients vs. control group ($p<0.05$), however, it was still higher than in the AR group ($p<0.05$).
The 10-day posttransplantation analysis showed a similar pattern, however, a significant increase in the concentration of peripheral Tregs in NONAR patients was observed ($p<0.05$), whereas no change was recorded in AR patients ($p>0.05$).
Conclusions: We found lower pretransplant levels of peripheral Tregs in both groups, AR and NONAR vs. control group. The deficiency of peripheral Tregs in investigated patients with end-stage renal failure might be due to the long-term

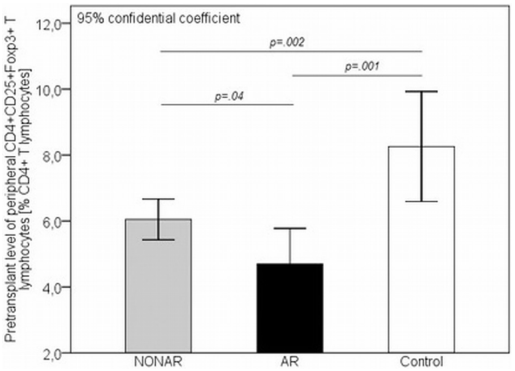

Figure 1. Mean levels of regulatory CD4+CD25+Foxp3 T lymphocytes in peripheral blood of non-rejection (NONAR) and rejection (AR) patients prior to the kidney transplantation [values shown as % CD4+ T lymphocytes].

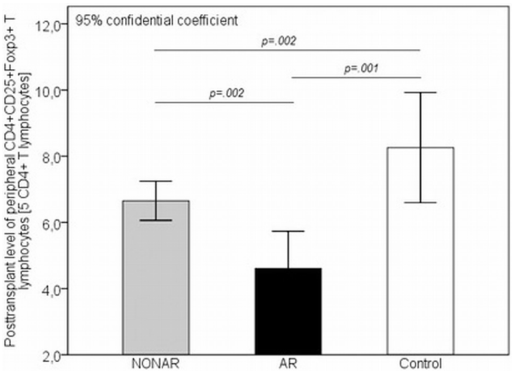

Figure 1. Mean levels of regulatory CD4+CD25+Foxp3 T lymphocytes in peripheral blood of non-rejection (NONAR) and rejection (AR) patients 10 days after kidney transplantation [values shown as % CD4+ T lymphocytes].

inflammatory processes adversely affecting the peripheral regulatory mechanisms, however, significantly lower levels of Tregs observed in AR patients might also be related to genetic predispositions. Our observation suggests that the size and possibly the functionality of Tregs in AR group was not sufficient to successfully control the immune response after kidney transplantation leading to acute rejection episodes.

P-241 DETECTION OF CITRATE SYNTHASE AUTOANTIBODIES IN RATS WITH CHRONIC ALLOGRAFT NEPHROPATHY

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Purpose: Citrate synthase (CS) is an important mitochondrial autoantigen and one of the key enzymes in citric acid cycle,which is central to the regulation of energy homeostasis and cell metabolism.We aimed to investigate CS autoantibodies in rats with chronic allograft nephropathy (CAN).
Methods: Fisher344 rat renal grafts were orthotopically transplanted into Lewis rats following the procedure of Kamada with our modification.All the recipients were given CsA 10 mg/kg^{-1} d^{-1} 10 d and then divided into 4 groups (each n=9): (1) Vehicle; (2) CsA: 6 mg/kg^{-1} d^{-1}; (3) FK506: 0.15 mg/kg^{-1} d^{-1}; (4) MMF: 20 mg/kg^{-1} d^{-1}. At 4w, 8w and 12w,renal allografts were harvested and sera were collected. The SCr was measured and the pathological changes were assessed according to the Banff 97 criteria.IgM and IgG isotype CS antibodies of all the recipients were detected by binding indirect enzyme-linked immunosorbent assay (ELISA).
Results: Both IgM and IgG isotype CS autoantibodies were found in the sera of all recipients before and after transplant,but the level of IgM CS autoantibodies are more obviously stable and higher than IgG isotype in all different blood samples. At 4w, the Banff scores in Vehicle, CsA, FK and MMF groups were 1.67±0.58,1.33±0.58, 1.00±1.00 and 0.67±0.58 respectively (P>0.05),and ΔOD values of IgG isotype CS autoantibodies in different groups were 0.068±0.007, 0.081±0.009, 0.083±0.003 and 0.056±0.006 (P>0.05). With progression of CAN (Banff score: 5.33±0.58 and 12.67±1.16 in vehicle group at 8w and 12w, respectively, P=0.001),and the ΔOD values of IgG were increased gradually (0.171±0.015, 0.335±0.009, respectively at 8w, 12w, P=0.005); in CsA group, with the progression of CAN (Banff score: 4.67±1.53, 13.33±1.53), IgG ΔOD was 0.137±0.001, 0.279±0.019 respectivly at 8w, 12w, p>0.5; in FK group, with the progression of CAN (5.67±0.58, 12.33±3.79 at 8w, 12w), the ΔOD values were 0.151±0.011, 0.291±0.009 at 8w, 12w, respectively, p=0.005; MMF could decrease significantly the formation of IgG (ΔOD values: 0.133±0.000 and 0.099±0.007 respectively, p=0.078) and the progression of CAN (1.67±1.16, 6.67±1.53) at 8w and 12w.
Conclusions: This study suggests IgG isotype CS autoantibodies may contribute to CAN after kidney transplantation,but IgM isotype autoantibodies may be physiological.

P-242 TACROLIMUS AND ANGIOTENSIN RECEPTOR BLOCKERS ASSOCIATED WITH CHANGES IN SERUM ADIPONECTIN LEVEL IN NEW ONSET DIABETES AFTER RENAL TRANSPLANTATION: SINGLE-CENTER CROSS-SECTIONAL ANALYSIS

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The purpose of this study was to confirm whether pre- and post-transplant low serum adiponectin levels are an independent risk factor for the development of new onset diabetes after transplantation (NODAT), and examine the relationships between serum adiponectin levels and therapeutic medications (immunosuppressive drugs and angiotensin receptor blockers (ARB)). A total of 98 previously non-diabetic patients who underwent renal transplantation between 1997 and 2007 were enrolled. Of those, 12 were diagnosed with NODAT and 86 without (non-NODAT). There was a significant inverse correlation between mean post-transplant serum adiponectin level and homeostasis model assessment for insulin resistance (HOMA-IR) (r=-0.22, p=0.03), and a positive correlation between follow-up duration after transplantation and HOMA-IR (r=0.28, p=0.005). The mean pre- and post-transplant serum adiponectin levels in NODAT patients were significantly lower than those in non-NODAT patients (13.3 vs. 21.0 μg/ml and 13.0 vs. 16.4 μg/ml, p=0.01 and 0.03, respectively). The post-transplant serum adiponectin level in patients treated with tacrolimus (TAC) was significantly lower than that in patients with cyclosporine (14.3 vs. 18.7 μg/ml, p=0.01). The pre-transplant adiponectin level in patients administered TAC who developed NODAT was significantly lower than that in non-NODAT patients (13.7 vs. 20.5 μg/ml, p=0.02). The post-transplant serum adiponectin level in patients treated with ARB was significantly higher than that in patients without ARB (17.9 vs. 14.7 μg/ml, p=0.01). The post-transplant adiponectin level in patients treated with ARB who developed NODAT was lower than that for non-NODAT patients (11.7 vs. 18.9 μg/ml, p=0.02). Our results indicate that post-transplant serum adiponectin levels are decreased after transplantation in association with insulin resistance in the development of NODAT. TAC administration decreased serum adiponectin levels, while that of ARB reduced the decrement of adiponectin.

P-243 DOES RELATIONSHIP EXIST BETWEEN CORONARY ARTERY CALCIFICATION AND SERUM CALCIUM, PHOSPHORUS, PTH LEVELS, AND CALCIUM-PHOSPHORUS PRODUCT IN RENAL TRANSPLANT RECIPIENTS?

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Coronary artery calcification (CAC) are present in about 2/3 of patients starting dialysis therapy. Serum calcium (Ca), phosphorus (P), parathormone (PTH) levels and calcium-phosphorus product (CaxP) are acknowledge factors for vascular calcifications in patients with chronic kidney disease (CKD). CAC is associated with increase of mortality in patients with CKD. The aim of the study was to evaluate the relationship between CAC and Ca, P, PTH levels and CaxP in renal transplant recipients (RTR).
The study group consisted of 104 RTR (31 females and 73 males), aged 49±12 years. All patients received graft from deceased donors. CAC was determined with multi-detector row computed tomography as total calcium score (CS) and calcium mass (CM). Serum Ca, P, PTH and CaxP product were analysed. Duration of renal replacement therapy (RRT) was also analysed. Glomerular filtration rate was calculated with abbreviated MDRD equation (eGFR). Results are shown as mean±SD in Table 1.
Results: CAC was found in 72 patients (69%). We compared RTR without CAC (CAC–) and those with CAC (CAC+).
No correlation was found between CS and CM and: Ca, P, CaxP and PTH either in whole analysed group or in CAC+ group.

Table 1

Parameter	CAC–	CAC+	P
Age (years)	41±11	52±10	<0,001
Gender (male)	17 (53%)	56 (78%)	<0,05
CS	0	765,6±968,1	<0,001
CM (mg)	0	128,2±13,7	<0,001
PTH (pg/ml)	82,1±41,7	113,5±116,9	NS
Ca (mmol/l)	2,37±0,17	2,38±0,18	NS
P (mmol/l)	0,99±0,16	1,0±0,19	NS
Ca×P	2,34±0,38	2,38±0,45	NS
eGFR (ml/min/1,73m^2)	55,9±18,1	55,1±16,8	NS
Duration of RRT (months)	63±42	75±48	NS

Conclusion: The prevalence of CAC in RTR is similar to that observed in patients starting dialysis therapy. No relationship was found between serum Ca, P, PTH, CaxP product and CAC. These results may suggest that CAC occurs before starting RRT.

P-244 THE RELATIONSHIP BETWEEN CORONARY ARTERY CALCIFICATION AND PULSE WAVE VELOCITY IN RENAL TRANSPLANT RECIPIENTS

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Coronary artery calcification (CAC) and increased pulse wave velocity (PWV) are responsible for high incidence of ischemic heart disease and other cardiovascular complications in patients with chronic kidney disease (CKD). PWV is a marker of arterial stiffness and independent cardiovascular risk factor in renal transplant recipients (RTR). Relationship between CAC and PWV was found in CKD patients and in non-renal population. The aim of the study was to evaluate the relationship between CAC and PWV in RTR.
The study group consisted of 104 RTR (31 females and 73 males), aged 49±12 years. All patients received graft from deceased donors. Total duration of renal replacement therapy (RRT) was 71±47 months. PWV between carotid and femoral artery was measured using Complior device. CAC was determined with multi-detector row computed tomography as total calcium score (CS) and calcium mass (CM). Glomerular filtration rate was calculated with abbreviated MDRD equation (eGFR). Results are expressed as mean±SD.
Results: CAC was found in 72 patients (69%). We compared RTR without CAC and those with CAC. Results are shown in Table.

Parameter	CAC–	CAC+	P
Age (years)	41±11	52±10	<0,001
Gender (male)	17 (53%)	56 (78%)	<0,05
CS	0	765,6±968,1	<0,001
CM (mg)	0	128,2±13,7	<0,001
PWV (m/s)	8,6±1,5	10,2±2,2	<0,001
eGFR (ml/min/1,73m^2)	55,9±18,1	55,1±16,8	NS
Duration of RRT (months)	63±42	75±48	NS

We found significant positive correlation between PWV and: CS (r=0,21; p<0,05), and CM (r=0,20; p<0,05). In multiple logistic regression analysis PWV was independent predictor of CAC – OR 1,82 (95% confidence interval: 1,18-2,31, p<0,01)
Conclusion: The study revealed high prevalence of CAC in RTR. PWV is an independent predictor of coronary artery calcification in RTR. Further studies are necessary to identify other than age and male gender pathogenic factors for both: CAC and increased arterial stiffness.

P-245 RESULTS OF SIMULTANEOUS AND SEQUENTIAL LIVER AND KIDNEY FROM LIVING DONORS: RENAL PERSPECTIVES

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Combined liver and kidney transplant (CLKT) has been increasing due to increase of end-stage hepato-renal disease. However, most of CLKT are performed from the deceased donors and there have been rare reports on CLKT from different living donors and comparisons with Kidney after liver transplant (KAL). So, the purpose of this study is to report our CLKT and KAL cases from living donors and to analyze its outcomes from the renal perspective.
From January 1999 to August 2008, 9 CLKT and 3 KAL were performed at our institution mostly from living donors except 1 cadaveric CLKT. Right after living donor LT, KT was performed through separate incision from living donors in case of CLKT.
All CLKT recipients were on dialysis at the time of transplantation and 3 KAL recipients were on impending dialysis at the time of LT. The mean interval from LT to KT in the 3 KAL was 20. 3 months (1.2-60 months). All patients were survived except 1 mortality at 8 months after CLKT due to HCC recurrence during follow up duration (0.5-9 years). 3 cases of acute rejections were reported (1 liver, 2 kidney) in the CLKT group and all the liver and kidney grafts were functioning well. Postoperative complications were developed in 3 patients in the CLKT group and managed conservatively. The length of ICU stay at the time of CLKT and first LT were similar and the recovery periods to normal creatinine level were significantly longer (10.3 vs 1.7 day) in CLKT than KAL.
Indication of CLKT from living donor would be much stricter than that of cadaveric CLKT. CLKT and KAL from living donors in appropriately selected patients can be performed safely and effectively for end-stage hepato-renal disease with comparable results.

P-246 MUCORMYCOSIS FOLLOWING KIDNEY TRANSPLANTATION: A MULTICENTER STUDY

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Background: Mucormycosis is an extremely rare and potentially fatal complication after kidney transplantation. Limited data are available on mucormycosis following living donor kidney transplantation.
Aim: The aim of this study was to determine the incidence of mucormycosis and to identify the clinical presentation and mortality rate in renal allograft recipients.
Methods: We conducted a retrospective survey of 7132 Iranian renal transplant recipients to find those with Mucormycosis in eight transplant centers from January 1990 to June 2008. A total of 22 patients had received kidneys from living donors were complicated with Mucormycosis. Mean follow up period after diagnosis was 9±13 (1-60) months.
Results: No significant differences were found between infection occurrence and gender (P=0.6). Patients with mucormycosis were older than those who had no infection (p=0.02) with the mean age at diagnosis 48±13 years. The diagnosis times since transplantation ranged from 1-84 (Median: 12) months. Mucormycosis was most likely to occur within 1 year after renal transplantation (n=13).The major form of disease in population studied was rhino-cerebral (n =11), followed by pulmonary (n=8), cutaneous (n=2), and disseminated (n=1). In addition, 9 patients have had the history of steroid pulse therapy. Diabetes mellitus was seen in 6 recipients with mucormycosis.
Conclusion: To our knowledge, the current study is the largest sample of renal recipients with mucormycosis in living donor renal transplantation. Augmented immunosuppression, especially with corticosteroids, older age and PTDM were the predisposing factors for the infection.

P-247 THE OUTCOME OF PATIENTS WHO DEVELOP CLOSTRIDIUM DIFFICILE INFECTION FOLLOWING SOLID ORGAN TRANSPLANTATION: A SINGLE CENTRE EXPERIENCE

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Purpose: *Clostridium Difficile* (*C. Diff*) is a gram-positive, anaerobic, rod-shaped bacterium responsible for most cases of hospital-acquired infective diarrhoea. It is very contagious, easily spread via direct contact. Immunocompromised transplant patients may be particularly vulnerable to it and may have a worse outcome.
The aim of this study was to find out the natural history of patients who develop *C. Diff*. within the first year following solid organ transplantation.
Method and materials: All patients who develop *C. Diff* are notified to the Microbiology Department. We identified all transplant patients who developed *C. Diff* within the first year of transplantation between 2004- 2008. We reviewed these patients' notes to identify when they acquired this infection, natural history and complications that occurred.
Results: Between 2004-2008 we performed 682 transplants: 433 deceased donor kidneys, 143 live donor kidneys, 18 pancreas only transplants, 88 simultaneous kidney and pancreas transplants. 25 patients developed *C Diff*. The median age was 46. All patients had standard induction prophylactic an-

tibiotics and immunosuppression. Only 5 patients were on antibiotics at time of infection. No single common antibiotic was identified. 2 patients developed fulminant colitis requiring urgent subtotal colectomy and ileostomy. Hospital stay was markedly increased at 15 days compared to 11 days for the general transplant population. When comparing first deceased kidney transplant the outcome of patient and graft survival at one year was worse for those who acquired *C.Diff.* (84% and 73% respectively) compared to the overall unit's results (95% and 94% respectively).
Conclusion: In our study 3.6% of transplant patients acquired *C.Difficile.* We didnt identify any common antibiotic or patient risk factor which increased the risk of acquiring *C. Difficile*. These patients had a markedly increased hospital stay, complication rate, poorer graft and patient survival.

P-248 ABO-INCOMPTIBALE KIDNEY TRANSPLANTATION IN TAIWAN – A SINGLE INSTITUTION EXPERIENCE

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Background: ABO-incompatible kidney transplantation (ABOiKT) is recognized as an effective way to expand the living related donation pool. The aim of this study was to assess the short-term result of this first ABOiKT program in Taiwan since 2004.
Methods: Thirteen patients underwent ABOiKT between January, 2004 and July 30, 2008. The initial protocol were 1. preconditioning immunosuppressive therapy with tacrolimus (0.05mg/kg), mycophenolate mofetil (MMF, 1g BID), and methylprednisolone (40mg QD) since 7 days before transplantation; 2. four to six times of double filtration plasmaphresis (DFPP) to remove A/B antibody (titer$<$1:4); 3. splenectomy on the operation day. After applying it for three patients, we abandoned splenectomy and changed the protocol with two doses of anti-CD20 antibody (200mg) on the 14 days before transplantation and the operation day. We analyzed short-term results of the program.
Results: The mean age of recipients was 46$\pm$11.93 years. Incompatibility in ABO blood group antigens was as follows: A$\rightarrow$O, 3; B$\rightarrow$O, 3; B$\rightarrow$A, 2; AB$\rightarrow$A, 1; A$\rightarrow$B, 1; AB$\rightarrow$B, 3. The numbers of HLA mismatches were 2.46$\pm$1.33. Two patients with upper gastrointestinal bleeding, one with MMF-related delirium, and one with deep vein thrombosis were found postoperatively. The mean follow-up was 25 months. The patients are all survived and the graft survival rate was 92.3%. We lost a graft because of BK virus allograft nephropathy at 8 months after the transplantation. One patient encountered cellular rejection and two patients with antibody-mediated rejection were found. Major infections was 23.1%, two with pneumonia and one with BK virus infection.
Conclusion: The short-term results of our ABOiKT program with pre-operative DFPP, two doses of rituximab, and a conventional triple immunosuppressive therapy seemed good. We should be aware of severe infections such as BK virus infection while using the protocol.

P-249 AUGMENTATION CYSTOPLASTY AND PYELOPLASTY WITH ENCRUSTED PYELITIS IN TRANSPLANTED KIDNEY

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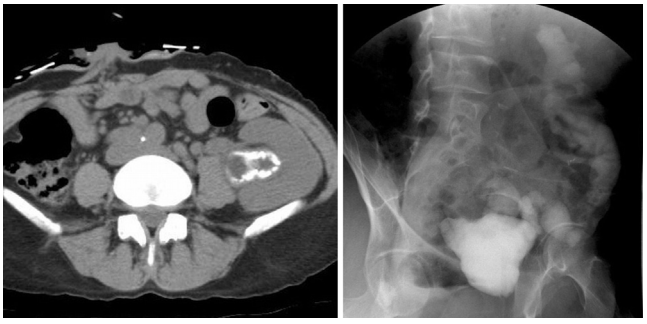
Encrusted pyelitis is characterized by mucosal inflammation and encrustations of the bladder or upper urinary tract. Such encrustations consist of deposits of ammonium magnesium phosphate and struvite. The *Corynebacterum urealyticum*, a gram-positive bacillus was identified as the most frequent causative pathogen. And encrusted pyelitis in transplanted kidney was caused graft failure or nephrectomy. We report surgical treatment of augmentation cystoplasty and pyeloplasty with encrusted pyelitis in transplanted kidney without transplanted nephrectomy. A 51-year-old female patient received kidney from her sister after both nephrectomy because of renal tuberculosis before 12 years. At that time, the transplanted ureter was anstomosed ileum in left lower abdomen and ileal conduit at opposite site. She had no problem for 12 years. On routine check, she complained abdominal pain, gross hematuria and increased debris in ileal conduit. The serum creatinine was elevated and her transplanted kidney developed hydronephrosis with calcified debris in sonography. The her transplanted kidney was not hydronephrosis and calcified debris in sonography before 6 months. We performed urine culture and abdominopelvic computer tomography, found hydronephrosis with encrusted pyelitis and ureteritis in transplanted kidney.
She was treated percutaneous nephrostomy and empirical antibiotics. The microorganisms in urine was *Proteus* and *Pseudomonas*, had no evidence of tuberculosis. We performed cytogram and the her bladder was not refluxed but small capacity in 50mL. After 3 weeks, we operated that the transplanted ureter was anastomosed remnant ileum in ileal conduit, augmentated cystoplasty with new ileum, remnant ileum was anastomosed with augmented bladder and removed ileal conduit.



After operation, the calcified debris was decreased and encrusted pyelitis was not found in sonogrpahy. If urinary tract infection is controlled, we think that ileocaliceal anastomosis is an alternative for the treatment of encrusted pyelitis.

P-250 SELF-EXPANDING METALLIC URETERAL STENT INSERTION FOR TREATMENT OF URETERAL STENOSIS AFTER URETEROURETEROSTOMY

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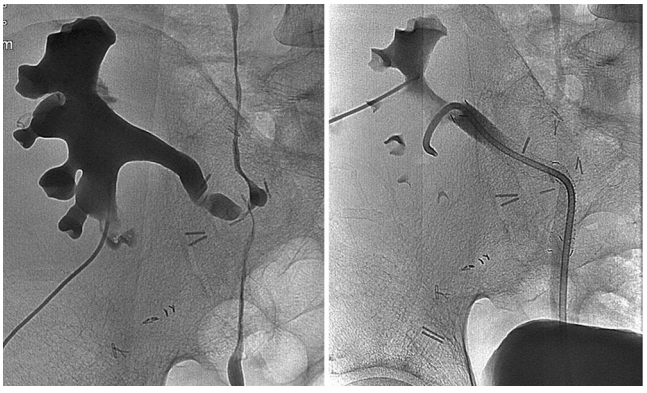
The obstruction of the ureterovesical anastomosis is the most common long-term urologic complication after renal transplantation. The incidence of stenosis has been reported as 2–10% of all renal transplant recipients. The common treatment for all these forms of ureteral stricture remains open surgery. Recently, the development of balloon catheters, stents and advances in percutaneous endourology has made percutaneous transluminal treatment of ureteral stenosis a safe and effective procedure. We report the successful treatment of metallic self-expanding stent in restenosis of transplanted ureter after ureteroureterostomy operation. A 37-year-old male patient received a living donor renal transplantation. He received regular follow-up at our hospital after surgery. After 8 months, the patient was admitted to the hospital for evaluation of abrupt elevated serum creatinine. We found hydronephrosis with transplanted ureteral stenosis from middle to distal transplanted ureter. We operated end to side ureteroureterostomy, proximal transplanted ureter with native right ureter and inserted D-J stent. After 1 month, we removed D-J stent. After 2 weeks, he was admitted to the hospital because of urinary tract infection with renal failure. He was treated antibiotics, then progressed renal failure. We performed abdominopelvic computer tomography and found new developed ureteral stenosis and diverticulum in anastomotic site.



We performed percutaneous nephrostomy and his renal function was recovered. We recommended reoperation of ureteral stenosis after controlled urinary tract infection, but the patient refused the reoperation. We performed balloon dilatation and self-expanding metallic stent insertion with D-J stent in ureteral stenosis.
At recent, 4 months after self-expanding metallic stent insertion, renal function was recovered before stent insertion. We recommend that ureteral stent implantation is the alternative for the treatment of ureteral stenosis in patients with refusing operation.

P-251 COMPARISON OF NEW ONSET DIABETES ACCORDING TO THE TIME OF ONSET AFTER KIDNEY TRANSPLANTATION IN KOREA

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Purpose: New onset diabetes is a common complication after kidney transplantation. However, the clinical course of post-transplant diabetes mellitus (PTDM) remains unclear. The aim of the present study was to analyze the natural courses and risk factors of PTDM according to the time of onset.
Methods: A total of 196 consecutive kidney transplant recipients were enrolled and patient medical records were investigated retrospectively. PTDM was defined as glucose $\geq$126mg without previous diabetic history. Patients were classified according to the onset: early PTDM (e-PTDM $<$12 months) and late PTDM (l-PTDM $\geq$12 months).
Result: PTDM was observed in 34 (17.3%) patients. The number of e-PTDM and l-PTDM patients was equal (17 vs 17). C-peptide, HbA1C, insulin were checked in PTDM (non-PTDM) patients. C-peptide was 1.75ng/ml (non-PTDM: 3.19); HbA1C, 3.3% (4.72); insulin, 6.21uU/ml (6.38). C-peptide, HbA1C, insulin in e-PTDM (l-PTDM) were 6.58ng/ml (3.9), 5.97% (6.7), 10.3uU/ml (8.4), respectively. T-score of BMD was -1.2 (e-PTDM); -0.95 (l-PTDM). The value of C-peptide in PTDM/non-PTDM was 5.6$\pm$0.9 vs. 6.3$\pm$1.4 (p=0.016). Compared with normoglycemic patients, the PTDM group was older (46.1$\pm$9.0 vs. 51.6$\pm$8.7, p=0.001). Pre-transplant BMI in PTDM/non-PTDM was 22.3$\pm$3.1 vs. 20.7$\pm$2.2 (p=0.049). The use of tacrolimus was associated with the development of e-PTDM (OR=4.87, 1.71-13.8 in 95% CI) but not l-PTDM (OR=0.34, 0.04-2.70 in 95% CI).
Conclusion: Recipient age, HbA1C and BMI were significantly correlated with the development of PTDM. The use of tacrolimus showed the significant correlation in development of e-PTDM.

P-252 NEWFOUND RISK-FACTORS FOR CMV-INFECTION IN KIDNEY TRANSPLANT PATIENTS

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Purpose: CMV infection is an important complication of solid organ transplantation. The aim of the study is to determine the correlation between susceptibility to CMV-infection and certain HLA-types, and to define if there are any other demographic parameters which influence this susceptibility.
Methods/Materials: Of 1213 investigated patients 129 were CMV-seronegative with seropositive donors. 38% developed primary CMV-infection in the first posttransplant year. The patients were homogenous in terms of CMV serostatus, immunosuppressive therapy and CMV prophylaxis. To determine whether CMV infection was related to any HLA specificities, the incidence of active CMV infection was analysed in relation to different HLA-types. The diagnosis of CMV infection was established by antigenemia test. HLA-typing was performed by standard NIH micro-lymphocytotoxicity method (NIH) and by DNA-based PCR-SSP technique.
Results: The occurrence of CMV-infection in patients with HLA-A2, -DR6 was higher, while this with HLA-B12 and -Cw7 was lower than that in patients negative for these HLA types, but the differences were not significant. However, a significant difference was found in the HLA-DQ3 positive group versus -DQ3 negative patients (P = 0.002). To determine whether these results were influenced by other risk factors, multivariate Cox regression analysis was performed.
Although the difference in the gender proportion was negligible among all 1213 recipients, this difference among CMV-seronegative patients was highly significant: of 163 seronegative patients 33% were females and 67% were males (P $<$0.001).
Conclusions: The study showed that the HLA-DQ3 positivity is an independent predictor of primary CMV-infection in high-risk transplant patients The cognition of HLA-DQ3 is useful in the prediction of acute CMV infection in high-risk patients. The number of females among seronegative patients was significantly lower, these data correlates with our previous study, which showed a higher CMV-seroprevalence among females supposing higher susceptibility of females to CMV-infection.

P-253 SERUM TISSUE INHIBITOR OF METALLOPROTEINASES 1 (TIMP-1) PREDICTS ORGAN RECOVERY FROM DELAYED GRAFT FUNCTION AFTRE KIDNEY TRANSPLANTATION FROM DONORS AFTER CARDIAC DEATH

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Donors after cardiac death (DCD) have recently become an important source of renal transplants to alleviate the shortage of renal grafts in kidney transplantation (KTx), although DCD kidneys often have complications associated with a delayed graft function (DGF). A microarray-based approach using renal biopsy samples obtained at 1 hr after KTx from DCD, identified the tissue inhibitor of metalloproteinases 1 (TIMP1) gene as a potential predictive marker for DGF. The current study measured serum TIMP-1 in patients undergoing KTx and analyzed the time-course after KTx. The average serum TIMP-1 level before KTx was 240$\pm$10 ng/ml (n=34). In patients undergoing KTx from a living donor (n=23), the serum TIMP-1 levels showed no increase after KTx (POD1: 226$\pm$12, POD2: 211$\pm$12 and POD3: 195$\pm$10 ng/ml), but in one case, the only patient who required post-KTx HD due to DGF, the level on POD1 was the highest among subjects (361 ng/ml). In contrast, patients undergoing KTx from DCDs (n=11), the serum TIMP-1 levels increased rapidly after a KTx (POD1: 418$\pm$32, POD2: 385$\pm$42 and POD3: 278$\pm$25 ng/ml). However, two patients who avoided post-KTx HD due to the immediate function of the graft, did not show increased levels ($<$370 ng/ml) on either POD1 or POD2. The peak serum TIMP-1 values appeared to correlate to the post-KTx dialysis period. Furthermore, the increment of serum TIMP-1 on the early POD was found to be predictive of immediate or delayed function of the grafts. These data suggest that monitoring of serum TIMP-1 levels allow the prediction of graft recovery and the need for HD after a KTx from a DCD.

P-254 HIGH FREQUENCY OF GASTRIC ULCER IN THE FIRST THREE POSTTRANSPLANT MONTHS

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Introduction: Upper gastrointestinal complications have historically resulted in considerable morbidity and mortality to solid organ transplant recipients.
Aim: Summarize the largest endoscopic database for kidney transplanted recipients.
Materials and methods: In a large transplant unit 2135 kidney transplants were carried out between 1994 and 2007. At that period, 672 upper endoscopies were performed for 543 of those patients with significant gastrointestinal complains. 56.9% were male, with a mean age of 49.5 years (16-78). All patients got ulcer prophylaxis long term following transplantation.
Results: Macroscopic findings included inflammation in 46.7%, oesophagitis in 24.7%, ulcer in 16.9%, and erosions in 14.8% of cases; 16% of all patients presented negative status. The presence of Helicobacter pylori (H.p) was verified by histology in 20.9% of cases, less than the 49% found by serology in the uraemic population ($p<0.0001$). Its presence was independent from the presence of erosions and ulcers. 29% of patients were examined in the first posttransplant year, and 58.5% of them in the first three months. 27 (29.3%) out of 92 ulcers developed in the first three months; 42 (45.7%) in the first year and all the others in a constant rate later on (p=0.0014).
Conclusions: More than 25% of all kidney recipients required upper endoscopy in their “posttransplant life”. The rate of clinically significant endoscopic findings was 84% and frequency of ulcer disease was 17%, both figures significantly higher than the ones found in the general population that required endoscopy ($p<0.0001$). The most vulnerable period was the first three months. The presence of H.p. was not associated with any specific endoscopic findings. Adopting a low threshold for endoscopy in a specialised centre revealed very frequent abnormalities that required medical intervention.

P-255 RHABDOMYOLYSIS IN KIDNEY TRANSPLANTATION INDUCED BY EXTREMELY HIGH LEVEL OF SERUM CYCLOSPORINE DUE TO THE DISORDER IN METABOLIC ENZYME AND TRANSPORTERS

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Aims: We treated a case of rhabdomyolysis induced by extremely high level of serum cyclosporine (CsA). The patient recovered after conversion of CsA to tacrolimus (TAC). We studied his genetic background of metabolism disorder and transporter polymorphisms to clear up the clinical obsevations.
Case: A 36-year-old man underwent ABO compatible kidney transplantation from his father. Three days prior to the operation, oral CsA was given at 5 mg/kg, while the CsA trough level elevated to 640 ng/ml and creatine kinase (CK) began to increase on the operative day. On post-operative day (POD) 2, CK and myoglobin (MG) in blood jumped up to 14019 ng/ml and to 6600 mg/ml respectively, with his complaints of general fatigue and lower limb muscle pain. We made a diagnosis as rhabdomyolysis caused by the rapid CsA elevation and then converted immunosuppressant to TAC (0.1 mg/kg), after which creatinine (Cr) gradually decreased, and CK and MG returned to normal ranges. His general condition and renal function improved. We investigated the cause of the high CsA concentration. His gene analysis showed the polymorphisms of the OATP1B1 1b/*15 and MRP2 -24T/T. These peptides were associated with a semi-defective form of hepatic uptake of CsA and defective form of bile excretion, respectively. Furthermore, our patient had the CYP3A5 *3/*3 polymorphism, which causes lower metabolism of CsA than CYP3A5 *1/*1 group. We thought these three factors induced high level of serum CsA in the case.
Conclusion: This is the first case study on coexistent polymorphisms of transporter and CYP3A5 affecting CsA metabolism, leading to extremely high level of serum CsA resulted in rhabdomyolysis. Additional studies of transporters and metabolic enzymes will enable individualized medical solutions.

P-256 TRANSPLANT GLOMERULOPATHY AFTER HLA ANTIBODY INCOMPATIBLE TRANSPLANTATION, REMISSION AND PROGRESSION

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Transplant glomerulopathy (TG) may be a chronic manifestation of antibody-mediated injury after HLA antibody-incompatible (HLAi) transplantation. It is generally regarded as carrying a poor prognosis, and there is concern that it may limit the longer term outcomes after HLAi transplantation.
Between 2003-2008, 67 patients received HLAi transplants in our centre. Six patients had renal biopsies that showed TG. These were performed at 3, 3, 16, 24, 34 and 41 months after transplantation. This represented 2/59 (3.4%) patients at risk at 3 months, and 5/27 (18.5%) at 24 months.
Mean creatinine at presentation with TG was 196 (range 158-237) umol/l, and protein-creatinine ratio (PCR) was 293 (range 36-696) mg/mmol, and the most recent mean creatinine was 236 (range 161-347) and PCR 179 (range 110-561). Treatment consisted of blood pressure therapy in all cases, and increase in immunosuppression in 5 cases. Three patients have had plasmapheresis. No graft has yet failed, though one patient has reducing function, and the follow up since biopsy is short (mean 10.2 months, range 3-22).
Development of TG was associated with donor specific antibody (DSA) levels pre-transplant. In patients at risk at 24 months post transplant, TG was present in 2/7 (28.6%) patients whose pre-treatment cytotoxic crossmatch (XM) was +ve, compared with 2/12 (16.7%) with flow cytometric (FC) XM +ve, and 1/8 (12.5%) with FC -ve. Four cases had DSA against HLA Class 1 only, and have stabilised function with current low DSA levels. The other two cases have ongoing production of high levels of DSA against HLA Class 2.
In summary, although the number of cases is small, it is possible that TG associated with HLA Class 1 DSA that modulate may carry a better prognosis than when it is caused by HLA Class 2 with ongoing high level production.

P-257 EFFECTIVENESS OF ULTRASONOGRAPHY SCREENING FOR RENAL CELL CARCINOMA IN RENAL TRANSPLANT RECIPIENTS

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Background: The incidence of malignancy is increased in renal transplant recipients, in which renal cell carcinoma (RCC) is found to be 15 times greater. However, there is no strong evidence to support regular screening using ultrasonography (USG). In our center, we started to arrange annually USG screening for our renal transplant recipients, particular for those with acquired cystic disease. We reported the effectiveness of the screening and the outcomes of the sub-clinical RCC.
Methods: All renal transplant recipients in our center were scheduled to have a USG scanning when they come back for follow up. The results of screening over a 10-year period were studied.
Results: Of the total 400 transplant patients, 6 tumors in the native kidneys (5 unilateral and 1 bilateral) were detected in 5 patients. The average ages at transplantation and diagnosis of RCC were 38.8±6.61 and 48.7±5.76 yrs, respectively. All tumors were detected by ultrasound scan and then confirmed by computed tomography with contrast. No biopsy was performed before nephrectomy. Patients were neither symptomatic nor polycythemia (Hb 14.0±1.0 g/L) and they were all undergone total nephrectomy. The median size of tumor was 3.5 cm (range 1.5 to 6.5). Cell types were 4 for papillary and 2 for clear cell, respectively. All tumors were Furhman grade 1 or 2 with stage 1 of the TNM staging. All patients are alive with stable allograft function and there is no evidence of recurrence on their latest follow up.
Conclusions: We have shown USG is an effective screening test to detect early stage of RCC. We recommend renal transplant recipients should have annually USG screening of their native kidneys such that earlier stage of tumor could be detected.

P-258 THE LOW DOSE OF RITUXIMAB IN ABO-INCOMPATIBLE KIDNEY TRANSPLANTATION WITHOUT SPLENECTOMY

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Purpose: A new protocol for ABO-incompatible (ABOi) kidney transplantation including rituximab instead of splenectomy was introduced since January 2005 in our institute. We started a dose of rituximab at 500mg/body at first. And then, we reduced a dose of the rituximab to 200mg/body since January 2007. We reviewed our results and evaluated the dose of rituximab.
Material and methods: Between January 2005 and November 2008, 45 de novo ABOi kidney transplantations were performed at Tokyo Women's Medical University. 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. The preconditioning protocol included plasmapheresis (PP) and a single dose of rituximab. The dose of rituximab was 500mg/body between January 2005 and December 2006 (Group I, n=23). Since January 2007, the dose of rituximab was reduced to 200mg/body (Group II, n=22). The periperal blood CD 19 levels were monitored regularly.
Results: Group I; The mean serum creatinine level of all the patients was 1.2 mg/dl. Antibody-mediated rejection (AMR) occurred in one patient. Group II; The mean serum creatinine level of all the patients was 1.3 mg/dl. AMR occurred in one patient. In both groups, effective elimination of the peripheral blood CD19 cells was recognized. Late-onset neutropenia was observed (Group I; 35%, Group II; 18%), nevertheless there was no serious infection. However, 24months after treatmen, the peripheral blood CD19 levels were still low in both groups. Esprcially, in Group I, 36months after treatment, most patients (67%) showed low level of the peripheral blood CD19.
Conclusion: Patients of Group II (200mg/body) showed an excellent result like patients of Group I (500mg/body). We suggest that the low dose of rituximab (200mg/body) is sufficient and optimal dose in ABOi kidney transplantation.

P-259 IMPAIRED RENAL FUNCTION IS ASSOCIATED WITH REDUCED ABILITY TO WORK IN KIDNEY TRANSPLANT RECIPIENTS

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Introduction: Occupational rehabilitation of Kidney Transplant (KTx) recipients is sub-optimal. Symptoms of reduced renal function may impair work ability, job performance and increase absenteeism. The association of renal function and Work Ability has never been studied in KTx recipients. We assessed the association of Glomerular Filtration Rate and Work Ability Index (WAI), a brief 7-dimension scale indicating the subjects' ability to perform their job with respect to work demands, health and mental resources.
Methods: This is an ongoing longitudinal study. We contacted KTx patients of 18-74 years of age followed at one Midwestern outpatient transplant clinic. For the present analysis, we selected a subset of patients excluding those with

multiple or multi-organ transplant, laboratory evidence of an acute cardiac ischemic episode in the month prior to assessment and those not in the working age. We matched WAI data to information extracted from clinical charts. Differences in WAI across CKD stages were tested by Spearman's partial correlation analysis adjusted for age, gender, race, family income, transplant vintage, serum albumin, hemoglobin, glycemia and markers of liver function.

Results: 275 (93%) patients completed the questionnaire and 53 met the exclusion criteria leaving 222 subjects. The Employment-to-Population ratio was 63% (n=144/222). Among employed subjects, those with more advanced CKD had lower albumin and hemoglobin levels and higher phosphatemia (table 1). Markers of liver functions were within the range of normality for all patients. WAI was negatively correlated to CKD stage even after adjusting for confounders (ρ= -0.24; p=0.04) (figure 1).

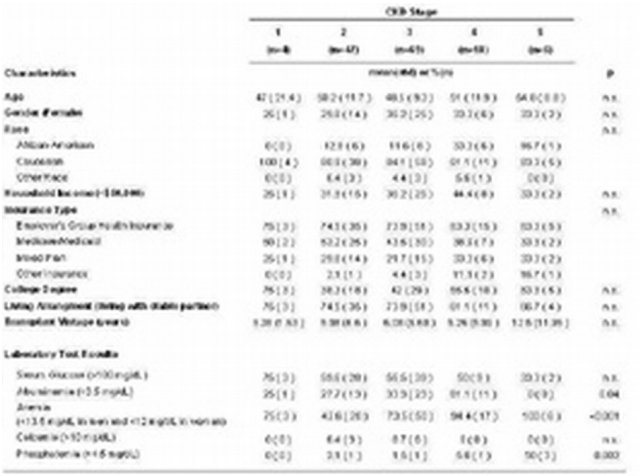

Table 1. Sample characteristics by CKD stage (KDOQI categories). CKD classification based on mean laboratory test results obtained in the 3 months prior to enrollment. P values based on χ^2 for categorical variable and Kruskal-Wallis test for continuous variables.

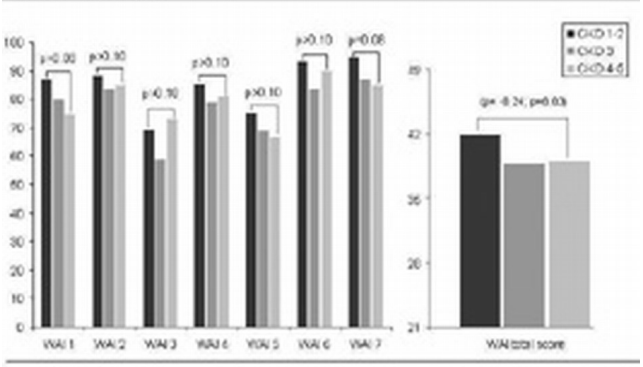

Figure 1. Work Ability index and Work Ability dimensions by stage of renal disease (KDOQI categories). Bars represent mean scores. We rescaled Work Ability dimensions to allow direct comparison (rescaled range: 0-100). P values refer to trends across categories analyzed by Spearman's rank correlation coefficients. All correlations adjusted for age, gender, race, family income, transplant vintage, serum albumin, hemoglobin, glycemia and markers of liver function. WAI 1: Current Work Ability compared to lifetime best; WAI 2: Work Ability in relation to physical and mental demands; WAI 3: number of comorbidities; WAI 4: Estimated impairment due to disease; WAI 5: Sick leaves in the past 12 months; WAI 6: own prognosis of Work Ability within 2 yrs; WAI 7: mental resources. WAI scoring classification: Poor (7-27); Moderate (28-36); Good (37-43); Excellent (44-49).

Conclusions: Work Ability may be affected by poor renal function after transplant. Previous evidence indicated that WAI is associated with absenteeism and early retirement. Further studies should investigate the relationship between renal impairment, indirect costs of kidney transplantation and patients' occupational outcomes.

P-260 A LONG TERM EXPERIENCE, OF A PROGRAM DEVOTED TO RENAL RE-TRANSPLANTATION

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One of the main problems in renal transplantation is represented by the immunological barriers; the candidates for a regraft often develop a high titer of anti-HLA antibodies that obstacles the regrafting. On the OPTN waiting list, 16.5% of patients are candidates for retransplantation but only 10.4% were transplanted in 2008. Since patient and graft survival is very close to that of first transplant, Transplant Centres are involved in specific programs to regraft these patients. This study evaluates retrospectively the kidney retransplant experience of the last 10 years (1998-2008), when 70 patients were retransplanted in our Centre; 4 of these were combined liver-kidney grafts. Allocation criteria for the second transplant was based on first transplant HLA mismatches exclusion, preformed anti HLA antibodies exclusion, identity on HLA class II, at least 2 compatibilities on HLA class I. 1 and 5 year actuarial graft survival of retransplanted patients was 90% and 83% (if combined were included) and 94% and 89% respectively, if not included. 1 and 5 year actuarial patient survival was 97% and 93% (if combined were included) and 94% and 89% respectively, if not included. Mean serum creatinine at the end of the first year was 1.45±0.59 mg/dl and rejection rate in the first 3 months was 15.5%. There were only small differences between immunized (39%) and non-immunized retransplant: graft survival was 2 points less (89 vs 91%), serum creatinine after 1 year was 1.52±0.4 vs. 1.38±0.5 mg/dl and the rejection rate was 21% vs 13% (p n.s.). This study showed that with an in-depth pre-transplant study of anti-HLA specificities and rigorous allocation criteria, the chance for a second or third graft, is quite similar to the first ones in terms of survival and renal function.

P-261 EFFECT OF MYCOPHENOLIC ACID MEDIATED APOPTOSIS IN HUMAN JURKAT CELLS VIA REGULATION OF HEME OXYGENASE-1 EXPRESSION

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Mycophenolic acid (MPA) is the active agent of mycophenolate mofetil (MMF). MPA is a selective inhibitor of inosine monophosphate dehydrogenase. Heme oxygenase-1 (HO-1), the rate-limiting enzyme of heme catabolism, is known to modulate various cellular functions, including cytokine production, cell proliferation, and apoptosis in stress-related conditions. However, the role of HO-1 in the immunosuppressive response system remains elusive. This study demonstrate that pharmacologic induction of HO-1 along with catalytic activation significantly modulated apoptosis of Jurkat cells induced by MPA. MPA induced apoptotic cell death showing nuclear fragmentation and sub G0/G1 phase arrest in Jurkat cells. 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. Decreased HO-1 expression on MPA treated-Jurkat cells after 36 hours. Change of mitochondrial membrane potential transition was also noted. Expression of Bax proteins was identified. CoPP, HO-1 inducer, induced expression of HO-1 proteins in MPA treated Jurkat cells. CoPP inhibited generation of H_2O_2. CoPP, significantly inhibited the MPA induced apoptosis. In conclusion, HO-1 inducer suppressed ROS generation, Bax protein expression and mitochondrial permeability transition in MPA-treated cells. This result suggests that the protective mechanism of HO-1 on MPA-induced cytotoxicity is associated with direct inhibition of ROS generation and mitochondrial permeability transition.

P-262 TACROLIMUS (FK506) INDUCED APOPTOTIC SIGNALLING WITH ENDOPLASMIC RETICULUM STRESS PATHWAY PROTEINS

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Tacrolimus (FK506) is an effective immunosuppressive drug used for the prevention of graft rejection in organ transplantation. We investigated the effects of FK506 on apoptosis, cell viability, measurement of H_2O_2 generation, intracellular accumulations of Ca^{2+} and NO, and western blotting of endoplasmic reticulum (ER) stress pathway proteins, such as phospho-PERK, PERK, CHOP, Grp78, Grp94, Bcl-2, and Bak proteins. 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 Ca^{2+} and NO production were identified in FK506 treated Jurkat cells after 24 hours. Expression of iNOS protein was also noted. Generation of H_2O_2 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. In conclusion, activation of caspase-12 and changes of other ER located proteins ascertained that ER stress mediated apoptosis. Also, FK506 increased NO production by iNOS expression. FK506 induced H_2O_2 generation revealed that cytotoxicity was achieved by generation of H_2O_2 which might modulate the expression of Bak protein. These data indicate that the effect of FK506 on ER stress mediated

apoptosis of Jurkat cells via generation of H_2O_2. Understanding of ER stress pathway would be a new approach to develop immunosuppressive drugs useful in organ transplantation cares.

P-263 PREDOMINANT Th1 AND CYTOTOXIC PHENOTYPE IN BIOPSIES FROM RENAL TRANSPLANT RECIPIENTS WITH TRANSPLANT GLOMERULOPATHY

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Purpose: Transplant glomerulopathy (TGP) appears to be a pathogenic feature of chronic antibody-mediated rejection, but the pathogenesis of this histologic entity is still poorly understood. Previous studies suggest the involvement of lymphocytes but the phenotypes of these cells have never been analysed. Here, we report the first study of mRNAs for specific markers of CD4+ T cells including Th1 (Tbet and INFg), Th2 (IL4 and GATA3), Treg (Foxp3) and Th17 (IL-17 and RORgt) subsets, cytotoxic CD8 T cells (Granzyme B) and B cell markers (CD20) in renal biopsies from renal transplant recipients suffering interstitial fibrosis and tubular atrophy (IF/TA) with or without TGP but with a similar inflammatory score and controls including transplant recipients with normal renal function.
Results: Only INFg, Tbet (both functionally defined markers of Th1 CD4 T cells) and granzyme B (a CD8 cytotoxic marker) were significantly more strongly expressed in patients with TGP than in patients without TGP and normal controls.
Conclusion: These results indicate a role of an active T-mediated inflammatory and cytotoxic process in the pathogenesis of TGP.

P-264 IMPACT OF HAND-ASSISTED LAPAROSCOPIC NEPHRECTOMY FOR LIVING DONOR TRANSPLANTATION ON DONOR'S QUALITY OF LIFE AND SOCIAL STATE

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Objective: Living donor kidney transplantation has gained widespread acceptance as an effective procedure for patients with terminal kidney disease. Laparoscopic donor nephrectomy has become the preferred method of choice in live kidney donation. The reason for this is the superior benefits of minimaly invasiveness nature of laparoscopic hand assisted nephrectomy for living donation.
Patients and methods: July 2003 to Jannuary 2009, a total of 48 hand assisted living donor nephrectomies had been performed at our institution. For evaluation of QoL, structured questionnaire has been mailed to the donors. The questionnaire was created at our center based on a combination of WHOQOL-BREF questionnaire and the 36-item health survey (SF-36) with slight modifications. The QoL scores were compared to data of German ordinary population. Mean follow-up time was 2.45 years.
Results: The QoL scores were higher than those of the normal population in all domains. The higher qualitiy of life in donors was independent of time since donation; we found no difference in mean QoL scores between those who had donated <1 year, or >5 years before responding to the survey. When asked to rate their health at the time of the questionnaire, 91% rated it as good, very good, or excellent; 6% rated it as fair, 3% rated it as poor. When asked to rate pain around their scar, 91% rated it as mild or absent, 6% as moderate, 3% as severe or very severe. 94% of the patients were likely to say they would donate again, if it were possible. For 6% of the patients was the overall experience very stressful.
Conclusions: Our study of assessment of QoL in living kidney donors after laparoscopic hand-assisted donor nephrectomy showed that the benefits of living donation exceed the risks.

P-265 EARLY AND LATE GRAFT FUNCTION AFTER LAPAROSCOPIC HAND-ASSISTED DONOR NEPHRECTOMY FOR LIVING KIDNEY TRANSPLANTATION: COMPARISON WITH OPEN DONOR NEPHRECTOMY

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Introduction: The laparoscopic donor nephrectomy has become the procedure of choice in the living kidney transplantation. However, longer warm ischemia time and application of pneumoperitoneum have raised concerns about the early and late function of the transplant graft. We report on our experience with laparoscopic hand-assisted donor nephrectomy.
Patients and methods: This study is a retrospective, non-randomized single-center analysis. Between oct. 1995 and jan. 2009, 86 patients with end stage renal disease have received kidney transplantation from living donors. Open living donor nephrectomy was performed in 38 donors, whereas 48 donors had undergone laparoscopic hand-assisted nephrectomy. Immediate graft function, and the biochemical marker of glomerular filtration rate (GFR), serum creatinine and serum cystatin C one year after the transplantation were evaluated.
Results: Both the rate of early graft function as well as kidney graft function parameters serum creatinine and serum cystatin C one year after transplantation showed no statistically significant difference between the two groups of patients.
Conclusions: Laparoscopic hand-assisted donor nephrectomy is safe and has compared with open donor nephrectomy no negative impact on the transplanted graft function.

P-266 A COMPARISON OF EFFECTS OF SHORT-TERM MAINTENANCE EXPOSURE OF ADVAGRAF AND NEORAL ON RENAL PERFUSION AND FUNCTION IN HEALTHY VOLUNTEERS

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Calcineurin inhibitor (CNI) nephrotoxicity remains an ongoing concern in recipients of all solid organ transplants. Previous studies have demonstrated that following administration of Neoral there is a strong correlation between the Cmax and decrease in both renal perfusion and GFR. The once daily preparation Advagraf has a similar AUC_{24} to twice daily Prograf, but a different PK profile, with a lower Cmax. Eighteen healthy Caucasian adult male volunteers were randomized to receive Advagraf and twice daily Neoral in a prospective, randomized, open label, 2 period, 2 sequence single crossover design. Outcomes included baseline and post- CNI exposure:effective renal plasma flow PAH (ERPF), iothalamate GFR, BP, AII, renin, urinary endothelin, TGFβ and urinary β2 microglobulin. Neoral was dosed at 5mg/kg/dy in divided dose for 10 days, targeted C2 of 700-1400 ng/ml; Advagraf was administered for 10 days at 0.1 mg/kg/dy as a single dose, targeted C0 of 5-10 ng/ml. All studies were repeated on day 10, followed by a 10 day washout period. BP, ERPF, GFR and renal tubular and hemodynamic markers were conducted pre-dose and over 6h post-dose, in concordance with PK of the respective CNIs. BP in mmHg at baseline was $119/77\pm8$ and on Neoral [C2=1200 ng/ml]or Advagraf [C0=8.7 ng/ml] was $125/83\pm10$ and $120/80\pm8$ p=0.016. The AUC_{6hour} ERPF for was 3251 ± 590 and 3782 ± 938 ml/1.73m^2, p=0.027 and the AUC_{6hour} GFR was 551 ± 82 and 616 ± 99 ml/1.73m^2, p=0.023, for Neoral and Advagraf, respectively. CNIs reduce both ERPF and GFR, these acute effects are attenuated with Advagraf compared to Neoral, and may correlate with the differing PK profile of these CNIs.

P-267 PROTEINURIA AMONG EGYPTIAN RENAL TRANSPLANT PATIENTS: ITS RELATION TO HCV AND GRAFT OUTCOME

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Background/Aims: Chronic Hepatitis C Virus (HCV) infection has been associated with glomerular disease in native and transplanted kidneys. Reports have suggested that HCV infected renal recipients may develop de novo glomerulonephritis. We evaluated the presence of HCV at the time of transplantation and occurrence of proteinuria in Egyptian renal transplant patients and its link with graft survival.
Patients and methods: The material of this work compromised 317 patients with end stage renal disease transplanted in Mansoura Urology and Nephrology Center Between 1993 and 1996. Their sera were routinely assayed for anti-HCV antibodies at the time of transplantation. The relationship between HCV and the development of post-transplantation proteinuria were evaluated and the effect of this proteinuria on long term graft survival was evaluated.
Results: 273 recipients fulfilled the inclusion criteria, 169 (62%) were positive and 104 (38%) were negative for HCV antibodies by third generation ELISA. The mean durations of post-transplant follow-up were 87.73 ± 26.79 (range 19-123 months) and 84.29 ± 28.55 (range 11-123) months for both groups respectively. Both groups were comparable regarding the incidence (56 patients out of 169 -33%-in HCV positive groups and 34 out of 104 patients-32%- in HCV negative group) and quantity (median, 0.6 gm/day in HCV positive patients and 0.4 gm/day in HCV negative patients, P=0.8) of proteinuria. Irrespective of the HCV infection, patients with nephrotic range proteinuria showed worse graft survival ($P<0.001$), higher frequency of chronic allograft nephropathy (p 0.05) compared with non proteinuric patients.

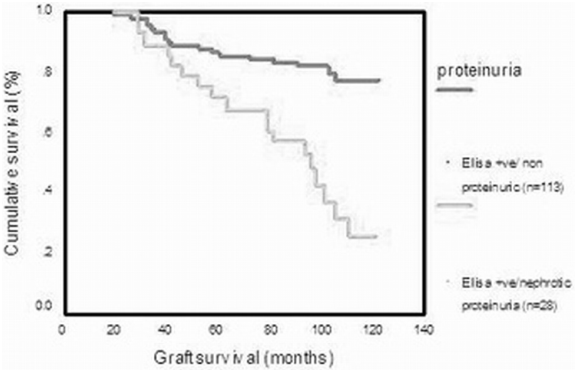

Figure 1. Graft survival in anti-HCV +ve according to proteinuria ($p<0.001$).

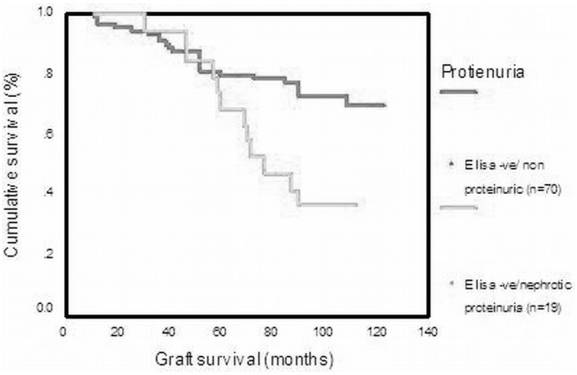

Figure 1. Graft survival in anti-HCV –ve according to proteinuria (p=0.005).

Conclusion: There is a high prevalence of HCV in our ESRD patients awaiting renal transplantation. The incidence and quantity of poteinuria do not increase by HCV infection, and nephrotic-range proteinuria is independently associated with chronic allograft nephropathy and a poorer graft outcome.

P-268 ALTITUDE AND LONG-TERM OUTCOMES OF KIDNEY TRANSPLANTATION

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Purpose: Recent research has indicated that dialysis patients live longer at higher altitude. It has been proposed that activation of hypoxia-induced factors may contribute to these better outcomes at higher altitude. Whether the outcomes of kidney transplantation differ by altitude is unknown.
Methods/Materials: We studied 75,400 patients who received a first kidney transplant in the United States between 1995 and 2004. We tested for any differences in patient or allograft survival (composite and death-censored) by residential altitude. Altitude was obtained by matching each patient's residential zipcode at time of transplantation with zip-code-specific information on average altitude from the US Geological Survey. We used multivariate Cox models for analysis, stratified by year of transplant, and adjusted for a large number of demographic, socioeconomic, comorbidity-related, transplant-related and donor-specific characteristics.
Results: While we did not find a clear association between altitude and mortality, the risk of allograft loss was markedly lower at higher altitude. Compared with patients living near sea level (<250 ft. or <76 m), patients living between 4000-5999 ft. (1219-1828 m) experienced a 13% (95% CI: 3%-22%) lower rate of allograft loss and those at ≥6000 ft. (>1828 m) had a 23% (95% CI: 2%-39%) lower rate of allograft loss including death with a functioning allograft. Similarly, patients living at ≥6000 ft. (>1828 m) had a 30% (95% CI: 1%-50%) lower rate of death-censored allograft loss compared with patients living at or near sea level. These results arose from models that carefully adjusted for differences in a large number of patient and donor-related characteristics.

Association between altitude and transplant outcomes

Altitude Stratum	Mortality	Allograft Loss	Non-Death Allograft Loss
<250 ft.	1.0 (Referent)	1.0 (Referent)	1.0 (Referent)
250-1999 ft.	0.99 (0.95-1.04)	1.01 (0.97-1.04)	1.03 (0.99-1.07)
2000-3999 ft.	1.07 (0.95-1.21)	0.99 (0.90-1.09)	0.94 (0.82-1.08)
4000-5999 ft.	0.88 (0.76-1.01)	0.87 (0.78-0.97)	0.89 (0.77-1.04)
≥6000 ft	0.84 (0.63-1.11)	0.77 (0.61-0.98)	0.70 (0.50-0.99)

Hazard ratios (95% Confidence Intervals).

Conclusions: Kidney transplant recipients living at higher altitude enjoyed longer allograft survival. Future research will aim to identify the causes and mechanisms underlying these superior transplant outcomes that were observed in patients living at higher altitude.

P-269 DGF AFFECTS REJECTION AND SURVIVAL OF HB BUT NOT OF NHB DONOR KIDNEYS

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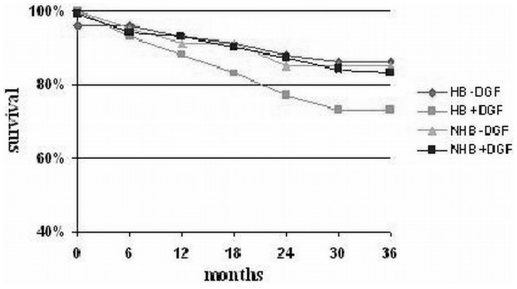
Kidneys derived from donors after cardiac death, i.e. non-heart beating (NHB) donors, are exposed to long warm ischemia times, which may result in tissue damage reflected in delayed graft function (DGF). As it has been suggested that DGF in heart beating (HB) kidneys might be associated with impaired long term graft survival, we wondered whether this negative effect of DGF could also be observed in NHB kidneys.
Methods: Data were prospectively collected from all 312 deceased donor kidney transplantations performed in our center between 2001 and June 2008. There were 133 NHB donor kidneys and 179 heart-beating (HB) donor kidneys. Recipient sex & age, donor age, cold ischemia time and HLA mismatches were comparable between the NHB and HB group.
Results: In the HB group a significantly larger amount of patients had direct graft function compared to the NHB group (64 vs 17%). The number of never-functioning grafts was the same in both groups (12%). DGF affected acute rejection (AR) rate only in HB donor kidneys. There was no significant difference in 3-year graft survival between HB and NHB kidneys without DGF (84 vs 83%). Graft survival after 3 years in HB kidneys with DGF was 73% compared to 83% in NHB kidneys with DGF.



Conclusion: DGF significantly affected AR rate and graft survival of HB donor kidneys, but not of NHB donor kidneys. This discrepancy may be explained by a pathofysiological difference in DGF between HB and NHB kidneys. While NHB kidneys may only suffer from extended long ischemia times, HB kidneys are also exposed to the consequences of brain death with its inherent cytokine storm and inflammatory reactions.

P-270 EMPOWERING NEW TRANSPLANT REGISTRY STUDIES: DESIGN, METHODS AND CENTER-SPECIFIC INFORMATION OF THE MYCOPHENOLIC ACID OBSERVATIONAL RENAL TRANSPLANT STUDY (MORE) REGISTRY

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The MORE registry is a prospective, non-randomized, observational study of center-specific (CS) practices and mycophenolic acid (MPA) immunosuppression (IS) strategies in *de novo* renal transplant recipients (RTR). PURPOSE: To describe the study methods and CS information
Methods: The MORE registry is conducted under normal clinical practice with physician-determined standard of care at 38 US sites with 400 *myfortic* and 200 CellCept patients followed for 3 years. To minimize potential patient selection bias, site investigators seek participation of all *de novo* adult RTR who meet eligibility criteria within 2 weeks of transplantation (Tx). Data is collected at specified post-Tx intervals (Months 1, 3, 6, 12, 24, and 36) including center-, donor-, recipient- and Tx-related information and IS compliance. The electronic data capture system includes an automated data quality review process followed by on-site 10% monitoring.
Results: As of July 31, 2008, 465 patients (61% received *myfortic*) from 38 centers have completed baseline assessments. All centers report use of an-

tibody induction therapy, most utilized in patients with high immunologic risk, DGF and ECD. Nearly 60% of the centers report use of conventional CNI exposure while 35% reduce CNI in early post-Tx and/or in maintenance. Conversely, 43% of the centers report maintenance steroid elimination and 24% report using conventional steroid exposure while 27% reduce steroids in early post-Tx and/or in maintenance. Only 2 centers report CNI elimination and 2 report universal steroid avoidance. Sixteen centers (42%) perform MPA monitoring; 31% utilize it routinely and 69% only for specific patients.
Conclusions: The MORE registry provides CS and patient level data to address clinical outcomes of kidney transplantation related to MPA therapy, providing clinicians with information about changing practices for the management of *de novo* RTR.

P-271 POST RENAL TRANSPLANTATION UROLOGICAL COMPLICATIONS

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Objectives: To explore incidence, risk factors, clinical presentation, management options, and outcome of post renal transplantation urological complications.
Patients and methods: Between November 1993 and December 2005, 646 renal transplantation procedures were performed at Hammed Al-Essa Organ Transplantation Centre. Recipients were 373 males, 273 females, 81 of recipients were children. Kidney grafts were obtained from 461 living and 185 cadaveric donors. The medical records were retrospectively reviewed for urological complications. Affected patients presented clinically with impaired kidney function and diagnosis was confirmed by ultrasound scanning, isotope renal scanning, MR- urography and antegrade urography. Ureteric stricture was managed by percutaneous antegrade ureteric dilatation and stenting, or by surgical reconstruction. Urine leak was treated by prolonged bladder drainage or surgical reconstruction. Renal stone was treated with ESWL.
Results: Urological complications were detected in 31 recipients (4.8%). Recipients were 21 males and 10 females, 4 of them were children. Kidney grafts were obtained from 19 living and 12 cadaveric donors. Urological complications were in the form of ureteric stricture in 15 (2.58%), urine leak in 15 recipients (2.58%), and Ureteric stone in one recipient (0.17%). There was no graft loss in this series secondary to urological complications.
Conclusions: In this series, the incidence of post-kidney transplantation urological complications was low (4.8%), they were more common in male recepients and following cadaveric kidney transplantation. While ureteric stricture presented late post transplantation, and was more common in children (4.23%), urine leak presented early and was more common in elderly (4.69%). All urological complications were successfully managed with no graft loss.

P-272 RENAL FIBRINOGEN-ALPHA AMYLOIDOSIS

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Fibrinogen amyloidosis is a type of hereditary amyloidosis characterized by amyloidogenic mutations in fibrinogen. In this study, we describe clinical features, renal biopsy findings and a novel diagnostic technique in 3 cases of renal amyloidosis that presented with renal insufficiency and significant proteinuria. Renal biopsy in all 3 cases showed glomeruli with massive mesangial expansion, the expansion was acellular resulting in large glomeruli filled with amorphous PAS and silver negative material with almost no discernable capillary lumen. Congo red staining was positive for amyloid in the glomeruli (with no interstitial or vascular involvement). However, immunofluorescence microscopy was negative for kappa and lambda light chains, ruling out AL amyloidosis. Electron microscopy showed non-branching amyloid fibrils measuring 8-10nm in thickness. Serum amyloid A component (SAA) staining for secondary amyloid was negative. To classify the amyloid we performed laser capture microdissection followed by liquid chromatography tandem mass spectrometry (LC MS/MS). Congo red positive regions of the glomeruli were microdissected and the extracted peptides were subjected to LC MS/MS. In all 3 patient samples, the most abundant peptides detected represented fibrinogen alpha chain, serum amyloid P component, and apolipoprotein E proteins confirming the diagnosis of fibrinogen alpha amyloid. Genetic testing of one case revealed a mutation in valine 526 position of the fibrinogen A-alpha chain. This case underwent a living related ABO incompatible kidney transplantation. The patient had a relatively uncomplicated course with gradual decline in renal function but no episodes of rejection for 5 years. 5-year protocol renal biopsy showed glomerular amyloidosis and laser dissection and LC MS/MS studies confirmed recurrent fibrinogen alpha amyloidosis. Thus, renal transplantation remains a viable treatment option for renal fibrinogen alpha amyloidosis since recurrence is slow to develop and progress, but to prevent recurrence it is likely that both renal and liver transplantation are required.

P-273 THE ROLE OF THE MALNUTRITION-INFLAMMATION COMPLEX SYNDROME IN POST-TRANSPLANT ANEMIA: RESULTS OF THE MALNUTRITION-INFLAMMATION COMPLEX SYNDROME IN TRANSPLANTATION-HUNGARY (MICSIT-HU) STUDY

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Introduction: The pathophysiology of post-transplant anemia (PTA) is not completely understood. The concurrent presence of malnutrition and inflammation called Malnutrition-Inflammation Complex Syndrome (MICS) is a frequent problem and it was associated with erythropoietin resistance in patients on maintenance dialysis. In our study, we examined the association between MICS and post-transplant anemia.
Materials and methods: 993 kidney transplanted patients were asked to participate. Socio-demographic parameters, laboratory results, transplantation related anamnestic data and medication were obtained from the charts. Malnutrition and inflammation were assessed by measuring serum leptin, Interleukine-6 (IL-6), Tumor Necrosis Factor-(TNF-α), C-Reactive Protein, albumin level and by using the Malnutrition-Inflammation Score (MIS). Anemia was defined according to the anemia guideline of the American Society of Transplantation.
Results: Mean age was 51$\pm$13 years, 57% was male, 21% were diabetics. The median time elapsed since transplantation was 72 months. The prevalence of PTA was 34% and 7% of the patients had a hemoglobin (Hb) less then 110 g/l. Serum Hb was significantly correlated with eGFR (r=0.434), the MIS (rho=-0.315), serum leptin (rho=-0.147), serum IL-6 (rho=-0.077), serum TNF-α (rho=-0.079), serum transferrin (r=0.299), serum albumin level (r=0.270) and abdominal circumference (r=0.261), $p<0.05$ for all. The proportion of anemic patients in quartiles of the MIS was 22%, 27%, 38% and 59%, respectively, $p<0.001$. In a linear regression model (R^2=0.382, $p<0.001$) age, gender, eGFR, serum ferritin, percentage of hypochrome reticulocytes and MIS were significantly and independently associated with Hb.
Discussion: MICS is independently and significantly associated with PTA and may contribute to the adverse outcome associated with anemia in the kidney transplanted population.

P-274 ASSOCIATION BETWEEN THE MALNUTRITION AND INFLAMMATION COMPLEX SYNDROME SCORE AND MORTALITY IN KIDNEY TRANSPLANTED PATIENTS

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Introduction: Chronic malnutrition and inflammation, termed Malnutrition and Inflammation Complex Syndrome (MICS) is frequent in patients with chronic kidney disease. The presence of MICS is associated with increased mortality in patients on maintenance dialysis. We have recently validated the Malnutrition and Inflammation Complex Syndrome score (MIS), which incorporates components of the Subjective Global Assessment (SGA) and other parameters, in kidney transplanted patients. Here we assessed the association between the MIS and mortality in a large sample of kidney transplanted patients.
Materials and Methods: Data from 993 transplanted patients were analyzed. Socio-demographic parameters, laboratory data, medical and transplant history, co-morbidity, type of immunosuppression, estimated glomerular filtration rate and MIS score were tabulated at baseline. The MIS score was ascertained during a brief patient interview, clinical assessment and by chart review. Data on 15-month outcome was collected prospectively.
Results: Mean age was 51$\pm$13 years, 57% was male, 21% were diabetics. The median MIS score was 3 (interquartile range 3). Both mortality and graft failure rate during the 15 months follow-up was significantly higher in patients who had high MIS score at baseline (mortality: 7% vs 1.6%; $p<0.001$; graft failure 8.7% vs 0.9%; $p<0.001$, for MIS$>$3 versus MIS$\leq$3, respectively). In multivariate Cox proportional hazard models the MIS score significantly predicted mortality ($HR_{1\ point\ increase}$ = 1.162; 95% CI: 1.043-1.295) and also graft failure ($HR_{1\ point\ increase}$ = 1.257; 95% CI: 1.134-1.393) after adjustment for several co-variables.
Conclusions: Our data suggest that the MIS score, which is a useful tool to assess the presence of MICS, is significantly and independently associated with mortality and graft failure in kidney transplanted patients.

P-275 ASSOCIATION OF TIME ON DIALYSIS PRIOR TO TRANSPLANTATION WITH LONG-TERM MORTALITY IN A PREVALENT COHORT OF KIDNEY TRANSPLANTED PATIENTS

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Introduction: Only little data is available on the effect of pre-transplant dialysis time on long-term outcome after transplantation. Previous long-term dialysis may contribute in premature mortality and graft failure in kidney transplanted patients due to increased cardiovascular risk. In our present prevalent cohort study (TransQol-HU Study) we examined the association between pre-transplant dialysis duration versus mortality; graft failure (return to dialysis) and combined outcome (mortality or return to dialysis) in kidney transplanted patients.
Methods: Data from 926 kidney transplanted patients followed at a single outpatient transplant center were analyzed. Socio-demographic parameters, laboratory data, medical history, donor characteristics and information on co-morbidities were collected at baseline. Data on 5-year outcome (graft failure, mortality) were collected.
Results: Significant association was found between pre-transplant time on dialysis and mortality ($HR_{\text{for each month increase}}$= 1.007; 95% CI: 1.003-1.011) in univariate analysis. In multivariate analyses, pre-transplant time on dialysis was a significant, independent risk factor of mortality ($HR_{\text{for each month increase}}$= 1.01; 95% CI: 1.005-1.015) and also of graft failure ($HR_{\text{for each month increase}}$= 1.008; 95% CI: 1.003-1.013) in kidney transplanted patients after adjustment for several co-variables. In the multivariate model patients with less than 1 year on dialysis (HR= 0.452; 95% CI: 0.281-0.728; p=0.001) and 1-3 years on dialysis prior to transplantation (HR= 0.592; 95% CI: 0.389-0.901; p=0.014) had significantly better survival after transplantation compared to those with more than 3 years on dialysis.
Conclusions: These findings expand on current knowledge about the significant association between longer pre-transplant dialysis duration and increased risk of mortality and graft failure in kidney transplanted patients.

P-276 ISCHEMIA-INDUCED COLLAPSING GLOMERULOPATHY IN RENAL TRANSPLANTS

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Collapsing glomerulopathy (CG) is an aggressive form of Focal and Segmental Glomerulosclerosis (FSGS) with rapid progression towards end stage renal disease. De novo CG has been rarely reported during posttransplant course, and has been associated in some cases with renal graft vascular lesions. This finding raises the important issue whether ischemia could induce podocyte transdifferentiation, an hypothesis supported by evidence of Hypoxia-Inducible Factor-induced podocyte proliferation in HIV associated nephropathy. We report here three HIV-negative renal transplant recipients, in whom early graft biopsy performed in the vicinity of segmental graft infarction, disclosed the typical features of CG. Podocyte transdifferentiation was characterized by hallmarks lesions such as loss of podocyte phenotype, podocyte proliferation and acquisition of a macrophage-like phenotype. Our investigations suggest that hypoxia-induced HIF-2a expression may be involved in both podocyte proliferation and myeloid differentiation. Altogether these data show that acute glomerular ischemia may lead to CG in renal transplants.

P-277 INTENSIVE AND PROLONGED TREATMENT OF FOCAL AND SEGMENTAL GLOMERULOSCLEROSIS RECURRENCE IN ADULT KIDNEY TRANSPLANT RECIPIENTS: A PILOT STUDY

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No treatment has consistently induced long-term remission of proteinuria in adult patients with FSGS recurrence after kidney transplantation. We undertook an open-label, non-randomized pilot trial of intensive and prolonged treatment of FSGS recurrence. Over an 18-month period, 10 adult kidney transplant recipients with FSGS recurrence received concomitantly high-dose steroids, intravenous cyclosporine for 14 days followed by oral cyclosporine therapy, and an intensive and prolonged course of plasma exchanges (PE). We compared this treatment with those of a control group of 19 patients with a FSGS recurrence transplanted between 1997 and 2005. Complete, rapid (mean 23±7 days) and sustained remission was obtained in 9/10 patients (90%) as opposed to 27% in the control group. At month 3 and month 12, proteinuria was 0.16g/day (range 0.05-0.3g/day) and 0.19 g/day (range 0.05-1g/day) respectively. Only one patient remained in partial remission at month 12 but he had already lost two previous grafts due to FSGS recurrence. PEs were stopped at month 9 in all patients except for the patient with a partial remission who remains PE-dependent. This small pilot study provides very encouraging results demonstrating that this treatment rapidly achieves complete and sustained remission in a high proportion of patients.

P-278 COLUMBIA CLASSIFICATION OF HISTOLOGICAL VARIANTS OF FOCAL AND SEGMENTAL GLOMERULOSCLEROSIS (FSGS) AND RISK OF RECURRENCE AFTER TRANSPLANTATION

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Recurrence of nephrotic range proteinuria in patients with idiopathic nephrotic syndrome (INS) and FSGS on native kidneys is associated with poor graft survival. Identification of risk factors for recurrence is therefore an important issue. In 2004, the Columbia University introduced a histological classification of FSGS that identifies five mutually exclusive variants. In non-transplant patients, the Columbia classification appears to predict the outcome and the response to treatment better than clinical characteristics alone. However, the predictive value of this classification to assess the risk of recurrence after transplantation has not been addressed. We retrospectively studied 77 patients with INS and FSGS on native kidneys who underwent renal transplantation. Of these, 42 recipients experienced recurrence of massive proteinuria. At time of recurrence, minimal change disease (MCD) was the main histological feature. On serial biopsies, the incidence of MCD decreased over time, while the incidence of FSGS variants increased. The variant type observed on native kidneys was not predictive of either recurrence or type of FSGS seen on the allograft. Patients with complete and sustained remission did not developed FSGS. In conclusion, the Columbia classification is of no help in predicting recurrence after renal transplantation or histological lesions in case of recurrence.

P-279 PREVALENCE AND RISK FACTORS OF POST-TRANSPLANT ANEMIA. A LONGITUDINAL STUDY

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Background: Posttransplant anemia (PTA) is a common complication after transplantation but its true incidence is not well known as it varies according to the criteria used in its definition. The purpose of the present study was to investigate the evolution of PTA during the first three years after transplantation, its treatment and the posible risk factors.
Patients and methods: 209 recipients with a functionig graft at 12 months were included in the study. 74% were on tacrolimus-based immunosuppression, 26% on cyclosporine-based immunosuppression and 79% also on treatmet with mycophenolate mofetil. Anemia was defined following the WHO criteria: hemoglobin (Hb) concentration $<$13 g/dl in men and $<$12 g/dl in women.
Results: The Hb concentration increased from 10.9 g/dl at 1 month to 13.5 g/dl at 12 months and to 13.4 g/dl at 36 months. The prevalence of PTA decreased from 88.5% at 1 month to 29.7% at 12 months and to 32.8% at 36 months. There were no differences in age, gender, dialysis treatment, primary renal disease, induction therapy, incidence of acute rejection and of delayed graft function and immunosuppression therapy between anemic and nonanemic recipients. There were no differences in concentrations of ferritin, vitamin B12 and folic acid. PTA at 12 months was associated with serum creatinine. At 36 months, PTA was associated with higher serum creatinine and also with lower serum albumin. At 12 months, only 19% of recipients with PTA were on

treatment with eritropoyesis stimulating agents and the percentage increased to 54% of recipients with Hb <11 g/dl.
Conclusions: PTA anemia defined according to WHO criteria is common and its incidence remained stable between 12 and 36 months. Variables associated with anemia were graft function at 12 months, and graft function and malnutrition/inflammation at 36 months.

P-280 MALIGNANCIES IN KIDNEY TRANSPLANT RECIPIENTS. INFLUENCE OF THE NEW IMMUNOSUPPRESSIVE THERAPIES

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Background: Solid organ transplant recipients are at higher risk of cancer than the general population. There are few data about the incidence of cancer with the newer immunosuppressant agents.The purpose of the present study was to investigate the incidence of malignancies in three immunosuppressive periods: azathioprin (AZA), cyclosporine (CsA) and tacrolimus (TAC).
Patients and method: 1029 first kidney allograft recipients performed between November 1979 and December 2007 were included in the sudy. The mean age at transplant was 44,6±14,9 years and the follow-up 94.1±84.2 months. Initial immunosuppression was AZA-based on 196, CsA-based on 526 and TAC-based on 307 recipients. Moreover, 277 were on mycophenolate mofetil (MMF) or an enteric-coated form of mycophenolic acid (MPA) and 102 patients received anti-CD25 induction.
Results: A total of 157 recipients had at least one tumour (15.2%), cutaneous in 92 recipients (8.9%) and noncutaneous in 65 recipients (6.3%) and 10 patients had more than one. The time of appearance was 70±58 and 102±75 months respectively (p=0.007). Among the cutaneous malignacies there wer 40 squamous cell carcinomas, 41 basal cell carcinomas and 7 Kaposi sarcomas. Among noncutaneous malignancies 15 were lymphomas, 14 digestive tract tumours, 11 kidney or urinary tract tumours and 10 lung cancers. The cumulative incidence at 5,10 and 15 years for cutaneos malignancy was 5%,10% and 16% and for noncutaneous malignancies 3%, 7% and 14% respectively. The multivariate analysis showed that age at transplant and male gender were the variables associated with cutaneous malignancies and age and treatment with OKT3 with noncutaneous malignancies. Moreover, malignancies were the cause of death in 18% of those who died with a functioning graft.
Conclusions: Posttransplant malignancies were an important cause of morbidity and mortality. Special follow-up is required in males with advanced age.

P-281 INCIDENCE OF ACUTE REJECTION AND GRAFT OUTCOME. AN HISTORICAL ANALYSIS

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Background: The new immunosuppressant agents have dramatically decreased the incidence of acute rejection. The objective of the present work was to investigate the evolution of acute rejection and its influence in graft outcome according to the immunosuppressive regime.
Patients and methods: 1029 first kidney grafts performed between November 1979 to December 2007 were included in the study. Basal immunosuppression consisted of azathioprine and steroids (AZA) in 196 recipients, cyclosporine and steroids with or without other immunosuppressant agents (CsA) in 526 patients and tacrolimus in different combinations (TAC) in 307 recipients.
Results: The characteristics of the three groups are expressed in the table 1.

	AZA	CsA	TAC	p
Age at transplant (years)	36.4±11.5	43.5±14,8	50.7±15.0	0.000
Time on dialysis (months)	34.6±25.0	33.6±33.9	27.4±28.3	0.007
Donor age (years)	29.0±14.7	37.7±12.3	47.5±16.6	0.000
HLA-DR mismatches (n)	0.5±0.6	0.9±0.7	1.3±0.6	0.000
Delayed graft function (n)	59	206	129	0,014
Acute rejection (n)	136	200	35	0.000
Serum creatinine at 6 months (mg/dl)	1.4±0.6	1.±0.8	1.6±0.6	0.000

Graft survival at 1, 5 and 10 years was 69, 56 and 46% on AZA; 82, 69 and 54% on CsA; 88, 77 and 60% on TAC (p=0.001). However, the differences disappeared when only grafts surviving more than 12 months were analyzed. The multivariate analysis showed that graft loss was associated with female gender, donor age, delayed graft function, acute rejection and immunosuppression with AZA or CsA. When only grafts surviving more than 12 months were included in the analysis age at transplant, male gender and higher serum creatinine at 6 months were the variables associated with worse graft outcome.
Conclusions: The new immunosuppressants have not improved graft outcome after 12 months. Their beneficial effects on graft rejection might be overcome by recipient age and a poor early graft function.

P-282 STUDY OF OPPORTUNISTIC INFECTIONS FOLLOWING RENAL TRANSPLANTATION AND THEIR CO-RELATION WITH IMMUNOSUPPRESSION PROTOCOLS

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The spectrum of infections, their chronological occurrence, and the risk factors are different developing countries from that of Western population. The present study aimed at examining incidence of various infections in renal transplant recipients and their co-relation with respect to underlying co-morbidities and type of immunosuppression.
A total of 1270 patients were studied for this project retrospectively (5 years) as well as prospectively (1.5 years) in this tertiary care hospital in north India. Total 231 infectious episodes were detected in 196 patients during the study period. This means that 15.5% patients had at least one episode of infection. Multiple infectious episodes were detected in 17 patients. The overall incidence of bacterial infections was found to be 6%. Bacterial infection (n=76) was the most common infection encountered followed by tuberculosis (n=63), viral infection (n=50) and fungal infection (n-28). UTI was the most common bacterial infection (86.7%) during immediate post transplant period while bacterial pneumonias and tuberculosis were predominant (32.5% each) six months after transplantation. Between 2 to 6 months of transplantation, viral etiology (CMV and herpes taken together) was the leading cause of infection (43.5%) Prevalence of HBV and HCV is 4% and 10.23% respectively The overall incidence of fungal infections was found to be 2.2%. Aspergillosis (32.1%) was the most common fungal infection followed by candidiasis and mucormycosis. Overall, zygomycosis and aspergillosis accounted for about 50% of all the fungal infections. There was statistical association between tacrolimus-MMF regime and occurrence of angioinvasive fungal infections, between recent antirejection therapy and viral infections. Significant correlation was also seen between CNI-MMF regime and occurrence of viral infections.
Infections are an important cause of mortality and morbidity in renal transplantation and more potent immunosuppression protocols predispose to more severe infections.

P-283 URINARY INTERLEUKINE PATTERN AND URINARY TRACT INFECTION AFTER KIDNEY TRANSPLANTATION

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Purpose: The early diagnosis and proper treatment of complications after transplantation, for instance allograft rejection and various infections, is important to obtain a good transplant function. Urinary tract infections (UTI's) often occur. We investigated, if urinary marker of inflammation can help to diagnose and monitor UTI.
Methods/Materials: The urinary interleukines 6 and 8 (IL6, IL8) and a marker of granulocytes in urine, the enzyme myeloperoxidase (MPO), were determined in 71 patients. In addition the patients classification “UTI” respectively “no UTI” based on the results of microbiological analyses. Statistical analyses were performed using the software “Statgraf for windows”. The receiver operating characteristic (ROC) analyses were performed using the software “Bias 8.1-2005“.
Results: The urinary IL6-, IL8- und MPO-level were significantly elevated in the UTI-group compared to the group “no UTI” (p<0,0005). The result of the ROC analysis indicated that MPO is the parameter with the best discriminatory power between the two patients groups followed by IL8 and IL6. The diagnostic sensitivity of MPO is 80%, IL6 56% and IL8 92%. The diagnostic specifity of MPO is 97%, IL6 100% and IL8 79%. After successful treatment there are no difference of the urinary IL6-, IL8- and MPO-concentrations between the two patient groups.
Conclusion: Elevated urinary concentrations of the inflammatory interleukines IL6 and IL8 and the granulocyte MPO are a sign of UTI in patients after kidney transplantation. IL8 is the marker of the best sensitivity, MPO has the highest diagnostic accuracy (minimal false positive and false negative results). The fast and simple method of determination allows an prompt control of treatment.

P-284 IMMUNOLOGICAL MONITORING AFTER KIDNEY TRANSPLANTATION: RESEARCH TO IMPROVE DIAGNOSIS OF REJECTION AND TO ESTIMATE RISK OF INFECTION

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Purpose: Not early enough treated immunological complications like infections and rejections can important compromise the success of kidney transplantation. For this reason a sensitive diagnosis is very important. The eligibility of selected cytokines and marker of inflammation to detect this complications was evaluated.
Methods/Materials: 32 patients was involved in our study. The determination of the serum parameter soluble interleukin 2-receptor (IL-2R), interleukine 10 (IL10) and CD30 as well as the urinary interleukine 6 (IL6), interleukine 8 (IL8), myeloperoxidase (MPO) and monokine induced by interferon gamma (MIG) carried out before transplantation and consecutively biweekly first month, than once monthly till 3 months after. A total of 314 serum and 309 urinary patient probes were obtained.
Results: The studied laboratory parameter contributed to diagnosis of complications in different way. Rapid decline of IL-2R, CD30 and MIG as well as no rise of IL10, IL6, IL8 and MPO characterized a uncomplicated course after transplantation. Rising concentrations of IL-2R and CD30 accompanied systemic bacterial and viral infections. Viral infections maybe cause a specific IL10-increase. UTI's cause pathological values of urinary IL6, IL8 and MPO. There are no UTI without rising IL8 and MPO. To detect rejection crisis urinary MIG is superior to the other parameters, but it is not specific. Also rising MIG-level were detected during periods of systemic bacterial and viral infections.
Conclusion: Preoperative determined values of the tested laboratory parameters didn't give a reference to an individual risk of transplant rejection or to the future transplant function. Unlike reported, MIG isn't a specific marker of transplant rejection.

P-285 PREVALENCE OF ANEMIA AND ITS CORRELATION WITH THE OUTCOMES OF KIDNEY TRANSPLANTATION

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Aim: To investigate the prevalence of anemia after kidney transplantation and its correlation with patients and allograft survival.
Methods: 330 patients who have lived for more than one year with functioning allograft after kidney transplantation have been studied. Maximum period of satisfactory functioning allograft was 19 years. The study is going on. The diagnosis of anemia was made in hemoglobin concentration less than 13 g/dl in men and less than 12 g/dl in women.
Results: Before kidney transplantation 98,7% of patients had anemia. In a one year after renal transplantation only 20% had anemia. In 3 years 28% of patients had anemia. Allograft and patients survival with normal hemoglobin level was accordingly in 2 and 1,7 times higher than in case of anemia. In 5 years after transplantation 37% of patients had anemia. Allograft and patients survival with normal hemoglobin level of blood was accordingly 1,9 and 1,1 higher than in case of anemia. In 10 years after kidney transplantation 45% of patients had anemia. Allograft and patients survival without anemia was accordingly 2,5 and 1,2 higher than in anemic patients. In 15 years of study 46% of patients had anemia. Allograft and patients survival without anemia was accordingly 3 and 1,3 higher than in anemic patients. In late period after kidney transplantation 9 recipients had erythrocytosis, but after mycophenolate mofetil were introduced into immunosupressive protocol (1998), no cases of erythrocytosis have been registered.
Conclusions: Kidney transplantation is effective method of treatment of anemia in chronic renal insufficiency. Absence of anemia correlate with substantial improvement of allograft and recipient survival in the late period after kidney transplantation.

P-286 PREVALENCE OF ARTERIAL HYPERTENSION AND ITS CORRELATION WITH THE OUTCOMES OF KIDNEY TRANSPLANTATION

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Aim: To investigate the prevalence of arterial hypertension (AH) after kidney transplantation and its correlation with patients and allograft survival.
Methods: 330 patients who have lived for more than one year with functioning kidney allograft have been divided into three groups. Arterial pressure (AP) in the first group was less than 140/90, in the second – 140-159/90-99; in the third – >160/100.
Results: Before the transplantation normal AP was in 1,8% patients, 9,2% made up the 2 group, 89% – the 3 group. In a one year after transplantation 27% had normal AP; 59% made up the 2 group; 14% – the 3 group. In 3 years 31% had normal AP, 58% made up the 2 group, 11% – the 3 group. Survival of allograft and patients with normal AP was accordingly 2,5 and 3,6 times higher than in AH. In 5 years 37% of recipients had normal AP, 59% made up the 2 group, 4% made up the 3 group. Survival of allograft and patients of the first group was accordingly 1,9 and 2,2 times higher than in AH case. In 10 years 45% had normal AP; the second group made up 53%, the third one – 2% of patients. Survival of allograft and patients with normal AP was accordingly 2,4 and 4 times higher than in AH case. In 15 years 54% of patients had normal AP, the second group made up 46%, AP>160/100 have not been registered. Survival of allograft and patients was accordingly 2,8 and 5 times higher than in the patients with AH.
Conclusions: Absence of AH correlate with substantial improvement of allograft and recipient survival in the late period after kidney transplantation.

P-287 CHANGES OF OXIDATIVE STRESS ON SKIN CANCER-SCREENED PATIENTS FOLLOWING SOLID ORGAN TRANSPLANTATION

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Transplant patients are at high risk of developing nonmelanoma skin cancer (NMSC). Ultraviolent radiation can generate oxygen free radicals (OFRs) leading to oxidative stress and carcinogenesis mainly under immunosuppression. In this study we examined changes of oxidative stress parameters on transplanted patients with or without NMSC.
116 adult, white skin-typed transplanted (kidney, simultaneous pancreas-kidney) patients have been involved. Dermatology follow-up have resulted 16 NMSC (13.8%). To monitor oxidative stress peripheral blood samples were collected to measure malondialdehyde (MDA), reduced glutathione (GSH), SH-groups, OFRs, and the activity of myeloperoxidase (MPO), superoxide dismutase (SOD) and catalase (CAT) by spectrophotometry.
Our results showed, that patients without NMSC MDA concentration significantly elevated compare to healthy controls ($p<0.05$). GSH level remained in the normal range, but SH-groups are significantly increased ($66.68\pm5,8$ vs. 40 nmol/ml). Total production of OFRs, CAT and MPO activity were in normal level. However, SOD activity elevated significantly (877 ± 25.9 vs. 500 IU/ml). These markers changed on the same tendency in patients with NMSC.
Preliminary research indicate that, exists an imbalance between pro- and antioxidant status on transplanted patients. According to examined parameters significant difference were not found in patients with or without NMSC. Thus, further studies are needed to elucidate these problems.

P-288 EFFECT OF THYMOGLOBULIN ON THE VARIOUS GRADES OF VASCULAR LESION IN ACUTE CORTICOSTEROID-RESISTANT REJECTION OF RENAL ALLOGRAFTS

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Introduction: In acute Rejection, vascular lesions are usually associated with corticosteroid resistance and poor prognosis. Although most of these rejections are mesured by antibody levels, humoral mechanism are not always involved, thus implying a different prognosis and treatment regimen.
Objectives: Analyze, in renal graft biopsies, performed for kidney function deterioration, the extent of vascular involvement in acute rejection, its association with the humoral mechanism, graft survival and response to thymoglobulin therapy.
Materials and methods: Restrospective analysis of 219 biopsies in 668 patients with renal transplant, carried out between January 1997 and september 2008 (N=36). The biopsies were classified according to the Banff Criteria (2005-2007). Two groups were analyzed: 1) Group I Biopsies with mild-to moderate or severe intimal arteritis (v1, v2) and 2) Group II biopsies showing humoral rejection. C4d staining was mesured by polyclonal and/or monoclonal antibodies and donos specific antibodies (DSA) were determined by flow cytometry.
Results: Thirteen (N=36%) of patients had renal retransplantation. 86% presented corticosteroid resistence. Twenty patients had delayed graft function. In 29 of 36 patients acute rejection ocurred shortly postransplant. transmural arteritis (v3) was a infrequent finding (N=1) whith a poor treatment response and graft loss.
Conclusion: Glomerular thromboses/HUS-Like vascular lesion correlates most closely to humoral rejection and is associated with poorer allograft sur-

Table 1

Rejection type	Group I (n=12)	Group II (n=24)
Predominant vascular lesion	arteritis v1=10; v2=2	Glomerular thromboses/ HUS_Like n=17 (70%)
DSA	n=2 (20%)	n=18 (80%)
Retransplantation	n=2	n=11 (46%)
Pretransplant panel-reactive antibody >50%	n=0	n=10 (42%)
Allograft survival	73% at 35 months	52% at 30 months
Thymoglobulin treatment	n=6 (50%). RESPONSE n=6 (100%). p=0.04	n=19 (79%). RESPONSE n=11 (57.8%)
Plasmapheresis treatment	n=0	n=9 (37.5%). RESPONSE n=4 (44%)
Resumption of dialysis	n=4 (33%)	n=13 (54%)

HUS: haemolytic-uremic like syndrome.

vival. Transmural arteritis is infrequent finding. Thymoglobulin treatment significantly improves graft survival in patients with mild-to moderate (v1) or severe (v2) arteritis.

P-289 RELATIONSHIP BETWEEN SERUM PARAOXONASE ACTIVITY, ADIPOKINES AND ASYMMETRIC DIMETHYLARGININE LEVELS IN OBESE RENAL TRANSPLANTED PATIENTS

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Increased oxidative stress and inflammation are associated with atherosclerotic coronary disease in renal transplanted patients. HDL-associated paraoxonase (PON1) prevents LDL-C from oxidation providing protection against atherosclerotic disease.

Our aim was to investigate the connection between serum paraoxonase activity, renal function, adiponectin, leptin and asymmetric dimethylarginine (ADMA) levels in renal transplanted patients. 38 male and 41 female patients (age: 49.01±14.00 ys) were included in the study. We examined fasting serum creatinine, cystatin C, homocysteine, CRP, glucose and lipids. PON1 activity was determined spectrophotometrically. Serum adiponectin, leptin and ADMA levels were measured by ELISA method.

Our patients had hypercholesterolaemia, high LDL and ApoB levels and parallel with improved renal function decreased cystatinC and homocysteine levels ($p < 0.001$). In obes pts (BMI > 30 kgm^2, n=14) was significantly higher LDL ($p<0.05$) and leptin concentrations (58.06 vs. 15.16 ng/ml, $p < 0.01$) than in malnourished pts (n=9). We did not find significant difference between serum adiponectin levels (15.12 vs. 17.34 μg/ml) and PON 1 activity (91.45 vs. 101.20 U/l) in obese and malnourished renal transplanted pts. Between serum leptin concentration and PON1 activity there was not significant negative correlation. After transplantation there was significant negative correlation between serum PON 1 activity and improved renal function ($p < 0.01$). Between PON1 activity and adiponectin levels there was a significant correlation (p=0.0276) and between PON1 activity and ADMA levels there was a negative, not significant correlation (p=0.2302). Connection between ADMA, leptin and CRP levels was positive not significant correlation.

Dyslipidaemic, obes transplanted pts have high LDL, leptin concentrations and paraoxonase activity and the correlation between leptin, ADMA and CRP levels is not significant. With improved renal function significant increased PON1 activity. Between serum PON1 activity and adiponectin levels there was a significant correlation.

P-290 TRENDS OF WEB BROWSING IN TRANSPLANT PATIENTS – A CAMBRIDGE SURVEY

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Background: Internet penetration in Europe is increasing rapidly and up to 79% of the Internet users seek health information online. The study aimed to explore the patient's trends of the Internet use in a transplant centre in the United Kingdom.

Methodology: A survey was conducted including renal transplant patients who used the Internet for transplant information within 6 months before their transplant. A 26 items survey questionnaire was used for this purpose which was developed and validated by a pilot study. Intraclass correlation coefficients (ICCs) were calculated to index test-retest reliability. Kruskal Wallis or student T-tests were used to compare different sub-groups by SPSS 15.0.

Results: Overall internet penetration in renal transplant patients was 59%. The study included 33 patients who used the Internet within 6 months before their transplant. The median age was 45 years (Range 21 to 70). The main source of information was General Practitioner (100%) followed by hospital doctors (90%). The Internet was relatively more popular (40%) as compared to books (30%, p=0.04) and magazines (38%, p=0.6). 53% of the Internet users could not find the information they required. Increasing level of education was associated with an increase in the use of the Internet (GCSE 40% and Masters 81%, p=0.001). The most popular topics explored were transplant complications 90%, treatment options 88%, pre-assessment 85%, indications 83% and immunosuppression therapy 83%. A majority of patients also explored life style topics such as post transplant exercise 80%, food 70% and travel 50%.

Conclusion: In the modern world, where e-technology becomes common place, transplant patients deserve e-services which are informative, trustworthy and useful. It is not only a challenge to but also a responsibility of transplant clinicians to make this happen.

P-291 POSTTRANSPLANT LYMPHOPROLIFERATIVE DISORDERS IN KIDNEY TRANSPLANT PATIENTS: REPORT FROM A SINGLE-CENTER OVER 25 YEARS

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Purpose: Posttranplant lymphoproliferative disorder (PTLD) is a fatal complication of organ transplantation and standard treatment is either ineffective or too toxic to tolerate. This study evaluated the characteristics of PTLD patients in kidney transplant patients from a single center, retrospectively.

Methods: There were 2,630 kidney recipients who underwent transplantation from April 1979 to June 2007 at Yonsei University Health System. And we retrospectively reviewed clinical manifestations of PTLD that developed among these subjects.

Results: Among 119 post-transplant malignancies from 2,630 renal recipients, 11 cases of PTLD were diagnosed during a mean follow up duration of 195.3±11.5 months (0∼388 months). PTLD predominantly occurred in males (Male:Female=10:1) and the mean age of PTLD patients at the time of diagnosis was 51±15 years (18∼71 years). Mean time interval to PTLD diagnosis was 126.6±74.8 months (6∼240 months). In aspect of the WHO classification, there were no early lesions, 1 polymorphic PTLD (9.1%), 10 monomorphic PTLD (90.9%). In aspect of involved organs, the gastrointestinal tract was involved in 1 case, lungs in 2 cases, bones in 2 cases, spleen in 2 cases, neck nodes in 2 cases, liver in 1 case, and multiple organs in 1 case.

Conclusions: Our findings showed that the prevalence of PTLD was 0.46%, which was less than reports from Western countries. We also found that the late onset PTLD was more common than early onset PTLD, which was another difference from previous reports.

P-292 A FRAMEWORK OF TRANSPLANT ONLINE SERVICES FOR PATIENT CENTRED CARE

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Background: The Internet has the potential to provide rapid and up to date communication, which patients can access at their convenience, and to enable patients to learn more about their disease and treatment options, therefore being better educated as consumers. The study aimed to develop a novel framework which can be used as a guiding tool to develop patient centred transplant Websites.

Methodology: Initially kidney transplants Websites were evaluated by four transplant clinicians independently with a weighted information scoring (IS). Then a 26 items survey questionnaire was used to explore the trends of the Internet use by transplant patients in Cambridge Transplant Unit. The method used was to extrapolate from the "research information" obtained from the Websites and from the survey and to bring this into the design of the framework. Intraclass correlation coefficients (ICCs) were calculated to index test-retest reliability. Kruskal Wallis or student T-tests were used to compare different sub-groups by SPSS 15.0.

Results: The quality of information on the kidney transplant websites was poor with overall median weighted IS for the 94 websites assessed was 21 (Inter-Quartile Range, IQR 0-61). The median weighted IS for both U.S.A and European websites 47 (IQR=21-61) and 45 (IQR=15-61, p= 0.27) respectively, were higher than other countries (median 22, IQR 6-30, p= 0.02). The patient's survey showed that 53% of the Internet users could not find the information they

Table 1. Framework for transplant online services

Heading	Subheading	Score	Total Score
Indications of kidney transplant	Hereditary	1	10
	Glomerulonephritis	1	
	Metabolic	1	
	Multisystem diseases	1	
	Toxic	1	
	Congenital	1	
	Irreversible Acute renal failure	1	
	Haemolytic uraemic syndrome	1	
	Reflux and obstructive nephropathy	1	
	Trauma	1	
Complications of end stage renal failure	Anaemia	1	10
	Bone diseases	1	
	Hypertension	1	
	Fluid overload	1	
	Pericarditis	1	
	Hyperkalaemia	1	
	Peripheral neuropathy	1	
	Infection	1	
	Insomnia, Anxiety and depression	2	
Treatment options	Haemodialysis	4	12
	Peritoneal Dialysis	4	
	Transplantation	4	
Transplant (Tx) team	Transplant coordinators	1	10
	Nurses	1	
	Transplant Managers	1	
	Nutritionists & Phlebotomists	2	
	Ward clerks	1	
	Ward assistants	1	
	Physicians & Surgeons	2	
	Anaesthetists	1	
Tx assessment	Medical and surgical history	2	14
	Physical examination	2	
	Routine blood tests, virology	2	
	Chest Xray, ECG/Echo	2	
	Ultrasound with Doppler	2	
	Tissue typing	2	
	Cross match and Plasma reactive antibodies	2	
Tx operation	Anaesthesia	3	10
	Incision	2	
	Steps of surgery	4	
	Picture	1	
Immunosuppression	Azathioprine & Cyclosporin	2	6
	Prednisolone & Tacrolimus	2	
	Mycophenolate & Monoclonal antibodies	2	
Tx complications	Anaesthetic complications	2	10
	Bleeding & infection	4	
	Rejection	4	
Followup	Exercise	1	8
	Food	1	
	Travel	1	
	Swimming	1	
	Minor injuries	1	
	Suspicious lumps	1	
	Surgery	1	
	Pets	1	
The donors	Living donation	5	10
	Cadaveric donation	5	
Total score			**100**

required and common topics explored were both medical and life style related. A framework was then developed consisting of 10 main items with 58 subheadings scored individually giving a total score of 100 as shown in Table 1.
Conclusion: A novel framework presented in the study may be used as a tool to develop structured online services for patient centred care.

P-293 CLINICAL OUTCOMES OF SPOUSAL DONOR KIDNEY TRANSPLANTATION: SINGLE CENTER EXPERIENCE

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Background: The supply of deceased donors is limited in Korea and most of kidney transplantations are performed using living related or unrelated donors. In this study, we investigated the clinical characteristics and outcomes of spousal donor kidney transplantation at our center.
Methods: From January 2000 to August 2008, we performed 909 cases of kidney transplantations. In this study, 475 one-haplomatch living-related donor (LRD) and 50 spousal donor kidney transplantations were retrospectively analyzed. We compared the outcomes of a spousal donor group with those of a one-haplomatch LRD group. We also compared the outcomes of husband-to wife with those of wife-to-husband subgroup.
Results: The number of human leukocyte antigen (HLA) mismatch was significantly larger in the spousal group (3.3±1.2) than in the LRD group (2.7±0.7). Tacrolimus use was greater in the spousal group (72.0%) than in the LRD group (26.6%). The incidence rate of delayed graft function was higher in the spousal group (4.0%) than in the LRD group (0.4%). There was no significant difference in the incidence of acute rejection between the two groups. Graft survival rates in the spousal group (98.0% at 1 year and 91.5% at 5 year) were comparable to those in the LRD group (99.6% at 1year and 98.7% at 5 year) (*P*=0.321). There were no significant differences in acute rejection and graft survival rates between the subgroups husband-to-wife vs. wife-to husband).
Conclusions: We achieved excellent outcomes by using spousal donors as an option to reduce the donor organ shortage.

P-294 THE EFFECTS OF GENDER ON HEALTH-RELATED QUALITY OF LIFE IN PEDIATRIC LIVE-DONOR KIDNEY TRANSPLANTATION: A SINGLE-CENTER EXPERIENCE

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Introduction and aims: A successful kidney transplant is the most effective renal replacement therapy for children with ESRD. Growth and development are maximized, and long-term results are excellent. The goal of organ transplantation is not only to strive for survival but also to give the patient the highest health related quality of life (HRQOL) possible. The domains of HRQOL are: physical, psychological, and social well-being. Health-related QOL refers to the capacity of an individual to perform social and domestic roles in order to meet the challenges of everyday living without emotional distress or physical disability. So, this study aimed at evaluation of the effects of gender on health-related quality of life (HRQOL) and overall health status in our pediatric kidney transplants.
Methods: We performed a cross sectional study in 77 children who received living renal allo-transplants in our center between 1981 and 2003. The patients were given questionnaire at a post-transplant visit. The questionnaire included demographic questions plus 57 multiple-choice questions designed to analyze various aspects of post-transplant life.
Results: Overall, the patients show satisfactory HRQOL. Most of patients lived with their parents (79.2%). The current health status did not cause difficulties at work in 70.1% and did not interfere with the social life in 62.3% of patients. Physical and sexual growth was delayed in 48% and 85.7% of patients respectively. 67.5% of patients had normal health life or minor symptoms with normal activity. There was no significant effect of gender on HRQOL except for onset of puberty, sexual function, practicing sports and obesity.
Conclusion: Overall, the patients show satisfactory HRQOL. There was mild significant effect of gender on HRQOL. These findings may help healthcare professionals to develop gender-specific interventions to optimize HRQOL of kidney transplants.

P-295 SKIN CANCER AFTER KIDNEY TRANSPLANTATION: A LARGE MULTICENTER STUDY

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Lifelong immunosuppressive treatments for sufficient graft function results in the reduction of immunosurveillance, with increased risk of various skin problems especially skin cancers. A retrospective study was conducted to appraise clinical and histological features of skin tumors in 10030 recipients who received allografts in 11 transplant centers between 1984 and 2008. Skin cancers were found in 0.47% (n=47) of the renal transplant recipients, amongst them, the most common types were Squamous cell carcinomas (n=32, 68.1%), Basal cell carcinomas (n=13, 27.7%), and Melanoma (n=2, 4.3%). The patients included 40 men and 7 women with a mean age of 53±11 (range 21-72) years and 6 to 211 (median 60) months after their transplantation. None of the recipients died of any kind of skin cancer in our study. All of our cases have had good allograft functions.
Although SCC is the most common of all skin cancers, its incidence is low in the large Iranian renal transplant recipient population. Early diagnosis and prompt wide local resection of these tumors are required in order to prevent morbidity and mortality in these patients.

P-296 STUDY OF CYTOKINE GENE POLYMORPHISM AND GRAFT OUTCOME IN EGYPTIAN LIVE-DONOR KIDNEY TRANSPLANTATION

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Background/Aims: The description of polymorphisms in many of the key immunoregulatory molecules involved in the rejection process (as cytokines) has offered a possible explanation for the individual variation in susceptibility to rejection and differences in allograft survival. We examined the relationship between recipient interleukin-2 (IL-2) and interleukin-10 (IL-10) genotype and clinical outcome in patients with surviving allografts for at least 5 years.
Patients and methods: The material compromised 50 patients with end-stage renal disease who received their first live-donor renal allografts between 2001 and 2003. All the patients received basiliximab induction and were maintained on prednisolone, sirolimus and MMF (38 recipients) or tarcolimus (12 recipients). 43 patients were subjected to protocol biopsy one year post-transplantation. Their sera were assayed for IL-2 (-330) and IL-10 (-1082) genotyping using real time-PCR amplification reaction. The relationship between IL-2 and IL-10 genotyping and the frequency of acute rejection episodes, chronic allograft nephropathy (CAN), results of protocol biopsies and survival of both patients and grafts were evaluated.
Results: The mean duration of post-transplant follow up was 72.48±6.28 months (range= 62-85). Analysis of the data in relation to IL-2 production showed insignificant relationship between IL-2 genotype and the frequency of acute rejections (P=0.357), CAN (P=0.181), results of protocol biopsies (P=0.768) and graft & patient survivals.
Similarly, insignificant relationship between IL-10 genotype and the frequency of acute rejections (P=0.578), CAN (P=0.964), results of protocol biopsies (P=0.465) and graft & patient survivals was found.
Combined analysis of both cytokines had insignificant relationship with the frequency of acute rejections (P=0.762), CAN (P=0.875), results of protocol biopsies (P=0.977) and graft & patient survivals.
Conclusion: There was no impact of IL-2 or IL-10 genotype and occurrences of acute rejection, CAN or graft & patient survivals in our Egyptian live-donor kidney transplant recipients.

P-297 MORPHOLOGY OF FOCAL AND DIFFUSE C4D-POSITIVE ACUTE ANTIBODY-MEDIATED (AAMR) KIDNEY ALLOGRAFT REJECTION (AR)

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Purpose: Morphological manifestations of focal and diffuse C4d-positive AAMR of kidney allograft were investigated.
Materials/Methods: 20 allograft biopsies from 20 patients with allograft dysfunction were evaluated retrospectively. Paraffin sections were stained with H&E, PAS, and immunoperoxidase labeling with antibodies to C4d, CD45R0 (T-lymphocytes) and CD68 (macrophages). H&E and PAS stained sections were assessed according to the Banff classification. Additional morphological changes, potentially related to AAMR, as well as the number of T-lymphocytes and macrophages in PTC, glomeruli, arterial wall, interstitium were also scored semiquantitatively.
Results: All biopsies were classified as C4d- (<10% of PTC; acute T-cells-mediated rejection (ATMR, N=3) and borderline changes (BC, N=1)), C4d+ (≥10-50% of PTC; AAMR only (N=2), AAMR+ATMR (N=3), AAMR+BC (N=4)), C4d++ (>50% of PTC; AAMR only (N=1), AAMR+ATMR (N=5), AAMR+BC (N=1). There were no significant differences in clinical data between groups.
Glomerulitis score in C4d++ biopsies (3 (2-3)) was higher than in C4d- (0,75 (0,25-1,5), p<0,01 and than in C4d+ (2 (1,5-2)), p<0,01. The presence of neutrophils in glomeruli (0% in C4d- vs. 44% in C4d+ vs. 71% in C4d++), and number of neutrophils per glomerulus (0 (0-0) vs. 0 (0-2) vs. 2 (0-3), respectively), number of T-lymphocytes per glomerulus (0 (0-0,7) vs. 0,73 (0,32-2,4) vs. 3,2 (2,2-8)) increased significantly only in C4d++ (p<0,05), but not in C4d+ AR. Capillaritis score was increased already in C4d+ (2 (1-3)), p=0,01, and also in C4d++ (2 (2-3)), p<0,01, compared with C4d- AR (0 (0-0,5)). The same pattern of changes was characteristics of diffuse capillaritis and interstitial macrophages score.
Conclusion: Glomerulitis index is increasing gradually according to the level of C4d-deposition in PTC. Increasing of neutrophils and T-lymphocytes in glomeruli are only characteristics of diffuse C4d-deposition in PTC. Diffuse capillaritis and interstitial macrophages infiltration appears already under focal C4d-deposition.

P-298 RENAL TRANSPLANTATION IN PATIENTS TREATED WITH CINACALCET

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It is know that the higher the serum PTH levels at transplantation the longer the time for recovery. Cinacalcet, a calcium sensing receptor antagonist, has been recently introduced to treat pts with ESRD with secondary iper PTH, but there are no data dealing with renal transplantation in subjects assuming the drug.
Purpose: To evaluate the behaviour of Ca-P metabolism after renal transplantation in patients treated with Cinacalcet.
Materials: 6 pts (5 F, 1 M); aged 53-66 years, on RDT since on 2.6 years average, underwent renal transplantation from cadaveric donor between 2005 to 2008. Causes of renal failure were: reflux nephropathy (2 pts), polycystic disease (2 pts), glomerulonephritis (1 pt),unknown (1 pt)
They all were treated with Cinacalcet (30 to 60 mg/d) since 3 to 12 months before transplantation. Immunosuppressive therapy consisted of basiliximab, methyl-prednisolone, tacrolimus (5 pts) or cyclosporin (1 pt), mycophenolate mofetil. Cinacalcet was withdrawn immediately before surgery
Results: All patients recovered a good renal function after grafting.
Only one patient required Ca supplementation in the first few days after surgery, to keep the values within the normal range. One week after transplantation the values were:Ca corrected for serum albumin: 8.22 mg/dl ± sd 0.69 (range 6.2-9.6 mg/dl), P 4.63 ± sd1.69 (range 1.9-8.8 mg/dl), PTH 269 pg/dl ± sd 154 (range 164-495 pg/dl). At 3 months follow up 2 pts were receiving calcitriol supplementation (0.25 mcg/d) while Ca supplementation was no longer needed in any pt. The mean values were: Ca 8.3 mg/dl ± sd 1.08, P 2.5 mg/dl ± sd 2.77, PTH 119 pg/dl ± sd 48.65.
Conclusion: Our results confirm that Cinacalcet is effective in reducing serum PTH to safe levels before surgery and that transplantation can be performed, stopping Cinacalcet administration, without serious Ca-P derangement in the post operative period.

P-299 MORPHOLOGICAL AND IMMUNOHISTOCHEMICAL MANIFESTATIONS OF KIDNEY ALLOGRAFT ACUTE REJECTION (AR) VARIANTS

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Purpose: Morphological manifestations of acute T-cells- (ATMR) and antibody-mediated kidney allograft rejection (AAMR) were investigated.
Materials/Methods: 20 allograft biopsies from 20 patients with allograft dysfunction were evaluated retrospectively. Paraffin sections were stained with H&E, PAS, and immunoperoxidase labeling with antibodies to C4d, CD45R0 (T-lymphocytes) and CD68 (macrophages). H&E and PAS stained sections were assessed according to the Banff classification. Additional morphological changes, potentially related to AAMR, as well as the number of T-lymphocytes and macrophages in PTC, glomeruli, arterial wall, interstitium were also scored semiquantitatively. Image analysis was used to quantitatively evaluate interstitial T-lymphocytes and macrophages infiltration.
Results: All biopsies were classified as C4d+ (≥10% of PTC; N=16) and C4d- (N=4). AAMR only (N=3), AAMR+borderline changes (N=5), AAMR + ATMR (N=8) were found in C4d+ biopsies. ATMR (N=3) and borderline changes were diagnosed in C4d– biopsies.
The key features of C4d- biopsies were: increasing of T-lymphocytes interstitial infiltration (62±28 per HPF vs. 16±9, p=0,0001) with the same level of macrophages infiltration (25±19 vs. 23±11) comparing with implantation biopsies, mild mononuclear glomerulitis and capillaritis; tubulitis.
The distinguishing morphological features of C4d+ vs. C4d– AR included: glomerulitis score, 2 (2,0-2,5) vs. 0,75 (0,25-1,5); p=0,039; neutrophilic glomerulitis, 56% vs. 0%; p=0,043; PTC capillaritis, 2 (1-3) vs. 0 (0-0,5); p=0,002; < 50% neutrophils in PTC, 56% vs. 0%; p=0,043; diffuse capillaritis, 81% vs. 0%; p=0,002; PTC dilatation, 13% vs. 0%; p=0,043; T-lymphocytes per glomerulus, 2,4 (0,3-8) vs. 0 (0-0,7); p=0,038, macrophages interstitial score under semiquantitative analysis 1 (1-1,5) vs. 0 (0-0); p=0,009, and macrophages number per HPF under quantitative analysis – 75±41; p=0,003, T-lymphocytes number per HPF, 144±94, p=0,001.
Conclusion: Routine staining for C4d, T-lymphocytes and macrophages with semiquantitative evaluation and quantitative image analysis is advisable for differential diagnostics of AR variants.

P-300 *PNEUMOCYSTIS* PNEUMONIA (PCP) AND *PNEUMOCYSTIS JIROVECII* CARRIAGE IN RENAL TRANSPLANT PATIENTS

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Introduction: Rising numbers of up to 25% of transplant patients suffer from *Pneumocystis* pneumonia (PCP). The PCP often occurs two to six months after transplantation in these patients.
Methods: Since 2001, we examined 22 patients with pneumonia after renal transplantation for the presence of *Pneumocystis jirovecii (P. jirovecii).* The laboratory diagnosis of PCP and *Pneumocystis* carriage was established by specific staining methods and nested PCR (mtLSU nPCR) from broncho-alveolar lavage and induced sputum.
Results: With mtLSU nPCR, 8 of 22 (36.4%) renal transplant patients had a PCP (both PCR steps positive), 5 (22.7%) had a *Pneumocystis* carriage (only second PCR step positive) and in 9 (40.9%) no *Pneumocystis* organisms or DNA were detectable. Five of 8 PCP patients had a delayed graft function after transplantation and 7 of 8 patients had a positive CMV antibody status; one patient showed a CMV reactivation. All five patients with *Pneumocystis* carriage had a positive CMV antibody status at the time of transplantation. The time interval from transplantation to PCP diagnosis ranged from six month up to three years.
Conclusions: PCP was present in 36.4% of transplanted patients with suspected pneumonia. Five of 8 patients received an immunosuppressive regimen with cyclosporine, mycophenolate mofetil (MMF) and prednisolone as basal immunosuppression, the three other patients were at high risk for acute rejection and received tacrolimus, MMF and prednisolone. In three of our patients with PCP, we retrospectively found an overlapping of hospitalisation times after renal transplantation in the same ward. Clinical onset of PCP infection occurred in all three patients nearly six months after transplantation. Thus, a person-to-person transmission seems to be plausible in these cases.

P-301 HYPERGLYCEMIA AFTER TRANSPLANTATION IN CALCINEURIN INHIBITOR TREATED INDIAN RENAL TRANSPLANT RECIPIENTS: INCIDENCE AND RISK FACTORS

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Purpose: Hyperglycemia after renal transplantation (HAT) is a major metabolic complication. We evaluated the incidence and risk factors for HAT in Indian patients receiving calcineurin inhibitor based immunosuppression.
Methods: All non-diabetic patients who received renal transplants, over a period of one and half years were included in this study and were followed up for minimum of one year. One hundred and twelve patients were eligible and were divided into two groups: Group1 (Cyclosporine-based immunosuppression, n=38) and Group2 (Tacrolimus-based immunosuppression, n=74). All patients in addition received one antimetabolite (azathioprine or mycophenolate mofetil) and steroids. Acute rejections were diagnosed clinically and substantiated by graft biopsy. New onset diabetes mellitus (NODM), impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) were diagnosed as per American Diabetes Association (ADA) criteria.
Results: The two groups were age and sex matched. All except two were living related transplants. There was no significant difference in acute rejection rates between the two groups. Antibodies to hepatitis C were detectable in 19.6% patients; however, none of them received interferon therapy prior to transplantation. Overall, HAT developed in 34.8% of cases (Group1- 13.2%, Group2- 47.3%, p=0.009). NODM occurred in 13.2% in group 1 and 39.2% in group 2 (p=0.009). Of these, 41% cases required oral antidiabetic agents, 5.1% required insulin while the rest were managed with dietary modifications. On multivariate analysis, use of tacrolimus (OR 15.3, p=0.002) and hepatitis C positivity (OR 8.7, p=0.003), emerged as significant risk factors for the development of HAT. One year patient and graft survival were not different in those who developed HAT as compared to normoglycemics.
Conclusions: Cyclosporine should be the calcineurin inhibitor of choice in Indian patients at low immunological risk because of the very high incidence of HAT with tacrolimus.

P-302 AN IDEA OF URETER RECONSTRUCTION OF RENAL TRANSPLANTATION IN LONG-TERM DIALYSIS PATIENTS

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Background: Urinary tract-related problems are reported in 2-10% of renal graft recipients as surgery-related complications. Urine leakage and bladder rupture due to a failure of the sutures are often reported when ureter-bladder anastomosis is performed using an atrophic bladder in long-term dialysis patients. Because the ureter is not atrophic in most cases even in long-term dialysis patients, however, we conduct ureter reconstruction by anastomosing recipients' own ureter and a transplanted graft ureter
Objective: Complications of ureter reconstruction performed through anastomosis of the patient's own ureter and a transplanted graft ureter were evaluated in renal graft recipients with a history of dialysis for 10 years or longer
Subjects: This reconstruction has been performed in 8 patients, 5 men and 3 women, since 2002. Seven received donated grafts and the other a live graft. The mean observation period was 48.8 months. Surgical method: Blood flow through the transplanted kidney was restored by arteriovenous anastomosis, and the patient's own ureter was exposed to make a 1.5 cm longitudinal incision for anastomosis after observing the flow of initial urine. End-to-side anastomosis with the graft ureter was performed. A 6-0 absorbable monofilament suture was used for suture. The ureteral stent is not left indwelling after anastomosis.
Results: None of the eight patients showed any complication such as urine leakage, stenosis and ureteral stones. Anastomosis remained patent for an average of 48 months or more. Ureteral occlusion due to intra-ureteral thrombi attributable to adenoviral hemorrhagic nephritis occurred in one patient. However, the anastomosed area remained patent with no stenosis when nephritis was cured.
Conclusion: The surgical method used in the present study made it possible to safely reconstruct the ureter. It is also satisfactory in terms of log-term patency.

P-303 OUTCOME OF RENAL TRANSPLANT RECIPIENTS WITH POST-TRANSPLANT LYMPHOPROLIFERATIVE DISORDER – 20 YEAR EXPERIENCE AT NOTTINGAM RENAL TRANSPLANT UNIT

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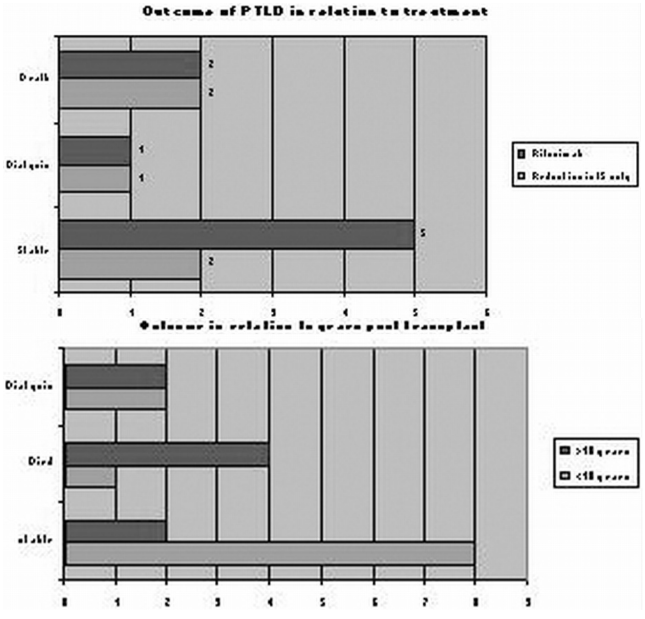
Purpose: To systematically look in to outcomes of renal recipients diagnosed with PTLD and identify factors affecting outcomes
Method: We retrospectively analysed cases over the last 20 years in our centre. 19 cases were identified from 741 adult renal transplant recipients. Analysis were carried out on demographic data (age, ethinicity & gender), variation in presentation, cumulative treatment doses and outcome. The cumulative dose of immunosuppresants was calculated as gram per month unit.
Results: Overall incidence of PTLD was 2.5%. All patients were caucasians. The time to diagnosis of PTLD ranged from less than 1 year to 20 years (mean 8.8 years) and cumulative dose varied widely with patinets on low dosage also developing PTLD. 79% of patients had extra nodal disease; the majority having GI/ intra-abdominal disease (63%). Patients presenting acutely had GI & CNS involvement whilst those presenting chronically had lung, allograft and other intra-abdominal & nodal involvement. Majority of them were B cell lymphoma (5% T cell lymphoma). Majority of them had insitu hybridization positive for EBV DNA in biopsy specimens. Treatment with rituximab had advantage over



reduction of immunosuppresants alone (62% versus 40% had stable kidney function) and fewer patients reached end stage (13% versus 20%).
Outcome was better in patients diagnosed within ten years of transplantation (9% versus 50% mortality).
The site of involvement didnot appear to influence the outcome.
Conclusions: Overall incidence was comparable with other reported data. Our data suggest survival advantage in rituximab treated patients compared to reduction of immunosuppresants alone. Outcome were worse in patients with PTLD diagnosed after ten years.

P-305 GASTROINTESTINAL CYTOMEGALOVIRUS INFECTION IN KIDNEY TRANSPLANTATION PATIENTS, PATIENTS WITH END-STAGE KIDNEY DISEASE AND IMMUNOCOMPETENT PATIENTS

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Aim: Cytomegalovirus is the most common viral pathogen affecting organ transplant recipients. The objective was to determine in which extent CMV can be found in the gastrointestinal tract in kidney transplant recipients and to compare them with patients in dialysis and randomly chosen otherwise healthy patients who were referred for oesophagogastroduodenoscopy (OEGD) or colonoscopy.
Patients and methods: Biopsies for CMV examinations were obtained from 130 oesophagogastroduodenoscopies and 54 colonoscopies performed on 82 kidney transplant recipients, 49 dialysis patients with chronic end-stage kidney disease and 53 immunocompetent patients because of clinical indications. CMV was demonstrated by immunohistochemistry, both in frozen sections using a monoclonal antibody against CMV-specific antigens (pp65 matrix protein) and in paraffin sections by means of a monoclonal antibody against the delayed early protein (p52).
Results: CMV positive cells were found in the gastroduodenal mucosa in 46 (68%) of the kidney transplant recipients, in 9 (31%) dialysis patients and in 15 (45%) of the immunocompetent patients, in the colorectal mucosa in 7 (50%), in 6 (30%) and in 9 (45%) of the patient groups, respectively. In the transplant recipient group, 4 patients had severe, and 10 patients moderate CMV infection in the gastroduodenal mucosa while all dialysis and immunocompetent patients had only mild involvement.
Conclusion: Kidney transplant recipients had more often and more severe CMV infection in gastrointestinal tract than other patients groups, especially in the gastroduodenal mucosa. In dialysis patients gastrointestinal CMV activation does not seem to be a significant risk factor. In immunocompetent hosts with gastrointestinal complaints CMV positive cells occur as often in the upper and lower gastrointestinal tract. CMV diagnostics is recommended always if biopsies of gastrointestinal tract are taken from kidney-transplanted patients.

P-306 ANTIBODY-MEDIATED ACUTE REJECTION (AMAR): AN IMMUNOLOGICAL AND CLINICAL STUDY FROM 14 FRENCH KIDNEY TRANSPLANTATION CENTRES IN 2007-2008

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A registry for AMAR was created, including14 French kidney transplantation Centres (Angers, Bordeaux, Brest, Caen, Clermont-Ferrand, Dijon, Grenoble, Limoges, Nancy, Poitiers, Reims, Rouen, Strasbourg, Tours). Diagnostic criteria were defined according to the 2005 Banff Classification. Clinical, histocompatibility and anatomopathology data were collected. In 2007 and 2008, 1984 kidney transplantations were performed in these centres. Over this period, 40 patients experienced AMAR and were registered (17F/23H, mean age = 45y). Range of transplantation was first for 23 recipients, second for 12 and third for 5, concerning only 2 living donors. 29 patients had prior sensitising events and 11 were considered to be naive. The prospective cross-match by complement-dependent cytotoxicity was IgG negative (on T and B cells) in all cases with current sera.
Mean creatinine level at diagnosis was 272 μmol/L. Apart from typical histological lesions, C4d deposits in renal transplant biopsies (36/40) and/or Donor Specific Antibodies (DSA) were present (31/40).
Twenty two AMAR cases occured during the first 3 months post-transplantation (group 1). They concerned 21 patients with history of sensitising events, and only one naive recipient. No clinical event (non compliance, transfusion, pregneancy, minimization of immunosuppression) was identified.
Eighteen cases occured between 3 months and 13 years after transplantation (group 2), including 10 naïve and 8 non-naïve recipients. For 13/18 patients, AMAR could be linked to clinical events (non compliance or minimization of immunosuppression for adverse events in 9 or 3 cases respectively). Interestingly DSA were present before transplantation (disregarded or retrospectivly found) in 14% of patients in group 2, versus 65% in group 1.
This registry is a useful tool to evaluate the incidence of AMAR. It seems that two groups with different immunological and clinical patterns likely exist.

P-307 PER OPERATIVE FLUID MANAGEMENT IN PREEMPTIVE RENAL TRANSPLANTATION:A CASE-CONTROL STUDY

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Peroperative fluid management in preemptive, ie non dialyzed, kidney recipients has never been defined. In non preemptive renal transplantation, maintaining adequate intravascular volume during surgery has been shown to be important to obtain appropriate graft function.
We compared peroperative fluid management between preemptive and non preemptive kidney recipients at our institution.
Patients and methods: Among the 666 recipients between 1999 and 2007, we identified all preemptive renal transplantations (n=31). We performed a case control study (2 controls: patients grafted before and after each case per case) to compare the peroperative fluid management and short term outcome (weight gain and renal function) between the two groups.
Results: Demographic characteristics of donors and recipients and the number of first renal transplantations were not significantly different between the two study groups. There were more living donors in the preemptive group (25% vs 3%,$p<0.01$). In preemptive transplanted patients, mean creatinine clearance (Cockroft formula) before transplantation was 12 mL/min. Perioperative fluid management was identical between the two groups (2450 mL vs 2470 mL,p=ns), with large amount of albumin (1403 mL vs 1474 mL,p=ns). Colloids were rarely used; for two recipients only in the control group. Post transplantation increase of weight was significantly lower in the preemptive group on day two (1.05 kg vs 2.5 kg,$p<0.01$) and on day five (0.28 kg vs 1.59 kg,$p<0.05$) but the difference did not remain significant. Serum creatinine was significantly lower on day 5 in the preemptive group (222 vs 351 micromol/L,$p<0.05$) but the difference did not remain significant at month 3 (133 ± 36 vs 138 ± 43 micromol/L).
Conclusion: At our institution, fluid management was not different in preemptive and non preemptive kidney recipients. Further studies are required to evaluate if specific management in these patients is needed.

P-308 INTERFERON-γ (γ-IF),INTERLEUKINE 10 (IL-10), TRANSFORMING GROWTH FACTOR-β (TGF-β) BLOOD LEVELS IN DIAGNOSIS OF CHRONIC RENAL ALLOGRAFT DYSFUNCTION

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There are several causes of late renal allograft dysfunction and accurate diagnosis is important for successfull treatment. So the search of non-invasive diagnostic tests is actual. The purpose of the study was to estimate the value of cytokine blood levels ixamination for diagnosis of chronic renal transplant pathology.
Blood levels of γ-IF, IL-10, TGF-β and their ratios were examined in 39 renal transplant recipients 1 to 4,5 years after surgery. The allograft state was evaluated according to biopcy data. The results were compared in five patient groups: I- normal function (n=10); II – chronic rejection (CR, n=8); III – calcineurin inhibitor toxicity (CIT, n=8); IV – recurrent nephritis (n=3); V – non specific interstitial fibrosis and tubular athrophy (n=10). The results are presented in table 1. The highest level of γ-IF was found in CR group and IL-10 – in CIT group. TGF-β level was significantly lower in CR group and higher in CIT group. To make clear the activity balance between different T limphocyte subsets we assessed the ratios: γ-IF/IL-10 and γ-IF/TGF-β in the studied groups. The results of analysis showed the highest γ-IF/IL-10 ratio in CR group and the lowest – in CIT group. γ-IF/TGF-β ratio was the highest in CR group and differed significantly from all other groups.
Conclusion: Determination of γ-IF, IL-10 and TGF-β blood levels may be usefull for the assessment of renal allograft state and the reason for chronic allograft dysfunction. The rise of γ-IF level and γ-IF/IL-10 ratio more than 1,5 as

Table 1. γ-IF, IL-10, TGF-β blood levels (pg/ml) and their ratio in renal transplant recipients

Groups	γ-IF	IL-10	TGF-β	γ-IF/IL-10	γ-IF/TGF-β
I	135±2,9	104±3,0	102±3,3	1,29±0,02	1,32±0,03
II	168±5,5	106±2,7	81±2,2	1,58±0,04	2,07±0,04
III	151±6,3	125±4,6	115±3,7	1,20±0,05	1,37±0,05
IV	136±6,7	96±6,1	100±6,3	1,31±0,05	1,36±0,03
V	148±5,2	110±5,8	107±4,1	1,35±0,04	1,38±0,05
	2-1,4,5 <0,05	3-1,2,4 <0,05	2-1,4,5 <0,05; 3-1,2,4<0,05	2-1,3,4,5 <0,05; 3-5<0,05	2-1,3,4,5 <0,05

well as γ-IF/TGF-β ratio more than 2,0 may be an additional sign of CR. The rise of TGF-β and IL-10 levels as well as decrease of γ-IF/IL-10 ratio lower than 1,2 is associated with CIT.

P-309 EVEROLIMUS IN MAINTENANCE RENAL TRANSPLANT RECIPIENTS: THE ASCERTAIN STUDY

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Chronic allograft nephrotoxicity (CAN), also described as interstitial fibrosis and tubular atrophy (IFTA) is a major concern with Calcineurin-inhibitor (CNI: cyclosporine, tacrolimus)-based immunosuppression. The ASCERTAIN study evaluates the effects of the proliferation signal inhibitor (PSI) everolimus, with simultaneous CNI-elimination or CNI-reduction on progression of renal dysfunction and development of atherosclerosis in maintenance renal transplant recipients (MnRTxR) with renal impairment.

Methods: ASCERTAIN is a 24-month, randomized, multicenter, open-label study. Key inclusion criteria were: age >18 years, primary or secondary renal transplant more then 6 months ago, unchanged immunosuppressive regimen for the previous 3 months and renal impairment defined as GFR 30–70mL/min/1.73m^2. Patients were randomized 1:1:1 to (A) continuation of current immunosuppressive regimen without everolimus or (B) initiation of everolimus (C-0h 8–12ng/mL; initial dose 4mg/day) with discontinuation of CNI or (C) initiation of everolimus (C-0h 3–8ng/mL; initial dose 3mg/day) with reduction of CNI blood levels by 70–90%. All patients received mycophenolic acid or azathioprine and steroids.

The primary study objective is the difference in renal function assessed by measured GFR (mGFR), between the groups at month 24. Secondary objectives are progression of CAN/IFTA by biopsy finding, graft and patient survival and incidence and severity of BPAR at month 24. Progression of atherosclerosis will be assessed at month 24 by carotid artery ultrasonography doppler examinations (intima-media thickness-IMT).

Results: 395 patients (65.8% male, mean age 48.9 years) at 5.6±4.1 years post-transplant were enrolled from 77 centers globally between February 2005 and August 2007. The study is ongoing and the data will be available in late 2009.

Conclusion: ASCERTAIN is the first study investigating the clinical impact of everolimus with CNI-elimination or CNI-reduction on renal function, on CAN/IFTA and on atherosclerosis by IMT in MnRTxR with renal impairment.

P-310 ROLE OF RESISTIVE INDEX MEASUREMENT IN DIAGNOSIS OF ACUTE REJECTION EPISODES FOLLOWING SUCCESSFUL KIDNEY TRANSPLANTATION

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Objectives: This study was performed to evaluate the role of resistive index (RI) in the diagnosis of rejection episodes following successful kidney transplantation.

Methods: One hundred and one unrelated living first kidney allograft adult recipients (75 male and 26 female) with the mean age of 39 years were enrolled in this study and followed for 6 months prospectively. The measurement of RI by Doppler ultrasonography was performed in all patients on days (3 and 7), months (1, 3, and 6) and when graft dysfunction occurred. Serum creatinine level as well as serum cyclosporine level were determined.

Results: Twenty-seven (26.7%) patients experienced 33 episodes of acute rejection during follow-up. There were statistically significant differences between mean RI in patients with normal graft function and rejecting graft (0.606±0.065 vs. 0.866±0.083, p<0.05) respectively. Overall, elevated serum level of cyclosporine, ischemic tubular necrosis and renal artery thrombosis was observed in 8, 5 and 3 patients, respectively. No association was found between these factors and RI.

Conclusion: RI was significantly higher in patients with acute rejection than others. Besides, it had no association with ATN or cyclosporine toxicity. Hence, RI could be used to diagnose acute renal allograft rejection following renal transplantation.

P-311 COULD PROPHYLACTIC MONOCLONAL ANTIBODY BLOCKER INJECTION HELP KIDNEY GRAFT SURVIVAL?

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Objectives: This study was designed to further evaluate the role of monoclonal antibody blocker injection (daclizumab) in early and late kidney graft survival and prevention of graft loss.

Material and methods: From 2007 to 2008, 57 kidney transplant recipients were enrolled prospectively in this case-control study at our center. Twenty-three patients (cases) received 1 mg/kg daclizumab (24 hours before and 14 days after transplantation) while 34 patients (controls) did not receive daclizumab. The same immunosuppressive protocol (oral prednisolone, mycophenolate mofetil and cyclosporine A) was administered for all participants. The evidence of delayed graft function (DGF), acute rejection, therapeutic pulse of prednisolone and/or anti thymoglobulin (ATG), cytomegalovirus (CMV) infection, urinary tract infection (UTI) as well as early and late graft function were evaluated and compared between two groups.

Results: The mean age in case and control groups was 39.7 (range 18-61) and 37.1 (range 13-60) years, respectively. The evidence of DGF was 4% vs. 3%, reversible acute rejection was16% Vs.14.5%, irreversible acute rejection was 0% vs. 9% (p-value <0.05) in case and control groups, respectively. Therapeutic ATG used in 21% vs. 23%, and pulse prednisolone 26% vs. 20% respectively. The average follow-up period was 9.3 months. In case and control groups, the mean creatinine level was 1.4 (range 0.9- 4) mg/dl vs. 1.35 (range 0.5- 3.5) mg/dl at discharge, while in the last follow-up session, it was 1.35 (range 1-2) mg/dl vs. 1.2 (range 0.5-2.7) mg/dl, respectively. CMV infection occurred in 30% vs. 35%, and UTI was observed in 17% vs. 19% of the cases and the controls, respectively.

Conclusion: The prophylactic administration of daclizumab has an effective role in the improvement of early graft survival and the prevention of irreversible acute rejection. Moreover, acute rejection might be handled better by using daclizumab.

P-312 ADIPONECTIN AND INSULIN RESISTANCE: COMPARISON OF HEALTHY SUBJECTS,UREMIC PATIENTS AND KIDNEY TRANSPLANT RECIPIENTS

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Introduction: Adiponectin, an important adipocytokine with antiatherogenic and anti inflammatory function, has been supposed to be inversely correlated with insulin resistance (IR) and variety of states associated with IR like cardiovascular disease and hypertension. Mechanisms involved in adiponectin metabolism are unknown but kidneys are suspicious to play a part. It is noteworthy that cardiovascular disease and IR are frequent complications after kidney transplantation (KT_x) which influence both patient and graft survival. To evaluate the importance of adiponectin in this regard and to investigate the possible role of kidney in adiponectin clearance.

Material and method: An observational study designed to contemplate the relationship between adiponectin, IR and kidney function in 20 healthy subjects and 26 end stage renal disease (ESRD) patients on hemodialysis and 14 days after successful KT_x. Plasma adiponectin levels were also compared in three different states.

Results: We found a remarkable higher adiponectin level in ESRD group in comparison with healthy subjects which remained high after KT_x ($p<0.001$). In addition, IR was much higher in ESRD patients than controls which increased to higher amounts after KT_x ($p<0.05$). There was no correlation between adiponectin, IR and kidney function in normal individuals, in uremic patients and in KT_x recipients.
Conclusion: Our results indicate that mechanisms other than kidney function are probably involved in adiponectin and IR status in uremic condition or immediately after renal transplantation.

P-313 CYTOMEGALOVIRUS INFECTION AND DISEASE FOLLOWING RENAL TRANSPLANTATION: PRELIMINARY REPORT OF INCIDENCE AND POTENTIAL RISK FACTORS

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Background: Cytomegalovirus (CMV) infection and disease are the major causes of morbidity and mortality after renal transplantation. However, the incidence and potential risk factors are different in developing countries. We sought to determine the precise incidence and potential risk factors of CMV infection and disease in our center. We also aimed at specifying the groups of recipients who may benefit from preemptive therapy.
Methods and materials: 40 renal transplant recipients were recruited and monitored regularly for CMV infection within 6 months after transplantation using CMV IgM and IgG titering, pp65 antigenemia and CMV DNA by PCR. Thorough laboratory and physical examinations were performed to detect CMV disease. We evaluated the role of different factors in CMV infection and the disease development using Cox regression and Kaplan-Meier statistical models.
Results: CMV infection and disease was detected in 33 (82.5%) and 10 (25%) subjects, respectively. The average time for the development of the infection to the disease was 4.7 and 11 weeks, respectively. PCR was the initial method of diagnosis in 22 (67%) cases. In comparison to other recipients, patients who received antithymocyte globulin (ATG) showed a significant decrease in the time of disease development (P=0.009). In multivariate survival analysis, ATG therapy remained an independent risk factor for CMV disease (OR: 6.8; P=0.02).
Conclusion: Due to low rate of CMV infection to disease progression, it does not seem reasonable to perform preemptive therapy in all infected cases. ATG therapy was an independent risk factor for CMV disease. Recipients under this treatment would be proper candidates to receive preemptive therapy.

P-314 -174 G/C INTERLEUKIN 6 GENOTYPE IS RELATED TO HIGHER RISK OF GRAFT LOSS AND GFR DECLINE IN 5-YEAR OBSERVATION IN KIDNEY GRAFT RECIPIENTS

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Aims: Polymorphisms of TNF-a, IL-10, IL-6, IFN-g and TGF-β_1 genes are related to the constitutional gene expression and production of appropriate cytokines. The aim of this study was to assess the impact of TNF-a, IL-10, IL-6, and IFN-g genotypes on GFR and long-term kidney graft outcome.
Methods: Genotyping was performed in 240 subsequent kidney graft recipients from January 1998 to December 2002. Genomic DNA was obtained from peripheral leukocytes. Identification of cytokine genotypes was based on PCR-SSP method for TNF-a at position -308 A/G, IL-10 at positions -1082 A/G, -819 T/C, -592 A/C, IL-6 at position -174 G/C, IFN-g at position +874 T/A and TGFβ1 in codon 10 (T/C) and 25 (G/C). Nineteen patients with primary graft nonfunction were excluded from the analysis. During 5-year follow-up period 17 patients died with functioning graft and 35 patients developed graft failure. The yearly eGFR decline was calculated from 6 months to 5 years follow-up period.
Results: Only IL-6 gene polymorphism had significant impact on kidney graft survival and decline of eGFR. In patients with CC genotype (determining low IL-6 production) only 6 out of 68 patients (8.8%) lost kidney graft while in the group with GG and GC genotypes (determining higher IL-6 production) 29 out of 151 patients (19.2%). The risk of graft loss (hazard ratio) was 2.38 (1.01-4.16), p=0.046 for GG or GC carriers. The frequency of death was similar in both groups (7.3 and 7.9%). eGFR decline was significantly faster in GG or GC carriers [-4.61 (-6.01- -3.21) ml/min/year] than CC carriers [-2.07 (-3.27- -0.88) ml/min/year], p=0.02.
Conclusions: IL-6 genotypes of the kidney recipient, determining higher IL-6 constitutional expression, are related to the increased risk of graft loss.

P-315 RENAL VASCULAR RESISTANCE MEASURED BY DOPPLER SONOGRAPHY IN THE EARLY PERIOD AFTER KIDNEY TRANSPLANTATION AS A PREDICTOR OF GRAFT LOSS AND CHRONIC GRAFT DYSFUNCTION – A 5 YEARS FOLLOW-UP STUDY

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Background: Resistive index (RI) measured by Doppler sonography during the early post-transplant period reflects interstitial oedema within the transplanted kidney. In the present, prospective study we have analysed the influence of RI measured shortly after kidney transplantation (KTx) on graft survival and kidney function during the 5 years follow-up period.
Patients and methods: RI was measured at 2nd-4th day after KTx in 389 out of 394 consecutive patients transplanted in our Centre. Twenty five patients with primary nonfunctioning graft or acute rejection were excluded from the study. Remaining 364 patients were divided into two groups: first, consisted of 152 patients with RI values below 0.75, and second one (N=212) with RI equal or above 0.75. The kidney graft function was analyzed using the MDRD formula 3 months after KTx and every 6 months of follow-up period.
Results: During the 5 years follow-up period 24 patients died (6 in group I and 18 in group II) and 57 lost their kidney graft (16 in group I and 41 in group II). Higher RI value measured in first days after transplantation was increasing the risk of graft loss by 93.7% [HR 1.937 (1.092-3.125); p=0.022] and the risk of graft loss or death by 106.1% [HR 2.061 (1.241-3.049); p=0.004). Patients in group II were characterized by lower eGFR during the whole follow up period, however the mean difference in eGFR between groups was diminishing from 9.2 ml/min after 6 months to 4.4 ml/min after 60 months of observation.
Conclusion: High intrarenal vascular resistance demonstrated by Doppler sonography shortly after KTx increases the risk of chronic graft dysfunction and almost double the likelihood of graft loss during the 5 years follow-up period.

P-316 INFLUENCE OF HEPATITIS C VIRUS IN THE DEVELOPMENT OF INFECTIONS IN KIDNEY TRANSPLANT RECIPIENTS. A PROSPECTIVE MULTICENTER STUDY

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Introduction: Kidney transplant recipients (KTR) infected by Hepatitis C Virus (HCV) present a reduced graft survival and a higher mortality. There is scarce information about the influence of HCV in the development of infections in KTR.
Methods: The Spanish research network for the study of infection in transplantation (RESITRA) prospectively registered the infections developed by a cohort of 1337 subjects that received a kidney transplant between September 2003 and February 2005. Wilcoxon test was used for calculating the risk of infection according to HCV status.
Results: There were 106 subjects infected by HCV in the cohort. KTR infected by HCV developed a mean of 0.85 infections per patient during follow-up versus 0.78 in those not infected by HCV (p=0.55). In those infected by HCV versus those not infected by this virus, no difference was found in total incidence of infections (Wilcoxon test Z=0.29), nor in the subgroups of infection by bacteria (Z=0.11), cytomegalovirus (Z=0.75), virus different from cytomegalovirus (Z=0.09) or fungi (Z=0.91). Incidence of infection by *Pseudomonas* was 8.5% in those infected by HCV versus 4.7% in those not infected (p=0.08). There were not differences found in the incidence of infection by *Staphylococcus aureus*. Incidence of pyelonephritis or renal abscess was significantly higher in those infected by HCV (12.2% vs 6.5%; $p<0.05$). Bacteraemia of any source was significantly higher in those infected by HCV (10.3% vs 3.3%; p=0.0018). There was not difference in the incidence of rejection (19% vs 14%; p=0.19).
Conclusions: KTR infected by HCV do not present a higher incidence of infections during the first years after transplantation than those not infected by HCV, but they present a higher risk for the development of complications (bacteraemia). Those KTR infected by HCV presented a higher incidence of upper urinary tract infections. A tendency to a higher incidence of infections by *Pseudomonas* was also detected.

P-317 IMPACT OF INTERSTITIAL FIBROSIS (IF) BY AUTOMATIC QUANTIFICATION AT ONE YEAR ON THE EVOLUTION OF RENAL FUNCTION IN TRANSPLANT RECIPIENTS WITH CYCLOSPORINE (CSA) DISCONTINUATION AND SIROLIMUS (SRL) INTRODUCTION

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We previously reported the results of a multicentric study showing that CsA conversion to SRL at W12 is associated with a significant improvement in renal function without difference of IF by automatic quantification on routine renal biopsy (RB) performed at W52. Clinical follow up is now available at M30.
This multicenter, prospective, randomized trial included 121 renal recipients randomized at W12 to be switched from CsA to SRL or to continue CsA. Routine RB was performed at W52 with a section imaged using a colour video camera and analyzed by a program of colour segmentation which automatically extracts green colour areas characteristic of IF. Results were expressed of % of IF and using Banff classification (grade I: $<$25%, grade II: 25-50% and grade III, $>$ 50%).
At W52, the mean IF percentage was 27.4% 15.4%. Using the quantitative analysis grading, 56 RB (45.4%) exhibited grade I fibrosis, 55 RB (46.2%) grade II fibrosis, and 10 RB (8.2%) grade III fibrosis. Of note, IF of grade $>$1 was identified in more than 50% of patients. During follow up, one patient died of pneumopathy and one patient lost his graft because of humoral rejection. Mean estimated glomerular filtration rate (MDRD) was 58.1$\pm$16.3 ml/min at W52 and 54.7$\pm$15.4ml/min at M30. There was a positive correlation between renal function at M30 and the percentage of IF on RB (p=0.04) at W52. Follow up of patients until 60 months is scheduled.
Conclusion: Automatic quantification of IF on routine renal biopsies at one year post-transplant is correlated with long-term allograft function and may assist early diagnosis of the renal function deterioration related to chronic allograft injury.

P-318 LONGITUDINAL ANALYSIS OF INTERSTITIAL FIBROSIS (IF) BY AUTOMATIC QUANTIFICATION IN SEQUENTIAL ROUTINE RENAL BIOPSIES (RB) AFTER RENAL TRANSPLANTATION (RT)

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Renal IF is the main histopathological feature of chronic allograft injury (CAI). IF is currently assessed by semi-quantitative analysis, but automatic color image analysis is more reliable and reproducible. The aims of this study was to measure quantitative IF on sequential routine RB at day 0, M3 and M12 RT to describe the natural history of CAI, possible risk factors and its functional consequences.
In 141 patients with RB between 2004 and 2006, a section was analyzed by a program of color segmentation imaging which automatically extracts green color areas characteristic of IF. Clinical and biological data between day0 and M36 were collected.
Mean donor age was 51 years. Mean cold ischemia time was 24.1 hours. At M36, graft survival was 97% and patient survival was 99%. At day 0, mean IF score was 20$\pm$10%. The IF score increased to 32$\pm$9% at M3, but remained stable at M12 (32$\pm$12%). Higher IF score at M12 was associated with a worsened eGFR at M36 (42,3 vs 62,0 ml/min). Diabetes mellitus (DM) was significantly associated with a higher percentage of IF at M12 (37.5$\pm$10.7% vs 29.61$\pm$1.5%, p=0.03). Biopsy-proven acute rejection (BPAR) occurring in 33% of patients, was associated with a lower eGFR at M36 (52$\pm$15.4 vs 61.3$\pm$15.4 ml/min, p=0.04) but no difference with IF at M12.
In conclusion, significant IF score is already present before RT and worsened at M3 but not between M3 and M12. DM is associated with worsened renal function and increased IF at M12. A specific analysis of progressors vs. non progressors will be performed to determine the risk factors for early worsening of IF lesions and to better understand the natural history of CAI.

P-319 INFLUENCE OF *CYP3A5* POLYMORPHISM IN DONOR AND RECIPIENT ON TACROLIMUS PHARMACOKINETICS AND CLINICAL OUTCOME AFTER RENAL TRANSPLANTATION

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Purpose: Tacrolimus is highly effective in preventing acute rejection after renal transplantation, but displays a narrow therapeutic index and high interindividual pharmacokinetic variations. Previous studies have reported that the dose-adjusted concentration of tacrolimus is much higher in *CYP3A5*3/*3* subjects than in **1/*1* or **1/*3* subjects. The aim of this study was to evaluate the contribution of recipients' and donors' *CYP3A5* genotype to tacrolimus pharmacokinetics and its impact on renal function.
Methods/Materials: This study included 153 consecutive renal transplant recipients (RTR) followed for 2 years. All patients initially received biological induction, tacrolimus (0.15mg/kg/d), MMF and steroids. Tacrolimus pharmacokinetics, renal function, Delayed Graft Function (DGF) and Biopsy Proven Acute Rejection (BPAR) were evaluated according to RTR and donors' *CYP3A5* genotype.
Results: CYP3A5 polymorphism frequencies were 20.7% (*CYP3A5*1/*1* + **1/*3*), 79.3% (**3/*3*) in RTR, and 14.6% (**1/*1* + **1/*3*), 85.4% (**3/*3*) in donors. Donor *CYP3A5* polymorphism was not associated with any pharmacokinetic parameters. For recipient CYP3A5 polymorphism, at all time-points during this survey, [1] the single tacrolimus dose per body weight was significantly higher for *CYP3A5*1* carriers (i.e at one year post transplant: 0.1$\pm$0.05 *vs* 0.08$\pm$0.04mg/kg/d, p=0.04); and the [2] dose-adjusted trough levels were lower for *CYP3A5*1* carriers (ie, at one year post transplant: 73$\pm$51 *vs* 124$\pm$81ng/mL/mg/kg/d, p=0.007). There was no impact of CYP3A5 polymorphism (donor or recipient) on renal function or incidence of BPAR. However, incidence of DGF seems to be associated with the *CYP3A5* genotype of the donor but not of the recipient (**1/*3* + **1/*1 vs *3/*3*: donor 5.9% vs 18.1%, p=0.06; recipient: NS)
Conclusion: Recipient's *CYP3A5* genotype significantly influences tacrolimus pharmacokinetics, but does not impact renal function or rejection rate. Donor's *CYP3A5* status seems to influence DGF.

P-320 KIDNEY TRANSPLANTATION IN POLICYSTIC KIDNEY DISEASE. IS NATIVE NEPHRECTOMY A RISK FACTOR FOR PATIENT AND GRAFT SURVIVAL?

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Purpose: Early and late results in patients with Autosomal Dominant Polycystic Kidney disease (ADPKD) who underwent native nephrectomy before or at the same time of kidney transplantation (KT).
Methods/Materials: From 1992 to 2008, 171 transplanted patients with ADPKD received a native nephrectomy. Main indications were: renal size, bleeding and infection. Sixty-four patients (M/F 41/23; mean age 50.1 years) received a nephrectomy before KT (Group A) while 107 patients (M/F 47/60; mean age 44.2 years) were submitted to concomitant nephrectomy and KT (Group B). Patient and graft survival in both groups was compared to a control group (Group C) of 1110 patients (M/F 542/568; mean age 45.3 years) submitted to KT for other causes.
Results: Perioperative mortality was 1.6% in Group A, 1.8% in Group B and 0.8% in Group C. Patient survival at 1-3-5 and 8 years was: 96.7%, 93.4%, 91.8% and 85.3% in group Group A, 92.8%, 91%, 91% and 91.0% in Group B group, 98%, 95.8%, 93.8% and 85.4% in Group C, respectively. At the same time points, graft survival was 86.9%, 80.3%, 78.7% and 70.5% in Group A group, 91%, 87.3%, 85.5% and 76.4% in Group B, 92%, 85.9%, 70.5% and 65.1% in Group C, respectively. Independently by group, cardiac accidents were the main cause of death and chronic rejection was the main cause of graft loss. Differently by Group C, pts with ADPKD had more postoperative and long-term complications because of colonic diverticula perforation (1.7%) and intracranial haemorrhage (2.3%). Specimen examination showed renal cell carcinoma in 4 cases (2.3%).
Conclusion: Patient and graft survival in ADPKD group is better than patients in the control group independently by native nephrectomy timing.

P-321 RISK FACTORS IN KIDNEY RE-TRANSPLANTATION. A 30-YEAR NIGUARDA HOSPITAL EXPERIENCE

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Purpose: We report our results of 160 first or subsequent Kidney Re-Transplants (re-KT) in a group of 150 patients (pts).

Methods/Materials: Eighty-five males and 65 females who had lost their first kidney graft, received a re-KT. The mean waiting time was 25.1 months at Kidney Transplant (KT) and 66.9 months at re-KT. In 48 pts first graft loss was early ($<$1 year) and in 102 pts was late. One hundred and thirty pts (86.7%) had a re-KT from standard donors and 20 pts (13.3%) from expanded criteria donors (ECD). Seventy-six pts were explanted (immunological factors 51 pts) and 74 pts had the first graft left in situ.
Results: Patient and graft survival rate at 1, 3 and 5 years in the 20 pts with a graft from ECD was: 90.0% and 65.0%; 90.0% and 65.0%; 90.0% and 65.0% respectively and was comparable to those pts with a graft from standard donor. In both groups the main cause of late graft loss was chronic rejection (80%).
Considering time of dialysis, among 74 pts with a follow up of more than 5 years, 23 lost their second graft for immunological reasons. Interestingly, 2 of them (8.7%) had had a time of dialysis $<$ 1 year, 10 of them (43.5%) between 1 and 2 years and 11 of them (47.8%) $>$ 2 years.
In the subgroup of 51 pts (34.0%) whose first graft was explanted for immunological reasons, 15 pts (29.4%) lost their re-KT for chronic rejection in respect to 13 pts (17.6%) out of 74 who had the first graft left in situ.
Conclusion: Long-term patient and graft survival in re-KT is negatively influenced by time on dialysis and nephrectomy of the first graft.
ECD does not seem to have adverse effects.

P-322 ABO INCOMPATIBLE (ABO-I) KIDNEY TRANSPLANTATION WITHOUT SPLENECTOMY: POSTTRANSPLANT PLASMAPHERESIS IS NOT A ROUTINE BUT ON DEMAND PROCEDURE FOR SAFE ENGRAFTMENT

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ABO-I kidney transplantation is a valuable option to overcome short organ supply. Excellent graft outcome has been reported in recent years but variable protocols exist in different centers, and whether doing or not doing plasmapheresis during posttransplant period is one of debating points.
Thirteen ABO-I living donor kidney transplantations with rituximab but no splenectomy were performed in our center. Anti-CD25 induction and tacrolimus-based triple drugs were used. Posttransplant plasmapheresis was performed only in indicated patients.
Median IgG ABO antibody titer at baseline was 32 (8-512), which was reduced to 2 (1-8) on transplant day by 5.9 (4-8) pretransplant plasmapheresis. Plasmapheresis during the critical posttransplant period (2 weeks) was done in not all but selected patients [n=5 (38%)] with high initial ABO antibody titer (256, n=2), rapidly rising titer during critical period (n=1), or increase in creatinine before pathology of graft biopsy reported (n=2). Mean number of posttrasnplant pheresis in these 5 patients was 1.8 (1-4).
Median follow up was 6.3 (3-25)months. No acute antibody-mediated rejection occurred. One case of reversed acute cellular rejection occurred. No patient or graft was lost. There was no CMV infection or other infection that requires hospitalization. Serum creatinine at last follow up was 1.2 (0.8-1.7)mg/dl.
We conclude that posttransplant plasmapheresis only in selected patients with higher probability of antibody mediated rejection is safe and cost-reducing strategy.

P-323 ASSOCIATION OF KIR GENOTYPES AND ACUTE REJECTION IN KIDNEY TRANSPLANT

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Purpose: The growth of biological knowledge about acute and chronic rejection of kidney transplants and the identification of new risk factors might allow to characterize innovative therapeutic approaches tailored to the single patient. It is well-known that innate natural killer (NK) cells as well as T cells contribute to graft rejection. Killer-cell immunoglobulin-like receptors (KIRs) belong to a polymorphic family of activating and inhibitory receptors expressed on the surface of NK cells and effector T cells and recognize human leukocyte antigen (HLA) class I ligands. It has been suggested that an overbalancing between activating and inhibitory signals, due to an HLA or a KIR mismatching, may lead to NK cell activation against the graft.
Methods: In this study, we evaluated NK cell alloreactivity based on KIR gene and HLA ligand analysis. To evaluate the impact of KIR/HLA, KIR/KIR and HLA/HLA compatibility in acute rejection, 95 patients who received kidney transplant between 1999 and 2005 were selected, 59 of them with stable graft function and 36 with at least one rejection episode. The patients in the two groups were matched for sex, donor and recipient age, time on dialysis, cold ischemia time and therapy. Donor/recipient pairs were analyzed retrospectively using HLA and KIR SSO genotyping test for the presence of single KIR gene and haplotypes.
Results: We found two nearly significant associations between NK cell alloreactivity based on KIR gene analysis and the occurrence of acute rejection. Specifically, KIR2DS1 was more present in patients who developed an acute rejection (O.R.=1.44, p=0.06), while KIR2DL2 was represented more in the control group (O.R.=0.47, p=0.08).
Conclusions: Our data suggest that the presence or absence of some specific KIR genes may influence graft short-term outcome after renal transplantation.

P-324 NATIVE KIDNEY FUNCTION AFTER COMBINED SOLID ORGAN TRANSPLANT (LIVER/KIDNEY, HEART/KIDNEY)

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Purpose: Pre-transplant renal failure represents a risk factor for mortality and morbidity in solid organ transplant programmes. There are no precise guidelines regarding the nephrological indications for combined transplants (liver-kidney LKT, heart-kidney) in patients with kidney failure. The objective of this study was to assess the functional contribution of native kidneys following the combined transplant of kidney with other solid organs.
Methods: At our transplant centre, 41 combined transplants (35 liver-kidney, 6 heart-kidney) were performed from January 1997. From 2004, 9 patients not on RDT at the time of transplant (age 50$\pm$8, creatinine 2.8$\pm$1.0 mg/dl) underwent combined transplant. The patients were suffering of chronic nephropathy and they were observed for 12$\pm$29 months before transplant. A scintigraphic functional study (Tc-99DMSA or Tc99mMAG3) was carried out 4$\pm$3 months after transplant to evaluate the functional contribution of both the native kidneys and the graft.
Results: Delayed graft function was not observed in any patient. All patients were given immunosuppressive drugs including calcineurin inhibitors (tacrolimus/cyclosporine). At the time of the scintigraphy, renal function in all patients examined was normal (creatinine 1.3$\pm$0.3 mg/dl). The functional contribution of the transplanted kidney was on average 77$\pm$15. Graft kidney function of $<$50% was noticed in only one patient (vascular nephropathy). At follow-up after 8-53 months patient and kidney survival was 100%.
Conclusions: The study confirms the good short and long term results of combined transplant programmes. Pre-transplant, close clinical and instrumental assessment is essential before proceeding with a combined transplant programme. In the light of our experience, when advanced chronic nephropathy is present ($<$30 ml/min creatinine clearance), the short-term risk of deterioration in native kidney function is highlighted.

P-325 PHYSICAL ACTIVITY IN SOLID ORGAN TRANSPLANT RECIPIENTS

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Purpose: Limited information has been published about sporting activities in solid organ transplant recipients. The aim of this study is to verify "in the field" the capacity for physical activity in transplant patients and the correlated metabolic and psychological aspects.
Methods: 16 transplant recipients (13 men, 3 women, 49$\pm$15yrs) who had undergone transplant (11 kidney, 4 liver, 1 heart) 84$\pm$67 months before participating in a day of alpine skiing were studied. The patients performed a countermovement jumping test to measure the power explosive (POW) of the lower limbs (Optojump). All patients wore a Sense Wear Armband (SWA), a portable device that monitors physiological parameters and calculates energy expenditure and physical activity. Body mass index (BMI) was calculated; body fat percentage was determined using plicometry (Jackson-Pollock equation). Functional health and well-being scores were obtained using the SF 36 health survey.
Results: The maximum displacement during the jumping test was 22.4$\pm$ 9.3cm (range 11-40 cm). The SWAs were worn for a period of 22hrs 12mins $\pm$ 2hrs 49mins; energy expenditure was 3376$\pm$2692 Kcal/24hr (men) and 2692$\pm$131 Kcal/24hr (women). Physical activity $>$3METs was recorded in all patients for a period of 2hrs 58mins $\pm$ 2hrs 8mins; energy expenditure in this phase was 915$\pm$713Kcal. BMIs were 24$\pm$2; body fat was 19$\pm$3% (men) and 27$\pm$11% (women). The SF36 scores relating to the perceived qualtiy of life were higher than those reported in the literature for transplant recipients.
Conclusions: The study confirms the efficacy of solid organ transplantation in terms of physical and social recovery. Even though results for POW and

level of physical activity were very varied, the performance of many patients was similar to those noted for the general population. Sporting activity helps to improve people's perception of their own well-being.

P-326 RENAL TRANSPLANT PROGRAMMES AND PREVIOUS BONE-GRAFT TRANSPLANTATION. IMMUNOLOGICAL IMPLICATIONS

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Purpose: In renal transplant programmes, pretransplant immunological screening is crucial in the study of patients on the waiting list. The main causes of immunization are previous solid organ transplantation, hemotransfusions, pregnancy. The immunogenicity can also be triggered by vascularized tissue grafts. Sensitization cryopreserved bone prostheses is still poorly characterized.
Case report: A 19 year-old patient with osteosarcoma underwent a resection of the left proximal tibia in 1997, followed by reconstruction using a cryopreserved (-80°C) human bone from a deceased donor. The donor HLA-typing was: A3, A29 (19) – B44 (12), Bw4 – DR13 (6), DR7, DR52, DR53. As established in the protocols for transplantation of cryopreserved bone allografts, no immunosuppression was administrated. During the anti-tumoral therapy, the patient underwent one red blood cell transfusion and developed cisplatin-induced renal failure. He initiated hemodialytic treatment in February 2005 and was accepted onto the waiting list for renal transplantation in November 2005. Pre-transplant immunological evaluation was performed using different screening techniques and revealed direct antibodies against all donor antigen specificities (Table 1).
Results: The immune status of the patient is currently monitored on the serum samples every three months, according to the standard procedures of the kidney transplant waiting list. The average percent PRA value was 54% using the CDC technique, with a peak value of 87%, while the flow cytometric method detected an average positivity of 69% on class I and of 80% on class II. As regards kidney allocation, it has been established that donors with HLA antigens shared with the previous bone graft donor must be excluded.
Conclusions: This case is the first reported regarding immune induction after the implantation of bone prosthesis in a kidney transplant candidate and underlines the importance of the availability of the HLA typing data of all human prosthesis donors.

P-327 KIDNEY TRANSPLANTATION (KT) FOR PATIENTS AFFECTED BY VON HIPPEL-LINDAU (VHL) DISEASE: EXPERIENCE OF AN mTOR INHIBITOR-BASED PROTOCOL

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Purpose: To describe the outcome of KT in three patients affected by VHL disease, transplanted and followed up at a single institution, focusing on immunosuppressive (ID) protocol and pre/post transplant working up.
Methods/Materials: The three patients underwent a single kidney transplantation at our Centre from June 2003 to March 2006. The charateristics of the patients are described below.

Pt	Age/sex	Diagn VHL/ before or after KT	Pheochromo-cytoma	Renal cell carcinoma (RCC)	Retinal angioma	Pancreatic lesion	Cerebellar angioblastoma
1	52/F	2004/after	yes	yes	yes	yes	no
2	46/M	1994/before	no	yes	no	no	yes
3	66/M	1999/before	no	yes	yes	yes	yes

An accurate pre-transplant screening was applied to exclude active malignancies and, in the case of Living Related Donor (LRD), a specific genetic test for VHL gene mutation was performed on the donor.
After transplantation the patients were subsequently followed up as outpatients.
Results: At January 2009 all the patients are alive and well, with a mean follow up of 56,7 months (range: 34–77). The grafts are currently well functioning, with a mean sCr of 1,3 mg/dL.

Pt	KT	Source of graft	Initial ID protocol	sCr at 1st month	Time to mTORi conversion	Current ID protocol	Current sCr
1	03/02/2004	DD	TAC+MMF+ster	1,1 mg/dL	1 yr (2005)	SRL+ster	1 mg/dL
2	19/06/2003	LRD	TAC+ster	1,6 mg/dL	2 yrs (2005)	SRL+ster	1,4 mg/dL
3	17/3/2006	DD	EVE+MMF+ster	2,1 mg/dl	15 days-no CNI (2006)	EVE+MMF +ster	1,8 mg/dL

Current ID regimen includes an mTOR inhibitor drug (sirolimus in two cases, everolimus in the other one) associated with steroids in low doses, and in one case also with mycophenolate mofetil.
The post-transplant follow up allowed us to promptly recognise and remove neoplasms that had worsened or occurred after transplantation: RCC, pheochromocytoma and pancreatic glucagonoma in patient 1, cerebellar emangioblastomas in patients 2 and 3. No metastasis were found.
Conclusions: On the basis of our experience we believe that kidney transplant can be safely offered to patients with VHL disease – also from LRDs – on condition that adequates pre-transplant screening and post-transplant intensive follow up are performed. At the best of our knowledge, an ID regimen including an mTOR inhibitor and excluding or minimizing CNI may contribute to improve patient and graft survival, thanks to its antitumoral and antiproliferative effect.

P-328 ARE ABO-IgA LEVELS IMPORTANT IN HLA INCOMPATIBLE RENAL TRANSPLANTS?

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In solid organ transplantation, non-HLA antibodies are thought to be responsible for both acute and chronic renal allograft outcomes. The most ubiquitous antigens to which patients are sensitized are the blood group antigens. There has not been any study looking at blood group antibodies in patients undergoing HLA desensitized transplantation.
We therefore analysed 30 patients who underwent HLAi renal transplant. Pre-transplant, patients were treated with 5 alternate day sessions of double filtration plasmapheresis.
Pretreatment with plasmapheresis, pretransplantation, antibody (Ab) rise, Ab peak, onset of rejection, resolution of rejection and late samples were the time points chosen for analyses. Plasma samples were analysed using flowcytometry for estimating IgG, IgM and IgA ABO antibodies against reagent cells and the relative mean fluorescence was calculated. The main DSA, cumulative DSA and the 3rd party Abs were analysed using Luminex. In patients with 'O' and 'B' blood group tested against 'A1' reagent and 'A' plasma tested against 'B'cells, if pre treatment IgA levels were high (> or equal to 2 RMF) irrespective of IgG levels 7/10 (70%) of patients had rejection. But if they were low (< 2 RMF) 7/20 (35%) had rejection. Similarly, if pre treatment IgG levels were high irrespective of IgA levels 6/12 (50%) of patients had rejection as opposed to 7/17 (41%) if they were low. Also, out of 17 patients with high pre-treatment peak DSA level (>5000), only 6 (35%) had high IgA ABO Ab. This was similar in relation to 3rd party as well. Thus, the correlation seemed to be independent to the level of DSA or 3rd party antibodies.
Thus, there seems to be a correlation between the pre-treatment levels of blood group IgA antibodies and occurrence of rejection, though the reason for this association is not clear.

P-329 VIRAL AND BLOODGROUP ANTIBODIES DO NOT FOLLOW DSA'S IN HLAi KIDNEY TRANSPLANTATION

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We looked at non HLA antibodies like viral and blood group antibodies in

Abstract P-326 – Table 1. Pre-transplant immunological evaluation

PRA screening (Complement-dependent lymphocytotoxicity, CDC)	First PRA: 63% (average value: 54%)
Flow cytometry (Luminex) for detection of anti-HLA antibodies and specificity to class I or class II HLA antigens	Anti-HLA antibodies (IgG) directed to HLA class I (A1, A3, A11, A36, B8, B44, B45) and HLA class II (DR7, DR9, DQ4)
Luminex single antigen (LSA) assay	Anti-HLA antibodies (IgG) directed to HLA class I (A1, A3, A29, A36, B8, B44, B45) and HLA class II (DR7, DR9, DR13, DR52, DQ4)

patients undergoing HLA desensitized transplantation, to see whether an HLA response affects viral and ABO antibodies. We analysed 30 patients. Pretransplant, patients were treated with 5 alternate day sessions of double filtration plasmapheresis. Using the Liason machine CMV, VZV and Anti-HBs IgG antibody were quantified from the corresponding serum samples. The main DSA, cumulative DSA and the 3rd party HLA Abs were analysed using Luminex. Plasma samples were analysed using flowcytometry for estimating IgG, IgM and IgA ABO antibodies against reagent cells and the relative mean fluorescence was calculated. The patients were divided into 2 groups; 1) higher post transplant peak DSA than pre-treatment levels and 2) had lower post transplant peak DSA than pre-treatment levels.

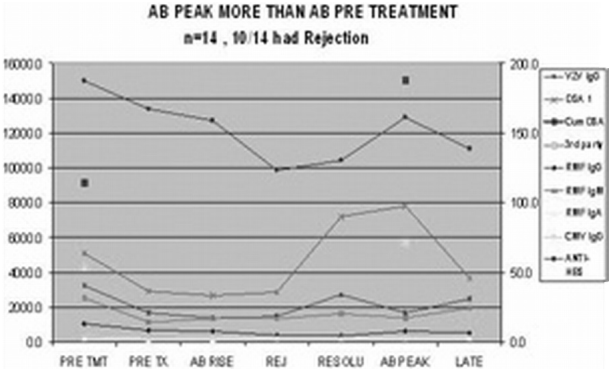

Figure 1. Patients with higher post transplant peak DSA than pre-treatment levels.

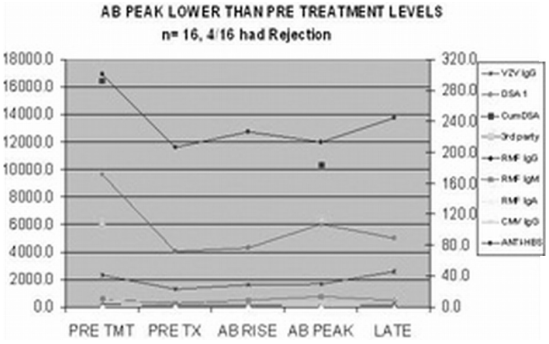

Figure 2. Patients with lower post transplant peak DSA than pre-treatment levels.

10/14 patients in group 1 had rejection as opposed to 4/16 in group 2. Inspite of the rises or falls in the cumulative DSA's and the peak DSA levels in the groups, there were no changes in the viral or the ABO abs in majority of these patients. Thus, viral or blood group antibodies do not follow DSA in desensitized transplants and the rise in DSA and 3rd party Abs seem to be HLA specific, at least in the acute period post transplant

P-330 PROGNOSTIC FACTORS IN ACUTE HUMORAL REJECTION OF RENAL ALLOGRAFTS AND THERAPEUIC DECISIONS BASED ON HISTOPATHOLOGIC FINDINGS

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Introduction: The clinical, histologic and immunologic criteria for acute antibody mediated rejection are well established. Most series report allograft survival below 50% at first year. Consequently, efforts should focus on finding an effective therapeutic approach that does no increase risk in patients with transplants.
Objetives: Analyze the clinical, histopathological and immunological factors associated with poor renal allograft survival and use the histopathologic findings as the basis for therapeutic management.
Materials and methods: Retrospective analysis of 219 biopsies performed for kidney function deterioration, between 1997 and september 2008 in 668 patients with renal transplant. 24 biopsies (10.9%) met the Bannf Criteria (2005-2007) for acute antibody-mediated rejection (AMR). C4d staining was mesured by monoclonal and/or polyclonal antibodies and donor specific antibodies (DSA) were determined by Flow Cytometry.
Results: N=24. C4d possitive in 100% biopsies. 18 patients had DSA. Allograft survival at 30 months was 51.8%. The postransplant presence of de novo DSA was significantly correlated to graft loss (p=0,006). Acute humoral rejection Type I (ATN_Like) responded well with Tymoglobulin or corticosteroid alone. Type III (v3) was and infrequently finding (N=1) with no response and graft loss. Type II (N=17) correlates most closely to humoral rejection. Association with cell acute rejection was in eight cases (33%). Of the 19 patients treated with Tymoglobulin 11 obtained good response and five of 19 cases were urresponsiveness to all antirejection treatment.

Table 1

Histologic lesion	Treatment	Response
Type I ATN (N=3)	thymoglobulin or corticosteroid alone	3/3 (100%)
Type II Glomerular thromboses (N=17)	Thymoglobulin +/- plasmapheresis +/- IVIG	9/17 (52.9%)
Type III Arterial v3	Rare, irremediable graft loss in all published cases	no response
Arteritis v1, v2 with C4d+ and DSA (N=3)	Thymoglobulin +/- plasmapheresis	2/3 (66.6%)

The histologic lesion can appear isolated or combined.

Conclusions: Postransplant detection of de novo DSA was significantly correlated to poorer graft survival. Thromboses glomerular (Type II AHR is the vascular lesion more frequently and requering more agressive therapies. Half patients responded to thymoglobulin

P-331 INCIDENCE OF NON-MELANOMA SKIN CANCER FOLLOWING HUMAN SOLID ORGAN TRANSPLANTATION

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Increasing evidence, that nonmelanoma skin cancers (NMSC) are the most frequent tumours in transplanted patients. The present study aimed to set going first Hungarian dermatological screening program to establish the incidence of NMSC after organ transplantations.
116 adult, white skin-typed transplanted (kidney, simultaneous pancreas-kidney) patients (70 male, 46 female; median age: 49.3 years) have been involved from September of 2008 on the Surgical Clinic of Pecs University. All patients were examined by one dermatologist for NMSC by a full skin examination, and they filled a standardized questionnaire.
Screening resulted 16 NMSC (13.8%, median age: 60 years, male/female=1:1) with a median duration since transplantation of 4.1 years. Histology showed 13 basal cell carcinoma (BBC), 3 squamous cell carcinoma (SCC), and the ratio of BBC/SCC was 4:1. Incidence of NMSC was significantly higher on patients using cyclosporine as immunosuppressant (16 vs. 1, $p<0.05$), who had more than 2 sunburn prior to transplantation (11 vs. 5), or had outdoor workplace (16 vs. 1).
These data indicate the relevance of skin cancer surveillance for transplant recipients and the closed-cooperation between Transplantation and Dermatological Centres. Our results correspond with the international statistics, excepting BBC/SCC ratio. So, further studies are needed to elucidate this difference.

P-332 A NEW APPROACH FOR THE TRANSPLANTATION OF SENSITIZED KIDNEY GRAFT RECIPIENTS AT A HIGH RISK OF ANTIBODY-MEDIATED GRAFT LOSS

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Sensitized kidney transplant recipients have a lower chance of receiving a suitable allograft, and if transplanted, they are at a higher risk of antibody-mediated graft loss.
Based on findings from the Collaborative Transplant Study, we adopted a new algorithm for the pretransplant identification and transplantation of high-risk presensitized patients. Thirty patients (mean age 49.0 years) who met the criteria shown in Table 1 and had an organ offer from 2006-2008 were treated with pre- and posttransplant apheresis, rituximab and quadruple-immunosuppression (basiliximab, tacrolimus, EC-mycophenolic sodium, steroids) and were monitored by donor-specific antibody (DSA) measurements and protocol biopsies.
Fifteen patients received their second, 6 patients their third and 2 patients their fourth transplant. Five patients had living-donor transplantation. Donor age was 52.6 years, mean cold ischemia time 14.3 hours. Patients received a mean of 8.5 apheresis sessions after transplantation. Delayed graft function was observed in 23 patients. The 1-year graft survival rate was 93.3%, functional graft and patient survival rates were 96.7%, respectively. Thirteen patients had at least one acute rejection episode. Cellular rejection was seen in 25 biopsies (mostly Borderline changes, N=21), which were treated by steroid pulse therapy. Two patients had antibody-mediated rejection with C4d-positivity and

Table 1. Patients defined to be at high risk for antibody-mediated graft loss

PRA	HLA class I antibody	HLA class II antibody	Retransplant	T-cell crossmatch	B-cell crossmatch
≥85%					
	Positive	Positive			
	Positive	Negative	Yes		
	Negative	Positive	Yes		Positive
				Positive	

demonstration of DSA. They were treated with intensified apheresis. Twenty-eight out of 29 patients alive had a functioning allograft on the last visit. Mean serum-creatinine was 2.96±2.00 mg/dl on day 14, 1.98±1.07 mg/dl on day 30, 1.59±0.91 on day 90, 1.58±0.84 on day 180 and 1.52±0.91 after one year. Infectious complications were infrequent.
In conclusion, we describe a new algorithm for the pretransplant identification and treatment of high-risk presensitized patients. This treatment protocol provided effective prevention of antibody-mediated graft loss at a low rate of side effects.

P-333 VALIDITY OF TWO SLEEP QUALITY ITEMS USED IN THE SWISS TRANSPLANT COHORT STUDY IN RENAL TRANSPLANT RECIPIENTS

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Purpose: Sleep Quality is not well studied in transplant patients and was therefore included in the Swiss Transplant Cohort Study (STCS) using 1 sleep quality (SQ) and 1 daytime functioning (DF) item. We assessed the validity of the 2 STCS Sleep-items.
Methods: Using a cross-sectional design, renal transplant recipients were included. SQ was assessed by the 3-factor model of the Pittsburgh Sleep Quality Index (PSQI) as the gold standard and the 2 STCS items (2 rating scales ranging from 0 (worst) to 10 (best); cut off = 6), depressive symptomatology by HADS and perceived health status by EQ-5D. Guided by the APA criteria we assessed content validity (CV-index), response processes (missing values, floor effect), internal structure (correlation SQ and DF) and relation to other variables (PSQI, HADS, EQ-5D).
Results: The study included 156 renal transplanted recipients (29% women; age: 52±12, range: 21-76; mean time since transplant was 2±1.6 years; range 1-5). Prevalence of poor SQ by PSQI was 48.4% (6.6±4.1) and 24.4% by the SQ item (7.1±2.1). 25.8% reported poor DF (7.1±2.2). Content validity was good for the SQ item (CV-I:. 81) and poor for the DF item (CV-I: 0.45). Large negative correlations were observed between the PSQI sub score perceived SQ and the SQ item (r: -0.737 $p<0.01$) and between the PSQI sub score daily disturbances and the DF item (r: -0.527 $p<0.01$). SQ and DF showed a significantly positive association with depressive symptomatology (r: -0.475 respectively r: -0.635, $p<0.001$) and perceived health status (r: -0.437 respectively r: -0.607, $p<0.001$).
Conclusion: The SQ item is a valid item to be used in the STCS as a general SQ screening. The wording of this DF-item needs to be improved.

P-334 THE ROLE OF SPOUSAL DONORS IN LIVING DONOR KIDNEY TRANSPLANTATION FOR DONOR POOL EXPANSION: SINGLE CENTER EXPERIENCE

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Background: The shortage of organ donors is one of the major problems of kidney transplantation today. Recent studies have shown that the graft survival rates of spousal donors are as high as living related donor groups. We examined the role of spousal donor groups for solution of donor shortage and expansion of donor pool.
Methods: Living donor kidney transplants between 1991 and 2005 were studied, retrospectively (n=593). We compared the graft survival rates of spousal transplantations (n=77) with those of sibling (n=125), other living related (n=142) or other living unrelated (n=249) donor groups. Also we analyzed the outcomes between husband to wife (n=25) and wife to husband (n=52) transplant groups. We compared the graft survival rate, acute rejection rate and post-transplantation complications among each groups.
Results: The 5, 10 year graft survival rates of spousal donors were 83.1%, 80.1%, those other living unrelated donors were 74.6%, 64.5% (P=0.019) and those of sibling and other living related donor were 82.3%, 75.9% (P=0.595) and 75.7%, 65.4% (P=0.032). Acute rejection rates of other living unrelated donors, 38.7% were more higher than those of sibling and other living related donors, 26.4% and 27.5% (P=0.032). In the post-transplantation infections, there was no difference between spousal donors and the other groups (P=0.250). In the multivariate analysis of donor groups, spousal donors were associated with a low relative odds of graft survival compared to other living donor groups (P=0.016). The graft survival, acute rejection rates between two spousal donor groups were no definite difference (P=0.488, 0.288). In psychologic aspect, the spousal donors had high secondary gain after donation.
Conclusions: The spousal donor groups had good graft survival rates and similar complication. We expect that the spousal donors are one of the good candidates for donor pool expansion.

P-335 CYTOMEGALOVIRUS INFECTION INFLUENCE ON THE KIDNEY GRAFT SURVIVAL

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Introduction: Cytomegalovirus infection (CMV) is an important pathogenetic factor in immunity alteration after kidney transplantation and therefore can contribute to the graft survival reduction. In this regard it is important to evaluate comparative evolution of the kidney transplant in the CMV positive and, respectively, negative patients.
Objective: Our study is centered on the CMV infection influence on the kidney graft survival.
Material and methods: A retrospective study of 81 patients, operated in our center between 1994 and 2003. Mean age 32,4±10,8. CMV infection was tested by corresponding antibodies determination and the following titers evaluation. CMV positive and negative groups were homogenous regarding age, gender, comorbidities and etiological spectrum.
Results: CMV infection activation was determined in 40 (49,4%) patients, with the viral titers being 5% in 13 patients, 10% – in 11 patients, 15% – in 10 patients, 20% – in 4 patients and more than 20% – in 2 patients. The longer previous hemodialysis duration (24,1±21,5 months vs 19,7±17,9 months) as well as the lesser kidney transplant survival mean duration (27,0±36,1 months vs 36,2±38,5 months) were characteristic for CMV infection activation. The viral titers correlated with the anterior dialysis treatment and the transplant survival was decreased in patients with the titers more than 15%. The CMV infection was associated with the lesser transplant survival on the moment of analysis: 10/41 (20%) vs 5/40 (40%) ($p<0,01$). The incidence of the chronic and acute rejection, infectious and post-steroid complications did not differ in studied populations. Clinically evident activation of the CMV infection was determined in 3 patients, being manifested mostly by hepatic and central nervous system lesions.
Conclusion: The CMV infection activation is a frequent complication of the kidney transplantation and is usually associated with less favorable prognosis both for graft and patient.

P-336 PREDICTION OF KIDNEY TRANSPLANT OUTCOME BY DONOR QUALITY SCORING SYSTEMS: EXPANDED CRITERIA DONOR AND DECEASED DONOR SCORE

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Purpose: Due to disparity between organ supply and demand, the use of kidneys form suboptimal donor has become increasingly common. To improve the stratification and the identification of deceased donor kidneys with an increased risk for graft dysfunction and graft loss, several donor quality systems have been developed. The purpose of our study was to compare the utility of Deceased Donor Score (DDS) and expanded criteria donor (ECD) status in predicting kidney transplant outcome in a single centre.
Methods/Materials: We analysed 298 deceased donor renal transplant procedures, collecting donor and recipient variables from the prospectively maintained institutional database. DDS and ECD were defined according to previously reported criteria. Delayed graft function (DGF) was defined as dialysis requirement during the first week postoperatively.
Results: Kidneys were obtained from marginal donors in 42.9% of transplant patients in accordance with DDS, while only in 27.9% defined by ECD. There was substantial agreement (kappa index = 0.698, $p < 0.001$) between both scores to define marginal donors. DDS-defined marginal donors were significantly related with the development of DGF compared with standard donors (38.6% vs. 26.8%, p =0.037), while ECDs were not related (35.6% vs. 29.7%, p =0.360). One year renal function was significantly worse in patients receiving kidneys from marginal donors (DDS-marginal donors 1.94±0.65 vs. 1.50±0.73

mg/dl, p < 0.001; ECD-marginal donors 1.95±0.77 vs. 1.59±0.74 mg/dl, p =0.002) than from standard donors.
Conclusion: DDS was related with DGF and one-year graft function, while ECD was only related with one-year graft function in our centre. Both systems provide a quantitative approach to evaluate deceased donors and can help to improve renal allocation.

P-337 TLR7 AND 9 EXPRESSION IN HUMAN KIDNEY TRANSPLANT BIOPSIES

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Toll-like receptors (TLR) are an emerging family of receptors that recognize pathogen-associated molecular patterns and promote the activation of leukocytes and intrinsic renal cells. Tubular epithelial cells, podocytes and mesangial cells are among the non-immune cells that express TLR. TLR have been shown to be involved in a variety of kidney diseases. We were interested in the expression pattern of TLR 7 and 9 in kidney transplant biopsies in humans.
Renal allograft biopsies were analyzed from patients with normal renal graft morphology (according to Banff 97 classification grade 1), antibody mediated rejection (Banff grade 2), acute cellular rejection (Banff grade 4), chronic allograft nephropathy (CAN, Banff grade 5), and various other lesions (acute tubular necrosis, pyelonephritis and arteriosclerosis). TLR 7 and 9 were localized by immunohistochemistry. Furthermore clinical data including laboratory values, immunosuppression and previous rejection episodes were available.
TLR 7 expression in tubules was low or absent in biopsies with Banff 1, 2 and 5, pyelonephritis and arteriosclerosis. The expression was significantly elevated in tubules of biopsies with acute rejection or acute kidney failure. TLR 7 expression in podocytes, glomerular endothelial cells or Bowmans capsule was detectable in most of the biopsies whereas the strongest expression in podocytes was seen in biopsies with acute rejection. Strong expression of TLR 7 was seen in vessels in all types of biopsies. TLR 9 expression was detected in tubules and glomerular cells of normal kidneys. Under pathologic conditions expression was increased in tubules and glomerular cells, strongest in biopsies with acute renal failure.
This is the first study describing the localization of TLR 7 and 9 in human renal transplantation. Our results point to a role of the innate immune system in the pathogenesis of renal allograft damage.

P-338 RISK OF INFECTIOUS AGENT TRANSMISSION BETWEEN DONOR AND RECIPIENT: WHAT IS THE VALUE OF PRETRANSPLANT MICROBIOLOGICAL SAMPLES?

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Purpose: Transmission of infection from donor to recipient is a significant risk in organ transplantation. There are no guidelines regarding graft microbiological sampling before transplantation.
Methods/Material: We routinely take multiple microbiological samples (MMS) of storage medium (M), perinephretic fat (PNF), renal artery (A), renal vein (V) and ureteral tissue (U) just before transplantation. We reviewed the results of theses samples between 2002 and 2006 to relate them to the occurrence of significant infection (SI: clinical infection or positive microbiological samples in recipients with concordant pathogen identification)
Results: 151 deceased-donor renal transplant were performed during the study period. MMS were all negative in 63% of the cases. One single sample was positive in 40%, 2 in 18%, 3 in 15% and 4 in 7% of the cases. 14 patients had 2 positive MMS: 5 with different agents and 9 with the same agent. Only the latter were pre-emptively treated. No untreated patients developed any SI. In contrast, all patients who developed posttransplant SI had 3 MMS positive for the same agent. Of those, one patient presented with multiple samples positive for Candida albicans. In spite of pre-emptive aggressive anti-fungal treatment, vacuum drain fluids remained positive for Candida albicans. Given the risk of mycotic aneurysm, a transplantectomy was performed on day 5 but graft cultures were negative.
Conclusion: MMS performed before transplantation are often positive. However, this does not seem to be predictive of posttransplant infection if one single sample is positive. Multiple samples should be routinely taken to allow for easier decision-making to avoid risks of life-threatening complications (mycotic aneurysms) and overreaction leading to undue transplantectomy. Only patients with multiple samples positive for the same agent should benefit from pre-emptive therapy.

P-339 PTH SUPPRESSION TEST PREDICTS PERSISTENT HYPERPARATHYROIDISM AFTER KIDNEY TRANSPLANTATION

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Background: Persistent hyperparathyroidism is frequent after renal transplantation whereas abnormalities of mineral metabolism are corrected progressively. Hyperparathyroidism can be complicated by hypercalcemia, hypophosphatemia, bone loss and fractures, and requires parathyroidectomy. High serum levels of parathyroid hormone (PTH) before transplantation are a well-known risk factor for persistent hyperparathyroidism. Our aim was to evaluate PTH secretion after a suppression test, and to describe the evolution of mineral metabolism according to the test results.
Methods: A PTH suppression test was performed prospectively at the time of transplantation in patients with PTH >100 ng/L during a hemodialysis session using a calcium-rich dialysate. Patients were divided in two groups according to the test results: group A (PTH decrease >50% of basal PTH) and group B (PTH decrease <50% of basal PTH). Mineral metabolism and clinical parameters were followed for 1 year post-transplantation.
Results: Forty-two patients were included in the study: group A (n=24) and group B (n=18). Mean PTH levels did not differ significantly between the groups before the dialysis session. The "non responders" group had a significantly higher incidence of persistent hyperparathyroidism, hypercalcemia, hypophosphatemia, higher serum concentrations of bone-specific-alkaline-phosphatase (BAP) and crosslaps, and more fractures during follow-up. Three parathyroidectomies were necessary in group B vs. none in group A. PTH decrease was correlated with PTH level, calcemia, phosphatemia, BAP and crosslaps levels after renal transplantation.
Conclusions: Low PTH suppressibility by calcium loading before transplantation predicts hyperparathyroidism persistence, hypercalcemia, hypophosphatemia, high bone turn-over, fractures, and need for parathyroidectomy.

P-340 INCIDENCE AND RISK FACTORS OF GLUCOSE METABOLISM DISORDERS AFTER KIDNEY TRANSPLANTATION: ROLE OF SYSTEMATIC SCREENING BY OGTT BEFORE TRANSPLANTATION

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Background: Transplant patients are at increased risk of developing diabetes after transplantation. Post transplant diabetes increases infectious and cardio-vascular complications and reduces both graft and patient survivals. We evaluate incidence of glucose metabolism abnormalities before and after kidney transplantation and studied risk factors for post-transplant diabetes using OGTT.
Patients and methods: 244 patients enrolled on the kidney waiting list from the 01/01/2005 to the 31/12/2007 at the University Hospital of Strasbourg (France) underwent an OGTT before transplantation. Patients with known diabetes were excluded. 106 patients received kidney transplantation and were screened for diabetes or glucose intolerance after transplantation. Diagnosis of new-onset diabetes after transplantation (NODAT), impaired glucose tolerance (IGT) and impaired fasting glucose (IFG) were based on American Diabetes Association (ADA) guidelines.
Results: IGT before transplantation was present in 19 (17.9%) of awaiting patients. NODAT occurred in 27 patients (25.5%) of whom 9 (47.4%) had an IGT before transplantation. OGTT done after transplantation also detected IGT in 13.2% of patients. Risk factors for NODAT were age, pre-transplant IGT, APKD, acute rejection and use of steroids after six months.
Conclusion: Our results suggest that the use of an OGTT before transplantation is a helpful tool to identify patients with risk of development of NODAT. Polycystic kidney patients are particularly exposed to glucose metabolism abnormalities after transplantation. For IGT and APKD patients, a adaptation of immunosuppressive treatment seems mandatory after transplantation. The benefit of steroid or tacrolimus avoidance needs to be precisely analysed in these populations.

P-341 DE NOVO SIROLIMUS-BASED REGIMEN IN ASIAN RENAL TRANSPLANTATION RECIPIENTS: A TWO-YEARS FOLLOW UP

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Calcineurin-inhibitor (CNI)-minimization with sirolimus (SRL)-based immunosuppression could reduce CNI-nephrotoxicity in Caucasian and African Ameri-

can kidney transplant recipients. There are insufficient data regarding the long-term effect in Asian.
A prospective single center regarding two-year outcomes were conducted in 21 recipients who received de-novo SRL-based with cyclosporine (CSA) minimization regimen (SRL-based regimen) during 2004-2008. The control group was a cohort of 82 recipients of CSA-based regimen (CSA, MMF, and prednisolone). Immediately post-transplantation, SRL-based group had received CSA, azathioprine, and prednisolone. Fourteen days post-transplantation, SRL was introduced, azathioprine was discontinued, and CSA dosage was reduced to maintain the recommended trough level of 100-150 ng/mL in the first three months. The target SRL levels were 8-12 ng/mL.
At 24 months, both regimens provided 100% patient and graft survival. The biopsy-proven acute rejection rates were comparable between the two groups (14.3% vs. 14.5%). The eGFR (abbreviated MDRD; mL/min/1.73m^2) in SRL-based group gradually increased to be more than CSA-based group, 56.3±14.3 vs 52.6±15.2 at 6th month (p=0.33), 66.2±27.3 vs 55.8±17.5 at 12th month (p=0.05), and 69.1±25.9 vs 55.4±17.6 at 24th month (p=0.01).
In SRL-based group, the CSA levels were 163 and 154 ng/mL at 1st and 3rd month. Forty-three percent of recipients underwent either protocol (19%) or clinical-guided (24%) allograft biopsy. The incidence of CNI-toxicity was 23.8%. The CSA levels were reduced to 46, 41, and 35 ng/mL at 12th, 18th, and 24th month. After 12 months, the number of CNI-toxicity was not increased. The eGFR of recipients with CNI-toxicity was improved from 42.1±17.8 at 6th month to 54.4±18.7 at 24th month (p=0.04).
De-novo SRL-based with CSA-minimization provides better renal function. The protocol biopsy can provide information for tailoring treatment. Further studies to identify the optimal CSA levels of SRL-based regimen for Asian are required.

P-342 TRANSPLANTATION IN ADULTS WITH PRIMARY HYPEROXALURIA: EXPERIENCE WITH 5 CASES

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Introduction: The incidence of primary Hyperoxaluria with End Stage Renal Failure (ESRF) in Europe remains around 1:120 000, with 80% of patients developing ESRF by the third decade. Primary Hyperoxaluria type 1 (PH1) is an autosomal recessive metabolic disorder caused by deficiency of the alanine-glyoxylate aminotransferase whilst Primary Hyperoxaluria type 2 (PH2) is caused by a defective D-glycerate dehydrogenase.
Methods: A retrospective review of five cases of Primary Hyperoxaluria managed at a major renal unit was performed. The cases were evaluated with a focus on presentation, symptoms, dialysis, transplantation, recurrence of disease and retransplantation.
Results: The 5 patients had a mean age of 32.2 years at time of first transplantation. The common presenting symptoms were urolithiasis (4), nephrocalcinosis (3), recurrent urinary tract infections (2) and uraemia (1). They all had signs of ESRF at diagnosis. 4 patients had PH1 and one had PH2. 3 patients had kidney only transplants (one live, 2 deceased donors) and 2 had segmental liver followed by delayed kidney transplantation. All 3 kidney alone (100%) failed, the first at 3 weeks (oxalate nephrocalcinosis and urolithiasis) the second at 9 years (recurrent urolithiasis) and the third at 13 years (chronic allograft nephropathy). Out of these three patients, one is now awaiting a live donor transplant, one underwent kidney alone retransplantation (failed 5 years later) and one had a combined deceased donor liver and kidney transplantation (remains well at 4 years). The 2 segmental liver sequential kidney transplant recipients remain well at 1 year and 3 years.
Conclusion: Primary Hyperoxaluria should be considered in calculus ESRF and remains a management challenge. Isolated deceased donor kidney transplantation invariably fails. Combined liver-kidney transplantation may be a better choice as the primary transplant procedure although living donor kidney transplantation after intensive dialysis is an option.

P-343 ASSOCIATION BETWEEN TWO POLYMORPHISMS IN IMMUNITY GENES AND CYTOMEGALOVIRUS REACTIVATION AFTER KIDNEY TRANSPLANTATION

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Purpose: Cytomegalovirus (CMV) infection is associated with morbidity after organ transplantation. IL-12 and PD-1 play a role in anti-infectious responses by stimulating and inhibiting IFNγ production respectively. An A-to-C polymorphism within the 3'UTR region of the IL-12p40 gene and a G-to-A polymorphism (called PD-1.3) within the intron 4 of the PD-1 gene were reported to be clinically relevant. However, their association with events after transplantation has never been reported. In this retrospective study, we assessed the association between these polymorphisms and the occurrence of CMV infection in kidney graft recipients.
Patients and methods: Restriction fragment length polymorphism method was used to genotype these polymorphisms in 469 Caucasian patients who had received a kidney transplantation at the University Hospital of Tours between 1995 and 2005. Then we assessed the occurrence of CMV infection, determined by pp65 antigenemia.
Results: The *IL12B* 3'UTR polymorphism and PD-1.3 were associated with CMV infection, especially in a subpopulation containing only the seropositive recipients before graft who did not receive any CMV prophylaxis (n=222; OR=1.91, p=0.021 and OR=2.60, p=0.006, respectively). In addition, multivariate analysis showed that the variant alleles were independent risk factors of CMV reactivation (OR=1.88, p=0.028 and OR=2.54, p=0.010, respectively). Interestingly, we found that the group bearing the PD-1.3 A allele regardless of the *IL12B* allele were at very high risk of CMV infection compared to patients having none of the 2 risk alleles (74% vs 43%, OR = 3.76, p<0.001).
Conclusion: We identified 2 new genetic risk factors for CMV reactivation after kidney transplantation. The analysis of these polymorphisms allowed us to stratify the risk of CMV reactivation into 3 groups according to *IL12B* 3'UTR and PD-1.3 genotype (high, low and intermediate). This result suggests that an adaptation of CMV prophylaxis based on genetic markers would merit further investigation.

P-344 EVOLUTION OF BONE DISEASE IN 2 YEARS AFTER TRANSPLANTATION; A PROSPECTIVE SINGLE CENTER STUDY

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Post transplant bone disease is caused by renal osteodystrophy (dialysis, IS drugs and metabolic factors after transplantation). Aim of study: to examine bone mineral density (BMD) and to identify factors preventing bone loss in patients (pts) in the first 2 years post transplant.
Material and methods: 90 renal allograft recipients (age 42,7±11,4 years), treated with cyclosporine/tacrolimus, azathioprine/MMF and prednisone. BMD of lumbar spine ((LS), femoral neck, Ward's and Trochanteric region were performed by DEXA in the third month and every 6 months for 2 years after Tx. Markers of bone remodeling: iPTH, calcitriol, osteocalcine and carboxyterminal telopeptide of type-I collagen were assayed on the third day, 1-st month and every 6 months.
Results: In the initial measurement, osteopenia (OSP) was found in 35% in the LS region and 52% in femur; osteoporosis in 8.3% (according WHO classification). Prevalence of OSP increased during the first year, then decreased to initial value, but frequency of osteoporosis did not change (8,3 vs. 6,0%). BMD and Z-score decreased during 1-st and increased in the 2-nd year; 27% pts achieved initial values and 38% higher than initial values.
BMD gain in LS and femur was found in pts with higher calcitriol level during first 6 months (P<0.01); higher osteocalcin level (P<0.05); higher eGFR during 1 to 24 months and in tacrolimus group. Improvement of LS BMD occurred in younger pts (38 vs. 46 years; P<0,027). BMD gain in femur correlated with higher level of iPTH 1-12 months (P<0,01);. Tacrolimus group had higher Z-score in lumbar and femur at 24 month in comparison to cyclosporine (p<0,05).
Conclusions: Two years after transplantation >60% of pts showed stability or gain in bone mass. Sufficient calcitriol level in early transplant period, adequate iPTH, renal efficiency and tacrolimus IS prevent progression post transplant bone disease.

P-346 VERY HIGH PREDITIVE VALUE OF BLOOD MIG LEVEL IN KIDNEY TRANSPLANT PATIENTS

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FlowCytomix Comboplex quantifies different growth factors in a small sample. We studied in KTx a group of cytokines/chemokines (IL-2, IL-10, IL-18, TNF-β, TNF- α, IFN-α, sCD40L, MIG, MIP-1α), which are important players in the alloimmune response and that can be modulated by different therapy.
Patients (n=49) were cadaver KTx, treated with CNI from the outset, excepted ATG group which started CNI post-day 7. Furthermore eight received IL-2R

αAb, and nine had RAPA plus CNI. Patients were divided into group I, rejection-free (n=36) and Group II, rejection (n=13). All rejections were confirmed by biopsy. Sera collected on day 7 post-KTx and on rejection day between day 7 and one year. Group I was further subdivided into Ia (ATG, n=8)), Ib (IL-2R αAb, n=9), Ic (Rapa, n=9)) and Id (triple immunosuppression, n=10).
No difference was found for demographics of donor-recipient, except in re-KTx that were significantly higher in Ia versus other I subgroups, but not different when comparing I vs II. A significant difference was observed in I vs II for IL-18 (392±228 vs 653±389 pg/mL, p=0.018) and MIG (276±578 vs 1578±2301 pg/mL, p<0.000, PPV for rejection 67% and NPV 93%) while IL-2, IL-10, TNF-β, TNF-α, IFN-α, sCD40L and MIP-1α showed no differences. In the I subgroups, MIG was significantly upregulated in Ia vs Id (531±923 vs 308±731pg/mL, p=0,043), and MIP-1α was higher in Ia (p=0.055) versus Id.
Our study shows that two important factors of the alloimmune response are upregulated in blood, which if confirmed in a larger group, would constitute a quick test to monitor the alloimmune response. Surprisingly, no differences were observed when comparing different therapies among stable KTx, but an upregulation of two important chemokines in ATG group, probably associated with cytokine release.

P-347 A MULTICENTER RCT OF DECEASED ORGAN DONOR PRE-TREATMENT WITH CORTICOSTEROIDS: RISK FACTORS FOR ARF IN STEROID PRE-TREADED DONORS

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We have recently shown in a RCT of 269 donors that steroid pre-treatment of the deceased donor changes the gene expression profile of inflammatory signatures in the transplant organ but does not reduce the rate or duration of ARF. The present paper sought to elucidate risk factors for ARF other than inflammation in all steroid pre-treated deceased organ donors.
We made use of 238 recipients of steroid pre-treated donor organs and analyzed genome-wide gene expression profiles of donor kidney biopsies with subsequent systems biology approaches such as transcription factors analysis, regulatory networks, and protein-protein interaction data.
At the time of abstract submission 20 randomly selected biopsy samples have been analysed. SAM (significance analysis of microarrays) yielded 101 significant down-regulated sequences associated with ARF that can be categorized according to PANTHER ontologies into two main biological processes: transport (p<0.001) and metabolism (p<0.001). Identified members of the process transport are nine solute carriers, AMN, LCN2 (NGAL) and APOD.
These preliminary genomics data suggest that reduced transport and metabolism are associated with ARF. A more precisely analysis of the clinical and transcriptional data will be presented at the meeting.

P-348 INCIDENCE AND CLINICAL CHARACTERISTICS OF POST-TRANSPLANT LYMPHOPROLIFERATIVE DISORDER DURING 38 YEARS OF KIDNEY TRANSPLANTATION AT THE SINGAPORE GENERAL HOSPITAL

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Purpose: We evaluate incidence and clinical characteristics of Post-Transplant Lymphoproliferative Disorder (PTLD)in kidney transplant recipients (KTX)at our hospital.
Method: The medical records of 1629 KTX between the period of 8th July 1970 and 31st December 2008 were reviewed for PTLD.
Results: The incidence of PTLD was 1.04% (n=17/1629) with a progressive incidence increase across the decades (0.65%, 1.10% and 1.19% during 1970-1987, 1988-1998 and 1999-2008 respectively). Median time of onset of PTLD was 9.2 (range 0.2-19) years. At diagnosis, median age was 48 (rage 37-81) years and 58.8% (n=10/17) were on cyclosporine-based immunosuppression. Patients on mycophenolate mofetil had shorter median time of onset of PTLD (1 year, 95% CI 0.46, 1.5)than those who are not (12 years, 95% CI 5.2, 18.8). Prior to diagnosis of PTLD, 47.1% (n=8/17) developed rejections, of which 50% (n=4/8) were treated with anti-lymphocyte serum. The most common presentation was extranodal disease (64.7%; n=11/17), which involved multiple-organ sites (64.7%; n=11/17) and were classified as stage 4 (52.9%; n=9/17). Most PTLD were of B-cell lineage (88.2%; n=15/17) and among 11 cases, 10 (90.9%) had tissue positivity for EBV. Immunosuppression was either reduced, withdrawn or switched to a mTOR inhibitor. As a result of immunosuppression reduction, rejection occurred in 23.5% (n=4/17) but graft loss from rejection was only 5.9% (n=1/17). Among 16 patients who had follow-up after treatment, remissions were complete in 56.2% (n=9/16), partial in 37.5% (n=6/16) and did not occur in one patient. At last follow-up, the median serum creatinine was 138 [range 69-348] mmol/L.
Conclusion: Reduction of immunosuppression for PTLD is associated with a low risk of graft loss.

P-349 IS DEFICIENCY OF 1,25-DIHYDROXYVITAMIN D3 A PREDICTIVE FACTOR OF POORER OUTCOME IN RENAL TRANSPLANTATION

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Calcitriol-l,25-dihydroxyvitamin D3, has multiple biological and immunomodulatory effects at the cellular level. In animal the efficacy of calcitriol in prolonging allograft survival was demonstrated. Deficiency of calcitriol is associated with cardiovascular and cancer morbidity in general population.
The aim of this study was to assess calcitriol status in renal allograft recipients and its impact on the outcome of transplantation.
Material and methods: The study entailed 90 patients transplanted between 2002-2005. All the patients received supplementation of Vitamin D before transplantation. The calcitriol levels were determined on 3rd day and at the 1st, 6th, 12th and 18th month after transplantation by radioimmunoassay.
Results: Severe calcitriol deficiency (7.3±3.3 pg/ml) was found in 83% of patients immediately after transplantation. From the 1st to 12th month the level increased almost 3-fold, and then remained constant at 18th month (Table). Only 50% of recipients reached a level >30pg/ml (similar as healthy control), and the remaining recipients had 17.2±6.4 pg/ml.
A high incidence of DGF occurred in patients with calcitriol deficiency (44% vs. 6%). Negative correlation of initial calcitriol level with serum creatinine on 3rd day and 6th month (p<0.03) was found. Similarly calcitriol level at 1-st month negatively correlated with creatinine levels at months 1 through 18 (p<0.01). Poor outcome was observed mainly in patients with deficiency of calcitriol: 2 developed cancer; 2 lost graft in 1st year, 3 in 2nd year; 4 died due to cardiovascular events.
Conclusions: Deficiency of calcitriol in renal allograft recipients was highly prevalent. Patients with calcitriol deficiency were at higher risk of DGF, and were more likely to lose their graft. This work points out at the necessity of adequate supplementation of vitamin D3 before and after transplantation.

P-350 OUTBREAK OF DISEASE OF SEVEN PNEUMOCYSTIS PNEUMONIA AT AROUND JUST SAME TIME AFTER RENAL TRANSPLANTATION

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There has been splendid progress about immunosuppressive drug in organ transplantation. However, the immunosuppressive therapy may cause serious infectious diseases after renal transplantation. In this paper, seven outbreaks of the interstitial pneumonia which were strongly suggested to be pneumocystis pneumonia (PCP) occurred among renal transplant recipients. The mean period from the transplantation to the occurrence was 15.9 months. Their chief complaints were high fever and dyspnea. Interstitial pneumonia was conjectured by plain chest CT in all cases. ST combination medicine was administered to all cases. Steroid pulse therapy was also performed in the cases with severe dyspnea. One case died and the other six cases were cured. The factors of higher age, the period after 2000 when the transplantation was performed and the use of immunosuppressants of BXM and MMF were associated with the occurrence of PCP-like pneumonia. It is suggested that the outbreak of the PCP-like pneumonia was the hospital-acquired infection because those patients were in the hospital at the same time or came to our clinic on the same day. We started to administer ST combination medicine prophylactically to new renal transplant recipients and PCP-like pneumonia has not occurred since then.

P-351 MANAGEMENT OF LOCALIZED PROSTATE CANCER BY RETROPUBIC RADICAL PROSTATECTOMY IN PATIENTS AFTER RENAL TRANSPLANTATION

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Purpose: The incidence of prostate cancer may be affected by long-term im-

munosuppression. However, when managing prostate cancer after renal transplantation, the presence of a pelvic renal graft and the potential for future transplants in the event of graft failure are to be considered. We present our experience with retropubic radical prostatectomy (RRP) for treatment of localized prostate cancer in renal transplant recipients.
Patients and methods: Data of 11 renal transplant recipients who had a RRP between 2002-2007 were retrospectively analyzed. DRE findings and/or elevated serum PSA levels, as well as TRUS-guided prostate biopsy were used for diagnosis. Postoperative follow-up consisted of physical examination and serial serum PSA measurements every 3 months. Follow-up was obtained in all patients with a mean follow-up time of 2.2 years.
Results: Mean time distance to the renal transplantation at the time of RRP was 81.2±19.1 months (range; 28–219 months). Mean age at surgery was 61.8±3.1 (53–71) years, and all patients have had cadaveric transplant. RRP was successfully performed and tolerated in all patients without pelvic lymph node dissection. No major complications occurred during or after the operation. There were two minor complications in two patients (prolonged haematuria and leakage). Mean operative time was 88.3±3.9 min (79–118 min), mean intra-operative blood loss was 384.1±203.1ml (128–1298 ml), and mean duration of hospital stay was 9.1±2.4 days (7–13 days). As shown by stable levels of serum creatinine as a measure of graft function, none of the patients had worsening graft function. At follow up, none of the patients had evidence of biochemical recurrence.
Conclusions: RPP is safe and feasible for management of localized prostate cancer in patients with kidney allograft being under immunosuppression. However, concern about impairment of graft function, infection and wound healing remain important.

P-352 IMMUNE FACTORS THAT INCREASE A CHANCE OF ACCEPTANCE OF ALLOGENEIC KIDNEY IN ELDERLY RECIPIENTS

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Introduction: The elderly are known as the population with compromised immunity. In this study we looked for biological markers that distinguish elderly recipients less prone to reject allogeneic kidney grafts and could possibly help finding a group in whom reduced immunosuppression can be administered.
Methods: We have analyzed 18 pairs of kidney transplant recipients from the same donors. Each pair consisted of old (ERP) and young (YRP) recipient, age $\geq$ 60 or $<$60, respectively. Peripheral blood CD4+ and CD8+ T cells were examined for the length of telomeres, the proportion of naïve (Tn) and memory (central memory and effector memory) subsets and the percentage of functional CD28+ cells. Mixed lymphocyte reaction with allogeneic stimulators and anti-CD3/CD28 beads was performed as functional test. Both, ERP and YRP were divided according to the onset of acute rejection (AR) in the past.
Results: History free of AR in ERP was associated with impaired condition of CD4+ T compartment (short telomeres and decreased proportion of CD28+ T cells). In contrary, rejecting ERP kept preserved telomere length and significantly higher number of functional CD28+ cells within CD4+ T subset. AR in YRP was different as it was associated with increased percentage of CD8+CD28- T cells, mainly in antigen-experienced effector memory subsets.
Conclusion: The feature that made the elderly less responsive to allogeneic kidney graft was the immunosenescence of CD4+ T cells. Rejection in ERP seemed to be associated with both preserved telomere length and significantly higher number of functional CD28+CD4+ cells, whereas in YRP AR was associated with increased level of CD8+CD28- T cells within differentiated memory cells, which is the feature of clonal expansion of CD8+ T cells.

P-353 THE ROLE OF ISOTOPE DIFFERENTIAL RENAL FUNCTION IN ASSESSING POTENTIAL LIVING KIDNEY DONORS

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Purpose: This study evaluated a possible correlation between Mercapto Acetyl Tri-Glycine (MAG3) differential renal function and kidney size measured by ultrasonography (US).
Methods: Between March 2003 and November 2008 a total of 81 potential kidney donors underwent the assessment process including 51-Chromium ethylenediaminetetraacetic acid scans for GFR measurement, 99-Tc MAG3 renograms for differential renal function and renal US to determine size. The donated GFR was calculated as a percentage of the total donor GFR according to the split function of the donated kidney. Transplant outcome [eGFR and creatinine (Cr) at 1, 3 and 6 months] was analysed according to the donor-recipient gender pairing (MM, MF, FF & FM), category of differential function (0% = A; 1-10% = B; 11-20% = C; $>$21% = D), donor sex and donated GFR.
Results: The mean donated GFR correlated significantly with categories of differential function (F=4.998, p=0.01). However, the mean GFR and mean Cr in recipients from the different categories at 1, 3 and 6 months were not significantly different. Donor-recipient gender pairing did not significantly affect eGFR or Cr at 1, 3 and 6 months post operatively. Right (r = 0.286, p = 0.01) or left kidney (r = 0.351, p = 0.035) length correlated significantly with GFR. Also, differential function correlated significantly with difference in length between right and left kidneys (r = 0.333; p = 0.005). However, in 7 donors kidney length was inversely related to the divided renal function. In 3 donors with differential function greater than 20% there were negligible differences in their lengths.
Conclusions: Donors could have their better kidneys removed if US alone is used. We advocate that differential renal function is used to assess all potential donors prior to kidney donation.

P-354 DONOR PERSPECTIVES IN LIVING KIDNEY DONATION

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Purpose: The aim of this study was to determine the overall experience (assessment, procedure and postoperative course) of kidney donors and to obtain their feedback about our service.
Methods: All 80 kidney donors at Derriford Hospital, Plymouth between 2003 and 2008 were sent a postal questionnaire to determine the level of satisfaction with the kidney donation process including postoperative pain (1, 4 and 12 weeks), return to fitness and whether they would consider altruistic donation or recommend living kidney donation to others. Fifty six completed questionnaires are the subject of this analysis. A qualitative analysis of the responses was also performed.
Results: Fifty-six donors (24 male, 32 females; 49 related, 15 unrelated & 2 altruistic) returned the questionnaires. Forty donors were employed, 10 retired, 3 unemployed, 2 carers and 1 disabled. The mean pain scores, time off work and loss of earnings are shown in Table 1. There was no correlation between pain at 4 weeks and loss of earnings (P = 0.132). Fifty-two (93%) rated their overall experience as excellent or good, and 48 (85%) had no regrets about donating. Fifty-five (98%) felt they had been given enough information before their operation and would recommend donation to their friends. Twenty six (46%) would have considered altruistic donation if they were unable to donate to their intended recipient. Qualitative analysis of responses showed a positive attitude to organ donation, with a willingness to encourage others, a request for chat facilities on the Unit's website and a more regular follow up.

Postoperative experience of kidney donors

Parameter	Number	Mean	Standard Error of Mean	Median	Range
Time off work (weeks)	40	9.75	0.722	8	0-24
Return to usual activities (weeks)	46	10.07	1.174	8	1-48
Pain score: 1 week	54	4.88	0.402	5	0-10
Pain score: 4 weeks	54	2.35	0.305	2	0-8
Pain score: 12 weeks	53	0.67	0.180	0	0-6
Loss of earnings	29	995.17	297.03	0	0-4800

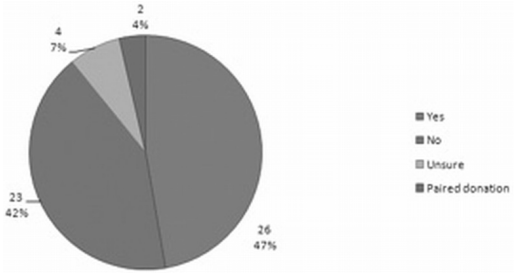

Figure 1. If unable to donate to loved one, would you consider altruistic donation?

Conclusions: To increase living kidney donation there is need to address the issue of compensation for loss of earnings. Forty-six percent of donors would have considered altruistic donation if they were unable to donate to their intended recipient.

P-355 PHARMACOKINETICS OF TACROLIMUS IN RENAL TRANSPLANT PATIENTS WITH PREVIOUS GASTRIC BYPASS SURGERY

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Aim: Tacrolimus is a vital immunosuppressant used in transplant patients. Ani-

mal studies have shown that absorption is throughout the gastrointestinal tract which is primarily through the jejunum followed by duodenum, ileum, colon then stomach. Patients who have undergone gastric bypass surgery have smaller stomachs, duodenal and jejunal surfaces for drug absorption. Hence we set out to investigate if altered pharmacokinetics of tacrolimus are observed in a renal transplant patient who had previously undergone gastric bypass.
Methods: A 45 year-old man who underwent gastric bypass for obesity, had a live donor transplant two years later. He was commenced on 4.5mg of Tacolimus with Mycophenolate Mofetil 750mg BD as immunosuppression. Whole blood Tacrolimus levels were taken at 0 (pre-dose), 1, 3, 6 and 12 hours. Samples were analysed by mass spectrometry. Results were compared to tacrolimus pharmacokinetic profile from study using renal transplant patients (n=6) also on the same combination of immunosuppression.
Results: Cmax was 23mcg/L at 1 hour post-dose, comparable to the control group 24.7 ($\pm$11.5). Cmin was 9mcg/L which was higher than the control group of 6.6 ($\pm$2.7). There was no significant difference in both parameters between the gastric bypass patient and control group.
Conclusions: Gastric bypass surgery does not significantly alter the pharmacokinetic profile of Tacrolimus. This indicates that the stomach and duodenum do not play as an important role in tacrolimus absorption as initially thought.

P-356 FRENCH REGISTRY OF PTLD AFTER KIDNEY TRANSPLANTATION: ANALYSIS OF GRAFT, BRAIN AND GASTRO-INTESTINAL TRACT LYMPHOMAS

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PTLD are a well-recognized complication after kidney transplantation. However, this complication is rare and analysis of large series are scarce.
Methods: The French Registry of PTLD enrolled 378 PTLD during 10 years. We studied characteristics of lymphomas developed in kidney graft, brain and gastro-intestinal tract.
Results: - 61 patients developed PTLD within the graft. 61% of graft PTLD arose during the first post-transplant year and the median of diagnosis is 13 months (vs. 90 months, $p<0.0001$). Acute renal failure is more frequent: mean creatininemia = 200 μmol/l vs 156 μmol/l, p=0.005. 70% of tumors were located in the graft only and 73% were EBV+. Patients survival was 61% at 10 years. Single site tumor, early onset lymphoma, polymorphic histology and EBV positivity in the tumor were associated with better survival.
- 48 patients developed a brain lymphoma. Brain PTLD were more frequent in women (sex ratio 0.8 vs. 2.1). Only 17% are early-onset lymphoma. However, brain lymphomas occurred sooner (median = 33 months vs. 88 months, p=0.001). Brain PTLD are localized in a single site in 83% and 82% were EBV+. Survival was 60% at 1 year and 33% at 10 years. Radiotherapy did not improve patient survival.
- GIT lymphomas occurred in 92 cases. It is the more frequent location. Majority of patients are men and most PTLD were late-onset. Most PTLD were located in the stomach and/or small bowel. Only half were found to be EBV+. Survival was 68% at 1 year and 37% at 10 years. Multiple sites PTLD was associated with a poor survival.
Conclusion: Analysis of subgroups of lymphoma permit to distinguish some particular features of PTLD in graft, brain and GIT and could help for the management of these patients.

P-357 CLOSURE OF HIGH-VOLUME ARTERIOVENOUS FISTULAS RESCUES RENAL ALLOGRAFT FUNCTION IN PATIENTS WITH RIGHT HEART FAILURE. A RETROSPECTIVE ANALYSIS OF 6 PATIENTS

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Background: Chronic right heart failure (CRHF) with consecutive venous congestion in patients (P) with chronic kidney disease (CKD) may reduce kidney allograft perfusion and may be associated with delayed graft function and poor prognosis. Since no data exist addressing this problem, we retrospectively analyzed 6 patients prior or after kidney transplantation (KTx) with chronic inferior vena cava and iliac congestion.
Methods: 6 CKD patients (64$\pm$8 years, m/f: 3/3) with primary unknown CRHF were analyzed: 1 patient prior (P_1) and 5 patients after kidney transplantation ($P_{2\text{-}6}$). All patients had normal left ventricular function (ejection fraction $>$ 60%)and were in good physical condition without history of chronic pulmonary disease. All patients underwent right heart catheterization. KTx patients had marginal graft function (GFR: 13$\pm$3 ml/min). Acute rejection was excluded by biopsy in all KTx patients.
Results: Hyperdynamic arteriovenous fistula (AVF) with mean fistula flow $>$ 2l/min was the underlying cause of CRHF in 5 patients ($P_{1\text{-}5}$), idiopathic pulmonary hypertension (IPH) was diagnosed in P_6. Flow reduction (P_1, P_2) or closure (P_3, P_4, P_5) of AVF reduced cardiac output by 21 $\pm$ 9% and reversed iliac congestion completely. Graft function increased significantly in KTx patients ($P_{2\text{-}4}$) by 26$\pm$8 ml/min (GFR) (table).

Patients	Before Intervention				After Intervention	
	MPAP (mmHg)	PCWP (mmHg)	GFR (ml/min)	CO (l/min)	GFR (ml/min)	CO (ml/min)
P1	26	24	$<$10	9.1	NT	6.8
P2	30	13	16	5.6	41	4.7
P3	25	19	14	6.4	32	4.7
P4	10	16	12	12.2	61	7.8
P5	27	18	15	9.1	28	7.1
P6	30	32	$<$10	6.3	$<$10	6.5

MPAP: Mean pulmonary artery pressure; PCWP: Pulmonary capillary wedge pressure; CO: Cardiac output; NT: not transplanted

Since treatment of IPH (sildenafil and tricuspid reconstruction) in P_6 was not able to reverse iliac congestion, the patient remained on dialysis without graft function.
Conclusion: Since untreated CRHF is associated with poor graft function we recommend screening all patients for chronic iliac congestion on the waiting list. Especially hyperdynamic AVF should be corrected prior KTx.

P-358 CARDIOPULMONARY EXERCISE TESTING COULD BE USEFUL FOR ASSESSING FITNESS FOR RENAL TRANSPLANTATION

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The ability to adapt to increased oxygen demand predicts the risk of early death and postoperative outcome. At present there are no methods to predict cardiac risk after renal transplant.
Aerobic capacity as a measure for left ventricular function was assessed by cardio-pulmonary exercise testing (CPET). This is predictive for mortality after other types of surgery and at altitude in healthy people. The anaerobic threshold (AT) expressed as oxygen consumption index to body mass (ml/min/kg) was compared to known predictors of survival in CKD patients.
Over 12 months CPET results were obtained on 110 patients, age 25-74 years (median 54.7) (female 22%) and AT range 5.6-30.8 ml/min/kg (mean 12.0); maximal oxygen uptake (peak VO_2) 6.6-34.6 ml/min/kg (mean 16.1), on average 55.9% of the predicted values. AT was correlated with age ($p<0.0001$), male vs female gender (13.4 vs. 10.5 ml/min/kg; p=0.003) and diabetic vs non-diabetic (9.5 vs. 12.3 ml/min/kg; p=0.02). Echocardiographical evidence (n=77) of left ventricular hypertrophy (LVH) resulted in a lower AT (p=0.02).
AT $<$11 ml/min/kg has been identified as mortality risk in other types of surgery, and 48% of our patents on the transplant list were in this category. They were older (p=0.02), had higher BMI (p=0.008), more had diabetes and evidence for left ventricular hypertrophy and diastolic dysfunction. CKD and dialysis duration, lung function, known history of coronary artery disease and haemoglobin levels were not different in the two groups.
To our knowledge this is the first study investigating the 'normal' range of AT in CKD patients. Almost half had a low AT putting them potentially at increased risk of peri-operative mortality. However, the threshold observed in non-renal patients may not apply. The usefulness of CPET as a predictive tool for CKD patients, replacing classical methods, is under investigation.

P-359 BETTER RENAL FUNCTION IN RENAL-TRANSPLANT RECIPIENTS TREATED WITH EVEROLIMUS PLUS CSA ELIMINATION COMPARED WITH CSA REDUCTION

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Use of the proliferation signal inhibitor everolimus (EVL) in combination with cyclosporine (CsA; Neoral®) elimination or reduction may improve renal function.

Methods: Two similarly designed multicentre, prospective, randomized studies (RAD A2419 and A2423) evaluated renal function in *de-novo* kidney-transplant recipients treated with EVL (C_0 levels 3–8ng/mL up to Month 3 [M3]), basiliximab, CsA and steroids. At M3, patients were randomized to CsA reduction (CsA-RD; C_2 target levels were 300–500ng/mL in A2419 and 350–450ng/mL in A2423) or CsA elimination (CsA-EL; by M4 in A2419 and M6 in A2423, with EVL C_0 target levels of 8–12ng/mL). The primary endpoint for comparison was renal function (glomerular filtration rate [GFR]) at M12. Key secondary objectives included composite efficacy failure (biopsy-proven acute rejection [BPAR], graft loss, death or loss to follow-up) and safety.
Results: Analyses of pooled data are presented for 170 enrolled patients (A2419, n=119; A2423, n=51). 54/170 (31.8%) patients discontinued treatment before randomization (mainly due to adverse events [18.2%]) and two patients were not randomized. 114 patients were randomized (55 CsA-EL and 59 CsA-RD). Prior to randomization, mean±SD CsA-RD C_2 levels were: A2419, 758.0±202.1ng/mL and A2423, 640.3±113.5ng/mL. CsA-EL C_2 levels were: A2419, 716.1±166.7ng/mL and A2423, 666.8±155.2ng/mL.
Mean cGFR (Nankivell) was comparable at M3 (CsA-EL: 69.2±18.4 *vs* CsA-RD: 68.5±19.9mL/min/1.73m^2) but was higher by M12 for CsA-EL *vs* CsA-RD (68.3±15.1 *vs* 63.6±14.6mL/min/1.73m^2; p=0.0289). Composite primary efficacy failure rate at M6 was CsA-RD: 12.3% *vs* CsA-EL: 9.4% and at M12, CsA-RD: 17.5% *vs* CsA-EL: 18.9%. All primary failures at M6 and M12 were BPARs. The incidence of AEs and serious AEs was comparable between groups at M12.
Conclusion: In this randomized study population, EVL allowed CsA elimination without compromising efficacy and provided a regimen leading to stable renal function.

P-360 THE EFFECT OF HEMODIALYSIS AND DIALYSIS ANTICOAGULATION BEFORE TRANSPLANT SURGERY ON EARLY RENAL ALLOGRAFT FUNCTION – A PAIR OF RANDOMIZED CONTROLLED TRIALS

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Background: Hemodialysis immediately before kidney transplantation has been suggested to adversely affect allograft function. We sought to assess the clinical impact of preoperative dialysis and dialysis anticoagulation in two related randomized trials
Methods: Eligible kidney transplant candidates with a serum potassium ≤5.0 mval/L were randomized to receive dialysis (heparin anticoagulation) or no dialysis prior to surgery. Patients with a potassium >5.0 meq/L were randomized to receive dialysis with heparin or with regional citrate anticoagulation. Pre-transplant dialysis consisted of euvolemic three-hour treatment with a polysulfone dialyzer. The primary endpoint was the estimated glomerular filtration rate (eGFR) at post-transplant day 5.
Results: The study population consisted of 220 recipients of a deceased donor allograft. The first comparison (56 versus 54 patients) revealed no effect of dialysis on estimated glomerular filtration rate (eGFR) at day 5 [12 (interquartile range: 5-36) versus 13 (5-37) mL/min/1.73 m^2, P=0.98], rates of delayed graft function (DGF, 22% versus 27%, P=0.66), early cellular rejection (20% versus 24%, P=0.65) and C4d-positive dysfunction (2% versus 9%, P=0.11), or 1-year death-censored graft survival (89% versus 91%, P=0.51). Comparing citrate with heparin anticoagulation (44 versus 66 patients), no differences in eGFR [17 (8-31) versus 14 (6-38) mL/min/1.73 m^2, P=0.57], DGF (21% versus 30%, P=0.28), cellular rejection (23 versus 33%, P=0.29) and graft survival (90% versus 88%, P=0.44) were found. For citrate anticoagulation, a trend towards lower C4d-positive rejection rates was observed (0% versus 8%, P=0.08).
Conclusions: Pre-transplant hemodialysis and anticoagulation mode may not affect early renal allograft performance.

P-361 RENAL GRAFT MASS AND TRANSPLANT OUTCOME

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Long-term kidney function depends on multiple factors. One of the factors that might affect survival and function of kidney graft is the functional mass of the graft.
In order to study whether graft mass may be a determinant of outcome after kidney transplantation we investigated the impact of the ratio between donor kidney weight (DKW) in grams and recipient body weight (RBW) in kilograms on creatinemia, creatinine clearance (MDRD formule) and proteinuria.
Delayed graft function, number of rejection episodes and graft survival were also considered. Donor and recipient data were collected at the time of inclusion and then at each follow-up (3, 6, 12, 24 and 36 months after transplantations).
One hundred fifty-four kidneys were weighted immediately before grafting; the donors were 95 males and 59 females, mean age was 49±14 years, and mean body weight was 72±15 kg while the recipients were 89 males and 65 females, mean age was 50±12 and mean body weight was 64±12 kg. The mean HLA incompatibility was 3±1. The mean kidney weight was 227±59 g.
The study evidenced a slight increase in creatinine clearance during the first six months of follow-up in the patients with DKW/RBW ratio <3g/kg, when recipient and donor sex and age, cold ischemia time, HLA mismatches, reject number, delayed graft function and time after transplantation were also considered. Moreover in the same period of follow-up we showed significantly greater occurrence of proteinuria (defined as >0.5g/24h) in the recipients with DKW/RBW ratio <2.5g/kg (Hazard ratio=3.6, p<0.001) by mean of Cox proportional-hazards model analysis.
These data showed a rapid impact of graft mass on filtration rate and proteinuria, which disappeared in the long-term follow-up.

P-362 EARLY RENAL ISCHEMIA-REPERFUSION INJURY IS PREVENTED BY IL-6 RELEASE FROM THE ALLOGRAFT

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Purpose: Ischemia-reperfusion (I/R) injury is the paradoxical exacerbation of tissue damage upon re-oxygenation of previously ischemic tissue and is the inevitable consequence of organ transplantation and vascular surgery. The pathophysiology of I/R injury is complex and its exact mechanisms have not been fully elucidated yet. We used human living donor kidney transplantation as a reproducible model of I/R to systematically study the processes involved in early organ reperfusion injury.
Methods: We measured arteriovenous differences of various biomarkers across transplanted living donor kidneys at fixed time-points during the first 30 minutes of reperfusion.
Results: Analysis showed significant IL-6 release, and some IL-8 release, but did not indicate release of the key inflammatory mediators TNF-a or IL-1b. Markers for platelet- (F1+2) and complement (sC5b-9) activation were released into renal venous blood and urine, respectively. No evidence was found for release of markers of oxidative damage (malondialdehyde, nitrotyrosine), endothelial activation (sICAM-1, vWF, P-selectin) or neutrophil activation (lactoferrin). Control arteriovenous measurements over non-ischemic kidney showed that IL-6 release, and platelet- and complement activation are all specific for I/R. Because IL-6 was most abundantly released from the kidney during reperfusion, we hypothesized that IL-6 may play a causative role in the pathophysiology of I/R injury. We tested this hypothesis in a mouse experiment of renal I/R injury. Treatment with neutralizing anti-IL-6 antibody significantly aggravated both functional and histological kidney injury as compared to non-treated mice.
Conclusion: This study shows that renal I/R in humans is dominated by local IL-6 release, rather than by oxidative/nitrosative stress. Neutralization of IL-6 in mice resulted in a significant aggravation of renal I/R injury, suggesting IL-6 exerts a protective effect in I/R injury.

P-363 INFLUENCE OF A MODIFIED PRESERVATION SOLUTION IN PROLONGING THE COLD ISCHEMIC PERIOD – A COMPARATIVE STUDY IN A PORCINE MODEL OF ALLOGRAFT KIDNEY TRANSPLANTATION

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Introduction: One of the big challenges following kidney transplantation (KTx) is the ischemia reperfusion injury (IRI).The magnitude of this injury correlates with the duration of ischemia.IRI is discussed to be caused by free oxygen

and/or nitrogen radicals that increase dramatically in tissue,during early post reperfusion phase.Therefore,it is of high relevance to find cell permeable antioxidants to scavenge these toxic products.To achieve this goal, a new modification of histidine-triptophane-ketoglutarate (HTK) has been formulated.Our aim was to evaluate this solution in a porcine model of allograft KTx with the cold ischemic period of 30 hours at 4°C.

Materials and methods: Forty eight Landrace pigs were divided in three groups (G1,G2,G3) and preserved respectively with the standardized HTK, (UW) and a new modification of HTK;in each group 8 donors and 8 recipients.After removing the native kidneys,implantation was carried out by vascular and ureteral anastomoses in right abdominal fossa.Pre and post reperfusion,3rd and 7th day post KTx the Cr of serum and urine and the urea of serum were examined.Additionally,tissue samples were taken to analyze histopathologically the degree of tubular injury and regeneration, pre and post reperfusion and in 7th day post-op.

Results: All laboratory data are summarized in Table 1. As it shows,although no significant difference depending on the preservation solutions can be seen,there is a trend in favor of the modified HTK.The histopathological assessment showed various degrees of acute tubular damage,regeneration and restoration of brush border of tubular epithelial cells in different phases in all groups without any significant difference.

Paerameters	Groups		
	G1 (HTK old)	G2 (UW)	G3 (HTK new)
Serum creatinin (mean±SEM)	10.08±4.77	12.05±7.14	8.46±5.11
Serum Urea (mean±SEM)	274±115	228±144	229±127
Urine creatinin (mean±SEM)	42.1±25.1	52.4±27.1	61.1±19.9

Conclusion: The implementation of a cell permeable antioxidant in HTK,in a porcine model of KTx did not improve the ischemia tolerance of the transplanted organs,significantly.The trend in favour of new HTK would be better to be evaluated in clinical setting.

P-364 MEASUREMENT OF MACULAR ANATOMIC ABNORMALITIES BY OPTICAL COHERENCE TOMOGRAPHY IN KIDNEY TRANSPLANTED PATIENTS

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Introduction: We observed the thinning of retinal volume in individual cases with chronic renal failure.

Purpose: Macular anatomic abnormalities were examined by optical coherence tomography (OCT), imaging in patients with kidney transplantation and compared to age-matched healthy volunteers.

Patients and methods: In a prospective case control study, transplanted patients (24-72 years of age, 51.8±12.9) were divided into two groups (group I: duration of haemodialysis (HD) before transplantation $>$ 1.0 years; group II: duration of HD before transplantation $\leq$ 1.0 year: year). Patients who underwent cataract surgery were excluded. All of the eligible 134 eyes had myopia $\leq$3D, best corrected visual acuity 0.9 (0.1-1.0±1.8). When both eyes of a subject were eligible for the study, one eye was randomly selected (67 eyes of 67 patients and 19 eyes of 19 volunteers in the control group). Retinal thicknesses of the macula measured by OCT3 were compared. The correlation between macular volume and duration of HD before transplantation, years after transplantation, type of immunosuppression therapy was determined.

Results: The mean values of macular volume (mm^3) in groups I, II and control were 6.55±0.27 (6.21-7.24), 6.84±0.28 (6.32-7.28), 6.82±0.38 (6.01-7.53), respectively. P values of Mann-Whitney U test for group I-control group, and for group I-group II were 0.012 and 0.024, respectively. The cut-off point of macular volume, determined by receiver operating characteristic curve was 6.40mm^3. The general estimating equation model statistics found no significant effect of either duration of HD, years after transplantation or the type of immunosuppression.

Conclusion: The macular volume of patients received HD for years before transplantation was significantly smaller compared to control subjects and to patients HD for maximum one year. Further study is required on patients waiting for kidney transplantation.

P-365 KIDNEY PAIRED EXCHANGE PROGRAMS AROUND THE WORLD

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Kidney paired exchange (KPE) idea was originally postulated by Rapaport in 1986. Paired exchange provides an alternative for potential living donor transplants unsuitable for the procedure because of an ABO blood group incompatibility or the presence in the recipient of HLA antibodies.

Although we can identify KPE programs in the four continents this procedure is not fully implemented around the globe mainly due to legal and logistic barriers. The first exchange donor program between two families was performed in South Korea, in 1991. Since then those kinds of programs have been available there in a single center basis. In Europe the first swap was performed in 1999, Basel, Switzerland where two married couples were involved, a Swiss and a German. After that no others exchanges where performed in Switzerland. KPE programs in the USA, Canada or Australia take place in a local or regional basis since 2000, 2003 and 2007 respectively. The experiences of the Rotterdam Erasmus medical center, which performed his first procedure in March 2003, were used to develop a national protocol for crossover kidney transplantation in the Netherlands applied since 2004. In Europe and before the Dutch experience also in Romania was implemented a crossover program but in a single center basis. A recent change in the UK legislation has allowed the development of a national program for paired donation and the first paired donation matching run took place in April 2007 been UK the second country in Europe and in the world with a fully implemented national KPE program. We were also able to identify kidney local or regional exchanges in Israel or Sweden meanwhile discussion about National programs take place in the USA, Australia, India and Portugal.

P-366 C4d-POSITIVITY AND OUTCOME FOLLOWING RENAL TRANSPLANTATION

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Background: The complement cleavage product C4d represents an attractive marker for the antibody-dependent classical pathway, as binding of C4d to target structures allows its detection in tissue sections over an extended period of time. Capillary C4d deposits in kidney allograft biopsies are associated with poor graft outcome and the appearance of post-transplant anti-donor antibodies, independent of morphological evidence of rejection. In the setting of chronic graft injury, endothelial C4d deposition is significantly associated with chronic transplant glomerulopathy.

Aims: To analyse the clinical relevance of C4d deposition in post transplant biopsies performed for clinical indications. Clinical outcome measures included creatinine at 3, 12 and 24 months, graft and patient outcome.

Materials/Methods: 232 consecutive kidney allograft recipients transplanted in the Royal Infirmary of Edinburgh between January 1999 and December 2005 were included. Patients were excluded if adequate renal tissue was not available (n=39) or C4d immunofluorescence was not performed (n=30). Follow up was for between 2 and 8 years. Statistics were performed using SPSS software.

Results: Biopsies from163 renal transplant patients were available. 122 patients received a deceased donor graft, 41 from a living donor. 71 women (44%) and 92 men (56%) were included. 32 of the 163 patients had C4d-positive biopsies (20%). There was a significant association between DR-mismatch and C4d-positivity (p=0.03). Serum creatinine at 3 and 12 months were not associated with C4d-positivity but a significant association was detected with creatinine at 24 months ($p<0.05$). C4d-positivity was also associated with increased risk of return to dialysis during the follow up period ($p<0.005$).

Conclusion: Our study demonstrates significant association between C4d-positivity and DR mismatch and with worse long term outcome. C4d staining is a potentially useful prognostic tool and a target for therapy.

P-367 OVERWEIGHT-ASSOCIATED HYPERFILTRATION DOES NOT AFFECT RECIPIENT RENAL FUNCTION

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Due to donor shortage, criteria for living kidney donors have become less strict, leading to an older and more overweight donorpool. Older age and overweight are known risk factors for renal function loss. Whether kidneys from overweight donors do worse after transplantation is unknown. Therefore, we investigated the effect of donor Body Mass Index (BMI) on recipient renal outcome 1 year after transplantation.

We analysed 213 living kidney donors (age 50±10 years, 45% male) and their recipients. Glomerular filtration rate (GFR) and effective renal plasma flow (ERPF) were measured as clearances of ^{125}I-iothalamate and ^{131}I-Hippuran, respectively, 4 months pre-donation in the donor and 1 year after transplanta-

tion in the recipient. Filtration fraction (FF) was calculated as GFR/ERPF. Data in recipients were analysed by break-up in donor BMI: normal weight (<25, n=89 (mean BMI 22,6±1,7) and overweight (>25 kg/m^2, n=114 (mean BMI 28,4±3,2).
Mean arterial pressure (MAP), GFR and FF were higher in the overweight donors, 90±9 vs 94±9 mmHg (p=0,003), 109±17 vs 119±21 mL/min (p=0,000) and 0,26±0,03 vs 0,27±0,03 (p=0,001). There was no difference.
Recipient age was 42±14 years (61% male). Remarkably, recipient BMI was significantly higher for the higher category of donor BMI: 25±4 vs 27±4 (p=0,010). GFR, MAP and FF, however, were similar in recipients for categories of donor BMI, 59±17 vs 61±18 ml/min; 104±12 vs 102±12 mmHg and 0.25±0.05 vs 0.26±0.04. On multivariate analysis, recipient GFR was determined by donor MAP and GFR.
Before donation, weight excess is associated with an unfavourable renal profile in the donor. After transplantation, the impact of donor BMI on recipient renal function disappeared. Donor MAP and GFR were the mean determinants for a lower recipient renal function. Thus, donor overweight does not affect recipient renal function at one year after transplantation.

P-368 RIGHT KIDNEYS AND MULTIPLE VESSELS ARE NOT CONTRA-INDICATIONS TO LAPAROSCOPIC LIVE DONOR NEPHRECTOMY

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Aims: Many laparoscopic surgeons remain reluctant to procure right kidneys and kidneys with multiple arteries. The aims of this study were to compare the outcomes of donor nephrectomy (LDN) and the subsequent renal transplants from right and left kidneys and kidneys with single and multiple renal arteries.
Methods: In a consecutive series of 235 transperitoneal LDN, 183 (78%) left and 52 right (22%) kidneys were procured. 194 (82.6%) kidneys had a single renal artery, 39 (16.6%) had two arteries and 2 (0.8%) had three arteries. Retro-caval dissection was performed in right kidneys where the renal artery bifurcated posterior to the IVC.
Results: Left kidneys had longer renal veins (38±11 vs 26±8 mm; P<0.0001), but there were no differences in arterial length (32±8 vs 30±6 mm; P=0.095). Three right kidneys required renal vein lengthening on the back table using recipient saphenous vein grafting. There were two conversions to open surgery during left LDN and none during right LDN. Operating time was shorter for right sided LDN (102±21 vs 145±27 min; P<0.001) and for kidneys with single renal arteries (135±24 vs 151±30 min; P<0.001). The only graft thrombosis in this series (0.4%) occurred in a left sided kidney with a single artery and vein. Comparisons between right and left kidneys and between allografts with single or multiple arteries showed no differences in delayed graft function, urological complication rates, renal function or allograft survival.
Conclusions: Shorter operating times suggest that laparoscopic procurement of right kidneys and kidneys with a single artery is technically easier. The need to procure the right kidney or a kidney with multiple arteries should not be regarded as contra-indications to transperitoneal laparoscopic donor nephrectomy.

P-369 SAFETY PROFILE OF A CONSECUTIVE SERIES OF 235 LAPAROSCOPIC LIVE DONOR NEPHRECTOMIES

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Introduction: Laparoscopic live donor nephrectomy (LDN) has the potential to overcome some of the disincentives to live kidney donation and is being increasingly widely adopted in the UK. This study presents the results of a consecutive series of 235 LDN from a single centre with an emphasis on post-operative complication rates.
Patients and methods: 235 live donors (143 women and 92 men; mean age 44 yrs) underwent transperitoneal LDN. There was no selection on the basis of donor body mass index (range 18-45 kg/m^2) or because of difficult vascular anatomy, although in general the left kidney was preferred to the right in view of renal vein length. Subcutaneous heparin and TED stockings were used for thromboembolic prophylaxis in all cases. All donors were reviewed 6 weeks post-operatively and complications were recorded prospectively.
Results: There was no donor mortality and no episodes of thromboembolic disease. Two operations were converted to open procedures, both because of bleeding (one from the renal artery and one port site bleed). There were no bowel perforations or splenectomies but 3 bowel serosal tears and 2 splenic capsular tears were repaired intra-operatively. Two patients required laparoscopic division of adhesions. Other post-operative complications were:
– Chest infection 15 (6.3%)
– Wound infection 11 (4.7%)
– Paraesthesiae of L1 9 (3.8%)
– Ileus 2 (0.9%)
– Testicular pain 6 (6.5%)
– Persistent wound pain 1 (0.4%)
– Wound hernia 3 (1.3%)
Conclusions: LDN is associated with a low rate of major or potentially life threatening complications but even in experienced hands there is an appreciable morbidity in fit healthy individuals undergoing LDN.

P-370 THE RETURN OF BIOSYNSORB ANTIGEN-SPECIFIC IMMUNOADSORPTION IN ABO-INCOMPATIBLE KIDNEY TRANSPLANTATION

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Background: It is well known that anti A/B antibodies in the recipient's serum cause acute antibody-mediated rejection (acute AMR) in ABO incompatible kidney transplantation. To perform successful ABO incompatible kidney transplantation, temporary elimination of the anti- A/B antibodies from recipient's serum is mandatory. There are several measures to remove anti A/B antibodies. PEX and DFPP are used in patients with ABO incompatible kidney transplants for elimination of anti A/B antibodies. However, there are some problems and complications. Biosynsorb was Antigen-Specific immunoadsorption and was designed to selectively remove anti A/B antibodies. This study of ABO incompatible kidney transplantation using Biosynsorb was started in our hospital in 2007.
Methods: Ten kidney recipients were enrolled in our study comparing two measures to remove anti A/B antibodies. Group I (n=4) patients received, as standard procedure (a low-dose CNI, low-dose MP, MMF started 1 month before transplantation and Rituximab without splenectomy), some sessions of Biosynsorb prior to transplantation until anti- A/B antibodies decreased to the level of 1:32 or below. Group II (n=6) patients received, as standard procedure, some sessions of DFPP prior to transplantation until same titers.
Results: Patient and graft survival at 1 month were no different between two groups. There was no significant difference in the incidence of acute rejection, acute AMR and anti- A/B antibody titers decreased between two groups. However, the removal of serum immunoglobulin IgG levels and fibrinogen were significantly reduced after Biosynsorb. Approximately 27.9% of Rituximab were removed by one Biosynsorb treatment that was significantly reduced in comparison with DFPP (40%) or PEX (63.5%).
Conclusion: In ABO-incompatible kidney transplantation can be successfully performed that anti A/B antibodies can be effectively and safely removed with the Biosynsorb. There is no difference between Biosynsorb and DFPP with regard to the effectiveness of antibody removal.

P-371 EVEROLIMUS WITH REDUCED-DOSE CYCLOSPORINE AS A STRATEGY FOR OPTIMIZING LONG-TERM RENAL FUNCTION: RESULTS FROM A RANDOMIZED STUDY IN 833 *DE-NOVO* RENAL-TRANSPLANT RECIPIENTS

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The development of immunosuppressive regimens that maintain low rates of acute rejection whilst minimizing calcineurin inhibitor-related nephrotoxicity is a major priority in renal transplantation. The proliferation signal inhibitor, everolimus, combines immunosuppressive and anti-proliferative actions, targeting the main causes of short- and long-term graft failure. Study A2309, the largest single registration trial ever undertaken in renal transplantation, is examining the efficacy and safety of everolimus with reduced-dose cyclosporine (CsA) as a strategy for improving long-term renal graft outcomes.
A2309 is a 24-month, multicentre, randomized, open-label, non-inferiority study comparing the efficacy and safety of three immunosuppressive regimens in *de-novo* renal-transplant recipients: two regimens of everolimus (EVL; 1.5mg/day targeting C_0 3–8ng/mL or 3.0mg/day targeting C_0 6–12ng/mL) with reduced-dose CsA *versus* a control group receiving enteric-coated mycophenolate sodium (EC-MPS) (1.44g/day) and standard-dose CsA (table 1). All patients receive basiliximab induction therapy. Corticosteroids are administered according to local practice.
The primary objective is to compare the composite efficacy failure rate (treated biopsy-proven acute rejection, graft loss, death, loss to follow-up) between the

Table 1. C_0 value ranges for CsA

Day/Month	EVL + reduced-dose CsA groups	EC-MPS + standard-dose CsA group
Day 5	100–200ng/mL	200–300ng/mL
Month 2	75–150ng/mL	100–250ng/mL
Month 4	50–100ng/mL	100–250ng/mL
Month 6	25–50ng/mL	100–250ng/mL

CsA: cyclosporine; EC-MPS: enteric-coated mycophenolate sodium; EVL: everolimus

everolimus and EC-MPS treatment arms at 12 months. Secondary objectives include comparisons of the incidence of graft loss, death, loss to follow-up, renal function and renal histology (in patients with proteinuria/suboptimal renal function) between the everolimus and EC-MPS treatment arms at 12 months. 833 renal-transplant recipients have been enrolled at 79 centres. The study is still ongoing and primary and secondary 12-month data will be reported for the first time at the ESOT meeting. Demographic data are summarized in table 2.

Table 2. Demographics

	EVL 1.5mg/day + reduced-dose CsA (n=277)	EVL 3.0mg/day + reduced-dose CsA (n=27)	EC-MPS + standard-dose CsA (n=277)
Patient characteristics			
Mean age, years	45.7	45.3	47.2
Male, n (%)	176 (63.5)	191 (68.5)	189 (68.2)
Race, n (%)			
Caucasian	193 (69.7)	180 (64.5)	190 (68.6)
Black	34 (12.3)	40 (14.3)	39 (14.1)
Asian	32 (11.6)	38 (13.6)	36 (13.0)
Other	18 (6.5)	21 (7.5)	12 (4.3)
Panel reactive antibodies			
≥20%, n (%)	17 (6.3)	13 (4.8)	11 (4.1)
Donor characteristics			
Living, n (%)	147 (53.1)	151 (54.1)	148 (53.4)

CsA: cyclosporine; EC-MPS: enteric-coated mycophenolate sodium; EVL: everolimus

The findings of this pivotal study will provide key information about the optimization of everolimus and CsA dosing in renal-transplant recipients as a strategy for improving long-term renal function.

P-372 DETERMINANTS OF PLASMA OXALATE IN NON-HYPEROXALURIA KIDNEY TRANSPLANT PATIENTS

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Background: We investigated plasma oxalic acid (oxalate) in patients admitted for kidney transplantation with diagnoses other than primary hyperoxaluria. The aim was to assess oxalate retention in unselected transplant recipients and identify factors that could predict plasma concentrations of oxalate.
Methods: We randomly investigated 212 patients, median age was 51,0 years (SD=15,7) and 49% had live donors. All received cyclosporine, mycophenolate and steroids. Plasma oxalate was measured at admission and 10 weeks after transplantation.
Results: The median plasma oxalate concentrations at transplantation was 35 mmol/l (95% central interval = 10.4- 93.9) with 98% of the values above the upper reference limit (median 5.4; reference interval 2.6-11.0). It was reduced almost fourfold to 9 mmol/l (4.0- 25.5) after 10 weeks but still 37% of the values were above the upper reference limit. We examined the bivariate Spearman correlation coefficients between plasma oxalate at transplantation and: preemptive transplantation, live versus diseased donor, donor and recipient age, creatinine, urea, phosphate, PTH, albumin and calcium. Oxalate at 10 weeks was tested with the same covariates and also with baseline oxalate, primary non-function, rejection episodes and measured GFR at follow-up. The significant associations were further tested in backward and forward multiple regression analyses. We found that independent positive determinators for oxalate at transplantation were: established dialysis treatment (p= 0,002) and creatinine ($p<0,000001$). Oxalate at 10 weeks was positively related to GFR (p=0,023), creatinine (p= 0,032) and donor age (p=0,027).
Conclusion: Plasma oxalate concentration is almost sevenfold increased in patients at the time of transplantation being highest in dialysis patients. The reductions in plasma concentrations 10 weeks after transplantation are determined by established graft function measured as GFR and also by donor age. Further studies are needed to elucidate long-term consequences of increased plasma oxalate concentrations following kidney transplantation.

P-373 SIROLIMUS INHIBITS LYMPHANGIOGENESIS IN RENAL ALLOGRAFTS – A NOVEL MECHANISM TO PREVENT CHRONIC REJECTION

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Lymphangiogenesis occurs in renal allografts but its significance is still unknown. Newly formed lymphatic vessels may be involved in the maintenance of the alloreactive immune response and thus participate in the pathogenesis of chronic rejection. Previously it has been demonstrated that sirolimus (SRL) is a potent antilymphangiogenic compound. Here we investigated the effect of SRL-treatment on lymphangiogenesis in renal transplants.
Physiological rat renal transplantation model was used. Kidney transplantations were performed from DA to WF rats. Allograft recipients were treated daily with cyclosporine A (CsA) 1.5 mg/kg s.c. or with SRL 2 mg/kg p.o. through orogastric tube. In addition SRL-treated animals were given CsA 1.5 mg/kg/d s.c. for the first 7 days after transplantation. Grafts were harvested 3, 7 and 90 days after transplantation for immunohistochemistry. LYVE-1 antibody was used to detect lymphatic vessels in paraffin sections. The density of lymphatic vessels was scored from 0 to 3.
In normal kidneys LYVE-1 staining revealed a dense lymphatic vessel network throughout the whole cortex (mean$\pm$SEM, 3$\pm$0). At 3 and 7 days after transplantation LYVE-1 positive lymphatic endothelium was lost and only few vessels were observed in both groups (control vs. SRL; 3 d 0,3$\pm$0,3 vs. 0$\pm$0; 7d 0,7$\pm$0,3 vs. 0,3$\pm$0,3). 90 days after transplantation the lymphatic vessel density remained low in SRL group (0,7$\pm$0,7) while lymphangiogenesis had occurred in control group and staining with LYVE-1 antibody was at least moderate (2$\pm$0).
Our results suggest that SRL efficiently prevents lymphatic vessel formation in kidney transplants. In our experimental model as well as in several clinical settings SRL has been shown to attenuate the progression of chronic rejection compared to calcineurin inhibitor based immunosuppression. Inhibition of lymphangiogenesis might be a possible mechanism mediating this positive effect.

P-374 PREOPERATIVE EVALUATION, MANAGEMENT AND SURGICAL APPROACH IN NON CONVENTIONAL KIDNEY TRANSPLANTATION DUE TO GRAFT VASCULAR ANOMALIES – 12 YEARS SINGLE CENTER EXPERIENCE

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Purpose: 12 years transplant experience, using normal and abnormal renal pedicle, preoperative evaluation and special anastomotic techniques represented the aim of this study.
Material and methods: From 06.1997-03.2009, 970 renal transplantations (775 living & 195 cadaver, 919 adults & 51 pediatric) with an average of 83/year (116 in 2007), were performed. General preoperative evaluation, immunological and vascular anatomy study and standard minimal lombotomy nephrectomy were performed in all living donor transplant. 304 cases (31%) had vascular graft anomalies, 182 abnormal arteries and 122 abnormal veins.
Results: No major complications in 773 nephrectomies and minor complic. were: renal artery spasm, bleeding, minor respiratory complic., pneumothorax, illeus, bladder voiding problems, UTI. Long-term complic.: persistent wound pain, parestezia and wound hernia. QOL after surgery assessed using SF 36 Health Survey Test was normal. Surgical approach to vascular anomalies: double T-T anast. – 109, T-L anast. – 10 (cadaver donors), combined anast. T-T and T-L – 3; single trunk made by 2 branches – 30, we used the epigastric artery in 4 cases. Minor aberrant vessels were excluded in 26 cases. Cava patch was used in 41 cases (21 from cadaver donors). Abnormal venous drainage was managed by classical T-L anast. to the external iliac vein.
Conclusions: Renal pedicle assessment, general and immunological evaluation, represented a must. No major complic. appeared in living donor nephrectomy, mortality was 0. It respects in our center the international accepted morbidity. Vascular renal graft anomalies appeared in 31% but TX was performed due to special anastomotic techniques which did not significantly increase the ischemia time and vascular complic. Accepting non optimal vascular donor, number of renal transplants could increase with 30%.

P-375 RECURRENT IgA NEPHROPATHY (IgAN) AFTER RENAL TRANSPLANTATION (rTx): A SINGLE CENTRE EXPERIENCE

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Aim: To retrospectively evaluate the incidence of IgAN recurrence (IgANrec) in a centre not performing protocol biopsies.
Methods: 107 rTxs performed in 102 pts with biopsy proven IgAN in native kidney, out of 2154 rTxs. Follow-up was 6.2±3.7yrs, age 46.5±12yrs, ratio M/F 81/21. RB was performed 6.8 yrs (1.0-15.1) post rTx, in 41% of the pts to investigate about increasing sCr and/or PTO≥1g/24 h.
Results: 43% showed IgANrec.

Case	ID at rB	Clinical presentation	sCr (mg/dl) at rB	PTO (g/24h) at rB	Treatment
1	Cya	↑sCr	1.9	0.3	none
2	Cya + MMF	↑sCr	2.3	0.3	oral steroid
3	Cya	↑PTO	0.8	2.3	oral steroid
4	Cya + st	↑PTO	2	2.5	+MMF
5	Cya + MMF	↑sCr	2.2	3	↑MMF
6	Cya + MMF	↑PTO	1.8	4	none
7	Srl + st	clinical trial	1.4	0.4	none
8	Cya + srl+ st	clinical trial	2.1	1	↑ACE
9	Cya + aza +st	↑sCr ↑PTO	2.5	2	+MMF
10	Tac	↑sCr	3.1	0.5	+ACE
11	Srl + st	↑PTO	1.5	1.3	+MMF
12	Tac + MMF	↑PTO	1.3	1	↑MMF
13	Tac + st	↑PTO	1.3	0.6	+MMF ↑ACE
14	Tac + st	↑PTO	1.3	1.9	+MMF
15	Cya + st	↑sCr	1.9	0.3	+MMF
16	Tac + eve+ st	↑PTO ↑sCr	4	3.6	IV steroid
17	Cya + st	↑PTO	0.8	1.1	+MMF
18	Cya + MMF + st	↑PTO ↑sCr	3	5	IV steroid

Follow-up 9.8±4.7yrs, age 42.7±12.4yrs, ratio M/F 16/2. At the time of RB: sCr 1.9±0.8mg/dl, PTO 1.2 g (0.3-5), 17/18 microscopic haematuria, 22% were in triple immunosuppressive protocol (ID), 61% in double ID, 17% in mono ID. 28% withdrew steroids 4.8±2.9yrs before IgANrec. The therapeutic strategies were: in 50% introduction/increasing MMF, in 11% re-introduction of steroid, in 11% ACE/ARB and in 17% none. 2 pts were treated with IV steroid for deteriorated renal function. Graft failure occurred in 3 pts: 2 due to IgAN (no crescents). Graft survival at 2, 3, 5yr were 100%, 94%,88% and sCrs at the same yr always 1.5mg/dl.
Conclusions: The majority of our pts run an indolent course. In literature no ID is known to affect the incidence of IgAN; yet a lower number of our pts on triple ID – including steroid – in comparison with double/mono ID developped recurrence (22% vs 78%). These results suggest us always to perform a RB when IgANrec is suspected: in 50% of pts we observed a stabilization of graft function associated with changes the ID. We are aware that data from literature show a variability of indications for RB and results are still lacking. Since clinical data alone are not predictable for outcomes, RB may be a useful tool to suggest whether basical immunosuppression should be changed or not.

P-376 THE IMPACT OF SLOW AND DELAYED GRAFT FUNCTION VS. IMMEDIATE GRAFT FUNCTION ON CADAVER RENAL TRANSPLANT OUTCOMES

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Introduction: According to the initial graft function (GF), kidney transplant pts. could be divided into 3 groups: immediate GF (IGF – postop. day 5 serum creatinine < 3 mg/day), slow GF (SGF) >3 mg/dl, no dialysis) and delayed GF (DGF – day 5 creatinine >3 mg/dl and dialysis). Our study assess the impact of the above 3 categories in TX outcomes, and factors involved in first days GF such was donor age and additional vascular reconstruction.
Methods: From 06.1997-03.2009, 970 renal TX (775 living & 195 cadaver, 919 adults & 51 pediatric TX) with an average of 83/year (116 in 2007), were performed. 86 cadaver TX entered in our study and renal RF developed as follows: 61 TX were IGF, 17 were SGF and 8 DGF. Acute rejection episodes (AR), serum creatinine level and graft survival (GS) were analyzed 3 mts, 6 mts. and 1 year after surgery.
Results: SGF pts. showed worse results considering AR, creatinine level and GS in comparison with IGF but better than DGF group. 1 year GS was better in IGF group than other 2 groups. Creatinine was worse in SGF group than IGF group – 1.8±0.8 mg/dl vs. 1.4±0.5 mg/dl, but better than DGF group – 2.1±0.6 mg/dl at 12 months, AR rate was 20% (12) in IGF group, 35.2% (6) in SGF group and 50% (4) in DGF group.
Conclusions: Pts. developing SGF have a worse outcome than pts. with IGF but similar, or in special cases better than pts. developing DGF. Despite they did not need dialysis, SGF pts. show worse creatinine level and GS and higher AR than IGF. Even mild to moderate post-TX dysfunction can have a negative impact in GF and survival.

P-377 CALCINEURIN INHIBITORS (CNI) RELATED OPTIC NEUROPATHY AFTER KIDNEY TRANSPLANTATION (KT): RESULTS OF CONVERSION TO AN m-TOR REGIMEN IN THREE CASES

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Purpose: To describe our Centre experience (in about 2200 KT performed from November 1981 to January 2009) about CNI related optic neuropathy.
Patients and methods: Main characteristics of the patients who suffered from this complication are described in Table 1 below.
Results: Therapeutic approaches and outcome are reported in Table 2.
Conclusions: Optic neuropathy is considered a very rare complication in KT recipient (6 cases in medical literature up to Jan '09). In our Centre, we noted 3 cases out of 2200 KT (2/3 at a month of distance) In 3 cases a clear correlation with CNI therapy, but not with CNI dose, was noted (in case 2, Tac levels were under the normal range). In our cases, CNI withdrawal, associated with conversion to m-TOR inhibitors was successful in 2/3 with a long f-up in one pt. We think that this complication, not life-threatening but seriously affecting the quality of life, is underdiagnosed and should be therefore carefully investigated. Withdrawal of CNI, and conversion to an m-TOR inhibitor regimen, when applicable, could be considered as an option for maintaining both graft function and acceptable visual acuity.

P-378 "SILENT" REJECTION DURING DELAYED KIDNEY GRAFT FUNCTION

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Aim: The aim of this study was to verify the presence and rate of "silent" rejections in cases of delayed renal graft function (DGF) and to determine the role of its treatment.
Materials and methodology: We analyzed 491 consecutive kidney transplantations that were performed in a single center between 01.01.2002 and 31.12.2008. The study included patients who developed delayed graft function (n=58). Patients were divided into three groups based on protocol biopsies

Abstract P-377 – Table 1

Patient	KT	Time of diagnosis	IS therapy at diagnosis and CNI level	sCr at time of diagnosis	Major comorbidities	Degree of visual impairment
F 65yrs	12/20/01	22 months	Tac: 7-15 ng/mL-EMIT	0.9 mg/dL	No	Decreased visual acuity in the right eye more than in the left one
F 64yrs	10/29/08	13 days	MMF + Steroids + Tac: 3.5-5 ng/mL-ACMIA	2.8 mg/dL	No	Decreased visual acuity in both eyes at the same extent
F 59yrs	09/30/08	9 days	MMF + Steroids + Tac: 13-18 ng/mL-ACMIA	3.8 mg/dL	Diabetes mellitus	Blindness

Pt: patient; F: female; DD: deceased donor; IS: immunosuppressive; Tac: tacrolimus; MMF: mycophenolate mofetil; sCr: serum creatinine.

Abstract P-337 – Table 2

Patient	IS therapy after diagnosis	Other therapies	Last follow-up	Outcome
1	Sirolimus + Steroids	MP 1 mg/kg/day	Jan '09	Bilateral improvement without restoration of the previous visual acuity
2	Sirolimus + Steroids	P 50 mg/day orally	Feb '09	Restoration of the previous visual acuity
3	Everolimus + Azatioprina* + Steroids	P 50 mg/day orally - Ganciclovir i.v.	Jan '09	No improvement - Blindness

MP: Methylprednisolone; P prednisone; *Aza was introduced instead of MMF due to severe gastroenteric intolerance

findings (Banff classification): A – with presence of "silent" acute rejection (AR) at biopsy with further treatment by intravenous steroids and/or polyclonal anti-lymphocyte antibodies (n=24); B – with presence of "silent" AR at biopsy without treatment (n=7); C – without "silent" AR (n=27). Groups were compared for the duration of DGF, stay in hospital, number of post-transplant dialysis, serum creatinine level at discharge, 1-year graft function.
Results: Histological examination revealed that 31 patients (53.4%) with DGF developed AR grade from IA to IIB. Comparison of DGF groups showed that patients treated for "silent" AR had less number of postoperative dialysis and shorter duration of DGF and hospital stay ($p<0.05$ for all). All group B patients later developed more severe histological and/or clinical AR within 1-2 months after transplantation. 1-year graft function had no significant differences for all groups.
Conclusion: "Silent" AR is the frequent complication during delayed kidney graft function. Treatment of AR during delayed kidney graft function may help to hasten function's recovery, to reduce number of postoperative dialysis and hospital stay. Further follow up is needed to determine long term outcomes in treated and non treated patients.

P-379 A SIX MONTHS STEROID BASED THERAPY FOR RECURRENT OR *DE NOVO* IgA GLOMERULONEPHRITIS (IgAGN) IN KIDNEY TRANSPLANTATION (KT): PRELIMINARY EXPERIENCE IN 3 PATIENTS (PTS)

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Purpose: To assess the use of the Steroids course proposed by Pozzi (The Lancet 1999) for IgAGN in native kidneys.
Patients and methods: Doses have been partially modified due to the concomitant immunosuppressive therapy (500 mg g/day of methylprednisolone intravenously for three consecutive days at the beginning of the Steroids course repeated at month 3 and 5; oral prednisone at a dose of 0.5 mg/kg every other day for 6 months). Main characteristics of the 3 pts are described in Table 1.
Results: The results at the end of the entire f-up (17, 18 and 12 months respectively) in 3 pts are summarised in Table 2 below.
Conclusions: The three pts, all with a f-up $\geq$12 months from 1st biopsy demonstrating IgAGN and data in favour of a deteriorating graft function, are well with improved sCr and proteinuria. Protocol biopsies after the six months steroid course demonstrated absence of crescents. Yet glomerular sclerosis increased. We are aware that 3 cases with a one year f-up should be considered a preliminary, not conclusive, result. Yet our favourable outcome in terms of patient and graft survival and of graft function, together with the absence of serious adverse side-effects, may be considered encouraging for the treatment of crescentic IgAGN in KT, a condition for which guidelines are still lacking.

P-380 COMPARATIVE QUALITY OF LIFE ASSESSED BY SF-36 HEALTH SURVEY IN DIALYSIS PATIENTS, ANEPHRIC PATIENTS FOR RENAL MALIGNANCIES, RENAL TRANSPLANT PATIENTS AND PATIENTS WITH MALIGNANT UROLITHIASIS

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Introduction: This study examine the quality of life (QOL) in 4 groups: pts. with RF in dialysis prog. with native kidneys, anephric pts. in dialysis progr. for renal malignancies, renal TX pts. in good condition, and non-dialysis CFR patients, secondary to uro-lithiasis.
Patients and methods: 223 pts. entered in our study: 74 in HD program, 12 anephric pts. for renal malign condition, 110 renal TX recipients and 27 suffered of severe urolithiasis complic. with CRF were included in study. 8 scales of SF-36 HS were scored: physical functioning (PF), role physical funct. (RP), bodily pain (BP), gen. health (GH), vitality (VT), social funct. (SF), role emotional funct. (RE), and mental health (MH).
Results: The scale scores of PF, RP, BP, GH, VT, SF, RE, and MH were as follows: 81.7, 65.7, 69.5, 49.2, 58.4, 72.7, 70.8, 72.2, for the pts. receiving HD, 82.6, 68.3, 70.2, 48.7, 62.2, 73.5, 71.6, 68.9 for anephric pts. secondary to a malignancy 83.7, 76.6, 78.2, 54.3, 63.1, 82.3, 80.1, 66.8, for the recipients of renal TX and 81.2, 71.5, 46.6, 51.3, 63.2, 71.1, 72.8, 72.2 for the pts. suffered of RF due to urolithiasis.
Conclusion: The BP score was the lowest in the malign. urolithiasis. Excepting the MH score, all the other 7 scores were better in the TX group. Considering a gen. pop. sample score as 100% (which rep. in reality 76.6% of the ideal score), the QOL was, 88.1% in the HD group, 89.1% in the anephric by renal malign. group, 94.5% in the TX group and 86.5% in the urolithiasis group. In our study, TX improved the QOL comparing to different causes of renal failure.

P-381 COMPARATIVE STUDY REGARDING QUALITY OF LIFE ASSESSED BY SF-36 HEALTH SURVEY IN OLDER VERSUS YOUNGER AND RELATED VERSUS NON-RELATED LIVE KIDNEY DONORS

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Introduction: SF-36 HS was designed to assess the health status in general. We compared quality of life (QOL) in 4 groups of kidney donors – related vs. non-related live kidney donors and younger vs. older. We defined border age of 65 (retirement in Romania) in order to compare the 2 age groups.
Methods: From 06.1997 – 03.2009, 970 kidney transpl. (775 living & 195 cadaver, 919 adults & 51 pediatric) have been performed, with an average of 83/year (116 in 2007). In all cases, general preop. evaluation, immunol. and vasc. anatomy study was performed. Standard min. lombotomy nephrectomy tech. was preferred. The SF36 eval. was done before, 1 month and 6 mts. after surgery. 65 young donors (mean age 43) were compared with 40 older donors (mean age 67), and 53 related were compared with 53 unrelated donors using the QOL questionnaire.
Results: 8 scales of SF-36 HS were scored in all 4 groups: physical functioning (PF), role physical funct.(RP), bodily pain (BP), general health (GH), vitality (VT), social funct. (SF), role emotional funct. (RE), & mental health (MH). Baseline QOL was better in younger vs. older group. PF, RP, VT and GH were deteriorated after 1 mth. in older group ($p<0.001$-0.003) and recovered close to baseline after 6 mts.
Conclusion: QOL in non-related vs. related donors returned at baseline following a slowly curve in the 1st group. BP scale in younger recovered less effective than older while QOL in general return close to baseline in older after 6 mts. following a slowly curve than younger donors. Considering that surgical results and graft function are comparable in all 4 groups, further expansion of borderline older donor pool is accepted.

P-382 OUTCOME OF RENAL TRANSPLANT RECIPIENTS WITH HEPATITIS B INFECTION AND PREEMPTIVE TREATMENT WITH LAMIVUDINE

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Purpose: Infection with hepatitis B virus has a big importance for transplant

Abstract P-379 – Table 1

Patient	Original disease in native kidneys	Tx	Tapering/stop steroids	IS therapy before steroid course	ACE-I/ARB therapy before steroid course
M 37yrs	Chronic GN	04/08/03 LD	06/2005	Tac monotherapy	no
M 35yrs	IgAGN	07/15/96 DD	07/2004	CyA + MMF + Steroids	yes
M 62yrs	Unknown	10/21/05 DD	10/2007	Tac monotherapy	no

LD: living donor; DD: deceased donor; IS: immunosuppressive; ACE-I: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker

Abstract P-379 – Table 2

Biopsy before Steroids course	sCr mg/dL	proteinuria g/d	Biopsy after steroids course	Latest f-up sCr/proteinuria	IS therapy	ACE-I/ARB
06/2007: Glomeruli with crescents: 2/11, sclerotic: 3/11	2.8	3	01/2008: Glomeruli with crescents: 0/15, sclerotic: 8/15	02/2008: 2.3/0.3	Tac + Steroids	no
05/2007: Glomeruli with crescents: 3/11, sclerotic: 3/11	5.2	8	04/2008: Glomeruli with crescents: 0/11,	02/2008: 3.6/1.8	CyA + MMF + Steroids	yes
11/2007: Glomeruli with crescents: 3/37, sclerotic: 1/37, fibrinoid necrosis: 1/37	2	1.3	06/2008: Glomeruli with crescents: 0/14, sclerotic: 2/14, fibrinoid necrosis: 0/14	02/2008: 1.2/0.3	Tac + MMF + Steroids	yes
	2	1.3				yes

recipients due to the risk of reactivation under immunosuppression, progression to chronic liver disease, development of liver cirrhosis and hepatocellular carcinoma.
The aim of the study was to analyze the influence of preemptive treatment with lamivudine in renal transplant HBV positive patients.
Method: We retrospectively analyzed 712 patients who received a renal allograft in our center between January 2000–December 2007. 20 patients (2.8%) were AgHBs positive at the time of transplantation. The median follow-up was 68.4 months. All received preemptive treatment with nucleosidic analog (lamivudine 100 mg/zi).
Results: 14 patients (70%) were DNA negative and 6 (30%) had mild viral replication at the time of transplantation. Discontinuation of antiviral was made for 14 after more than 12 months therapy, DNA negative and liver enzymes in normal range.Reactivation of HBV infection (viral replication ± elevated liver enzymes) occured in 14 patients; 8 had reactivation of viral replication after more than 6 months of lamivudine withdrawal and 6 have developed resistance to lamivudine after a mean 44 months therapy (min 12 mo/max 72 mo); patients with resistance were converted on entecavir. All patients with reactivation after lamivudine withdrawal restart therapy with viral response for 6. No deaths related to hepatitis B were seen and only one patient lost the graft for surgical cause. We havn't noticed any significant adverse reaction on lamivudine.
Conclusions: Our study shows that immunosuppressant therapy is associated with a significantly high risk of hepatitis B virus reactivation but does not decrease patient or renal allograft survival if they receive preemptive antiviral therapy. Long time therapy with lamivudine is associated with drug resistance and viral replication.

P-383 EARLY GRAFT DYSFUNCTION DUE TO VASCULAR ANOMALIES, VESSELS RECONSTRUCTION AND SPECIAL ANASTOMOTIC TECHNIQUES IN KIDNEY TRANSPLANTATION

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Purpose: The aim of this study was to evaluate one week renal graft function consecutive to additional arterial and venous reconstruction and special anastomotic techniques during renal transplantation.
Material and methods: 12 years transplant experience (June1997 – March 2009) was assessed considering 970 renal transplantations (775 living and 195 cadaver, 919 adults and 51 pediatric) with an average of 83/year (116 in 2007). In all cases, general preoperative evaluation, immunological and vascular anatomy study was performed. 305 cases (31%) had vascular graft anomalies, 183 abnormal arteries and 122 abnormal veins.
Results: Special anastomotic and reconstruction techniques were used as followed: double T-T anastomosis – 109 cases, T-L anastomosis – 10 cases (cadaver donors), combined anastomosis – 3 cases; single trunk made by two branches – 30 cases and we used the epigastric artery for small branches in 5 cases. Minor aberrant vessels were excluded, feeding a minor area of parenchyma. Cava patch and venous reconstruction were used in 41 cases (21 from cadaver donors). Abnormal venous drainage was managed by classical T-L anastomosis to the external iliac vein. One week vascular graft failure occurred in 1.4% cases – one arterial reconstructed graft (0.6%) and one venous reconstructed pedicle (0.8%), proving a reasonable result.
Conclusions: Vascular anomalies of renal pedicle were founded in 31% but transplantation was performed due to special reconstruction and anastomotic techniques. Arterial and venous reconstruction combined with special anastomotic procedures did not increase the risk of early graft failure. One week graft function remained in very good condition. Accepting the borderline vascular donor, the number of transplantation could increase with 30%.

P-384 LOW DOSE IMMUNOSUPPRESSION IS NOT SUFFICIENT TO AVOID ACUTE REJECTIONS IN OLD FOR OLD KIDNEY TRANSPLANT RECIPIENTS: A ONE YEAR PROSPECTIVE MULTICENTER RANDOMIZED CONTROLLED TRIAL

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Background: Kidney transplantation (KTx) in the elderly is a challenge since patient's co-morbidity and the decreased injury threshold of older grafts may limit the benefits of transplantation in these patients. To compare favourable effects between low dose tacrolimus (LD-Tac) and mycophenolate-mofetil (MMF) we conducted a one year prospective multicenter randomized controlled trial.
Methods: 90 kidney transplant recipients (KTR) > 65 years with cadaveric grafts (> 65 years) from 5 centers were enrolled and received baseline IS with daclizumab induction (1mg/kg), LD-Tac (trough level 5-8ng/mL), MMF (2g/d) and steroids. After three months 52 patients were centrally randomized either to MMF (1-2g/d) and steroids (23 patients) or to LD-Tac and steroids (29 patients). Protocol biopsies were performed after one year.
Results: Of the 90 patients enrolled, 38 KTR dropped out within the first three months due to severe rejection (10%), intolerance of MMF dose (12%), out of target Tac level (7%) or other protocol offences (15%). One year patient and graft survival was 98% and 90%, respectively. Delayed graft function occurred in 23% and acute rejections in 32% of the KTR. Plasma creatinine (P-Crea) was significantly lower in the MMF group after 6 ($p<0.05$) and 12 months ($p<0.05$) compared to the LD-Tac group (table). P-Crea within the LD-Tac group significantly increased within the observation period ($p<0.01$, table).

	3 Months	6 Months		12 Months	
		LD-Tac	MMF	LD-Tac	MMF
Creatinie (μmol/L)	169±100	170±97	127±17	195±144	146±70
GFR (mL/min)	38±11	37±10	44±9	37±9	40±6
Rejection (%/patients)	32/29	21/4	25/3	5/1	0/0
Infction (%/patients)	13/12	21/4	8/1	15/3	11/1
Blood pressure systolic (mmHg)	140±17	144±19	137±14	138±14	141±16
Blood pressure (mmHg)	76±10	80±10	74±8	73±10	76±12
Hemoglobin level (g/L)	114±14	128±13	120±14	126±15	127±16
LDL-Cholesterol (mg/dL)	213±54	207±58	170±38	204±46	211±42

Conclusion: If tolerated, MMF based calcineurin-inhibitor free maintenance immunosuppression (>3 months after KTx) improves graft function without increasing the rate of late rejections. Nevertheless the high incidence of early rejections within the first 3 months after KTx demonstrate that a low dose immunosuppression protocol in this early phase after transplantation is not sufficient for older patients.

P-386 INFLUENCE OF PERIOPERATIONAL ACID-BASE BALANCE DISORDERS ON 1-YEAR GRAFT FUNCTION IN KIDNEY TRANSPLANTATION

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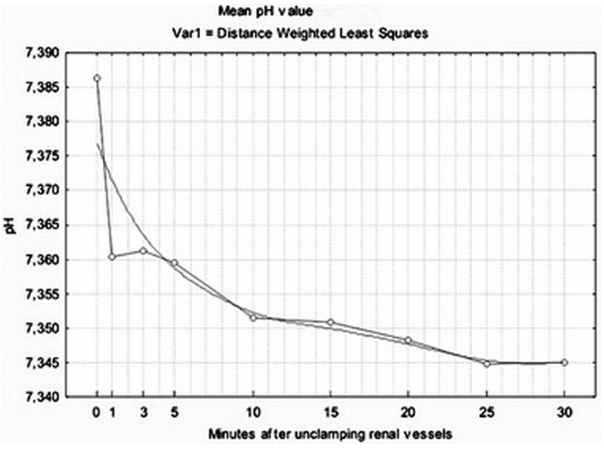
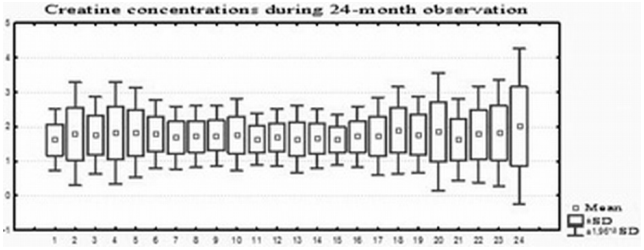
Introduction: The reperfusion is a very crucial moment to the kidney transplantation, connected with many metabolic changes which are the result of the kidney's initial condition, preservation and perioperational course. We observed acid-base balance (ABB) disorders during reperfusion, their correlation with preoperational factors and their influence on graft's function during 1-year observation.
Aim: The study's purpose was the examination of ABB dynamics during 30 minutes of reperfusion basing on arterial blood samples, the evaluation of ABB relationship with donor related factors, matching and the evaluation of ABB influence on kidney's function based on 1-year observation of blood parameters and events e.g. graft loss.
Material and methods: The examined group consisted of 54 recipients. Full arterial blood gasometric analysis was made 0, 1, 3, 5, 10, 15, 25, 30 minutes after unclamping renal vessels. Postoperatively we analyzed factors: donor gender, donor age, HLA mismatch, ischemia time, kidney's side, order of operation, blood parameters after pretrasplant dialysis, delayed graft function





(DGF) occurrence. During 1-year observation period we observed graft loss occurrence and serum concentration of creatinine, urea and uric acid. Statistical significance was analyzed using repeated-measures ANOVA followed by Tukey post-hoc test as well as U Mann-Whitney's and Spearman's ranges correlation tests.
Conclusions: Reperfusion is the cause of increasing metabolic acidosis with mediocre respiratory component. Higher acidosis is related to complete antigen mismatch in HLA-DR and to male recipient. In postoperative course higher acidosis is related to higer DGF occurrence and higher serum creatinine concentrations. ABB disorders during reperfusion are not related to ischemia time and serum concentration of creatinine, urea and uric acid in 1-year observation.

P-388 A SINGLE CENTER EXPERIENCE UTILIZING KIDNEYS FROM DECEASED DONORS WITH TERMINAL ACUTE RENAL FAILURE

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Transplantation of kidneys from deceased donors (DD) with terminal acute renal failure (ARF) is uncommon.
Methods: ARF DD kidneys were defined as either a doubling in admit serum creatinine (SCr) or a terminal SCr level >2.0 mg/dl.
Results: Between 1/07 and 10/08, we transplanted 25 kidneys from 17 ARF DDs including 22 from standard criteria DDs; all were refused by multiple centers. Mean DD age was 33 years (range 20-65). Causes of DD death included trauma in 8 (47%), anoxia in 5 (29%), and stroke in 4 (24%). Mean admit and terminal DD SCr levels were 1.3 mg/dL and 3.2 mg/dL, respectively (mean calculated Cr clearance 43 ml/min). All kidneys were placed on pulsatile perfusion with a mean cold ischemia time of 27.4 hours (range 11-41). The patient (pt) group included 18 men and 7 women with a mean age of 49 years (range 27-70) and a mean waiting time of 24 months (range 1-68). All pts received antibody induction in combination with tacrolimus, MMF, and tapered steroids (52% had early steroid withdrawal). Pt and graft survival rates are 100% and 92%, respectively, with a mean follow-up of 12 months. Delayed graft function occurred in 9 pts (36%), primary nonfunction in 1 (4%), and the mean length of initial hospital stay was 6 days. Four pts (12%) had acute rejection episodes, while 8 (32%) developed infections. Reoperation was required in 3 (12%) pts. Mean 1, 6, and 12 month pt SCr levels and glomerular filtration rates (GFR) were 1.9 mg/dl (45 mL/min), 1.6 mg/dl (50 ml/min), and 1.5 mg/dl (52 mL/min), respectively.
Conclusion: Kidneys transplanted from DDs with terminal ARF have excellent short-term outcomes and represent another potential method to safely expand the donor pool.

P-389 A SEVEN YEAR EXPERIENCE WITH 222 EXPANDED CRITERIA DONOR KIDNEY TRANSPLANTS AT A SINGLE CENTER

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The purpose of this study was to review outcomes in expanded criteria donor (ECD) compared to concurrent standard criteria donor (SCD) kidney transplant (KT) patients (pts) using a standardized approach with similar immunosuppression.
Methods: Single center retrospective analysis of 578 adult deceased donor (DD) KTs performed from 10/01 to 07/08, including 222 (38%) from ECDs and 357 (62%) from standard criteria donors (SCD).
Results: ECDs were characterized by older DD age (mean 62 yrs ECD vs 34 SCD) and more pump preservation (PP, 84% ECD vs 56% SCD, all p<.05). Estimated DD creatinine clearance was lower in ECDs (mean ECD 77 ml/min vs SCD 98, p<.01). ECD KT pts were older (mean age 58 yrs ECD vs 49 SCD) and had fewer 0-antigen mismatches (9% ECD vs 25% SCD) and a shorter waiting time (mean 22 months ECD vs 28 SCD, all p<.01). Mortality (13% ECD vs 8% SCD, p=.06) and death with functioning graft (DWFG) rates (10% ECD vs 6% SCD, p=.10) were slightly higher in ECD KT pts. Actuarial graft loss (GL) rates (27% vs. 17%, p=.004) and death-censored (D-C) GL rates (19% vs. 11%, p=.02) were greater in the ECD KT pts with a mean follow-up of 33 months. Delayed graft function (DGF) was greater in SCD KTs (26% vs 18%, p=.02). Acute rejection rates were slightly higher in SCD KT pts (15% ECD vs 21% SCD, p=.09), whereas major infections were higher in ECD KT pts (32% ECD vs 23% SCD, p<.01). Mean 24 month calculated GFR was higher in SCD pts (ECD 43 mL/min vs SCD 55, p<.01).
Conclusions: A systematic approach based on age and nephron mass matching between DDs and pts may improve utilization and outcomes with ECD kidneys.

P-390 HISTOMORPHOLOGICAL AND IMMUNOHISTOCHEMICAL EVALUATION OF PERFUSED AND PRESERVED KIDNEY WITH EC OR UW SOLUTION STUDIED WITH AN EXPERIMENTAL MODEL OF THE PRE-TRANSPLANTATION PERIOD

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Ischemic injury of the donor's kidney taking place prior to grafting plays an important role in the pathogenesis of chronic nephropathy of the graft and may also serve as a key prognosticator for the fate of the grafted organ basing on standardized histologic criteria which reflect the extent of injury. Experimental evidence for this possibility has been offered while clinical studies have demonstrated that perfusion and preservation with UW solution results in fewer cases of delayed renal graft function as compared with EC solution.
This work was undertaken to describe structural lesions in renal tubules and interstitium of rat kidneys perfused and subsequently preserved with EC or UW solution, as compared with the KON control group.
Histologic lesions in the kidney were assessed using criteria for the tubulo-interstitial area only and replacing the original Shih index with its simplified version according to Remuzzi. Each component of the tubulo-interstitial injury index (IUCS) and its final value were studied, basing on following: *inflammatory cellinfiltrate* – I, *tubular necrosis* – T, *interstitial fibrosis* – F. Immunohistochemistry was done to reveal the presence of antigens specific for macrophages/monocytes, B and T cells using murine monoclonal antibodies against CD68, CD79a, and CD45-RO, respectively.
Table presents histologic findings in rat kidneys from KON, EC, and UW groups obtained at the end of the warm ischemia period.

Tubulo-interstitial injury index (IUCS) and its variables

Variable	KON	EC	UW	ANOVA p
I	0,12±0,35	0,62±0,52	0,75±0,46*	<0,05
T	4,00±0,00	2,37±0,52*	1,25±0,46*#	<0,05
F	0,00±0,00	0,00±0,00	0,00±0,00	NS
IUCS	1,37±0,12	1,00±0,25*	0,67±0,25*#	<0,05

I, inflammatory cell infiltrate; T, tubular necrosis; F, interstitial fibrosis; KON, control; EC, Euro-Collins solution; UW, University of Wisconsin; NS, not significant

Conclusion: 1. Perfusion in situ of renal kidneys with UW solution followed by preservation for 24 hours at 4°C was much more potent in limiting the extent of tubular necrosis as compared with EC solution.
2. Renal immunohistochemistry with antibodies specific for macrophages and lymphocytes has shown that T cells represent the major fraction of the cellular infiltrate.

P-391 IS ABO-INCOMPATIBLE RENAL TRANSPLANTATION A RISK FACTOR FOR MALIGNANCY?

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Introduction: Malignant tumor is a troubling onset complication of renal transplantation, which may affect upwards of 8% in the current era of immunosuppression. The risk factors for the development of this problem appear to be a history of using cyclophosphamide and induction therapy (muromonab-CD3 monoclonal antibody or anti-thymocyte antibody). However, no studies have

demonstrated that ABO-incompatible renal transplantaion (ABOi LDRT) is a risk foctor for malignancy due to over-immunosuppression.
Method: We have performed ABOi LDRT in 88 patients since 1993. To minimize the risk of humoral rejection, we performed a splenectomy 2 weeks before transplantation, eliminated anti-A and/or anti-B antibodies by double-filtration plasmapheresis (DFPP), and administered a potent immunosuppressive regimen consisting of cyclophosphamide (until 10 days after transplantation then convert to mycophenolate mofetil or mizoribine), anti-CD25 monoclonal antibody, calcineurin inhibitor and prednisolone. The calcineurin inhibitor dose was adjusted by monitoring $AUC_{0\text{-}4}$ target values (60 patients received cyclosporine based regimen and 28 patients received tacrolimus based regimen).
We investigated the incidence of malignancy between ABOi LDRT and ABO-compatible renal transplantation group (n=177).
Results: The overall incidence of malignancy after transplantation was 4.5% (4/88, gastric, host kidney, prostate and lymphoma) in the ABOi LDRT group as compared with 5.1% (9/177, 3 colons, 2 host kidneys, breast, bladder, prostate and lymphoma) in the ABO-compatible group (p=0.848). There were no significant differences in the clinical profiles such as mean duration of hemodialysis before transplantation, recipient age, donor source and follow-up period in both groups. The overall graft and patient survival rates were also no significant in both groups.
Conclusion: Although total immunosuppression might be generally potent in ABOi LDRT, our center protocol of ABO-incompatible renal transplantation might be a suitable regimen without increasing the incidence of malignancy.

P-392 AREA UNDER THE CURVE SERUM CREATININE 7 DAYS POST TRANSPLANT DETERMINES GRAFT OUTCOME IN LIVE DONOR KIDNEY TRANSPLANTATION

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Introduction: Live kidney donation is considered the best mode of treatment for patients with end stage renal failure. However, there is a degree of variability in graft function in the immediate post transplant phase that may influence graft outcome. We investigated whether the calculation of Area under the curve serum creatinine (AUC_{Cr}) in the first 7 days post transplant could predict graft outcome in live donor kidney transplantation.
Methods: One hundred and eighty live donor renal transplants were retrospectively analysed. The AUC Cr values in the first 7 days post transplant was calculated and the data divided into two groups (AUC_{Cr} $<$2000: n= 106 and $>$2000: n=82). Donor demographics, intra-operative details and recipient demographics were recorded and compared. Factors that influenced AUC Cr and correlated AUC Cr with one year graft function were also determined.
Results: The mean values of AUC_{Cr} were 1479$\pm$347 in the $<$2000 group and 2718$\pm$790 (AUC_{Cr} $_{\mu}$mol/L.day) in the $>$2000 group. There was a significantly higher number of female donors to male in the $>$2000 group (P=0.0001). Serum creatinine levels were significantly higher in the $>$2000 group at 12 months post transplant (179$\pm$146.1 vs 124$\pm$6.2$_{\mu}$mol/L; P=0.0001) and eGFR significantly lower (47$\pm$15.0 vs 53.9$\pm$4.6; P=0.004). AUC_{Cr} significantly correlated with 12 month serum creatinine levels (0.478; P=0.0001). Independent variables that correlated with AUC_{Cr} were donor gender, donor Isotope GFR, cold ischaemic time and recipients that were on dialysis prior to transplantation.
Conclusion: The simple calculation of AUC_{Cr} levels 7 days post transplant is a valuable and reliable means to assess acute graft function in live donor kidney transplantation. It predicts poorer graft function at 12 months which is known to influence long-term graft survival. This study also highlighted the need for careful donor selection.

P-393 IMPACT OF OXIDATIVE STRESS AND INFLAMMATORY CYTOKINES ON SHORT TERM KIDNEY TRANSPLANT OUTCOME

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Purpose: Oxidative stress is the result of an imbalance between pro- and anti-oxidant factors in favour of the former leading to potential damage. The inflammation processes distinctive to haemodialysis treatment leads to an increased ROS production promoting oxidative stress. The aim of this study is to estimate oxidative damage and apoptosis in the early follow-up period after kidney transplantation measuring DNA oxidation and DNA fragmentation of peripheral lymphocytes. Serum levels of cytokines related to the oxidative processes were also quantified to better understand how oxidative stress is involved in the follow-up of renal transplantation.
Methods: Blood samples from 15 kidney transplant recipients were collected before transplantation and 2 days, 1 and 6 months after transplantation. Oxidative DNA damage and DNA fragmentation was measured through Comet Assay. Plasma levels of IL1β, IL4, IL6, IL8, IL10, IFNand TNFα were measured through the Searchlight Custom Human 7-Plex Array.
Results: Our data show a significant reduction in oxidative DNA damage and DNA fragmentation 6 months after kidney transplantation compared with pre-transplant ($p \leq 0.0001$). After 6 months a decrease in IL-6 plasma levels was observed with a p_value of 0.006. Biochemical and haematological features show an ameliorating of clinical conditions 6 months after transplantation (creatinine decrease $p<0.0001$; albumin increase p=0.0001; haemoglobin increase $p<0.0001$). Cytokine correlation analysis highlights a strong association between pro-inflammatory cytokines, in particular between INF, IL1β, IL4, TNFα (correlation coefficient between 0.65 and 0.88, $p< 0.01$). Finally we found that IL-6 influences DNA oxidation (p_value = 0.0052) and also DNA fragmentation (p_value = 0.0149).
Conclusions: Replacement of renal function through kidney transplant ameliorates oxidation and apoptosis index 6 months after transplantation. Evaluation of inflammation factors such as cytokine levels confirm this data showing a reduction of inflammation parameters within 6 months of follow-up.

P-394 TRANSIENT DISAPPEARANCE OF DONOR-SPECIFIC ANTIBODY ON POST-TRANSPLANT DAY 1 MAY INDICATE HIGH RISK FOR ANTIBODY MEDIATED ACUTE REJECTION FOLLOWING KIDNEY TRANSPLANTATION IN SENSITIZED RECIPIENTS

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Introduction: Pre-transplant donor specific antibody (DSA) positive recipients have a high risk for antibody mediated acute rejection (AMR) and acute rejection (AR) following kidney transplantation. However, AMR does not always occur in these so-called sensitized recipients following renal transplantation.
Purpose: To elucidate the risk factors for AMR/AR in pre-transplant DSA positive recipients.
Materials and methods: DSA was determined in 11 pre-transplant DSA positive recipients who underwent renal transplantation on postoperative day (POD) 1, 14, and 60. The onset of AMR/AR was evaluated.
Results: Four patients were negative for DSA on POD 1, and then positive on POD 14 and 60, of whom 3 developed AMR. No AMR was observed in 4 patients positive for DSA on POD 1, 14, and 60, though late onset AR developed in 3. No rejection of either type was seen in 3 patients negative for DSA on POD 1, 14, and 60.
Discussion: Transient negative findings for DSA on POD 1 in sensitized recipients may be caused by a high affinity to DSA by the graft, which leads to rejection. Furthermore, a low affinity to DSA by the graft may result in continuous positive findings for DSA from POD 1.
Conclusion: Our results suggest that a negative finding for DSA on POD 1 that is subsequently positive on POD 14 and 60 after renal transplantation may be strongly correlated with AMR in pre-transplant DSA-positive renal transplant recipients.

P-395 BELATACEPT DEMONSTRATES SUPERIOR COMPOSITE PATIENT/GRAFT SURVIVAL IN DIABETIC KIDNEY TRANSPLANT RECIPIENTS VS CSA: RESULTS FROM THE BENEFIT AND BENEFIT-EXT STUDIES

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Introduction: An increasing number of kidney transplant patients have pre-transplant diabetes mellitus, which is associated with poorer outcomes post-transplant. We assessed outcomes in diabetic kidney transplant patients utilizing pooled data from two Phase III studies assessing belatacept-based immunosuppressive regimens vs a cyclosporine (CsA)-based regimen.
Methods: Patients with a pre-transplant history of diabetes or who were taking anti-diabetic medication at baseline were assessed from BENEFIT and BENEFIT-EXT, 3-year, randomized, Phase III studies. Patients were randomized 1:1:1 to receive a more intensive (MI) or less intensive (LI) regimen of belatacept, or CsA; all patients were treated with basiliximab induction, MMF, and corticosteroids. Endpoints through 12 months included composite patient/graft

survival, composite renal endpoint (measured GFR [mGFR] <60 mL/min/1.73 m^2 at Month 12 or a decrease in mGFR ≥10 mL/min/1.73 m^2 from Month 3 to Month 12), incidence of acute rejection (AR), and prevalence of chronic allograft nephropathy (CAN). A descriptive analysis of a subgroup of diabetic patients is presented.
Results: Across both studies a total of 336/1209 patients (28%) with diabetes prior to transplant were randomized and transplanted (n=180 BENEFIT; n=156 BENEFIT-EXT).

Diabetic patient outcomes	Belatacept MI (n=114)	Belatacept LI (n=97)	CsA (n=125)
Composite patient/graft survival, n (%)	103 (90%) [p=0.03 vs CsA]	90 (93%) [p=0.01 vs CsA]	101 (81%)
Mean measured GFR, mL/min (SD)	61.2 (22.1) [p=0.0005 vs CsA]	66.1 (39.3) [p<0.0001 vs CsA]	46.4 (20.2)
Acute rejection, n (%)			
BENEFIT	13/63 (21%)	12/58 (21%)	5/59 (9%)
BENEFIT-EXT	13/51 (26%)	8/39 (21%)	13/66 (20%)
CAN prevalence, n (%)			
BENEFIT	6/63 (10%)	14/58 (24%)	18/58 (31%)
BENEFIT-EXT	22/51 (43%)	18/38 (47%)	38/66 (58%)

The incidence of AR in diabetic patients was consistent with the overall study population.
Conclusion: In a descriptive analysis of diabetic transplant patients, belatacept regimens were associated with superior patient/graft survival and renal function vs CsA. The incidence of AR observed in these patients was consistent with the overall population. The renal benefit in the population may translate to better long-term outcomes, which will be evaluated further in these 3-year studies.

P-396 BELATACEPT IS ASSOCIATED WITH PRESERVATION OF RENAL FUNCTION AND STRUCTURE AT 1 YEAR COMPARED TO CYCLOSPORINE IN KIDNEY TRANSPLANT PATIENTS (BENEFIT STUDY)

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Introduction: Post-transplant renal function at 1 year and chronic allograft nephropathy (CAN) correlate with long-term graft function and patient/graft survival. Belatacept is being investigated as part of a non-nephrotoxic immunosuppressant regimen in kidney transplant recipients to replace calcineurin inhibitors. This abstract focuses on renal endpoints.
Methods: BENEFIT is a 3-year, randomized, Phase III study of belatacept in adults receiving a kidney transplant from a living or deceased donor with an anticipated cold ischemia time <24 hours. Patients were randomized 1:1:1 to receive a more intensive (MI) or a less intensive (LI) regimen of belatacept or cyclosporine A (CsA); all patients received basiliximab induction, MMF, and corticosteroids. The primary renal endpoint was composite renal function (measured glomerular filtration rate [mGFR] <60 mL/min/1.73 m^2 at Month 12 or a decrease in mGFR ≥10 mL/min/1.73 m^2 from Month 3 to Month 12). Secondary renal endpoints at Month 12 included mGFR, calculated GFR (cGFR), and protocol biopsies to assess for chronic allograft nephropathy.
Results: 666 patients were randomized and transplanted. More CsA patients had reduced renal function vs belatacept regimens as shown by the composite renal endpoint.

	Belatacept MI (n=219)	Belatacept LI (n=226)	CsA (n=221)
Composite renal function impairment endpoint, n (%)	115 (55%) (P<0.001 vs CsA)	116 (54%) (P<0.001 vs CsA)	166 (78%)
Mean mGFR, mL/min (SD)	65.0 (30.0) (P<0.0001 vs CsA)	63.4 (27.7) (P<0.0001 vs CsA)	50.4 (18.7)
Mean cGFR, mL/min (SD)	68.3 (19.2) (P<0.0001 vs CsA)	68.1 (19.0) (P<0.0001 vs CsA)	53.6 (16.9)
CAN prevalence, n (%)	40 (18.3%) (P=0.001 vs CsA)	54 (23.9%) (P=0.058 vs CsA)	71 (32.4%)

Differences in cGFR were apparent 1 month post-transplant and were maintained through 1 year. There was concordance between overall mGFR and cGFR over the first 12 months.
Conclusions: Belatacept regimens demonstrated superior renal function and had a favorable impact on the development of CAN at 12 months compared with CsA. Differences in renal function were observed soon after transplant, were maintained through 1 year, and will be followed during the 3-year study.

P-397 LIMITED IMPACT OF ACUTE REJECTION ON GRAFT OUTCOMES IN BELATACEPT-TREATED KIDNEY TRANSPLANT RECIPIENTS (BENEFIT/BENEFIT-EXT)

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Introduction: Belatacept-based immunosuppression is associated with superior renal function and similar patient/graft survival vs cyclosporine (CsA) in two Phase III trials in kidney transplant recipients. This descriptive analysis characterizes the impact of acute rejection (AR) on 1-year outcomes.
Methods: BENEFIT assessed belatacept in patients receiving kidney transplants from a living or deceased donor; BENEFIT-EXT in extended criteria donor recipients. Each assessed belatacept in more intensive (MI) and less intensive (LI) regimens vs CsA. All patients received basiliximab, MMF, and corticosteroids.
Results: 1209 patients were randomized and transplanted (n=666 in BENEFIT; 543 in BENEFIT-EXT). In BENEFIT, 22% (MI), 17% (LI), and 7% (CsA) of all patients exhibited AR by Month 12. 10% (MI), 5% (LI), and 1% (CsA) of all patients had Banff Grade≥IIb AR. In BENEFIT-EXT, AR rates were similar across arms: 17% (MI), 18% (LI), and 14% (CsA) of all patients exhibited AR by Month 12. 8% (MI), 5% (LI), and 3% (CsA) of all patients had Banff Grade ≥IIb AR. The proportion of patients with AR who had post-AR serum creatinine recovery to within 110% of pre-AR nadir was 59% (MI), 72% (LI), and 54% (CsA) in BENEFIT, and was 61% (MI), 73% (LI), and 71% (CsA) in BENEFIT-EXT. 12-mo outcomes below.

	Belatacept MI		Belatacept LI		CsA	
	+AR	–AR	+AR	–AR	+AR	–AR
Mean measured GFR, mL/min (SD):						
BENEFIT (n=666)	61.8 (25.4)	66.2 (32.1)	60.6 (43.7)	65.1 (25.4)	48.3 (17.4)	50.8 (19.4)
BENEFIT-EXT (n=543)	45.9 (19.9)	53.8 (22.3)	38.8 (19.2)	51.3 (27.0)	34.4 (16.4)	47.5 (22.3)
Survive w/functioning graft, n (%):						
BENEFIT (n=666)	45 (94%)	164 (96%)	36 (92%)	182 (97%)	15 (94%)	190 (93%)
BENEFIT-EXT (n=543)	28 (88%)	130 (86%)	25 (81%)	129 (90%)	18 (69%)	138 (87%)

Conclusions: The impact of AR on graft function and survival in the belatacept groups was limited, despite higher grades of AR in the belatacept groups vs CsA. Measured GFR in the belatacept patients with AR remained similar or higher than measured GFR in CsA patients with AR in each study. Furthermore, belatacept patients with AR had better renal function at 12-mo compared with CsA patients without AR in the BENEFIT study. Long-term effects of AR continue to be assessed over the duration of these 3-year trials.

P-398 NON-SKIN MALIGNANCIES AFTER RENAL TRANSPLANTATION: ONE CENTRE EXPERIENCE

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Background: During the last several decades, renal transplantations (RT) have been performed with increasing success. However, RT recipients are predisposed to greater number of late complications including neoplasia caused by graft-preserving immunosuppressive therapy.
Objective: The objective of the research was to estimate the number and the type of *de novo* cancers among kidney grafts recipients.
Material: We reviewed the medical records of 913 patients (568 males and 345 females) who underwent RT in our transplantation centre between 1980 and 2008.
Results: During the follow-up 30 (3.3%) of RT recipients were diagnosed with non-skin malignancies. 4 lymphomas and 26 solid malignancies were recognized (7 genitourinary, 5 lung, 4 gastrointestinal, 3 liver, 2 breast, 1 pancreas, 1 brain, 1 larynx, 1 suprarenal gland and 1 of unknown origin). Affected group included 23 (76%) males and 7 (24%) females, they mean age at diagnosis was 54.3±13 (range 24 – 79) years. The mean time since transplantation to cancer diagnosis was 66.2±58.9 (range 6 – 228) months. The immunosuppressive protocol consisted of: prednizone (P) + azathioprine (AZA) + cyclosporine A

(CsA) in 14 (46%) patients, P + mycophenolate mofetil (MMF) + tacrolimus (TAC) in 6 (20%) patients; P + CsA + MMF in 4 (13%) patients, P + AZA in 1 (3.3%) patient; P + CsA in 3 (10%); P + TAC in 1 (3.3%) patients; patients and TAC alone in 1 (3.3%) patient. Twelve (40%) of patients died. All patients with lymphoma died (8 – 44 months after diagnosis). Four (13%) patients lost their grafts due to cancer.
Conclusions: Genitourinary cancer, lung cancer and lymphoma were diagnosed most frequently. Almost 50% of cancer patients received P, AZA and CsA. Life expectancy after cancer diagnosis was short.

P-399 SEMI-QUANTITATIVE ANALYSIS OF FOXP3

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Introduction: Some of recipients with long-term stable graft function could possibly minimize immunosuppression, if “almost tolerance”state is taken. However, useful assays for assessing immune status have not been established. Foxp3 is a transcription factor of CD4+CD25+ regulatory T cell that play a key role in immune tolerance. We investigated the clinical meaning of FoxP3 mRNA measurement.
Methods: (i) FoxP3 mRNA expression (normalized beta-actin or CD4) was compared with the number of FoxP3+ cells in peripheral blood. (ii) FoxP3 mRNA was successively measured pre and post renal transplantation. Moreover, Foxp3 expression treated with everolimus (RAD) was compared with mycophenolate mofetil (MMF). (iii) Maintenance recipients were classified into 4 groups according to immunosuppressive regimens including calcineurin Inhibitor (CNI), MMF and prednisolone (PRD). The effect of immunosuppressive drug on FoxP3 mRNA was examined in 4 groups and patients with HLA antibody.
Results: (i)FoxP3 mRNA significantly correlated with the rate of Foxp3+ cells. (ii) After tansplantation,FoxP3 mRNA were reduced immediately and gradually recovered.

Foxp3 mRNA expression pre and post transplantation

	Pre	1w	2w	3w	1m	2m
Foxp3/CD4	1.6	1.1	1.2	1.3	1.2	1.2
Foxp3/beta-actin	3.1	1.4	1.8	2.2	2.2	2.2

No apparent difference in Foxp3 expression was observed between RAD group and MMF.(iii) Only CNI-free recipients showed significantly higher Foxp3 expression than other groups and patient with de novo HLA antibody ($p<0.05$), although no significant difference was observed in renal function.

Foxp3 expression according to immunosuppressive regimens

	CNI free	PRD free	CNI+PRD	CNI+PRD+MMF
Foxp3/CD4	1.4	1	0.9	0.9
Foxp3/beta-actin	3.4	2	2.1	2.1

Discussion: FoxP3 expression was significantly interfered by CNI. However, no obvious correlation to renal function was observed. Significant difference in Foxp3 was not observed between RAD and MMF, although RAD has been recently reported to promote Treg expansion. The Foxp3 mRNA was considered to reflect the number of FoxP3+ regulatory T cells. The semi-quantitative analysis of peripheral blood mRNA would be easy and promising method, because not only FoxP3 but also potential biomarkers could be analyzed in future. The study on clinical value of FoxP3 mRNA and the search of other biomarkers are in progress.

P-400 SKIN AND SOLID ORGAN CANCERS IN KIDNEY TRANSPLANT RECIPIENTS: WHEN SHOULD CANCER SCREENING BE CLOSER?

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Cancer is the second cause of mortality in kidney transplant recipients.
Aim: The aim of the study was to analyse the annual incidence in the early (<18 months (m)), median and late (>14 years (y))post kidney transplantation period and the cumulative incidence of non melanoma skin cancers (NMSC), solid organ cancers (SOC) and lymphoproliferative disorders (LPD) and the standardized incidence ratios (SIRs) in a cohort of kidney transplant recipients.
Patients and methods: 525 consecutive patients transplanted between 1987 and 2005 were included and followed until 31-12-2007 or until graft failure or/and death.The mean follow-up was 7.7±4.7y. The immunosuppressive threrapy included Antithymocyte globulins induction (ATG) and tritherapy with steroids, azathioprine (n=223) or mycophenolate mofetil (n=302), and anticalcineurins: ciclosporine A (n=410) or tacrolimus (n=98).Patients with early graft loss or death were excluded (n=47).
Results: 110 out of the 478 patients (23%) had at least one cancer and 189 cancers were observed in 3687 patient-years of follow-up: 117 NMSC, 25 LPD, 47 SOC. The cumulative incidence at 15y was 46.6% [37.1-54.7] for all cancers, 19.3% [11.8-26.1] for solid organ cancers, 11.9% [5.9-17.6] for LPD, and 27.7% [19.2-35.4] for NMSC. Risk factors for all cancers in a multivariate analysis were age, body mass index, EBV primo-infection (RR=1.92) and azathioprine exposure (RR=1.47).

Annual incidence of cancer (Kaplan Meier)

	<18 months	18 months - 14 years	>14 years
All cancers	**5.4±1.4**	2.8±0.3	**3.2±0.1**
SOC	0.8±0.2	1.0±0.1	**1.3±0.1**
NMSC	**2.2±0.9**	1.4±0.2	**1.9±0.1**
LPD	**3.2±0.8**	0.7±0.2	ND

Comparing to the French General Population (InVS 2002), the SIR for all non NMSC cancers was 6.54 [5.12-8.23].
Discussion: This study shows an overrisk for NMSC and LPD, but not for SOC, in the early post-transplantation period,and an overrisk for NMSC and SOC after 14y. It confirms the high cumulative incidence and the high SIRs of cancer after kidney transplantation and allows to adapt their screening according to the age and the time after transplantation.

P-401 DEVELOPMENT OF MARGINAL DONOR SCORING SYSTEM IN KOREA

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The use of marginal donors has increased worldwide to address the shortage of deceased donor organs. However, the use of marginal kidneys may result in delayed graft function, prolonged hospitalization and reduced graft survival. A scoring system was devised to predict the outcomes and assist the allocation of marginal kidneys.
Records of 172 deceased renal transplant recipients between January, 2006 and December, 2008 at 6 medical centers were studied retrospectively. Six donor variables (Donor age >50 years old, history of hypertension, Body mass index ≥25 kg/m^2, cerebrovascular accident induced brain death, history of cardiopulmonary resuscitation, estimated glomerular filtration rate before procurement <60 ml/min) before procurement were assessed. The quality of donor kidneys were stratified into 3 grades by its cumulative score (grade 1, 0-1 point; grade 2, 2-3 points; grade3, 4-6 points). For 38±13.1 months of mean follow-up, 37 (21.5%) patients experienced delayed graft function. There were 11 patient deaths. The six donor variables showed a tendency to be associated with delayed graft function, but were not independently significant. However, by integrating the six variables, the scoring system was useful in predicting the early graft function after deceased donor renal transplantation. Delayed graft function was significantly observed in kidneys with increased donor score and grade ($p<0.05$). The characteristics of deceased donors in Korea are different than those from other countries. Therefore there is a need for a modified definition and criteria for Korean deceased marginal donors.

Incidence of delayed graft function (DGF), acute rejection and graft failure by donor scoring system

	No.	DGF	Acute rejection	Graft failure
Grade 1 (0-1)	69	8 (11.6%)	4 (5.8%)	4 (5.8%)
Grade 2 (2-3)	92	19 (20.7%)	13 (14.1%)	7 (7.6%)
Grade 3 (4-6)*	13	7 (53.0%)	2 (15.4%)	2 (15.4%)
Total	172	37 (21.5%)	19 (11%)	13 (7.6%)

*p=0.002 versus Grade 1 and Grade 2

Our scoring system is a simple, practical and also compatible with posttransplant renal function. This system allows efficient evaluation of marginal kidneys and may improve allocation of these organs in Korea.

P-402 MULTIPLE SEQUENTIAL NEOPLASM IN KIDNEY ALLOGRAFT RECIPIENTS

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Introduction: Cancer is the second leading cause of death in renal allograft recipients with a 3,5-4,6 of relative risk for first malignancy compared to general population. This higher incidence is related to immunosuppressive therapy, viral infection, age and sex of the patient. A percentage of recipients manifest a second malignancy after the first one and fewer has multiple sequential malignancies.
Materials and methods: We have studied type and incidence of second malignancy in kidney allograft recipients in the period between 1968 and 2007 (1351 cases). We have defined as second cancer a malignancy arising in a patient already treated for a primitive form.
Results: 138 patients showed cancer (10%). 26 (19%) developed a second neoplasm after a median lapse of 764 days from first one. (min 96 – max 2327). 4 recipients developed a third cancer. 60% of secondary diseases was cutaneous (10 squamous cell carcinoma and 5 Bowen-like cancer). The remaining 40% was visceral or haematological (3 PTLD, 1 seminoma, 1 breast cancer, 1 HCC, 1 thyroid cancer and one lung cancer). The two groups of patients (those with one cancer and those with two or more cancer) was similar in age, gender, time of dialysis, number of HLA mismatch, PRA percentage and time of follow-up. Stratifying the risk of second neoplasm for type of immunosuppressive therapy (azathioprine + corticosteroid *vs* CsA/FK + MMF $\pm$ corticosteroid) cumulative incidence rate was not statistically meaningful.
Discussion: In our set 20% of patients have second neoplasm after a median time of about 2 years from first cancer. We found no relation between risk of onset of second and multiple tumor and demographic characteristic or immunological factor or type or immunosuppressive therapy. Second cancer, except for skin cancer, is not related to first one in kidney transplantation recipients analysed in our study.

P-403 CLINICAL SIGNIFICANCE OF 25-HYDROXYVITAMIN D (25-OHD) DEFICIENCY IN RENAL TRANSPLANT RECIPIENTS

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Background: Vitamin D deficiency is prevalent in chronic kidney disease (CKD) patients. Vitamin D deficiency has been reported to be associated with the risk of insulin resistance, diabetes, albuminuria and cardiovascular disease, which is the major cause of mortality in CKD patients. Renal transplant recipients may also be susceptible to vitamin D deficiency. However, this association in renal transplant recipients is not clear.
Purpose: To investigate the prevalence of 25-OHD deficiency and its association with insulin resistance, proteinuria, and other indicators of cardiovascular disease, such as PWV, ABI, FMD and Carotid IMT in renal transplant recipients.
Patient and method: Cross-section of 95 our renal transplant patients with mean age of 48$\pm$10 (25-70) years, and mean posttransplantation months of 103$\pm$53 (15-201) was performed during November and December in 2007. We compared Insulin resistance (HOMA-IR) and the prevalence of proteinuria (random urine protein-creatine ratio $\geq$ 0.2mg/mg) between 25-OHD deficiency ($\leq$30ng/ml, N=19) and normal control group ($>$30ng/ml, N=76).
Results: Mean 25-OHD (ng/ml) was 40.2$\pm$12.6, Of 95 transplant recipients, 19 (20%) have 25-OHD deficiency. Mean posttransplant month was significantly longer 126$\pm$49 in 25-OHD deficiency than 97$\pm$53 in normal 25-OHD (P=0.049). The prevalence of proteinuria was significantly higher 47.4% (9/19) in 25-OHD deficiency than 19.7%(15/76) in normal 25-OHD (P=0.019). Vitamin D deficiency is a significant risk factor of proteinuria, independent of age, posttransplant month, gender, and BMI (OR= 3.93, P=0.03). No association of vitamin D deficiency with Insulin resistance and cardiovascular (CV) parameters was observed.
Conclusion: We concluded that 25-OHD deficiency is not uncommon and is significantly associated with an increased prevalence of proteinuria in renal transplant recipients. Additional studies are needed to clarify the causal relationship of vitamin D with proteinuria and determine whether vitamin D therapy prevents or improves proteinuria, or markers of kidney and cardiovascular risk.

P-404 ANEURYSM SCREENING IN LONG TERM TRANSPLANT RECIPIENTS MAY PREVENT LETHAL COMPLICATIONS

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Purpose: Following the death of a longstanding renal allograft recipient (known external iliac artery aneurysm), from catastrophic rupture of concomitant gastro-duodenal artery aneurysm, we speculated that such patients might be at increased risk of aneurysm formation in unusual sites.
Method/Materials: To investigate this hypothesis, we reviewed 182 renal allograft recipients under follow-up with a minimum allograft age of 20 years. Patients at highest risk were targetted for initial screening; aged $>$40 yrs with a history of major adverse cardiovascular events, steroid-containing immunosuppressive regimens, a primary diagnosis of hypertension, diabetes or renovascular disease. The abdominal and pelvic vasculature was screened using magnetic resonance or CT angiography, followed by intra-arterial digital subtraction angiography where indicated.
Results: A cohort of 54 patients judged high risk were identified. Median patient and graft age were 52.5 yrs and 24 yrs respectively. A total of 22 recipients have been screened to date. Aneurysms have been detected in 3/22 patients thus far (13%). Two further patients with grafts surviving $>$10yrs were also incidentally identified to have aneurysms.
Conclusion: This small pilot survey demonstrates a significant prevalence of aneurysm in long-surviving renal allograft recipients. This phenomenon is hitherto unreported and ours is the first attempt to define the prevalence of such aneurysms in this population. The pattern of aneurysm formation appears different from the general population. Repair of such aneurysms is not without risk. Further information about the natural history of these lesions is needed to inform our decision-making. It is conceivable that aneurysm rupture is an important but unrecognized cause of patient mortality in the late post-transplant period.

P-405 ROUTINE PERIOPERATIVE ANTIBIOTIC PROPHYLAXIS IN RENAL TRANSPLANTATION: IT MAKES NO DIFFERENCES IN BACTERIAL INFECTIONS

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Purpose: Although there is consensus in the use of preventive antibiotics because it may prevent infections following renal transplantation, it would increase cost, resistant micro-organisms and adverse effects. The effect of infections that do not routine use of perioperative antibiotic prophylaxis has not been well studied. Therefore we evaluated the differences in routine use of antibiotics or not.
Methods/Materials: We reviewed retrospectively 106 renal transplantations (cadaver donor 42, living donor 64)performed from January, 2006 to December, 2008. They were divided into two groups: Group A (n= 41; 38.7%), without prophylactic antibiotics and Group B (n= 65; 61.3%), received prophylactic antibiotics. We analyzed infectious complications within 1 month after renal transplantation.
Results: There were 66 (62.3%) male patients and 40 (37.7%) female patients. In Group A, most patients (62 cases, 95.3%) used 1st generation cephalosporin. There were 2 (1.8%) cases of wound infection, 1 case in Group A (1/64) and 1 case in Group B (1/39) but no significant difference. Bacteremia (3 cases, 2.8%), hematoma (1 cases, 0.9%) infection and urinary tract infection (2cases, 1.8%) occurred only in Group B. Pneumonia and central catheter related infection were not occurred in both Groups. There were no clinical correlation between recipient diabetes, vesico-ureteral reflex, ESRD duration, operation time and infectious complication. But CAPD patients had higher wound infection (2 cases, P=0.031) and urinary tract infection (2 cases, P=0.031). And donor infection affected recipient post transplantation bacteremia (1 cases, P=0.02).

Abstract P-404 – Table 1. Patient & aneurysm data

Age (yrs) & Sex	Graft age (yrs)	Aneurysm(s)	Outcome	Complications
69 M	31	1 $\times$ gastroduodenal artery, 1 $\times$ external iliac artery	graft nephrectomy	death on rupture of gastroduodenal artery aneurysm
48 M	20	1 $\times$ external iliac artery	surgical repair of aneurysm	loss of graft, post-op MI
46 F	20	1 $\times$ internal iliac artery	observation	none
21 M	16	1 $\times$ abdominal aorta, distal to anastomosis site	surgical repair of aneurysm	none
58 F	11	1 $\times$ external iliac artery, 1 $\times$ native renal artery	graft nephrectomy, native nephrectomy	none

Conclusion: The results of this study demonstrate that prophylactic use of antibiotics do not make a difference in bacterial infections although renal transplantation is clean-contaminated surgery. Further studies are needed to evaluate proper indication of prophylactic antibiotic use, especially CAPD patients and previous donor infection.

P-406 RENAL FUNCTION AND SAFETY ARE WELL-MAINTAINED AFTER CONVERSION FROM TWICE-DAILY PROGRAF® TO ONCE-DAILY ADVAGRAF® IN STABLE KIDNEY TRANSPLANT PATIENTS: A PHASE IIIB STUDY

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Purpose: Once-daily immunosuppression doubles the likelihood of post-transplant adherence, which improves graft protection. We assessed 12-week renal function and safety of stable kidney transplant patients upgraded from twice-daily (Prograf®) to once-daily prolonged-release tacrolimus (Advagraf®).
Methods: In this multicentre, open, crossover study, stable adult kidney transplant patients on unchanged Prograf dose $\geq$12 weeks were converted to Advagraf (morning dose) on a 1:1 mg:mg basis after a 6-week Prograf-treatment phase. Patients remained on Advagraf for 12 weeks with minimal dose changes. The primary endpoint was the change in steady-state creatinine clearance (CrCl; Cockcroft–Gault) between Prograf and Advagraf. Secondary endpoints included: adjunct immunosuppression use and efficacy and safety parameters.
Results: 114 patients (mean age 48.9 years; mean time post-transplant 48.9 months) completed the study; 91 without major protocol deviation. Mean daily dose was 0.06mg/kg and 0.07mg/kg for the Prograf and Advagraf phases, respectively; 79.2% of patients required $\leq$1 dose change post-conversion. Mean trough level was 7.2ng/mL before conversion, 6.3ng/mL at Week 1 and 7.0ng/mL at Week 12. Mean CrCl was 72.5mL/min and 72.1mL/min for Prograf and Advagraf phases, respectively (relative difference -0.7% [95% CI: -1.8; 0.5], N=91). Concomitant immunosuppression treatment remained unchanged throughout; 48/91 (52.7%) patients took corticosteroids (4.7$\pm$1.3mg/day). No deaths, graft losses or acute rejection episodes occurred. Adverse events were few and none led to dose modifications or withdrawals.
Conclusions: Stable kidney transplant recipients can be conveniently converted from Prograf to a once-daily Advagraf regimen, while maintaining efficacy, safety and good renal function.

P-407 VACUUM-ASSISTED CLOSURE THERAPY (VACT) IN THE MANAGEMENT OF WOUND INFECTION AFTER RENAL TRANSPLANTATION: A SINGLE CENTRE EXPERIENCE

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Introduction: Wound infection in the setting of an immunosuppressed state such as after renal transplantation (RT) causes significant morbidity from sepsis, prolongs hospital stay and is expensive. Vacuum-assisted closure therapy (VACT) is a new technique of management of wound based on the principle of application of controlled negative pressure. The aim of this study was to assess the efficacy of VACT in the management of wound infection following RT.
Methods: This is a prospective study of a cohort of 237 consecutive RTs performed over a period of 5 years, where the data were retrieved from a prospectively maintained computerised database and case-notes.
Results: 11 of 250 (4.4%) patients developed deep wound infection following RT leading to cavitations and dehiscence with copious discharge, which refused to heal with conventional treatment. All 11 cases were treated with VACT. The VACT system was removed after a median of 9 (range 3-120) days when discharge from the wound ceased. Six patients were discharged home with portable VACT device and managed on an outpatient basis, where the system was removed after a median of 7 days (range 3-116) days. The median hospital stay after initiation of VACT was significantly shorter (4, range 2-12 days) than on conventional treatment prior to VACT (11, range, 5-20 days). Complete healing was achieved in all cases. No complications related to VACT such as haemorrhage and intestinal fistulae were observed in this series.
Conclusions: The use of VACT is an effective and safe adjunct to conventional and established treatment modalities for the management of deep wound infection and dehiscence following RT.

P-408 THE ANSWER IS IN MACHINE PERFUSION: ANALYSIS OF MACHINE PERFUSION ON DONORS AFTER CARDIAC ARREST

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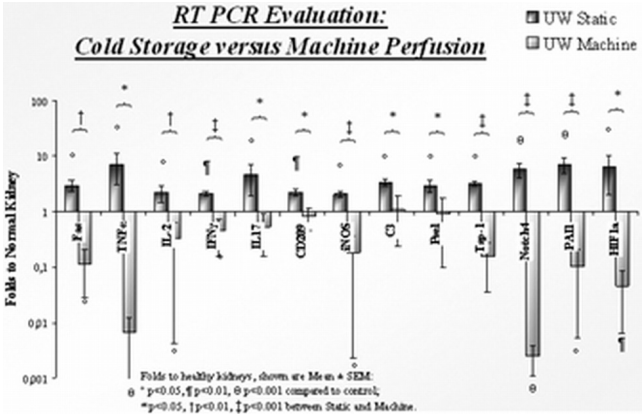
Purpose: The rift between the number of patients waiting for a graft and donations keeps expanding, increasing the pressure for new sources of organs. Deseased after cardiac arrest donors (DCAD) represent such a source. Due to the warm ischemia before preservation, these organs must be preserved using machine perfusion (MP), which improves graft early function. However, to date no analysis of the mechanistic impact of MP versus cold storage (CS) has been established.
Methods: We evaluated kidney grafts 3 months after transplantation in Large White pigs, for which warm ischemia was induced 60 minutes before 24h hours of either CS or MP conditions, using UW as preservation solution.
Results: After 3 months, kidney function was improved in grafts preserved with MP, as significant decreases were observed in plasma creatinine (209.8$\pm$19.4 vs. 459.0$\pm$37.0 μmol/L in CS, $p<0.01$) as well as proteinuria (0.7$\pm$0.1 vs. 4.5$\pm$0.4 g/24h in CS, $p<0.001$). MP had a definite impact on survival: 71.4% in MP group vs. 28.6% in CS, as well as graft fibrosis (31.7$\pm$5.2 vs. 53.3$\pm$2.8% Sirius Red staining in CS, $p<0.001$)
RT-PCR analysis revealed that MP decreased cytotoxicity marker Fas, and inflammatory cytokines TNFα, IL-2, IFNγ and IL-17, denoting a protection from both Th1 and Th17 immune responses. Decreased CD209 denoted lower dendritic cell invasion. iNOS levels evidence oxidative stress decrease. Downregulation was also evidenced in inflammation markers C3, P selectin and Thrombospondin (Tsp1); pro-injury marker Notch4 as well as fibrinogenesis marker PAI-1, and hypoxic stress marker HIF1α.



Conclusion: Machine perfusion on DCAD kidney graft appears to be beneficial for a wide range of lesional mechanisms: inflammation, oxidative stress, endothelial activation and fibrinogenesis.

Liver & intestine I

P-409 DEVELOPMENT AND VALIDATION OF A SURGICAL CHALLENGE SCORE WITH SIGNIFICANT IMPACT ON RESULTS AFTER LIVER TRANSPLANTATION

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Background and aims: Results of liver transplantation depend on many non-surgical factors. In this context the impact of surgical challenge at the time of transplantation is difficult to assess. The goal of this study is to develop and validate a surgical challenge score (SCS-score).
Material and methods: Clinical data of 2114 consecutive liver transplants performed between 1983 and 2005 was collected retrospectively and used to develop and test model scores. The data set was randomized in Groups 0 and 1. Group 0 was used for score design with variables with significant impact on outcome. Group 1 was used for score validation. The versatility of the validated score was further tested with different subgroups of the complete data set.

Findings: The binary variables (no=0, yes=1) portal vein thrombosis, portal vein interposition graft, aortal anastomosis, splenectomy, and retransplantation at the time of transplantation were used in the SCS-score by arithmetical adding. This SCS-score demonstrated in both Groups 0 and 1 a significant influence ($p<0.001$) on 30-day-mortality, 5-year patient and graft survival as well as long-term patient (Exp(B)=1.6) and graft survival (Exp(B)=1.5). Subgroup analysis confirmed this significant influence on patient and graft survival for full-size ($p<0.001$) and spilt-liver transplantation ($p<0.005$), age groups 1-18 years ($p<0.05$), 19-60 years ($p<0.001$) and >60 years ($p<0.05$) as well as eras 3 ($p<0.001$) and 4 ($p<0.001$) (era 3 and 4: 01.01.1994–31.12.2005).
Conclusion: Surgical challenge is a significant factor with impact on outcome after liver transplantation and can be quantified with the SCS-score.

P-410 NONPERSISTENT EFFECT OF BISPHOSPHONATE TREATMENT FOR PREVENTING FRACTURES THREE YEARS AFTER LIVER TRANSPLANTATION

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Introduction: We recently showed that high-dose zoledronic acid (ZOL) prevents bone fractures after orthotopic liver transplantation (OLT). The aim of the present study was to evaluate whether this high-dose bisphosphonate treatment exhibited a persistent prevention of fractures.
Methods: A group of 96 liver transplant recipients were equally randomized to the control (CON) group, which received the Ca/VitD supplementation or to the zoledronic acid treatment (ZOL) group additionally intravenous zoledronic acid with a total dose of 32 mg within twelve months. Patients were followed for three years by sequential determination of X-ray, bone mineral densitometry and specific biochemical markers.
Results: Bone fractures after OLT occurred between the first and until three years only in the ZOL group (n=3). From month six to three years after transplantation, both treatment groups exhibited an improvement of bone mineralization. The increase in BMD t-scores of the lumbar spine in the same time interval reached statistical significance in both groups (p=0.006). No statistically significance differences could be detected in BMD t-scores of the femoral neck in both groups over 36 months after OLT (p=0.125). Osteoprotegerin, c-telopeptide, calcitonin, and iPTH were not significant different at 12 and 36 months after OLT between both groups. 1,25 (OH)-VitD occurred within twelve months in both groups and continued to be sufficient within the next two years. Osteocalcin (OCN) and bone specific phosphatase (bsPh), which correlate with bone formation, were suppressed in the ZOL group at twelve months compared with the CON group (OCN: p=0.005, bsPh: p=0.003) and returned to normal levels afterwards.
Conclusion: The one-year preventive benefit of high-dose bisphosphonate treatment for fractures was not persistent at three year post-transplantation.

P-411 EXCELLENT OUTCOME AFTER LATE RETRANSPLANTATION OF THE LIVER DURING THE LAST DECADE

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The need for late retransplantation (RTx) grows in parallel with better long-term survival after liver transplantation. In contrast to early RTx for primary graft non- or dysfunction, late RTx is traditionally considered a challenging procedure because of massive perihepatic adhesions, recurrent portal hypertension, and effects of long-term immunosuppressive medication. The present study analyzes the results of late RTx at our institution during the last decade. Outcome parameters were patient and graft survival, morbidity, and operative parameters. Between January 1995 and June 2008, 56 patients underwent late RTx (>1 year after the first transplant). The main cause of late RTx was non-anastomotic biliary strictures (32%). The median time period between the initial transplant and late RTx was 5.9 years (range 1.1-18.2 years). Overall 1- and 5-years patient survival after RTx was 86% and 78%, respectively. Overall graft survival at the same time points was 70% and 60%, respectively. Median blood loss during RTx was 5.4 l (0.4-65.0) and median RBC transfusion was 6.5 units (0-44). Five patients (9%) did not require any RBC transfusion. Postoperative complications occurred in 75% of the patients and among them infectious complications were the most common (39%). In univariate analyses, the following variables were significantly associated with mortality after RTx: the need for a second or third RTx, pretransplant CPT score, surgical technique, posttransplant ICU stay, intubation time, septic complications, and the need for reinterventions. However, after multivariate Cox regression analysis only septic complications remained as a significant independent predictor of patient survival. In conclusion, excellent short- and long-term survival can be obtained after late RTX of the liver. Postoperative sepsis is the main risk factor for poor outcome, indicating that adequate antimicrobial prophylaxis and microbiological surveillance are of great importance after late RTx.

P-412 LIVER FAILURE AND THE NEED FOR TRANSPLANTATION IN THREE PATIENTS WITH HEPATOPORTAL SCLEROSIS

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Introduction: Hepatoportal sclerosis (HPS) is a clinicopathologic condition that causes noncirrhotic portal hypertention. Several different synonyms are used for this entitiy such as obliterative portal venopathy and idiopathic portal hypertention In general the main presenting clinical symptoms are those of portal hypertension (PH) and only mild abnormalities in liver enzymes are seen. Hepatic synthetic function is mostly well preserved and hepatic encephalopathy is rare and relief of PH with TIPS (transjugular intrahepatic portosystemic shunt) is the treatment of choice. Rarely patients with HPS may need to undergo liver transplantation.
Herein we discuss the clinical and pathologic aspects of 3 patients with HPS that were diagnosed on microscopic examination of the explanted liver.
Results: Over a 2 year period (2004-6), 3 liver transplant patients were diagnosed as having HPS based on histologic examination of the explanted livers. Major clinical presenting symptoms were variceal bleeding with concomitant ascites and jaundice. Table-1 shows lab and clinical findings of these three liver transplant patients.

The major clinical and paraclinical data in the three patients with hepatoportal sclerosis

case	No-1	No-2	No-3
Age/sex	14/M	35/M	47/M
Persumed liver disease	Cryptogenic cirrhosis	Cryptogenic cirrhosis	PSC
Major presenting symptom	Variceal bleeding and Asites	Variceal bleeding and Asites	Jaundice and Asites
Duration of symtoms/y	5	7	2
PT	14	16	17
Alb gr/dl	3.1	3.5	4
Bl mg/dl	2	2.7	4
Alk U/L	311	448	646
AST U/L	26	53	51
ALT U/L	13	49	43
Phlebosclerosis	Present	Present	Present
Weight of liver	700	815	950

Discussion: The first report of HPS was from Mikkelsen et al in 1965. Until now, most of the reported cases had normal or near normal liver synthetic activity. The severe phlebosclerosis seen in these livers may in part explain the hepatic parenchymal loss that causes hepatic synthetic failure.
Recently several other reports such as our patients were published. Similar to our study, the diagnosis of noncirrhotic portal hypertension was made only after the explanted livers were examined, So careful review of the liver explants is always necessary. Pre-liver transplant diagnosis in most of the previous reported cases as ours had been cryptogenic cirrhosis and rarely they have been diagnosed as autoimmune hepatitis, primary sclerosing cholangitis, chronic hepatitis B and even alcoholic induced cirrhosis.

P-413 LIVER TRANSPLANTATION FROM A DECEASED DONOR WITH SEVERE RHABDOMYOLYSIS

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Many deceased donors have intracranial lesions and that may trigger seizures, which can induce rhabdomyolysis. In donors with severe rhabdomyolysis, the kidneys often cannot be transplanted due to damage from rhadomyolysis. But, whether the liver can be transplanted safely is not clear. Most serum markers of liver function deteriorate markedly with severe rhabdomyolysis so that it is very difficult to evaluate hepatic viability. We transplanted a liver to a stuporous recipient with fulminant hepatic failure from a donor with severe rhabdomyolysis. When the donor management began, the serum lactate dehydrogenase and total creatine kinase were 661 IU/L and 16,559 IU/L, respectively. Rhabdomyolysis was diagnosed based on a high serum myoglobin level of 42,554 ng/mL. The serum urea nitrogen and creatinine level were 42 mg/dL and 4.6

mg/dL, respectively and the serum AST/ALT was 225/67 IU/L. The PT INR was also prolonged to 2.14. Hydration and urine alkalization were attempted to protect the kidneys and FFP was transfused to normalize the PT. However, the serum creatinine increased so that kidneys were abandoned. The PT did not improve and the AST and ALT increased steadily to 1,156 and 256 IU/L, respectively. Nonetheless, we agreed to make a final decision after an intraoperative assessment. Grossly, the liver was very dark brown, but its texture was good. On frozen section, no cellular necrosis or severe fatty change was observed. We decided to attempt transplantation. After transplantation, the recipient's hepatic function improved rapidly despite the poor preoperative function, and the recipient completely recovered her health. In conclusion, the liver of a donor with severe rhabdomyolysis should not be discarded based on the preoperative laboratory results and the final decision should be made after an intraoperative assessment.

P-414 HEALTH-RELATED QUALITY OF LIFE IN ADULT TRANSPLANT RECIPIENTS MORE THAN 15 YEARS AFTER ORTHOTOPIC LIVER TRANSPLANTATION

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Background: With continuously rising survival rates following orthotopic liver transplantation (OLT), health-related quality of life (HRQOL) of transplant recipients becomes increasingly important.
Methods: Recipients more than 15 years after OLT were studied retrospectively. HRQOL in 104 adult liver transplant recipients surviving more than 15 years after OLT was assessed using the German Version of the 36-Item Health Survey (SF-36).
Results: Liver transplant recipients surviving more than 15 years after OLT scored lower in all categories of SF-36 revealing a poor HRQOL in comparison to the German reference population. A statistical significance was reached in almost all SF-36 categories with the exceptions of mental health and bodily pain, where our study population scored similarly to the reference population. Job rehabilitation after OLT had a positive effect on HRQOL. Patients who returned to their job during the first year after OLT scored significantly higher in the SF-36 categories of physical functioning and role physical. Marital status and the immunosuppression used didn't affect HRQOL as there was no statistical significance reached in any of the comparisons performed.
Conclusions: More than 15 years after OLT, long-term survivors present a poor HRQOL comparable to the reference population. Occupational rehabilitation was the only factor shown to positively influence long-term HRQOL.

P-415 *DE NOVO* AUTOIMMUNE HEPATITIS AFTER LIVER TRANSPLANTATION

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Background: *De novo* autoimmune hepatitis (AIH) after liver transplantation has been described in children and adults. We reviewed our experience with 1349 transplants performed.
Material, methods and results: Twelve patients with suspected *de novo* HAI by the International Autoimmune Hepatitis Group scoring system were identified, all of them without a prior history of autoimmune liver disease. Seven patients had definitive (score >15) and five had probable (score 10-15) AIH at the time of graft dysfunction. All patients had a biopsy with periportal hepatitis and lymphocytic inflammatory infiltrate. The indications for transplantation had been alcoholic cirrhosis (one patient), hemangioendothelioma epiteloide (one), tyrosinaemia (one), primary biliary cirrhosis (one), extrahepatic biliary atresia (one), cryptogenic cirrhosis (two), HCV cirrhosis (four) and HBV cirrhosis (two). Four patients had been treated with pegylated interferon plus ribavirin for recurrent hepatitis C after liver transplantation. Sustained virological response was achieved in three patients who had completed treatment 17 months ago. Nine patients were females. The median age at presentation was 55 years in recipients with IFN+RIB and 35 in the other group. Eight patients had significant title of autoantibodies >1/80 (six with positive ANAS, one with AML and one with AML and antiLKM autoantibodies). Six patients showed HLA DR3/DR4. We had analyzed the cross-match and missmatch. Six patients had episodes of acute rejection and 2 developed chronic rejection. Five recipients had recently decreased immunosuppression and 6 had low levels of calcineurin inhibitors. Nine patients were treated with corticosteroids and 8 was achieved a biochemical response. Of the 4 patients who discontinued steroids, 3 had a recurrent AIH. Two recipients developed autoimmune diseases, 5 developed cirrhosis and one patient was retransplanted.
Conclusions: *De novo* HAI should be included in the differential diagnosis of unexplained graft dysfunction. *De novo* HAI could be an alloimmune attack preceded by isolated episodes of acute rejection. The treatment with PEG IFN+RIB could lead to development of *de novo* HAI in HCV transplant recipients.

P-416 OUTCOME OF LIVING DONOR LIVER TRANSPLANTATION FOR INCIDENTALLY FOUND HEPATOCELLULAR CARCINOMA

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Background: Hepatocellular carcinoma incidentally found in the explanted liver were observed despite advances in the imaging techniques. The purpose of this study to evaluate the impact of incidental lesions on the patient's outcome post LDLT.
Methods: 25 adult recipients underwent LDLT for HCC in Dar AL-Fouad Hospital, Egypt in the period between August 2001 and January 2007, demographic and laboratory data for the recipients were evaluated. Survival of patients was presented by Kaplan-Meier curves. Radiologic findings prior to transplantation and pathologic findings of the explants liver were compared
Results: Incidental lesions were detected in 11/25 (44%), mean size of nodule was 1.7 cm $\pm$ 1 (0.5-3.5 cm) while mean size of nodules detected radiologically was 2.5 cm$\pm$ 1.5 (0.5-6 cm), 19/25 (76%) of our cases were within the Milan criteria. All cases showed well differentiation and only 2/25 (8%) showed portal vein invasion. HCC recurrence was only 2/25 (8%). The 5 years survival rate in HCC patients was 56% (14/25), incidental lesions and operative difficulties were the only predictors for poor outcome, 8/11 (72.7%) mortalities showed incidental nodules
Conclusion: Incidental HCC could have poor outcome post LDLT.

P-417 EVALUATION OF THE APACHE III SCORE IN COMPARISON TO MELD SCORE AND KING'S COLLEGE HOSPITAL CRITERIA FOR FULMINANT HEPATIC FAILURE

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Introduction: Whilst the MELD score and the King's College Hospital (KCH) criteria are accepted evaluation models in patients with fulminant hepatic failure (FHF), the impact of the APACHE III score on outcome after orthotopic liver transplantation (OLTX) has not been defined yet. Aim of this study is to compare these early indicators for liver transplantation and investigate their predictive efficacy.
Patients and methods: The study included 111 patients with FHF, listed for OLTX between 1996 and 2007. MELD score, KCH criteria and APACHE III score were retrospectively defined for the day of listing for transplantation.
Results: We devided the cohort according the 1-year outcome. Group 1 included 11 patients who were delisted from the liver waiting list due to improved clinical condition as well as 73 patient who were transplanted and survived the procedure. Group 2 included 11 patients who died while waiting for a suitable graft and 16 patients dying after transplantation. In Group 1 compared to group 2 the mean MELD score was 32$\pm$8 vs. 34$\pm$7 and the APACHE III was 61$\pm$17 vs. 75$\pm$21, respectively. In group 2 the KCH criteria were positive in 56% of the patients. The ROC analysis revealed that compared to MELD score and KCH criteria, the APACHE III score was a better indicator of prognosis in patients with FHF (AUC: 0.66, 0.55 and 0.83 respectively).
Conclusion: This study is the first that shows that the APACHE III score is superior to MELD score and the KCH criteria in prognosing the clinical outcome in patients with FHF.

P-418 130 LIVER TRANSPLANTATIONS FOR FULMINANT HEPATIC FAILURE: RESULTS OF A HIGH VOLUME CENTER

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Introduction: Fulminant hepatic failure (FHF) is a rare but life-threatening clinical syndrom. Despite impovements in medical therapy, orthotopic liver transplantation (OLTX) remains the treatment of choice. Purpose of this analysis was to evaluate the outcome after liver transplantation, the incidence of recurrent diseases and the optimal timing for liver transplantation in a high volume transplantation center.
Patients and methods: This retrospective analysis included 135 patients with FHF who underwent OLTX between 1988 and 2007. Etiology of FHF, patient's demographic variables and laboratory values were analyzed and compared with the outcome after transplantation. Postoperative liver specific laboratory values were assessed.
Results: In the cohort of 135 transplantated patients, 44 (32.6%) were males and 91 (67.4%) females with a mean age 32±17 years at time of transplantation. In most instances cause of FHF remained unclear (44%) followed by hepatitis B infection (22.2%) and drug-induced hepatic failure (13.3%). The mean waiting time for a suitable graft was 2±2 days. Cold and warm ischemia time were 525±174 min und 44±13 min respectively. Nine grafts showed initial non-function. The mean hospital-stay was 47±32 days. The 1 year survival was 82%. Gender and etiology of FHF did not correlate with posttransplant outcome (p=NS). At the 14th POD most patients had a sufficient graft function indicated by liver specific laboratory values (bilirubin 8,9±9 IU/L, INR 1.16±0.23 und ALT 92±81 IU/L).
Conclusions: This analysis demonstrates that OLTX after FHF has a 1-year survival over 80% with excellent postoperative graft function. OLTX represents the best therapeutic option for patients with irreversible FHF and the indication for liver transplantatino should be set early in the process.

P-419 A SINGLE CENTER EXPERIENCE OF 50 LIVING DONOR LIVER TRANSPLANTATIONS FOR ACUTE LIVER FAILURE

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Purpose: To analyze the clinical outcomes of 50 living donor liver transplantations (LDLTs) for acute liver failure (ALF) in a major Japanese transplant center.
Methods: Retrospective analysis was performed.
Results: The etiologies included unknown cause (n=28, 56%), hepatitis B (n=15, 30%), Wilson's disease (n=3, 6%), autoimmune hepatitis (n=2, 4%), hepatitis C (n=1, 2%), and acute fatty liver disease of pregnancy (n=1, 2%). The graft types were as follows: left lobe (n=38, 76%), right lobe (n=11, 22%), and lateral segment (n=1, 2%). Left lobe graft is the first choice for transplantation if its graft volume (GV)/standard liver volume (SLV) is over 35%. The 1- and 5-year survival rates were 77.1% and 66.1% for grafts, and 81.4% and 72.4% for patients. The 1-year survival rate was 75.0% in patients who received grafts with GV/SLV $>$ 40%, and 74.4% with GV/SLV $<$ 40% (p=N.S).

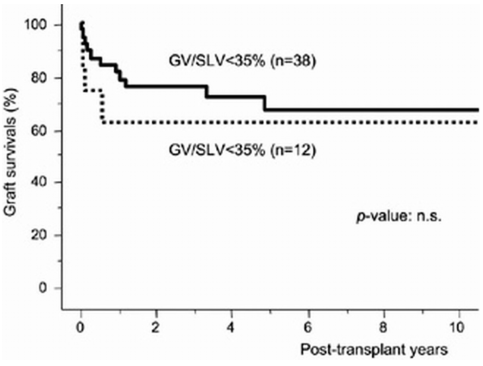

Figure 1

Five patients received extra-small grafts with GV/SLV$<$30% (23%, 26%, 27%, 29%, 29%). The patients who received GV/SLV of 23% died with severe graft dysfunction, however other patients are alive with normal liver functions. Blood type incompatible LDLT grafts were transplanted in 3 patients, and 2 patients (67%) are alive. Causes of mortality after LDLT for ALF included adult T-cell leukemia (ATL, n=4), hepatic artery thrombosis (n=2), acute or chronic rejection (n=3), sepsis (n=3), neurological problems (n=2), recurrent acute liver failure (n=1), and esophageal cancer (n=1). Donor complication rate was 28% (14/50).
Conclusion: The outcome in LDLT for ALF, even with the positive use of left lobe grafts, is fairly acceptable despite severe general conditions and emergent transplant settings.

P-420 THE EFFECTS OF ULTRASONOGRAPHY EXAMINATION ON THE MICROSURGICAL RECONSTRUCTION OF THE HEPATIC ARTERY IN LIVER TRANSPLANTATION

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Objectives: Microsurgical reconstruction of hepatic artery is the essential but challenging technique in liver transplantation (LTx). Especially on living-donor LTx (LDLTx), compared with cadaveric donor, hepatic artery is short, the intimal damage is severe, and usable vessel grafts are limited. To overcome these difficulties we performed back wall support suture technique with double needle sutures. We placed two sutures at the deepest, most difficult points in the artery for backside support. Each stitch was placed from inner side of the arterial wall to outer side with double needle sutures. The purpose of this study is to examine the effects of this technique using ultrasonography examination.
Methods: From July 1991 to December 2008, we performed 128cases of LTx (LDLTx=126). In the 87 cases, 91 arteries, we reconstructed using conventional twist technique. In the 41 cases, 42 arteries, we reconstructed using back wall support suture technique. We performed ultrasonography examination every day after LTx until 14 days and examined pulsatile index (PI: peak systolic-end diasto!ic/ mean velocities), resistive index (RI: peak systolic-end diastolic/peak systolic velocities) and the time-to-maximum velocity.
Results: Total ratio of hepatic artery thrombosis (HAT) was 6.8%(9/133). In the conventional twist technique group, HAT occurred in eight patients (8.8%, 8/91). On the other hand, in the new technique group, it occurred only one case (2.4%, 1/42). This case had intimal dissection in recipient original artery. The values of PI and RI in the new technique group were similar to those in the conventional group. In the HAT cases of both groups, the values of PI were decreased (PI$<$0.4), and the time-to-maximum velocities were delayed over 100 millisecond.
Conclusion: Our technique was safe for intimal adaptation. Ultrasonography examination is useful to anticipate the risk of HAT.

P-421 ACUTE GRAFT FAILURE AFTER LIVING-DONOR LIVER TRANSPLANTATION SUGGESTING THE INVOLVEMENT OF APOPTOSIS BY ACTIVATION OF Fas/Fas-L

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The term 'seventh'day syndrome' derived from cases that suddenly developed graft failure around postoperative day seven. Here, we report a case of acute graft failure after living-donor liver transplantation, which is similar to the clinical course of seventh-day syndrome. The patient was a 5-year-old girl who had biliary atresia. We performed a living-donor liver transplant, with her father as the donor. At the time of transplantation, we anastomosed the middle hepatic vein and left hepatic vein separately. After reperfusion, vein reconstruction was required because of left hepatic vein obstruction. The lateral segment was congested for about 4 hours. The postoperative course was good, including hepatic blood flow, but a high fever developed suddenly on the fifth postoperative day. The liver function worsened on the sixth postoperative day and the portal vein blood flow subsequently stopped. We performed an exploratory laparotomy, but there was no stenosis of the portal vein or hepatic vein anastomosis. We performed a retransplantation, but the patient died of sepsis. Primary nonfunction, acute cellular rejection, arterial thrombosis, and a major infection are reported causes of acute graft failure in the early phase after liver transplantation. However, our case did not show any findings to suggest these causes. Many TUNEL-positive cells were found in the resected liver graft and a DNA ladder was observed on DNA electrophoresis. Apoptosis appeared to contribute to the graft failure. Immunostaining for Fas showed many Fas-positive cells in comparison with the graft time-zero biopsy. Fas/Fas-L activation was the apoptosis pathway involved in our case. The relationship between the intraoperative hepatic venous outflow obstruction and Fas/Fas-L activation is not clear. But it may have been triggered by the liver congestion.

P-422 ELDERLY VS YOUNG LIVER TRANSPLANT RECIPIENTS: PATIENT AND GRAFT SURVIVAL

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Introduction: This study analyzed two Centers experience comparing patients over 63-years old and less than 40, suggesting as the only age cannot be considered a contraindication to LT.
Materials & methods: From 1996 to 2008, 500 LT have been performed at University of Udine and Ancona. 42 patients, aged over 63 years old (group A), were compared with 32 patients aged between 18/40-years old (group B). In group A there were 31 male, and 11 female, (median age 65-years old; median MELD score 12). Indication for LT was: hepatitis-C cirrhosis 15 patients, 14 HCC, 8 alcoholic-cirrhosis, 2 PSC, 1 PBC 1 ALF, and 1 metabolic disease. In group B, 21 were male and 11 female, (median age 37-years old, median MELD score 12). Indication for LT was: hepatitis-C cirrhosis 10 patients, 7 HCC, 1 alcoholic-cirrhosis, 3 PSC, 3 hemocromatosis, 1 PBC, 4 ALF, 1 Wilson disease, 1 alpha-1-antitrypsin-deficiency-related, and 1 Budd-Chiari syndrome. No statistically differences were evidenced considering preoperative patients comorbidity. Donor characteristics were similar except. Statistical analysis was performed using the log-rank test. Multivariate analysis was performed by logistic regression. P was considered statistically significant if the value was <0.05.
Results: 1, 3, 5, and 10 years patient survival was 75% vs 78%, 65% vs 78%, 65% vs 78%, and 52% vs 65% in group A and group B, respectively (p= 0.4). Graft survival was 66% vs 74%, 60% vs 68%, 60% vs 60%, and 50% vs 62% (p=0.99). Multivariate analysis confirmed that age was not a negative prognostic factor for patient/graft survival (p=0.3).
Discussion: Based on the findings of our study there seems to be no difference in patient/graft overall survival with age stratification above 63-years old vs less than 40, suggesting that LT provides acceptable long-term outcomes for selected older recipients.

P-423 HUMORAL REJECTION AFTER LIVER TRANSPLANTATION; DELAYED ONSET AND PROGNOSIS

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Humoral rejection (HR) in liver transplant (OLTx) recipient belongs to the category of difficult diagnosis and poorest prognostic factor of the survival and late graft function. Despite all efforts to develop the effective treatment and active use of all kinds of immunosuppressive drugs as well as plasmapheresis and immunoglobulin the overall outcome is still very poor. Originally HR was described as very early complication developing immediately after reperfusion or in the first hours after OLTx. The main blood groups mismatch in donor/recipient combination as well as positive cross match reaction is the prognostic factor. Our current experience may suggest that HR diagnosis could be the case also in blood group compatible cases and with onset "far" from day of Tx. Some data may also suggest that the negative cross match test on the day of transplantation do not exclude the HR late episode. In our retrospective study among 242 OLTx performed between July 2000 and December 2008 we have identify 3 cases of possible delayed onset humoral rejection. The primary diagnosis of liver disease in these cases was HCV – 2, PBC – 1. In 2 cases we found the blood group mismatch in the remaining 1 the identical combination was registered. The time from Tx to first symptoms and diagnosis vary from day 11 to day 175. The diagnosis was based on routine biochemistry, liver biopsy, platelets count drop and vascular study. The treatment consisted of pulses methylprednisolone, MMF, plasmapheresis, high doses of polyvalent immunoglobulin as well as Maptera. All responded to the treatment. All 3 patients were discharged home with stabile relatively good liver function but 2 had recurrent deterioration 3 months (acute cellular rejection) and 6 months later (recurrent HCV hepatitis).

P-424 EFFICACY OF NUCLEOSIDE ANALOGUE MONOTHERAPY FOLLOWING ONE-YEAR COURSE OF HEPATITIS B IMMUNOGLOBULIN PLUS NUCLEOSIDE ANALOGUE IN PREVENTING HEPATITIS B VIRUS RECURRENCE AFTER LIVING DONOR LIVER TRANSPLANTATION

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Purpose: We report the efficacy of nucleoside analogue monotherapy following one-year course of hepatitis B immunoglobulin (HBIG) plus nucleoside analogue after living donor liver transplantation (LDLT).
Materials and methods: From July 1991 to February 2007, 105 LDLTs were performed in our hospital, we had eight patients with chronic hepatitis B, three with fulminant hepatitis, and three whose donors were positive for anti-HBc antibody. From the operation to POD 2, 40,000 units of HBIG was administered and then the level of anti-HBs Ab was maintained at around 150 IU/L for one year by monthly administration of HBIG. After one year, HBIG was withdrawn. A nucleoside analogue (lamivudine: 11 cases, lamivudine+adefovir: 2 cases), was administered daily from just after LDLT and it was continued up to the present. One recipient out of 3 anti-HBc Ab positive donors, who had transplanted in 1993, had no prophylaxis. Other two recipients of anti-HBc Ab positive donor had the same prophylaxis of chronic hepatitis B patients. The mean follow-up period was 55 months.
Results: Two out of 14 recipients, including one who did not receive the prophylactic therapy, experienced HBV recurrence. One recurrent recipient, who had our prophylactic protocol, treated with entecavir because of YMDD mutant 3 years after LDLT. One recipient, who had HB hepatitis transmitted by an HBc Ab(+) donor, became HBV DNA negative after treatment with lamivudine and adefovir. Two recipients died; one due to a liver abscess and the other because of recurrence of HCC. The other 12 recipients are alive and in good conditions.
Conclusion: Nucleoside analogue monotherapy after one-year course of HBIG plus nucleoside analogue is feasible and cost-effective in terms of preventing HBV recurrence.

P-425 SINGLE CENTER EXPERIENCE IN LIVER TRANSPLANT FOR HIGH MELD RECIPIENTS

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Background: MELD score is the criteria to allocate grafts in Brazil. Donors are critical issue with just 7.0 donors per million people.Patients are frequently very sick becoming high risk recipients. Increasing experience of a single center can improve results.
Aim: Analyze results of a single center in recipients with MELD score $\geq$ 30, in the last 3 years.
Casuistic and methods: Single center data collected prospectively of 33 liver transplant recipients with MELD score $\geq$ 30 transplanted from May 2005 to September 2008.
Results: Donor's characteristics (medians): age 42 years (range 18 – 76), 54.6% with 1 vasopressor, 42.4% with >1 vasopressors, BMI was 25 kg/m^{2,} sodium 153 mEq/L (range 133 – 189), ALT 42.0 U/L, AST 44.0 U/L, 63.6% had a cardiac arrest and 42.4% had a controlled infection. Causes of death: 42.5% had a cranioencephalic trauma, 48.5% hemorrhagic cerebral vascular accident and 9% other causes.
Graft's characteristics: 33.3% had grade I liver steatosis, 51.5% grade II and 15.2% had grade III. Arterial anomalies were present in 26.7%. Median cold ischemia time: 490.5 minutes and median warm ischemia time was 59.5 minutes. Recipient's characteristics (medians): age was 56 years, MELD score: 33%, 39.4% HCV, 30.3% Laennec's cirrhosis, 21.2% auto-immune liver disease and 15.2% cryptogenic cirrhosis. Median intra-operatory blood transfusion was 3, median intensive care stay was 3 days, median length of hospital stay was 20.5 days. Three patients with mild, one with moderate and one with severe acute rejection. Two patients had vascular complications: one with hepatic artery thrombosis (retransplanted) and other with hepatic artery stenosis (endovascular stent).
Graft survival rate was 76.5% in the first year. Patients survival were 84.2% in 3 months, 74.6% in one year and 69.3% in two years.
Conclusion: Liver transplant can have acceptable results in high meld recipients.

P-426 BRAZILIAN SINGLE CENTER SURVIVAL RATES AFTER LIVER TRANSPLANT DUE TO FULMINANT HEPATIC FAILURE

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Background: Fulminant hepatic failure (FHF) represents 5% of liver failure in UNOS-Data and 17.4% in our program. FHF are prioritized for a liver graft, but donors are a critical issue (7.0 donors/million).This high risk situation could compromise results
Purpose: Analyze results of liver transplant (OLT) for FHF within the last 3 years.
Casuistic and methods: Twenty six patients (from 36 with FHF) were trans-

planted from May 2005 to September 2008. Retrospectively were analyzed data from a single center.
Results: Donor characteristics (medians): age 40.5 years, 42.3% with 1 vasopressor, 38.5% with >1 vasopressors, BMI was 24.0 kg/m^2, sodium 155 mEq/l, ALT 39 U/L, AST 53.5 U/L, cardiac arrest 42.3% and controlled infection 19%. Causes of death: 42.3% cerebral bleeding, 38.5% cranioencephalic trauma, 3.8% ischemic cerebral vascular accident and 11.5% others. Grafts characteristics: 73.1% grade 1 liver steatosis, 19.2% grade 2, 3.8% had grade 3. Arterial anomalies in 19.2%, median cold and warm ischemia time: 452.5 minutes and 54 minutes. Ten patients died waiting for OLT. Recipient's characteristics (medians): age: 44 years, intra-operatory time: 400 minutes, intra-operatory blood transfusion: 2 red blood packages, ICU stay: 11 days after transplant, length of hospital stay: 19.5 days. Three recipients (11.5%) needed retransplant. Five patients (19.2%) died post OLT. One year graft and patient survival rate was 73,08% and 82,61% respectively. Survival curve from State of Sao Paulo, shows 55,36% and 58,8%, respectively for grafts and patients.
Conclusion: Liver transplant has satisfactory survival rates in FHF in specialized center.

P-427 TESTING OF POST-TRANSPLANT LIVER FUNCTION AND VIABILITY BASED ON PORTAL FLOW

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Studies of factors responsible for early liver graft function were conducted in our institutions. Aim of the study was to identify most simple and useful test for predicting early liver graft function.
Methods: Fifty-six livers were classified as transplantable based on routine donor demographics, hemodynamics and biochemistry as well as macroscopic assessment by the surgeon on retrieval. Morover, portal, arterial and parenchymal hepatic blood flow as well as HE histology, ketone index, bile acids chromatography, arachidonic acid metabolites were also studied. Post-transplant early liver function was categorized based on modified Neuhaus classification (2 poins assigned for each of: bile output <50ml/d, AST>1800 IU/L, ALT>1600 IU/L, INR>1.7 despite plasma infusions, poor initial function (PIF) was diagnosed with score >6).
Results: Of 56 patients, only 4 had PIF. No primary nonfunction was seen. Neither histology, nor biochemical tests prooved useful in prediction of this complication. Of multiple methods of flow assessment, portal blood flow (PF) 30 minutes after reperfusion was the most reliable factor. It differed significantly between good (GF) and poor initial function groups.
Portal flow 30 minutes after reperfusion:

GF (L/kg/min)	PIF (L/kg/min)	p<
1,74±0,6	1,05±0,44	0,04

PF showed significant, strong correlation with good liver graft function (R=0,677). It was also a significant predictive factor of early liver function in logistic regression model (model p=0,002). The model predicted graft function correctly in 94,4% of cases.
Conclusions: Portal blood flow is sensitive and reliable factor for prediction of early liver graft function, however clinical criteria applied so far allow for safe liver transplantation at minimal risk of nonfuction for the recipient.
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P-428 INTENT-TO-TREAT SURVIVAL ANALYSIS OF CANDIDATES FOR LIVER TRANSPLANTATION IN ISRAEL

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Introduction: The growing gap between the number of candidates for liver transplantation (LT) and the number of donors is associated with a prolonged wait for transplant subsequently leading to increased waiting list and post-transplant mortality.To better evaluate a patient's chance of survival after listing, an intent-to-treat survival analysis that combines waiting list and post-transplant mortality was designed.
Patients and methods: Data on adult patients (>18 yr) registered for LT between 2001-2005 was drawn from our electronic database. Patients with acute liver failure and re-transplants were excluded, giving a cohort of 197 patients for the analysis with a follow-up until 1/2008. We classified patients as transplanted (Tx, n=123) or not transplanted (non-Tx, n=74) and compared the groups for clinical and laboratory parameters at the time of registration. Actuarial survival was calculated using the Kaplan-Meier method.
Results: One- and 5-yr survival for all patients were 67% and 54%, respectively. One- and 5-yr survival were 85% and 75%, respectively, in the Tx patients vs. 40% and 19%, respectively, in the non-Tx group. The mean waiting time for Tx was 33.6 months. The mean MELD score at transplant was 22.1. Patients in the non-Tx group were significantly sicker at registration (MELD score 19.65±8.64, vs. 17.20±5.35 in the Tx group) and had more frequent events of hepato-renal syndrome (20.3%, s. 7.3% in the Tx group).
Conclusions: The low donation rate in Israel has a detrimental effect on outcome, with an estimated 67% chance of survival at 1-year after listing for liver transplantation. Performing an intentto-treat survival analysis of candidates for transplant gives a more accurate estimate of survival that combines both organ donation and transplantation outcomes.

P-429 THE VENOUS RECONSTRUCTION AT LIVING DONOR LIVER TRANSPLANTATION IN CHILDREN AND ADULTS

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Introduction: Feature of living donor liver transplantation (LDLT) is deficiency of functional weight of a graft in adult and autovenous a plastic material for performance of vascular reconstruction.
Aim: Aim was studying efficiency of venous reconstruction at LDLT.
Materials and methods: 65 patients with end stage liver diseases received LRLT from August 2003 till 2009, there were 30 adults (46,2%) and 35 (53,8%) patients in the pediatric age group. From 22 patients with biliary atresia in 1 case took place agenesis of the portal vein, in 1 – congenital fibrosis of the portal vein. From 31 patients with right lobe LDLT, in 6 cases the cirrhosis of a liver with PVT was observed. In all cases of right lobe liver transplantation the donor's remnant liver volume was not less than 35% of standard liver volume.
Results: From 65 LRLT venous reconstruction was made at 40 patients. In 2 cases cavaportal transposition was made. For this purpose suprarenal part of IVC was anastomosed with left portal vein of a graft. Cavaportal transposition used in one case of right lobe LDLT at the patient with viral liver cirrhosis and total portal veins system thrombosis.In 8 cases adults LDLT right lobe harvested with middle hepatic vein (MHV). Reconstruction of MHV carried out by recipient's portal vein bifurcation. At 5 cases right lobe LDLT large venous tributary from Sg5 and Sg8 inserted to recipient's iliac vein graft which sutured with stump MHV and left hepatic vein of the recipient.
Conclusion: Venous reconstructions of a grafts allows to expand indications to donation parts of a liver from the alive donor, to made LDLT of patients with a portal vein thrombosis which were considered unpromising earlier and to provide adequate graft function.

P-430 THE VENOUS OUTFLOW RECONSTRUCTION IN ADULT LIVING DONOR LIVER TRANSPLANTATION USING THE RIGHT HEPATIC LOBE WITHOUT THE MIDDLE HEPATIC VEIN

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Purpose: Hepatic venous reconstruction is the key procedure in adult living donor liver transplantation (ALDLT). There is currently no clear consensus about the optimization of venous outflow in right lobe ALDLT. We describe our experience and analyze our results in the outflow reconstruction in ALDLT using the right lobe without harvesting the middle hepatic vein (MHV).
Patients and methods: From May 2001 to November 2008 clinical records about 49 ALDLT were retrospectively reviewed. All of them underwent ALDLT using right lobe grafts without the main trunk of the MHV. All MHV tributaries with a diameter equal or larger than 4 mm were drained. Twenty-two reconstructions were performed either by jumping graft or by one-orifice venoplasty. Sixteen V5, V6 and V8 branches were anastomised end-to-side with the inferior vena cava (IVC) by an interposition graft. One V7 and five right inferior hepatic vein (RIHV) were reconstructed in one-orifice venoplasty when they were relatively close to the IVC.
Results: The 3-5 years graft and patient survival rates were 78.9% -77.4% and 86.8%- 82.9% respectively. The causes of death were: massive pulmonary bleeding in one, severe sepsis in 2, cardiac arrhythmia in one, pleural empyema in one. Four recipients underwent liver re-transplantation from deceased donor: 3 because of arterial thrombosis, 1 for small-for-size-syndrome and 1 for recurrence of primary sclerosing colangitis.

Post-operative complications in the donor were: 1 pulmonary thromboembolism, 1 acute appendicitis, 4 biliary collections spontaneously resolved in 3 patients and radiologically treated in one. No donors received homologous blood transfusion.
Conclusions: Aggressive MHV tributaries reconstruction in ALDLT using right lobe without harvesting the middle hepatic vein is a viable option and gives good results in term of donor safety and long-term survival outcome.

P-431 BACTERIAL AND FUNGAL INFECTIONS IN LIVING DONOR LIVER TRANSPLANTATION

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Background/Aim: Infection is one of the leading causes of morbidity and mortality in living donor liver transplantation recipients.
Method: In this study, 105 consecutive living donor liver transplantation recipients were prospectively studied for postoperative infections from August 2002 to October 2008. The risk factors for postoperative infections that occurred within 3 months after surgery were evaluated by univariate and multivariate analyses.
Results: A total of 58 episodes of postoperative infections occurred in 42 (40%) of the 105 living donor liver transplantation patients. Of these 42 patients, 22 (21%) had secondary bacteremia. Univariate analysis revealed that postoperative infections were associated with biliary leakage, a repeat surgery, prolonged duration of surgery, biliary reconstruction with Roux-en-Y, previous upper abdominal surgery, use of small-for-size grafts (graft-to-recipient weight ratio$<$0.7), the National Nosocomial Infections Surveillance risk index, and that adoptive immunotherapy using liver allograft-derived Natural Killer cells was associated with a reduction in the incidence of postoperative infections. Mutivariate analysis revealed that small-for-size grafts and biliary leakage were independently associated with postoperative infection. The adoptive immunotherapy was independent protective factor from postoperative infections by multivariate analysis. In addition, the 1-year survival rate was significantly higher in patients without infections (98%) than in those with infections (66%).
Conclusions: The indication for transplantation may need to be more restrictive when a small-for-size graft is available. Aggressive management, including adoptive immunotherapy, would reduce the mortality in the living donor liver transplantation recipients.

P-432 LIVING DONOR LIVER TRANSPLANTATION: EFFECT OF THE TYPE OF LIVER GRAFT DONATION ON DONOR MORTALITY AND MORBIDITY

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Objective: To investigate whether the type of liver graft donation has an influence on the mortality and morbidity of the donors.
Methods: Eighty-seven consecutive living donor liver transplantations performed between 01.06.1997 and 01.07.2008 were retrospectively analyzed. We tested whether the donation of liver grafts that involve central liver structures like segments 1, 4, 5 and 6 is associated with significantly more frequent complications or more serious complications such as biliary leakage.
Results: No donor mortality was present in this series. Fifty donor procedures were associated with blood transfusions (57.5%). Four of 87 donors (4.6%) developed bilioma, nine (10.3%) had to be readmitted to hospital after initial postoperative discharge and six donors (6.9%) required some form of reoperation related to the liver donation. Reoperations related to previous liver donation included hernia repair in five cases (5.7%), repair of biliary leakage in one case (1.1%) and segmental colon resection combined with hernia repair in one case (1.1%). Donors who donated grafts which involved central liver segments had a significantly longer hospital stay, required more autologous blood transfusions and underwent an operating procedure of longer duration, compared to donors who donated only liver segments 2 and 3. There was no statistical significance noticed regarding hospital readmission, operative revisions and the development of complications. Interestingly, donors who donated only liver segments 2 and 3 presented a higher frequency of bilioma (5.9% versus 2.8%) although the difference was not statistically significant.
Conclusions: Living donor liver transplantation can be performed safely with excellent donor results. Donation of central liver segments is associated with prolonged hospital stay, increased need of blood transfusions and prolonged operating times. The frequency of complications did not have any correlation to the type of liver donation.

P-433 THE EFFECTS OF DESFLURANE AND SEVOFLURANE ON POSTOPERATIVEHEPATIC AND RENAL FUNCTIONS AFTER RIGHT HEPATECTOMY IN LIVER DONORS

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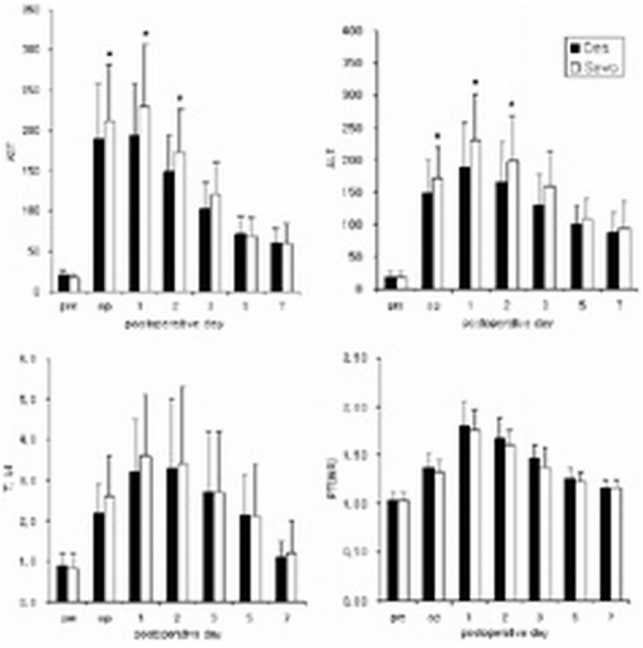
Background: Various volatile anesthetics with different degree of hepatic metabolism have been used in hepatectomy in living donors. The aim of this study was to compare the postoperative hepatic and renal functions between volatile anesthetics with desflurane and sevoflurane in living donors undergoing right hepatectomy.
Methods/Materials: Seventy adult patients were randomly allocated into two groups: Des group (Desflurane group, n=35) and Sevo group (Sevoflurane group, n=35). Aspartate aminotransferase (AST), alanine aminotransferase (ALT), prothrombin time (PT), total bilirubin (TB), blood urea nitrogen (BUN), creatinine (Cr), and estimated glomerulofiltration ratio (GFR) were analyzed at preoperative period, immediately after operation, and on the first, second, third, fifth, and seventh postoperative days (POD).
Results: Demographic and surgical data were similar between two groups.

Demographic and Surgical Data

	Group Des (n=35)	Group Sevo (n=35)
Gender (male/female)	19/16	25/10
Age (yrs)	31.6±10.7	32.2±11.5
Height (cm)	165.8±8.7	170.0±9.0
Weight (cm)	62.3±10.1	67.6±11.7
GV (ml)	652±145	708±115
RLV (%)	34.9±6.8	34.4±3.2
Surgical time (min)	368±51	365±51
Anesthetic time (min)	411±52	409±49
Remifentanil (mg)	1.69±0.76	1.87±1.06
Crystalloid (ml)	2269±527	2387±579
Estimated blood loss (ml)	489±261	431±145
Urine output (ml)	313±204	394±280

Abbreviation: GV, graft volume; RLVR, remnant liver volume ratio ([TLV-GV]/TLV) × 100

AST and ALT levels were significantly higher in Sevo group until POD 3. TB and PT (INR) levels were similar between two groups.



Renal function tests were similar between two groups.
Conclusions: In conclusion, the results of our study suggest that living donors for liver transplant may have a better outcome following anesthesia with desflurane. However, further testing will be necessary to prove this hypothesis.

P-434 MAGNESIUM DEPLETION AFTER LIVER TRANSPLANTATION UNDER CYCLOSPORINE A OR TACROLIMUS IMMUNOSUPPRESSION

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Purpose: Magnesium (Mg) is the second most abundant intracellular cation in the body. It plays an important role in numerous enzymatic reactions. Calcineurin inhibitors (CNI) cyclosporine A (CSA) and tacrolimus are widely used immunosuppressants in liver transplantation. They both are regarded to cause hypomagnesemia (1,2), by renal wasting (3). Serum ionized Mg and even more often serum magnesium may be normal despite of total body Mg deficiency. Intravenous loading tests are regarded reliable assessing Mg status (4). The magnesium mean uptake in healthy subjects between 18-66 years was 6.3%±10.3 and in this work pathological value was regarded to be 28% (5). This was little larger than previously suggested 20% (6). It is obvious that the significant magnesium depletion can occur with uptake values less than 28%.
Methods/Materials: Ten patients on CSA and eight patients on tacrolimus for immunosuppression were given intravenously Mg sulphate 30 mmol. Uptake of Mg was assessed by calculating the ratio between the amount of Mg excreted in urine (dU) to the given dose of Mg.

Demographics

	CSA	Tacrolimus
Age (years)	51±17.6	46±14.5
Time from transplantation (months)	49±29.1	21±17.6
Drug concentration (μg/l)	143.5±49.9	10.2±3.8
INR	1.2±0.4	0.9±0.1
TT (70-130%)	80±28	106±18
ALAT (10 U/l female, 10-70 U/l male)	57±98	27±17
P-creatinine (40-90 μmol/l female, 50-100 μmol/l male)	85±18	85±22
P-Urea (2.6-6.4mmol/l female, 3-8.5mmol/l male)	7.5±3	8.0±1.7

Results: In CSA group the mean uptake of Mg was 20.3±14.1% and in tacrolimus group it was 19.6±12.9%.

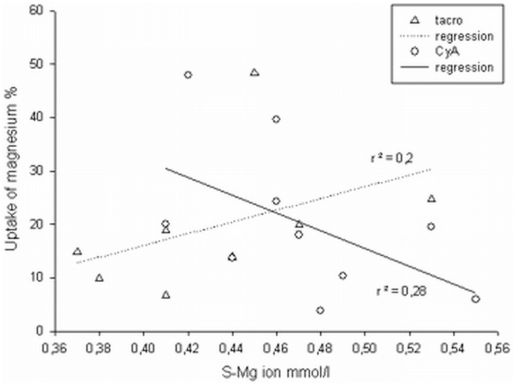

Figure 1. Uptake of magnesium vs Mg-ion before loading test.

Conclusions: There are no data on use of Mg loading test to determine magnesium status in liver transplantation patients. In our work both CNI:s utilized the given Mg similarly. According to our work the magnesium wasting is equal if the drug concentrations are within the therapeutic window. Despite of the immunosuppressants causing Mg wasting our patients uptook Mg amounts that reveal magnesium deficiency. Measurement of serum ionized magnesium does not reveal magnesium deficiency.
References: 1. Transplantation 1993;56:847; 2. Nephron 1996;72:59; 3. Transplantation 2005;2780(8):1046; 4. Clin Chim Acta Apr 2000;294(1-2):1; 5. Scan J Clin Lab Invest 1994;54:23; 6. Magnesium 1985;4:137.

P-435 CMV-REACTIVATIONS IN ADULT LIVER TRANSPLANT RECIPIENTS MONITORED BY QUANTITATIVE PCR

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Cytomegalovirus (CMV) is a significant infectious agent, mostly appearing within 3 first months, in transplant patients. To prevent CMV, most liver centers use prophylaxis for high risk patients of CMV-seronegative recipients receiving an organ from a seropositive donor (R-/D+) and many centers even for all seroposive recipients (R+). Preemptive treatment is mainly used for those at a moderate or low risk of CMV. Preemptive therapy is based on the screening for CMV by monitoring of viral load. CMV-reactivations, demonstrated by PCR-monitoring, of adult CMV-seropositive liver transplant recipients were studied.
Patients and methods: Of 211 consecutive adult liver transplant recipients most 176 (84%), were CMV-seropositive (R+). The basic immunosuppression consisted of CNI inhibitors, azathioprine/MMF plus steroids. High risk patients received valganciclovir (or ganciclovir) prophylaxis, i.v. ganciclovir was used for preemptive therapy for (R+) patients, and in the case of symptomatic CMV. The patients were frequently monitored for CMV by a real-time quantitative plasma PCR. Of those, 161 (R+) patients with a follow-up over six months were studied.
Results: In most cases, 98/161 (61%) no evidence of CMV was seen, and just 63/161 (39%) developed CMV-DNAemia during the post transplant six months. Only 25/63 reactivations exceeded 5000 copies/ml considered as cutoff level for preemptive treatment (median 21500, range 5100-813300 copies/ml), and most had self-limiting, low-level CMV-DNAemia (median 850, range 234-4000 copies/ml). Thus, low-level temporal CMV-reactivation occurred in 38/161 (R+) patients (23.5%), and only 25/161 (15.5%) demonstrated significant viral loads. No correlation to immunosuppression regimen was found. No patient or graft was lost due to CMV.
Conclusions: Most CMV-seropositive adult liver recipients do not develop CMV-reactivation, and even if reactivations occur, most of them are temporal, low-level DNAemias. Thus, universal prophylaxis for all R+ patients would not seem to be reasonable in this patient population.

P-436 INCIDENCE OF HEPATIC VENOUS OUTFLOW OBSTRUCTION IN "PIGGY-BACK" LIVER TRANSPLANTATION: COMPARISON OF THREE KINDS OF GRAFT'S OUTFLOW RECONSTRUCTION

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Background: The "piggy-back" liver transplantation (PBLT) has gained worldwide acceptance. However, the hepatic venous outflow obstruction usually be reported as one of the main complications of the operation. Its incidence often relate with the technical errors such as small-caliber anastomosis of the suprahepatic vena cava, twisting, or kinking.
Objective: We compared the three kinds of graft's outflow reconstruction: end-to-end anastomosis of the graft hepatic veins to the recipient's hepatic veins (E-E style), end-to-side anastomosis of the graft vena cava to the recipient's vena cava (E-S style) and side-to-side anastomosis of the graft vena cava to the recipient's vena cava (S-S style), in order to find a most satisfied one to minimize the incidence of the hepatic venous outflow obstruction.
Material and method: From 2001 to 2008, 120 cases of piggy-back liver transplantations were performed in our center. According to the difference kinds of the graft's outflow reconstruction style, all the 120 patients were divided into 3 groups: E-E group 34 cases, E-S group 36 cases and S-S group 50 cases. There were no differences in mean age, gender, UNOS or Child-Pugh score, and indications for liver transplantation.
Results: The incidence of the hepatic venous outflow obstruction in the 3 group were as follows: E-E group (35.3%, 12 cases), E-S group (22.2%, 8 cases) and S-S group (8.0%, 4 group) respectively. The side-to-side anastomosis style has an obviously fewer incidence of the hepatic venous outflow obstruction than the other 2 styles ($p<0.05$).
Conclusions: In our PBLT series, hepatic venous outflow obstruction were more frequent in cases in which E-E or E-S anastomosis style were used than S-S style was used. So we recommend the S-S style when performing the graft's outflow reconstruction.

P-437 FEASIBILITY OF USING GRAFTS FROM MARGINAL DONORS IN LIVER RETRANSPLANTATION. A SINGLE-CENTER ANALYSIS

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Purpose: Use of grafts from marginal donors in patients undergoing liver retransplantation (ReLT) is controversial because of the use of grafts with worse expected function in patients with lower expected survival compared to primary liver transplantation (LT). We analyzed graft characteristics in patients undergoing ReLT in our center and compared the survival of marginal grafts vs. non-marginal grafts in these patients.
Methods and materials: From June 1988 to January 2006, 1118 patients un-

derwent LT in our center and 108 ReLT were performed (98 patients received a second graft, 9 a third graft and 1 a fourth graft). ReLT were divided in urgent (first week after previous LT: 24 patients), semiurgents (second week to 3 months: 14 patients) and non-urgent (more than 3 months: 70 patients) and in two periods of equal duration: first period (June 1988 to March 1994: 53 ReLT) and second period (April 1994 to January 2006: 55 ReLT). Grafts were divided in non-marginal (Donor risk index (DRI) under 1.8: 79 grafts) and marginal (DRI equal or over 1.8: 29 grafts).
Results: Donor age and DRI were higher in the second period (32±17 vs. 48±18 years, $p<0.001$ and 0.86±0.63 vs. 1.32±0.72, p=0.001 respectively). No differences in overall graft survival were found when comparing marginal and non-marginal grafts. Graft survival in patients with MELD under 19 or a high Rosen score was lower in marginal graft compared to non-marginal grafts. Marginal grafts showed poorer survival compared to non-marginal grafts only in non-urgent ReLT.
Conclusion: The use of grafts from marginal donors has increased in the last times. Although the use of grafts from marginal donors is not associated with a worse survival, in order to improve ReLT results recipient conditions should be taken into account when using these grafts.

P-438 PREVENTION OF BILIARY STENOSIS AFTER DUCT-TO-DUCT RECONSTRUCTION IN LIVING DONOR LIVER TRANSPLANTATION WITH A BIOABSORBABLE POLYMER STENT

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Background: Duct-to-duct biliary reconstruction in liver transplantation is now adopted for mainstream use, even though biliary strictures occur at increased frequency during the procedure
Aim: Our group attempted to develop a self expandable bioabsorbable polymer stent preventing anastomotic stenosis in the duct-to-duct biliary reconstruction
Methods: The procedure was performed with a bioabsorbable polymer stent (BAPS) made from a polyglycolic acid fashioned into a self-expandable tube with a 5-mm bore diameter, and a targeted degradation time of about 4 weeks after implantation. Hybrid pigs were laparotomized under general anesthesia. After baring the extrahepatic bile duct and sectioning it with an electrical scalpel, the divided ducts were anastomosed at the stumps. The animals were divided into a silicone tube stent group (STS) and BAPS group. The animals were re-laparotomized at 12 weeks after the operations for radiological and histological studies
Results: In the STS group, we found a narrow segment on cholangiography and trapped sludge on gross examination at the anastomotic site. Histological studies revealed abruptions of epithelial cells, abundant connective tissue, and abundant infiltrating inflammatory cells. The anastomotic site in the BAPS group was free of any observable stricture on cholangiography and was indistinguishable from the native extrahepatic bile duct on gross examination. Histological studies in the BAPS group revealed consecutive epithelial cells, with fewer connective tissue and inflammatory cells compared to the STS group. Conclusions: This study demonstrated that the BAPS could induce appropriate duct-to-duct regeneration of the anastomotic site. We suggest that the BAPS insertion, a simple procedure with minimal loss quality of life for the patient, can prevent biliary stenosis after duct-to-duct reconstruction in living donor liver transplantation.

P-439 THE SURVIVAL BENEFIT OF LIVER TRANSPLANTATION IN PATIENTS WITH HEPATOCELLULAR CARCINOMA

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Background: There are no studies evaluating the survival benefit of liver transplantation (LT) over alternative therapies (AT) for patients with hepatocellular carcinoma (HCC).
Methods: The present study evaluated data collected prospectively on HCC patients listed for LT (n = 135). The short- to mid-term survival benefit was calculated by comparing the mortality rates of transplanted patients with those of patients on the waiting list undergoing to AT.
A Markov prediction model was then created to estimate the long-term survival benefit of LT (gain in life expectancy) over AT. The long-term survival rates in the LT group were calculated using the Metroticket website calculator (http://89.96.76.14/metroticket/calculator/).
Results: The short- to mid-term analysis indicated that LT afforded no significant short- to mid-term survival benefit in the group of HCC patients as a whole (hazard ratio = 1.229, 95% confidence-interval 0.544-2.773, p=.6200). The benefit was concentrated in patients with a poor initial response to AT (hazard ratio = 3.137, 95% confidence-interval 1.428-6.891, p=.0044).

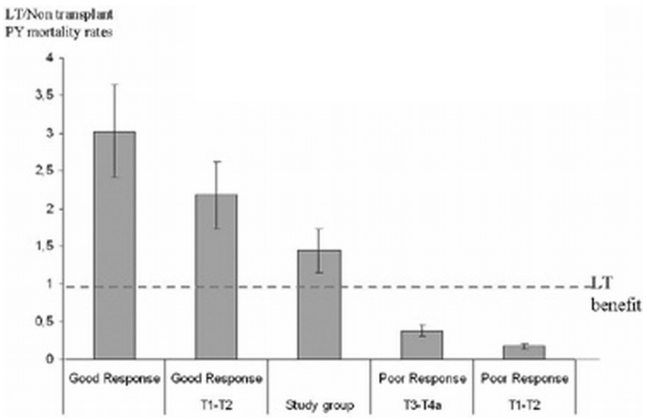

Figure 1. Ratio between transplant (LT) and waiting list (non transplant) patient-years mortality rates by response to non transplant therapy category and by UNOS TNM stage. Median follow-up of non transplant patients was 10.4 months (3.1–79.2); median follow-up of LT patients was 27.6 months (0.3–99.0).

In the long-term analysis (Markov model), the gain in life expectancy after LT with respect to AT was 6.115 years (base-case analysis). Applying the calculated range (Metroticket website) of LT 5-year survival rates (52%-68%), the 5-year survival prospects after AT and the patient's age were the main determinants of gain in life expectancy.

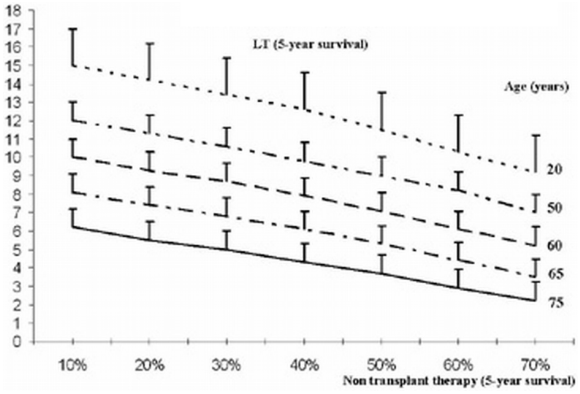

Figure 2. Three-way sensitivity analysis applied to the base-case scenario: long-term survival benefit of LT (gain in life expectancy, left y-axis) according to patient's age (right y-axis), non transplant therapy related 5-year survival (x-axis) and LT (vertical bars) related 5-year survival.

Conclusions: When the survival benefit endpoint is applied to the complex field of LT for HCC, the patient's age and the effectiveness of AT emerged as crucial prognostic tools to consider for both patient selection and prioritization.

P-440 CONGESTION OF REMNANT LIVER AFTER PROCUREMENT OF AN EXTENDED LEFT LOBE GRAFT IN LIVE DONORS

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Background and aim: The congestion of right lobe graft without middle hepatic vein is known to cause critical outcome in living donor adult liver transplantation. However, little has been reported about congestion of remnant liver after procurement of an extended left lobe graft in live donors. The aim of this study is to clarify the impact of congestion in live donors.
Patients and methods: Ten live donors were enrolled in this study, who underwent an extended left hepatectomy (with middle hepatic vein). The estimated congestion volume (CV) was calculated using MD-CT data and Region growing software (Hitachi Medical Corp., Japan). The estimated CV was compared with actual CV, which was determined by postoperative CT (dysper-

fusion area). Then, patients were divided into 2 groups, according to actual CV/(remnant liver volume (RLV)) at postoperative day 7; high CV group (n=5), over 10% of CV/ RLV and low CV group (n=5), with less than 10% of CV/RLV.
Results: The estimated CV and CV/RLV were 226.8±93.1 ml and 31.1±7.1%, respectively. On the other hand, the actual CV and CV/RLV at POD7 were 84.4ml and 9.5%, respectively. The actual CV and CV/RLV were all less than the estimated CV and CV/RLV. There was no difference in operative time, blood loss, diameters of middle hepatic vein, postoperative liver function tests, and regenerative rate of RLV at POD 7 and 14 between high and low CV groups. The diameter of superior right hepatic vein tended to be larger than that in low CV group (10.3mm vs. 12.8mm).
Conclusions: Those findings suggested that the congestion of remnant liver after procurement of an extended left lobe graft does not affect any serious complications in live donors.

P-441 PREVENTION OF HBV INFECTION AFTER LIVER TRANSPLANTATION IN PATIENTS WITH HBV OR HBV+HDV CIRRHOSIS

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To prevent the liver transplant infection after OLT due to HBV or HBV+HDV cirrhosis, a specific HB-Ig in combination with nucleoside analogs have been routinely used.
Methods: The protocol of prevention therapy is generally accepted and aimed at eliminating HBs Ag and maintaining the anti-HBs rate in the recipient's blood serum higher than 100 IU/l. The treatment duration is 12 months, and the total Hb-Ig dose for this period makes 75 000 IU.
Results: Among 18 patients with OLT due to HBV or HBV+HDV cirrhosis, 12 pts (1st group) received the complete course of HB-Ig with lamivudin or entecavir (12 months). Two of them received Antihep® (Russia), the other 10 pts received Neohepatect ®(Germany). Three pts (2nd group) received an incomplete course of HB-Ig (4000-8000 IU) in combination with lamivudin. Three pts (3rd group) with HCC and liver cirrhosis received a lamivudin monotherapy without HB-Ig.
All the patients of the 1st group had a rapid virologic response with HBs Ag, HBV DNA, and HDV RNA disappearance (the longest follow-up after OLT was 64 months). Three pts from the 1st group died due to the causes unrelated to HBV recurrence. There was reappearance of Hbs Ag in one pt from the first group after 18 months of complete course of HB-Ig. Two pts from the 2nd group and 2 pts from the 3d group became Hbs Ag negative, but in one case (3rd group) Hbs Ag reappearance was noted at 18 months after the OLT.
Conclusion: The prolonged treatment with HB-Ig and nucleoside analogs given to the pts after the OLT due to HBV or HBV+HDV cirrhosis prevent liver transplant HBV reinfection in 83.3% cases.

P-442 LONG TERM OUTCOME OF LIVER TRANSPLANTATION VS RESECTION FOR ADVANCED HCC

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Transplantation (LT) and hepatic resection (HR) are both considered standard approach for treatment of HCC. The aim of this study is to retrospectively analyze the long-term outcome of LT vs HR for HCC outside the Milan criteria at histology.
Patients & methods: retrospective chart review of all cases of LT vs a group of HR resulted outside the Milan criteria at histology at a single teaching center from 2001 to 2008
Results: Presented as 23 LT vs 20 HR cases. Gender was male in 22 vs 17 cases (p=0.009). Median age at surgery was 58 (range 41-65) vs 57 (range 40-66) years-old (p=0,595). Viral hepatitis was present respectively in 74% vs 60% (p=0.33). More patients were Child A in the HR group (90% vs 61% p<0.001). Preoperative alfa-feto protein was 66±83 vs 133±151 (p=0.20). The number and diameter of nodules at histology was 4±2 and 5.7±2.3 cm vs 1.6±0.9 and 7±2.4 cm (p<0.0001 and p=0.63 respectively). HCC grading was 3-4 in 26% vs 60% of cases respectively (p=0.02). Vascular invasion was present in 22% vs 50% of cases (p=0.052). HCC recurred in 30% vs 40% of cases (p=0.511). The estimated 1, 3 and 5 years overall and disease free survival was respectively 93%, 57%, 40% and 87%, 70%, 62% vs 53%, 34%, 34% and 69%, 45%, 45% for LT and HR (p=0.11 and p=0.15 respectively). The median survival was 47 vs 21 months for LT vs HR.
Conclusion: both LT and HR are available options for the treatment of HCC outside the Milan criteria, although LT seems to have better long results with longer median survival. However, the use of donor's liver for HCC outside the Milan criteria is still a matter of debate due to organ shortage.

P-443 SOTRASTAURIN: PHARMACOKINETICS AND CLEARANCE IN LIVER TRANSPLANTION

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Sotrastaurin, a selective protein kinase C-inhibitor, undergoes hepatic metabolism and excretion via the bile. We characterized the pharmacokinetics, protein-binding, and biliary clearance of sotrastaurin and its *N*-desmethyl-metabolite in 13 *de novo* liver transplant recipients (LTxR) with bile drainage *via* T-tube. Recipients received two single doses of sotrastaurin 100mg; once between days 1-3 and again between days 5-8 post-LTx.
Results: Sotrastaurin absorption appeared adequate with blood total drug AUC in the range observed earlier in healthy subjects (HS; 3544±1434 *vs* 4531±1650 ng.h/ml, p=0.24). Due to elevated plasma levels of the sotrastaurin-binding protein, α1-acid-glycoprotein (AAG), the free sotrastaurin fraction in blood was lower in LTxR than in HS (0.7±0.2% *vs* 1.4±0.3%, p=0.0002). Therefore, free (nonprotein-bound) drug exposure was compared between LTxR and HS (Table): sotrastaurin C_{max} and AUC remained stable between days 1-3 and 5-8, whereas metabolite AUC decreased over time. Free sotrastaurin AUC was significantly correlated with AAG (r^2=0.45, p<0.001). Since LTxR had higher AAG levels (more AAG bound drug) the free sotrastaurin AUC was 60% lower than in HS (p=0.001). Free metabolite AUC was 2-4 fold higher in LTxR (p=0.01) early post-LTx but normalized to HS levels by days 5-8 (p=0.31).

Parameter	LTxR (day 1-3)	LTxR (day 5-8)	HS
Sotrastaurin Cmax (ng/ml)	3.6±2.6	3.8±2.0	8.6±1.5
Sotrastaurin AUC (ng.h/ml)	26.0±13.0	23.0±19.0	61.0±15.0
Sotrastaurin t1/2 (h)	8.7±3.5	9.5±4.5	9.2±2.9
Metabolite AUC (ng.h/ml)	11.0±8.0	6.0±10.0	3.0±1.0

Excretion of sotrastaurin and its metabolite in bile was minimal (1% and 3% of dose) consistent with the fact that sotrastaurin is extensively metabolized. Presumably, other unmeasured metabolites constitute the biliary eliminated products.
Conclusion: In the first week post-LTx elevated levels of the acute phase protein, AAG, contributed to higher sotrastaurin protein-binding. Subsequently, free drug levels may be low. As AAG normalizes over time, free drug exposure is anticipated to increase. The need for a higher sotrastaurin dose short-term post-LTx will depend on the overall immunosuppressive regimen in which sotrastaurin is used.

P-444 ADULT CIRRHOTIC LIVER EXPLANTS: DIAGNOSIS OF UNDETECTED CHOLANGIOCARCINOMA

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Background & aims: Liver cirrhosis, heavy alcohol consumption and chronic HCV infection are possible risk factors for intrahepatic cholangiocarcinoma. Because of major recent advances in imaging techniques of the liver, it is relatively easy to detect hepatocellular carcinomas (HCC) in cirrhotic livers. Nevertheless, small cholangiocarcinoma nodules might be undiagnosed, or misdiagnosed as HCC, in the context of liver cirrhosis. The aim of this study was to determine the prevalence of undetected cholangiocarcinomas in liver explants of adult cirrhotic patients undergoing liver transplantation.
Methods: From December 1985 to November 2008, a first liver transplantation was performed in 700 adult cirrhotic patients in Edouard Herriot Hospital, Lyon, France. All liver explants were analyzed for the presence of macroscopically atypical nodules, which were then pathologically described as non-neoplastic nodules, HCC, and/or cholangiocarcinoma.
Results: In the cohort of 700 consecutive patients, the diagnosis of HCC was made from liver explants in 225 cases (not recognized before LT (= incidental) in 66 cases), *i.e.* in 32.1% of the patients. Similarly, an intrahepatic cholangiocarcinoma was identified in 7 (1%) patients, with a mean size of 28±17mm. The mean age at transplantation was 57.6 years (range 43 – 66). The indication for LT was alcoholic cirrhosis (58%, n=4), HCV-related cirrhosis (14%, n=1), or HCC (28%, n=2). The mean follow up duration after LT was 27 months (range 6 to 61). Presence of cholangiocarcinoma was associated with an older age (57.6 Vs 51.0, p<0.05), but not with gender, HCC or indication for transplantation. Post transplant tumor recurrence was observed in 1 patient (14.3%), leading to death.
Conclusions: Our results suggest that unrecognized intrahepatic cholangiocarcinoma complicating liver cirrhosis is a rare entity. Nevertheless, this can significantly influence post-transplantation survival in case of recurrence.

P-445 LONG TERM RESULTS OF LIVER TRANSPLANTATION FOR WILSON'S DISEASE

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Background/Aims: Orthotopic liver transplantation (OLT) is the ultimate therapeutic option for the treatment for Wilson's disease. The aim of this retrospective study was to review our experience over a 20-year period of time, especially regarding long term outcome.
Methods: Long-term follow-up data were obtained for 8 adult and 7 children patients (median age 20 years ranging 8-53, 8 women and 5 men) who underwent OLT between 1987 and 2006 for Wilson's disease associated with severe liver disease. The diagnosis of Wilson's disease was made in all cases before OLT.
Results: The indication for OLT was a chronic liver disease in 61.5% of the cases or an acute liver failure in 38.5% of the patients. One patient had associated neurological symptoms before OLT. The median follow-up after OLT was 10 years, and the overall patients' survival was 100% and graft survival was 92% (one retransplantation was performed after 13 years). In all cases, copper metabolism normalized after OLT. None of the patients with liver failure without neurological symptoms (n=12) did receive chelating agents and did experience neurological manifestations of Wilson's disease after OLT. The patient with severe neurological symptoms did not improve.
Conclusion: Our experience confirms that OLT can be safely performed in patients with Wilson's disease, with excellent long-term results and survival. Moreover, OLT does reverse the copper metabolism abnormalities and their consequences. The indications of OLT in case of progressive neurological deterioration despite no hepatic insufficiency, in patients with Wilson's disease who do not improve with medical treatment remains widely debated.

P-446 STUDY ON COMPLEMENT ACTIVATION DURING LIVER REPERFUSION IN PATIENTS WITH ATYPICAL HEMOLYTIC UREMIC SYNDROME OR OTHER INDICATIONS FOR LIVER TRANSPLANTATION

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Purpose: Atypical hemolytic uremic syndrome (aHUS) is often caused by loss-of-function mutations in plasma protein complement factor H (CFH). Since CFH is produced nearly totally by liver combined liver-kidney transplantation has been proposed for treatment of these cases. Initially the procedure was associated with complications but after massive plasma exchange (PE) therapy a total of seven successful combined liver-kidney transplantations are generally known to be performed, three of these in our institution.
Methods/Materials: Serial EDTA plasma samples were collected from systemic circulation, portal vein, and hepatic vein before and during reperfusion of the liver graft in two aHUS patients and three adult patients. Complement markers C3, C3a, iC3b, C3d, SC5b-9, factor B, Bb, C4, and C4d were measured.
Results: According to the concentration of the activation markers in peripheral blood complement was activated during all the LTX procedures. In the early reperfusion most activation was seen in the portal samples while 15-60 min after portal declamping activation markers were high also in the hepatic vein samples of most patients. In most cases the activation was first mediated via the alternative pathway followed by activation of the classical/lectin pathways. The concentrations of the activation markers returned to low levels within 24 hours after the reperfusion. The highest ALT levels of both the aHUS patients stayed below 50 for the first 72 hours and thus the high complement activation seen in the female aHUS-patient did not reflect in ALT levels.
Conclusions: PE therapy together with excellent liver graft quality seems to impede thrombotic complications in transplantations for aHUS. Complement activation during LTX in aHUS patients after extensive PE did not differ from patients with LTX performed for other reasons.

P-447 ALBUMIN DIALYSIS MARS IN ACUTE LIVER FAILURE: PREDICTIVA CRITERIA FOR OUTCOME

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Background: In the era of liver transplantation many researchers want to have some methods for estimating what the probability for success will be in the short or long term in Acute Liver Failure patients. In this study, we examined whether the Molecular Adsorbent Reciclyng System (MARS) can be seen as a predictor of survival in patients with ALF.
Methods: In Intensive Care we treated 45 patients with Fulminant Hepatitis. During treatment the concentration of albumin and albumin bound-toxins changes both in the circuit and in the patient from hour to hour. We found ideal concentrations for every patient supported by a study among our clinical data and the mathematical model. Continuous MARS treatment was carried on all patients with kit change every 9 ± 3.2 hours. Blood flow rate was 180 ± 30mL/min, depending on the hemodynamic status of the patient. The kit preparation and the release of albumin circuit was 60 minutes to remedy the mixing with the dialysis bath that dilutes the albumin concentration up to 50%.
Results: Of the 45 patients, thirty two of which survived, 19 went to the transplant while 14 have continued extracorporeal method for a maximum period of 15 ± 2.5 days indicating a positive resolution of the clinical condition. When we obtain an improvement of GCS (from 7-8 to 10-11), lactates levels$<$3mmol/L, a reduction of cytokines levels and a change in hemodynamic instabilty from hyperkinetic to normal kinetic condition between 30 and 50 hours with the treatment MARS, we decide to continue extracorporeal treatment. Twelve patients have died, including 3 before transplant for multi organ failure, while nine after transplantation.
Conclusion: In our Department the MARS is standard bridging therapy in association with Intensive Care Unite for FH patients.

P-448 DEVELOPMENT OF AN ARTIFICIAL BILE DUCT MADE OF BIOABSORBABLE POLYMER TO BE USED FOR TREATMENT OF BILIARY STENOSIS AFTER LIVING-DONOR LIVER TRANSPLANTATION

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Along with the recent widespread use of living-donor liver transplantation, complications involving the biliary system are increasing. Stent or T-tube insertion is a common treatment for bile duct stenosis by which the papilla of Vater can be preserved. However, there are some disadvantages with both stents and T-tubes, and new means of treatment have been called for. We investigated whether an artificial bile duct made of bioabsorbable polymer could substitute for a narrowed bile duct.
Methods: Hybrid pigs were laparotomized and the extrahepatic bile duct was identified. Then a portion of the duodenal side of the bile duct was resected, 3 cm in major axis, and substituted by a bioabsorbable polymer tube of the same size. It was made of a P (CL/LA) 50:50 reinforced with a PGA fiber mesh and was designed to degrade in six to eight weeks in the body. There was no prior cell seeding onto the graft. Animals were re-laparotomized three months after implantation and gross, histological and blood chemical studies performed.
Results All recipient pigs survived until they were sacrificed for collection of graft sites three months after implantation. All of them gained weight. On gross examination, the artificial duct was found to have been absorbed and the graft site was indistinguishable from the native extrahepatic bile duct. Stricture was not found on cholangiography, adhesion to surrounding tissue was mild and the graft site could be freed manually. Histology revealed a neo-bile duct growing in the graft site with the epithelium of highly uneven thickness and increased accessory glands compared with the native duct. Blood chemistry data at three months post implantation did not show change from baseline values.

P-449 DEVELOPMENT OF A NEW TREATMENT FOR BILE DUCT STENOSIS USING TISSUE ENGINEERING TECHNIQUES – DEVELOPMENT OF A BILE DUCT PATCH MADE OF BIOABSORPABLE POLYMER –

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Along with the recent widespread use of living-donor liver transplantation, complications involving the biliary system are increasing. Stent or T-tube insertion is a common treatment for bile duct stenosis. However, there are some disadvantages with both stent and T-tube, and new means of treatment have been called for. We investigated whether a bioabsorbable polymer patch that dilated the narrowed bile duct could be available for the treatment of bile duct stenosis. (Materials and Methods) Hybrid pigs were laparotomized and the extrahepatic bile duct was identified. Then a portion of the duodenal side of the bile duct was resected, 3×2 cm in size and spindle in shape, and substituted by a patch made of bioabsorbable polymer of the same size. Animals were re-laparotomized four months after implantation to recover graft sites for gross, histological and blood chemical studies. (Results) All recipient pigs survived until they were sacrificed for collection of graft sites four months after implantation. On gross examination, the patch was found to have been absorbed and the graft site was indistinguishable from the native extrahepatic bile duct. Stenosis did not occur, adhesion to surrounding tissue was mild and the graft

site could be freed manually. Histology revealed a neo-bile duct growing in the graft site with the epithelium of highly uneven thickness and increased accessory glands compared with the native duct. Blood chemistry data at four months post implantation did not show change from baseline values. (Conclusion) This study demonstrated that the patch could be used for the treatment of bile duct stenosis. Thus, dilation of the bile duct with this patch can be a substitute for T-tube insertion in transplantation surgery.

P-450 CLINICOPATHOLOGICAL STUDY OF EXPLANTED LIVERS IN TRANSPLANTATION FOR ADULT POST-KASAI BILIARY ATRESIA

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Background: Because of the improvement in results of Kasai operation, biliary atresia (BA) cases that reach their adulthood without liver transplantation are increasing in recent years. Thus we have more patients with post-Kasai BA undergoing liver transplantation in their adulthood.
The aim is to characterize the clinicopathological feature of adult post-Kasai BA in one institution in Japan.
Patients and results: There were 6 adults in 43 BA cases undergoing living donor liver transplantation (LDLT) from1998 to 2008. The mean age of the patients was 27.3 years. They had undergone Kasai at 68.5 days of life in average. The treatment after the Kasai to the LDLT included that for the variceal bleeding, portal hypertension, adhesive intestinal obstruction and recurrent cholangitis in each one case. Two cases had had no additional treatment until the transplantation. Pre-LDLT serum hyaluronic acid was extremely high (400 ng/ml or more) in 4 cases. The explanted liver macroscopically presented with intrahepatic cholelithiasis in 3 cases. Patency of the perihilar bile duct to the Roux-en-Y limb could not be confirmed macroscopically in all cases. Microscopic findings of the explanted livers showed definite liver cirrhosis (F4) in 3cases, moderate liver fibrosis (F3) in one and mild fibrosis (F1-2) in the other two. All cases have been doing well after LDLT in the mean follow-up of 17.8 months.
Summary: Long uneventful period through the adolescence after Kasai did not ensure the life without liver transplantation. Pathological findings of the explanted livers at the adult LDLT for BA showed liver fibrosis of various severities.

P-451 ARE THE PROTECTIVE FACTORS OF PRECONDITIONING TRANSFERRABLE?

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Purpose: Ischemic preconditioning (IP) defined as brief periods of ischemia and reperfusion cycle(s) preceding the prolonged periods of ischemia has been reported to maintain a protection against ischemic injury. Moreover ischemic preconditioning of liver is known to protect renal tissue from ischemia-reperfusion injury. Considering the beneficial remote effect of preconditioning, in this present study we evaluated whether the transfusion of plasma obtained from a rat exposed to ischemic preconditioning would be beneficial in reducing the ischemic injury of another rat liver and plasma.
Methods/Materials: Spraque-Dawley rats were divided into five groups: group I; sham, group II; normal plasma transfusion, group III; hepatic ischemia, group IV; normal plasma transfusion following hepatic ischemia, group V; IP factors containing plasma transfusion following hepatic ischemia. Ischemias were performed with hepatic pedicle clamping for 45 minutes in liver and IP was created by 10 minutes of brief hepatic ischemia and 10 minutes of reperfusion. The normal plasma was obtained from blood of eight rats catheterized through inferior vena cava. IP containing plasma was obtained from four additional rats previously subjected to ischemic preconditioning by clamping the hepatic pedicle for 10 minutes.
Results: The results of the study revealed that liver functions were influenced less in group V. The histopathological injury of liver tissue was also less in group V than in group III and IV. The IP factors containing plasma transfusion produced also less TNF-α, IL-2 and LDH responses as compared to groups III and IV at 45 min.
Conclusion: We concluded that the beneficial factors of preconditioning observed after brief period and reperfusion are transferrable and may reduce the ischemic injury of another rat subjected to sustained peridos of ischemia and reperfusion.

P-452 ALCOHOL-METABOLIZING ENZYME GENE POLYMORPHISMS IN ALCOHOL LIVER CIRRHOSIS AMONG POLISH INDIVIDUALS

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Aim: The aim of the study was to find in the Polish population the ADH1B, ADH1C, ALDH2 and CYP2E1 genotypes, which are likely to be responsible for higher susceptibility to alcohol liver cirrhosis.
Material and methods: The ADH1B, ADH1C, ALDH2 and CYP2E1 genotype and alleles frequencies were examined in 202 patients: 77 with alcoholic liver cirrhosis, 64 alcoholics without damage to gastrointestinal organs and 61 non-drinkers (control group). Genotyping of the ADH, ALDH2 and CYP2E1 was performed using PCR-RFLP on white cell DNA.
Results: The genotype ADH1C*1/*1 and allele ADH1C*1 were found to be significantly more frequent in alcohol abusers compared to non-drinkers. Frequency of ADH1C*1 allele in alcohol liver cirrhosis group was 62,8%, and ADH1C*1/*1 genotype was observed in 45,4% and was significantly higher than in the control group. The differences between of the group of patients who abuse alcohol were not statistically significant. In the group of nondrinkers ADH1B*2 and ADH1C*2 alleles were more frequent in comparison to the alcohol liver cirrhosis patients and alcohol addicts. All examined patients were ALDH2*1/*1 homozygotic, so we could not show correlation with alcohol cirrhosis. In the examined population the c2 allele was present only in 1.5% of patients and was found only in alcohol abusers. The c2 allele frequency in alcohol liver cirrhosis group was statistically significantly higher than in the controls. But the differences between of the group of patients who abuse alcohol were not statistically significant.
Conclusion: Our studies suggest that in the Polish population examined ADH1C*1 allele and ADH1C*1/*1 genotype favor developing alcoholism and alcohol liver cirrhosis. However ADH1B*2 allele is likely to protect against them. The c2 allele frequency among Polish individuals is low, however, they pose the risk of alcohol liver cirrhosis. The Polish population examined is monomorphic ALDH2*1.

P-453 GRAFT PRECONDITIONING WITH LOW-DOSE TACROLIMUS (FK506) AND NITRIC OXIDE INHIBITOR (AGH) REDUCES ISCHEMIA/REPERFUSION INJURY AFTER LIVER TRANSPLANTATION IN THE RAT

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Purpose and methods: Ischemia/reperfusion (I/R) injury is a main cause of primary dysfunction or non-function after liver transplantation (LTx). Recent evidence indicates that an increase in nitric oxide (NO) production after LTx is associated with I/R injury. The aim of this study was to demonstrate that low-dose FK506 in combination with aminoguanidine (AGH), which leads to a reduction of NO levels, has a protective effect by reducing I/R associated injury after LTx.
Materials: Fortyone DA-(RT1av1) rats served as donors and recipients for syngenic orthotopic arterialised LTx. They were divided into 4 groups: controls without pre-/treatment (I), pre-/treatment with high-dose FK506 (II), pre-/treatment with AGH only (III), and pre-/treatment with low-dose FK506 in combination with AGH (IV). After LTx the laboratory parameters and liver biopsy were performed.
Results: The levels of transaminase (ALT) in groups I, II and III were significantly higher on day 3 after LTx compared to group IV ($p=0.001$, $p=0.001$, $p=0.000$). In group IV the I/R-associated liver necrosis rate was reduced significantly.
Conclusion: Our results demonstrated that a combined dual pharmacological pretreatment (group IV) reduced I/R injury of the graft after LTx in a rat model.

P-454 HEPATIC ARTERY RECONSTRUCTION WITHOUT MICROSCOPE IN LIVING DONOR LIVER TRANSPLANTATION. TECHNICAL ASPECTS

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Background: In living donor liver transplantation (LDLTx) hepatic artery (HA) anastomosis still remain a challenge. Indeed arterial reconstruction using a microscope has been advocated to decrease the incidence of hepatic artery thrombosis (HAT). However microscope itself is not considered compulsory by many surgeons. We herein describe our experience of arterial reconstruction without the microscope.

Methods: From March 2001 to December 2008, 49 LDLTx were performed at our institution using the right graft without the middle hepatic vein. All the arterial anastomosis were performed using the "parachute " technique, after an arteriotomy on both arterial stumps, with one running 7/0 prolene suture using 2.5X surgical loupe magnification. Arterial flow is re-established before the suture is tied to allow further expansion at the anastomosis site. The arterial anastomosis was performed with the right hepatic artery in 22 cases and with the proper hepatic artery in 27 cases. In 2 cases an interposition arterial conduit was used.
Results: Data have been retrospectively analyzed. HAT occurred in 2 patients (4%).One of them has been retransplanted while the second one underwent an urgent surgical revision within 8 hours after transplantation. A thrombectomy and a new anastomosis using an aortic conduit have been performed. The HA developed a new thrombosis. Four months after transplantation an intra hepatic biloma has been drained. Patient is alive with a biliary stent in place and normal liver function tests.
Conclusion: Our results show an overall arterial complication rate of 4%. These data are comparable to other previous published series that report a negative arterial complication rate between 1.6% and 22% using a microscope. Although the use of microscope allows more precise and easy arterial anastomosis in LDLTx, an accurate surgical technique using 2.5X surgical loupe magnification can assure remarkable results.

P-455 LIVER TRANSPLANTATION FOR HCC. A COMPARATIVE ANALYSIS OF PATIENTS TRANSPLANTED WITH GRAFT COMING FROM DECEASED OR LIVING DONORS

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Introduction: The liver transplantation (LTx) waiting list drop out due to HCC progression is increasing world wide as a consequence of organ shortage. In this scenario the living donor (LD) LTx is considered a valuable option even if it use in patients with HCC remains controversial.
Methods: From January 2000 to December 2007, 179 patients with HCC have been transplanted in our Unit. Among them 25 (13.9%) received a LD graft (Group-A), while 154 (86.1%) received a deceased donor graft (Group-B).The mean days in waiting list before Tx were significantly less for patients transplanted with a LD (264 days vs. 404 days). In group-A 21 patients (84%) and 107 (69,4%) in group-B underwent an aggressive downstaging procedure prior to LTx. As far as Milan criteria are considered 15 (60%) patients in group-A and 107 (69,4%) patients in group-B were "Milan in" at time of Tx.
Results: No significant differences appeared from long-rank test comparing the 5 years long term survival rate (60.0% vs. 77%) and the disease free survival rate (88.1% vs. 89.4%) between the two groups. The neoplastic recurrence itself as cause of death is different between the 2 groups but has no statistical relevance Two patients (8%) developed HCC recurrence in group A and they are still alive, while 16 patients (10,3%) had HCC recurrence in group B showing a mortality rate of 7,1%.
Conclusions: Our data show the same long term survival and disease free survival rate between patients with HCC transplanted using graft coming from living or deceased donors. Moreover an aggressive HCC downstaging policy while on waiting list for transplantation and an intensive use of graft coming from LD, are able to decrease the drop out rate that follows neoplastic progression.

P-456 LIVER RESECTION FOR HCC PRIOR TO LIVER TRANSPLANTATION DOES NOT AFFECT PATIENTS OUTCOME

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Introduction: HCC downstaging seems to improve liver transplant (LTx) long term cumulative and disease free survival. HCC downsizing can be achieve throughout transarterial chemoembolization (TACE), radiofrequency ablation (RF), alcohol injection (PEI), as well as liver resection (LR). The role of LR prior to LTx is not accepted worldwide because of several concerns related to various technical difficulties to perform LTx.
Methods: From January 2000 to December 2007 out of 475 LTx performed in our Unit 179 (37.6%) patients had HCC on cirrhosis. Among them, HCC downstaging was performed in 128 (84.2%) cases prior to LT. 102 (79%) patients underwent TACE, 48 (37.5%) RF, 7 (5.4%) PEI and 19 (14.8%) LR. Fourteen out of 19 resected patients LR was associated to previous or subsequent HCC ablative treatment. One patient underwent 2 LR. One hundred ninety nine (66,4%) recipients where "Milan in" at time of transplantation according to the explanted liver's histology.
Results: Comparing the group of patients resected versus the one of patients transplanted without any previous LR the 5 year overall survival rate (77.2% vs 71.9%) and disease free survival rate (88.2% vs 87.9%) was not significantly different. The operation duration time, the intraoperative blood loss, the intra and post-operative blood transfusion did not show any significant differences.
Conclusions: In our experience, liver resection represents a valid HCC downstaging treatment in selected patients as bridging to LTx. Mortality and morbidity does not increase among LTx recipients who underwent previous LR, moreover long term survival and disease free survival rate is similar between resected versus non resected patients. In patients listed for liver transplantation liver resection should be taken into consideration and performed at best by the same surgeons who will perform the LTx in order to minimize the surgical liver manipulation.

P-457 HCC RADIOLOGICAL PROGRESSION AFTER DOWNSTAGING ALSO IN PATIENTS INSIDE MILAN CRITERIA CORRELATE WITH A HIGH HCC RECURRENCE RATE AFTER TRANSPLANTATION

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Introduction: An aggressive hepatocellular carcinoma (HCC) downstaging policy while on waiting list for transplantation (Tx) is routinely run out also in patients who meet the Milan criteria.In order to optimize the transplant's results within Milan criteria, they can be integrated by other factors such as tumoral progression after downstaging.
Methods: One-hundred-eighteen among 179 patients with HCC transplanted in our unit from January 2000 to December 2007 represent the study group. All of them underwent one or more downstaging procedures such as liver resection (LR), radiofrequency ablation (RF) or transarterial chemoembolization (TACE). The response to these procedures monitored by CT-scan/MRI before Tx has been defined as: progressive (increasing HCC nodule's number and their dimension) group-A; complete (no evidence of HCC) group-B; partial (partial nodule ablation with no HCC progression) group-C; stable (no significant nodule ablation, no HCC progression), group-D. Forty two patients (35.5%) were in group-A, 39 (33%) in group-B, 10 (8.4%) in group-C; 27 (22.8%) in group-D. In our analysis we compared the patients in group-A with all the other patients (group-B,C and D) forming group-BCD.
Results: With a median follow-up of 41.2 months the cumulative overall-survival rate at 3- and 5-years is 65.5% and 48.9% for group-A and 84.8% and 74.6% for group-BCD (p-value 0.01). The cumulative disease-free-survival rate at 3 and 5-years is 74% for group-A and 95.7% and 93% for group-BCD (p-value=.007).
Conclusion: Following an aggressive HCC downstaging throughout LR, RF or TACE a tumoral radiological progression while on waiting list for Tx was a strong predictor of high HCC recurrence rate also in patients who meet Milan criteria. On the contrary the lack of radiological tumoral progression can help in selecting good transplant candidates for HCC along with Milan criteria.

P-458 LARGE-FOR-SIZE STEATOTIC LIVER GRAFTS CAN BE SAFELY REDUCED

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Background: In order to expand organ pool, steatotic livers are being increasingly used. However large steatotic grafts are often difficult to transplant, with increasing duration of anastomoses. Resection of the left lateral liver segments can facilitate the surgical procedure. We present herein the outcome of reduction of large-for-size steatotic liver grafts.
Methods: From 1999 to 2008, among 30 patients who received a large-for-size (GW/BW ratio $\geq$ 2.5%), steatotic liver graft (macrovacuolar steatosis $>$30%), 12 cases underwent a liver reduction (RL) by an ex-situ left lateral + S1 resection and were compared with the group who received the whole liver (WL). The two groups had similar recipient and donor characteristics.
Results: Mean time of reduction was 60$\pm$20 min. Macrovacuolar steatosis was higher in the RL group (58$\pm$13% vs 43$\pm$16% p=0.01). Mean GW/BW ratio decreased in the RL group from 2.95$\pm$0.4 to 2.24$\pm$0.8 (-24%) and was significantly lower to the WL group (2.24$\pm$0.8 vs 2.87$\pm$0.3; p=0.003). Comparing RL to WL, the two groups showed similar duration of transplantation, cold ischemia time, warm ischemia time, intraoperative bleeding and number of transfusion. WL experienced a significantly higher rate of delayed abdominal wall closure (25 vs 61%; p=0.05), a significantly higher rate of early biliary complication (0 vs 33%; p=0.025) and a higher rate of arterial thrombosis (8 vs 33%). One year survival (92 vs 88%), did not differ in the two groups.
Conclusion: Results of this study showed that reduction may improve the tolerance of large-for-size steatotic grafts and should be considered systematically before discarding these livers.

P-459 HEPATIC SURGERY IN TRANSPLANTED PATIENTS: IS IT DIFFERENT FROM ROUTINE LIVER SURGERY?

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Background: Liver resections (LR) on transplant recipients are extremely rare. We present the patterns of postoperative outcomes after LR in 7 transplantation recipients.
Methods: Retrospective analysis of prospective data on transplanted patients from 1997 to 2008 was performed. Of 850 liver transplantation recipients and 8 renal transplantation recipients, 6 had LR on the transplanted liver and one patient with a renal transplant underwent 1 LR. Demographic data, indications of surgery and post operative course were analyzed.
Results: The indication for surgery in the 7 cases was: recurrent HCC (n=2); persistent fistula from posterior sectoral duct (n=1) and recurrent cholangitis due to anastomotic stricture of posterior sectoral duct (n=1); hydatid cyst (n=1) and large biliary cyst (n=1) and polycystic liver disease (n=1). The LR was 5 to 41 months after LT (mean 23 months) including one right hepatectomy, one left hepatectomy, one right posterior hepatectomy; two left lobectomy; one pericystectomy and one biliary fenestration. Morbidity was seen in 5/7 (71%) patients including subphrenic infection in 2 patients treated by percutaneous drainage and systemic infection treated by antibiotics in 2 patients. One patient had postoperative ascites due to hepatic insufficiency and pleural effusion while 3 patients experienced renal insufficiency which settled with medical management. There was no postoperative mortality. All the patients are alive till date (2 months to 10 years after LR). Both cases of HCC are disease free 10 and 7 years after LR. The other patients did not have recurrent cholangitis or recurrent cysts.
Conclusion: LR in transplanted patients is associated with high rate of specific complications due to immunosuppression including severe infection and renal insufficiency. Therefore we recommend that LR in transplanted patients should be performed in experienced liver units.

P-460 FIBRINOLYSIS AFTER LIVER GRAFT REPERFUSION: INCIDENCE ANALYSED WITH ROTEM

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Purpose: Hyperfibrinolysis occurs during liver transplantation and many centers are using antifibrinolytics prophylactically. The risk of this treatment is not negligible. The aim of our study was to detect hyperfibrinolysis early using Rotem analysis, and decide whether it requires treatment.
Method: During one year we studied 53 patients (37 men, 16 women), mean age was: 54±12.8years. Rotem analysis was done at the beginning of the surgery, at the end of anhepaty and after 30 minutes reperfusion. The usual coagulation parameters were noted (INR, activated cephalin time, platelets count, fibrinogen dosage) as well as metabolic indicators (Ph, ionized calcium, lactate) and graft parameters (cold ischemia time, anhepaty). We realized: Extem, Intem, Fibtem and Aptem test (aprotinine additional): fibrinolysis was recognizing when CT-Extem >80s and CT Aptem >10% shorter than CT-Extem, and/or CLI30 <50%, and/or CLI60 <85% corrected with Aptem test.
Results: Among the 53 patients, 8 (15%) presented a hyperfibrinolysis after the graft reperfusion, diagnosed with Rotem, 4 patients had Child C disease, 2 Child B and 2 Child A. Only three of them had already a hyperfibrinolysis treated just before surgery. Hyperfibrinolysis after reperfusion was not dependant of cold ischemia (p=0.07, Anova) or duration of ischemia (p=0.6) and Child status (p=0.12, χ^2). Hyperfibrinolysis after graft reperfusion was not related with hyperfibrinolysis before surgery (p=0.054, χ^2) in our study, but could be with a largest population. Biological parameters as: Ph, ionized calcium and lactate level were not related to hyperfibrinolysis occurence (p=0.64, p=0.07, p=0.79, Anova). But hyperfibrinolysis after reperfusion is correlated with the total blood loss (p=0.02, Anova).
Conclusion: The systematic prophylactic used of antifibrinolytics seems not justifiable. The disease liver severity does not appear to be an available parameter. The incidence of hyperfibrinolysis on the bleeding shows that the early diagnosis and adapted treatment are essential.

P-461 RISK FACTORS FOR POST-TRANSPLANTATION MALIGNANCY IN LIVER AND SMALL INTESTINE TRANSPLANT RECIPIENTS REPORTED BY UNOS 1988-2006

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Purpose: The aim of this study was to investigate the risk factors for development of post-transplant malignancy in liver and small intestine transplant recipients.
Methods: United Network for Organ Sharing (UNOS) and Organ Procurement and Transplantation Network (OPTN) data* as of 25/02/2008 was used. Age, gender, ethnicity, donor-recipient ABO match, history of pre-transplant malignancy, type of malignancy, number of years between transplant and cancer diagnosis and immunosuppression were analysed. Odds ratio (OR) or relative risk (RR) were calculated.
Results: Of 81642 liver (male=49424, female=32218, M/F=1.5) and 1320 small intestine (male=669, female=651, M/F=1.0) transplant recipients, 6.5% of liver and 5.8% of small intestine transplant recipients developed malignancy post-transplantation. Malignancy was diagnosed within 3 years of transplantation in 46% of liver and 73% of small intestine recipients to develop cancer and after 6 years in 28% of liver and 13% of small intestine cases. Where reported, the most common post-transplant malignancy in liver transplant recipients was skin cancer, and lymphoma and oropharyngeal cancer in the case of small intestine recipients.
Caucasian ethnicity, previous history of cancer, immunosuppression with cyclosporine, OKT3, steroids and azathioprine were associated with increased risk of post-transplant malignancy (Table 1). Afrocarribean ethnicity was associated with reduced risk in the case of liver recipients but not in the case of small bowel.

Odds Ratio or Relative Risk of post-transplant malignancy in liver and small intestine transplant recipients

Increased Risk			Decreased/Equal Risk		
Odds Ratio	Liver	Small Intestine	Odds Ratio	Liver	Small Intestine
Caucasian Ethnicity	1.8	1.2	Afrocarribean Ethnicity	0.5	(1.1)
Pre-Transplant Malignancy	2.8	3.5			
ABO Identical	1.3	1.9			
Immunosuppressant (Relative Risk)			Immunosuppressant (Relative Risk)		
Cyclosporine	1.4	1.1	Sirolimus	(1.0)	0.5
OKT3	1.6	2.5	Mycophenolate	0.9	(1.0)
Steroids	2.0	1.6	Daclizumab	–	0.7
Azathioprine	1.8	3.2	ATG	0.4	–
Tacrolimus	(1.0)	1.2			
Daclizumab	1.1	–			

Conclusion: Caucasian ethnicity, certain immunosuppression medications and history of pre-transplant malignancy were risk factors for post-transplant malignancy in liver and small intestine transplant recipients from 1988-2006. The continuing development of malignancy greater than six years post transplantation has implications for the close follow up and screening of transplant recipients.
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P-462 HEPARINOIDS DETECTION AFTER LIVER GRAFT REPERFUSION WITH ROTEM ANALYSIS

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Purpose: During liver transplantation, haemostasis disturbances are well known, especially after the graft reperfusion. The origin seems to be multifactorial. The ROTEM analyses help us to appreciate the mechanism of coagulation abnormalities. The aim of this study was to determine the presence of heparinoids after the graft reperfusion in liver transplantation.
Method: We did ROTEM analysis in 43 patients undergoing liver transplantation. The tests were done at the beginning of the surgery, at the end of anhepaty and after 30 minutes reperfusion. The Rotem test was done with 5ml of patient's blood immediately after sampled. The population characteristics are in table 1. Typical sign of heparinoids effect is a CTintem>240s. We try to find a relation between this increasing of CTintem and Anhepaty, cold ischemia, activated cephalin time (TCA), ionized calcium (Ca++) and total blood loss.
Results: Among the 43 patients, 38 (88%) presented a CTin>240s, 30minutes after the graft reperfusion. Statistical analyze show that the increasing of CTintem was related to the TCA ($p<0.001$, wilcoxon) and to the lactate level after reperfusion ($p<0.001$). The cold ischemia was associated with an increase in CTintem ($p<0.001$, wilcoxon), as well as the duration of anhepathy ($p<0.001$, wilcoxon). The value of ionized calcium, and Ph after reperfusion were not related to the CTintem (p=0.23, p=0.81).The abnormal CTintem after reperfusion was not related with an increase in bleeding (p=0.71).
Conclusion: A heparin effect (CTintem>240) after the graft reperfusion is observed in 88% of the patients undergoing liver transplantation, without incidence on the clinical bleeding.The endogenous or exogenous origin of this Heparin is not clear. The reason of prolonged CTintem as to be clarified to avoid unnecessary coagulation factors replacement. The realisation of a Heptem test could be helpful to test the protamine effect

P-463 INCIDENCE OF ABNORMAL FIBRINOLYSIS IN PATIENTS UNDERGOING LIVER TRANSPLANTATION- ROTEM ANALYSIS

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Purpose: The ROTEM allows evaluation of the coagulation as a dynamic process. It provides detection of fibrinolysis, fibrinogen, platelets and plasma factors insufficiency and effect of heparine. The aim of our study was to appreciate the incidence of hyperfibrinolysis in those patients.
Method: Rotem analysis was done, after anesthesia induction, before any coagulation disorders correction. The usual coagulation parameters were noted. We realized Extem and Aptem test (aprotinine additional): fibrinolysis was recognize when CT-Extem>80s and CT Aptem>10% shorter than CT-Extem, CLI30<50%, and CLI60<85% corrected with Aptem test.
During one year we studied 53 patients (37 men, 16 women), mean age was: 54±12.8years. The liver diseases were: 23 alcoholic cirrhosis, 10 viral hepatitis, 4 biliary diseases, fulminant hepatitis 4, other 12.
Results: Among 53 patients, 8 (15%) presented an abnormal fibrinolysis: 5 child C, 2 child B and 1 child A. All the patients were treated with aprotinine or tranexamic acid. We found no relation between fibrinolysis incidence and Child status (p=0.65, χ^2) or MELD score (p=0.81, Anova). Regarding biological results of the patients before surgery, we found no relation between fibrinolysis and INR (p=0.3, Anova), platelets count (p=0.98, Anova), and fibrinogen dosage (p=0.13, Anova). The total blood loss was not related to hyperfibrinolysis (p=0.43, Anova). Before surgery, 22 patients received an antifibrinolytic treatment (14 without fibrinolysis), with no effect on the total blood loss (p=0.57, Anova). 50% of the patients Child C, received antifibrinolytic before surgery (10 vs 9) without difference on the total bleeding and the incidence of hyperfibrinolysis after reperfusion (2 vs 2)
Conclusion: Abnormal fibrinolysis is present in 15% of the patients undergoing liver transplant, not related to the liver disease severity, and the biological coagulation status. The ROTEM analysis seams to be helpful to diagnose and treat those patients.

P-464 NK-CELL CHIMERISM IS A UNIQUE FEATURE OF LIVER TRANSPLANTATION AND MAY MODULATE THE RECIPIENT'S IMMUNE RESPONSE AGAINST THE GRAFT

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Liver grafts have tolerogenic properties, as shown by low incidence of chronic rejection and the possibility to discontinue immunosuppressive medication in about 20% of liver transplant (LTx) recipients. We hypothesized that this unique property of liver grafts may be related to their high content of organ-specific NK cells. In the present study we determined whether hepatic NK-cells of donor origin migrate into recipients after clinical LTx, and characterized NK-cells that detach from human liver grafts.
Using antibodies that recognize donor HLA-alleles, we found that 1% – 8% of circulating NK-cells in LTx-recipients (n=13) are of donor origin for an average time of 15 days after LTx. In contrast, no NK cell chimerism was observed in renal transplant (RTX) recipients (n=6). NK-cells that detach from liver grafts were characterized using cells present in perfusion fluid obtained during routine vascular perfusion of liver grafts before transplantation. Perfusate mononuclear cells contained 31±9% NK-cells, of which 46±6% belonged to the CD56bright/CD16- subset, reminiscent of NK-cells present in human decidua and lymph nodes. Hepatic CD56bright NK-cells were highly activated (95±3% CD69+, versus 12±4% CD69+ of blood CD56bright NK cells; p<0.001), and had an increased perforin- and granzyme-content compared to their counterpart in blood. Purified hepatic NK-cells showed a two-fold increased capacity to kill MHC class I-devoid K562 cells compared to blood NK-cells, and both CD56dim and CD56bright hepatic NK-cells showed CD107a degranulation.
Conclusions: After clinical LTX, but not after RTX, donor NK cells migrate into the recipient. NK-cells that detach from liver grafts are enriched for CD56bright NK-cells, which are highly activated and cytotoxic. These donor-derived NK-cells may combat rejection of the liver graft by killing recipient Antigen-Presenting Cells and T-cells.

P-465 EARLY PREDICTION OF ACUTE OR CHRONIC ALLOGRAFT REJECTION IN FK506 TREATED RAT INTESTINE TRANSPLANT RECIPIENTS

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Early noninvasive rejection markers would greatly improve post-transplant monitoring after intestinal transplantation (ITx). Accordingly, we assessed the novel tolerance marker "tolerance associated gene 1" (TOAG-1) as early predictor of allograft rejection in a high responder rat model of ITx.
Methods: Intestines from Dark Agouti were transplanted into Lewis rats receiving single dose tacrolimus (TAC) (1, 3 or 5mg/kg; low/medium/high dose). Untreated recipients and non-transplanted/TAC treated animals served as controls. Grafts were recovered after 7, 14, and 45 days. PBMCs and graft tissue were analyzed by real-time RT-PCR on days 1, 3, 5, and 7 after ITx for TOAG-1, perforin, mannosidase, and CD3. Graft biopsies were subject to histopathology and immunohistology assessment.
Results: Naive controls, medium, and high dose treated recipients revealed long-term survival and only minor histological changes, whereas untreated and low dose recipients died 8-10 days after ITx due to severe acute rejection (score day 7: low vs medium/high dose; p<0.05). ITx survival was 50% in the medium and 100% in the high dose group after 45 days, which coincided with the extend of chronic allograft changes (p<0.001). The non-invasive marker TOAG-1 discriminated between non-rejectors in the high dose group (5mg TAC) vs. rejectors with 1mg and 3mg TAC, and controls (no TAC) by demonstrating significantly higher TOAG-1 gene expression on days 5 and 7 (0mg/1mg vs. 5mg ;p< 0.01; 3mg vs. 5mg; p<0.05). Perforin, CD3, and mannosidase failed to do so.
Along with the differences in histopathology, significantly higher numbers of graft infiltrating dendritic cells, macrophages, CD4+ and CD8+T-cells were detected in the rejecting groups.
Conclusion: Intestinal allograft rejection correlates with a significant early downregulation of TOAG-1. Monitoring of this gene may be beneficial for the prediction of acute and chronic allograft rejection.

P-466 A SIMPLIFIED FUNCTIONAL VENOPLASTY OF MIDDLE HEPATIC VEIN IN RIGHT LOBE GRAFT LIVER TRANSPLANTATION

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Aim: We have developed a simplified functional venoplasty. To evaluate efficacy of this procedure, we analyzed the surgical complications (short and long-term) and graft survival following living donor liver transplantation with right lobe graft (RLG) with middle hepatic vein (MHV).
Background: There is a trend towards complex venoplasty of MHV including redundant venoplasty using cryo-preserved vein grafts which needs total clamping of inferior vena cava (IVC) with/without veno-veno bypass.
Patients: From December 2004 to January 2009, forty-one patients (mean age 50.1 years old, mean MELD score 18.5) underwent living donor liver transplantation with RLG with MHV. The Mean GRWR was 0.99% and the mean ratio of remnant liver volume of the donor was 36.2%. The 12.5% of RLG needed the reconstruction of MHV depend on our criteria of graft selection during this study.
Methods: We selected RLG with MHV when the regional volume of both V5 and V8 drainage were greater than 40% of the total RLG. Right hepatic vein (RHV) was connected to MHV to make a common and then one simple venous patch taken from the explanted liver was anastomosed to the anterior wall of the common orifice in back table. The common orifice with an anterior patch was anastomosed to the stump of the recipient RHV in nearly end-to-side fashion with half clamping of IVC.
Results: Thirty-seven patients (90.2%) are alive both with good graft function and with good outflow of RHV and MHV without any treatment except one whose MHV was injured in second laparotomy of biliary reconstruction (the mean follow-up 1026 days).
Conclusion: In conclusion, a simplified venoplasty provides excellent short-term and long-term patency of MHV and end-to-side (short) anastomosis didn't hamper the patency of both RHV and MHV even when liver graft regenerated.

P-467 RESULTS OF LIVER TRANSPLANTATION IN ALCOHOLIC CIRRHOSIS: ARE THE SAME THAN WITH OTHER ETIOLOGIES?

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Introducction: Alcoholic cirrhosis is one of the most frequent indications for liver transplantion (LT) in Europe with good long-term results.
Objective: Analyze, if in our experience, the results of LT for alcoholic cirrhosis are the same than with other etiologies and look for risk factors for alcoholic recurrence.
Patients and methods: From January 2002 to December 2003 we perfomed 147 LT and we study 95 of them with three groups: A: alcoholic cirrhosis (28 patients); B: alcoholic+other ethiologies cirrhosis (20 patients);C: non-alcoholic cirrhosis (47 patients).Between the group B 70% were VHC+ and 44% in the group C.
Results: With a mean follow-up of 44.69±11.24 months 76 patients are alive (80.1%) with a mean survival time of 55 months and an 1 and 3 years actuarial survival of 95.8% and 92.9% respectively. Three patients recurrence the use of alcohol (8.8%). Between alcoholic patients (A+B group) there are more male rate (81.3% vs 61.5%, p=0.07), smokers (90.6% vs 45.2%, p=0.0001), with ascitis (71.1% vs 51.4%, p=0.08) mainly in alcoholic alone (83.3%), with encephalopathy (48.7% vs 1.6%, p=0.01), and lower rate of hepatocellular carcinoma (10.4% vs 25.5%, p=0.05). There are no differences in morbidity or mortality but the alcoholic patients need more transfusion (91.4% vs 80.6%, p=0.1). There are no differences in long-term mortality although is shorter in alcoholic patients (16.7% vs 23.4%). Liver disease recurrence is larger in alcoholic patients (28.6% vs 41%) with significance differences comparing the three groups (9.5% vs 57.1% vs 41%, p=0.008). There are no differences in mean survival or actuarial survival. There are no association between alcoholism recurrence and abstinence and there are no relation with long-term mortality.
Conclusions: Liver transplant for alcoholic cirrhosis get same results than other etiologies. Alcoholic recurrence is shorter than 10% and it is not correlated with abstinence time. Alcoholic patients are more smokers and have more ascitis and encephalopathy.

P-468 CONVERSION FROM TWICE-DAILY PROGRAF TO ONCE-DAILY ADVAGRAF IS STRAIGHTFORWARD IN STABLE LIVER TRANSPLANT RECIPIENTS

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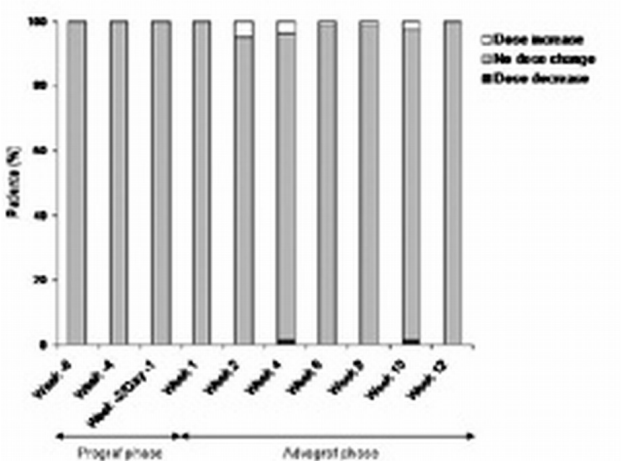
Purpose: Once-daily tacrolimus prolonged-release (Advagraf®) may improve adherence and, therefore, graft survival compared with the established twice-daily (Prograf®) formulation. This study assessed renal function and safety in stable liver transplant patients receiving Advagraf for 12 weeks after conversion from Prograf.
Methods: In this multicentre, open, crossover study, stable adult liver transplant patients (≥12 months post-transplant, on unchanged dose of Prograf ≥12 weeks) received Prograf for 6 weeks (Week –6 to Day –1) then were converted to Advagraf (morning dose; Weeks 1–12) on a 1:1 mg:mg basis. Patients remained on Advagraf for 12 weeks, with dose adjusted if trough levels deviated >20% or clinically indicated. The primary endpoint was change in steady-state creatinine clearance (CrCl, Cockcroft–Gault) between treatments. Secondary endpoints included tacrolimus dose and trough levels, concomitant immunosuppression use, and adverse events (AEs).
Results: Eighty patients without major protocol violations were evaluated (of 98 patients receiving study drug). Mean total daily dose was 0.05±0.03mg/kg throughout the Prograf phase, remained unchanged after conversion to Advagraf, and was maintained at that level to Week 12. Mean tacrolimus trough levels were 7.5ng/mL before conversion, 6.2ng/mL at Week 1 and 6.3ng/mL at Week 12. Following conversion, 86% of patients did not require any dose change (Figure) and no patients required a change in concomitant immunosuppression. At Week 12, 51% of patients were receiving Advagraf monotherapy. Mean CrCl was 85.7 and 85.5mL/min for Prograf and Advagraf phases, respectively (relative mean difference –0.0%; 95% CI –1.4%, 1.3%). AEs reflected the known profile for tacrolimus. Arterial blood pressure improved significantly from Day –1 to Week 12 (Table).
Conclusions: Conversion of stable liver transplant patients from Prograf to a once-daily Advagraf regimen is straightforward, well tolerated and renal function is well maintained.

Change in mean blood pressure between Advagraf (Week 12) and Prograf (Day -1) (per-protocol set)

	Mean (standard deviation)		Mean difference (95% confidence intervals)
	Prograf (Day -1)	Advagraf (Week 12)	
ABP (mmHg)[†](n=84)	101.9 (9.0)	100.0 (8.7)	-2.0 (-3.4, -0-5) p=0.0084
SBP (mmHg) (n=84)	138.0 (13.9)	136.0 (13.5)	-2.0 (-4.0, -0.1)
DBP (mmHg) (n=84)	83.9 (7.7)	81.9 (7.1)	-2.0 (-3.4, -0.5)

ABP, Arterial blood pressure; SBP, Systolic blood pressure; DBP, Diastolic blood pressure.
[†]Derived from 24-hour ambulatory blood pressure monitoring

Figure: Proportion of patients requiring a dose change during the Prograf and Advagraf treatment phases (N=80)



P-469 ADULT LIVING-DONOR LIVER TRANSPLANTATION WITHOUT GRAFT COLD PRESERVATION; NON-RANDOMIZED PROSPECTIVE STUDY

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Purpose: The aim of this study was to evaluate the outcome of transplant patients receiving liver graft without cold storage in living donor liver transplantation.
Methods/Materials: 40 adult patients who underwent living-donor liver transplantation from April 2008 to December 2008 were included in this study. Living-donor liver transplantation without cold preservation (n=20) was performed as timely matching both donor and recipient operation. In this group, liver graft was only washed with 700cc of HTK solution at room temperature and directly transplanted to the recipient without bench procedure. In both groups, warm ischemic time was under 60 minutes.
Biochemical parameters before operation and post-reperfusion 1, 3, 12, 36, 60 hours, 7 days and 1 month were analyzed. Clinical outcome such as post-transplant biliary complication were also studied.
Result: Post-reperfusion 3-hour CRP and 1-, 3-hour post-reperfusion CPK levels were significant lower in the no cold preservation group (p= 0.048, 0.041, 0.004 respectively). LDH 1 month after transplantation was also significantly lower in the no cold preservation group (p=0.008). There were no significant differences between the cold preservation and no cold preservation groups when serum total bilirubin, AST, ALT, ammonia, prothrombin time, creatinine level at each sampling time were compared. In no cold preservation group, AST and ALT levels at reperfusion 30, 60 hours were lower than the other group, however, it did not reached statistically significance (Fig 1 & 2). Incidence of biliary complications was not influenced whether or not cold preservation method was used.
Conclusion: In adult living-donor liver transplantation, some of the biochemical parameters after no cold preservation of liver graft were better; however, clinical outcome did not differed. No cold preservation method may be a way to minimize graft injury in the living-donor liver transplantation.

P-470 ROLE OF LIPOCALIN 2/LCN2 IN LIVER REGENERATION

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Purpose: Small-for-size syndrome is a limiting factor in living donor and split liver transplantation. Maximization of liver regeneration represents a promising strategy to overcome the risk of liver failure due to insufficient liver mass in either the donor or the split graft recipient. Growing evidence suggests that lipocalin 2 has a role in regenerative processes.
Methods: To establish the role of lipocalin 2 in liver regeneration $lcn2^{+/+}$, $lcn2^{+/-}$ and $lcn2^{-/-}$ mice were subjected to 2/3 partial hepatectomy. Hepatic proliferation was measured by BrdU and PCNA immunohistochemistry. Hepatic lcn2 expression was analyzed by qRT-PCR and western blots. Serum levels of lcn2, Il-6, and TNF-α were determined by ELISA.
Results: Hepatic regeneration in $lcn2^{+/+}$ mice was analyzed at 24, 48, 72 and 96h after partial hepatectomy. The peak of hepatic proliferation as indicated by the number of BrdU- and PCNA-positive cells was confirmed to be at 48h post surgery.
Analysis of hepatic lcn2 expression showed a 140-fold up-regulation only 24h after liver resection in $lcn2^{+/+}$ animals with a stepwise reduction during the observation period (48h 15.7-fold, 72h 5.5-fold, 96h 5.8-fold). Western blots confirmed significant lcn2 protein over-expression 24h after partial hepatectomy. Also, serum lcn2 levels were significantly elevated upon liver resection.
To determine the biological relevance of lcn2 induction on liver regeneration, hepatocyte proliferation was analyzed in $lcn2^{+/-}$ and $lcn2^{-/-}$ mice 48h after partial hepatectomy. The number of BrdU- and PCNA-positive cells did not differ significantly between the groups. However, $lcn2^{-/-}$ animals exhibited a significantly elevated baseline liver regeneration (6.6-fold $lcn2^{-/-}$ vs $lcn2^{+/+}$, $p<0.05$).
Conclusion: Up-regulation of lipocalin 2 after murine partial hepatectomy is striking but without significant impact on hepatocyte proliferation. Our results imply that lcn2 induction upon liver resection either constitutes a redundant pathway or simply displays an epiphenomenon.

P-471 IMPACT OF LEFT LOBE GRAFT ON ADULT-TO-ADULT LIVING DONOR LIVER TRANSPLANTATION

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Background/Aim: Operative mortality for a right lobe (RL) donor in adult-to-adult living donor liver transplantation (LDLT) is estimated to be high as 0.5-1%. To minimize the risk to the donor, left lobe (LL)-LDLT might be an ideal option in adult-to-adult LDLT. The aim of the study was to assess the feasibility of LL-LDLT in adult patients.
Patients: Between February 2005 and February 2009, fifteen consecutive LDLTs were performed at Tokushima University Hospital, Tokushima, Japan. Of the 15 adults, 12 patients underwent LDLT using LL grafts with (n=10) or without (n=2) the caudate lobe. Four of 7 patients with HCC had HCC beyond the Milan criteria. A case with ABO-incompatible LDLT was included.
Results: The mean graft weight of LL grafts was 458g (range 385-520g), and a graft volume-to-recipient standard liver volume (GV/SLV) was 39% (range 33-47%). Graft-to recipient weight ratio (GRWR) was 0.77% (0.61-0.91). Seven of 12 patients (58%) had <40 GV/SLV or <0.8 GRWR value. Postoperative complications were dissection of hepatic artery (n=1), sepsis (n=1) and small-for-size syndrome (n=1). One patient with HCC had recurrence in the graft 3 years after LDLT and partial hepatectomy was performed. The overall 1- and 3-year patient survival rates in LL-LDLT were 100%, which were superior to those of RL-LDLT, though follow-up period was not long.
Conclusion: Adult-to-adult LL-LDLT was found to be feasible without affecting patient and graft survival rates. Further utilization of LL grafts should be undertaken to keep the chance of donor morbidity and mortality minimal.

P-472 STRATEGIES FOR PREVENTING THE SMALL-FOR-SIZE SYNDROME IN LIVING DONOR LIVER TRANSPLANTATION: A CLINICAL STUDY OF 39 CASES

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Introduction: To present our experience of LDLT with 39 cases, and propose several strategies for preventing the small-for-size syndrome.
Methods: From May, 2005 to Dec, 2008, 39 LDLTs were performed in our centre, including 22 cases of right lobe graft without MHV, 10 cases of right lobe graft with MHV and 1 cases of LDLT using dual graft. The most common indications were end-stage liver disease due to HBV (42.9%) and HCC (36.7%). All the recipients and the donors underwent 3D CT volumetry to ensure the safety of donors. We measured the portal venous pressure by puncturing the blood vessels on the major omentum. The splenic artery ligation (SAL) was performed when the pressure was higher than 20mmHg (27cm H2O).
Result: All donors' remnant liver volumes were over 35% of the total liver volume. There was no donor mortality. No serious complications occurred after the operation and the median hospital stay was 11.7 ± 1.7 days. Of the 39 recipients, with a median follow-up period of 13.8 ± 1.7 months in adult and 18.9 ± 2.3 in child, the actual survival rate was 78% and 87.5%. 12 (30.7%) experienced complications that required treatment and 3 (7.7%) died within 3 months post operation. 14 qualified recipients were subject to SAL. And there was significant difference between two groups in decreasing of PVP after SAL, but there was no significant difference between two groups in PVF. The SAL can significantly reduce spleen volume, the spleen volume decreased by 30% after three months.
Conclusion: The study demonstrates that LDLT can be done safely with good results for a variety of liver diseases. Several strategies were already reported to prevent the occurrence of SFSS. It is hoped that as the pathogenesis of SFSS being continuously studied, improved outcomes in LDLT will be seen.

P-473 MARGINAL ORGANS DO NOT IMPAIR LIVER ALLOGRAFT RECIPIENT ONE YEAR OVERALL AND ORGAN SURVIVAL

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Background: The number of patients awaiting LT is increasing with a growing shortage of donors. A large number of organs allocated are marginal organs (MO). They have to be accepted to be able to overcome organ shortage
Patients and methods: Between 2003 and 2007 a total of 179 OLTs were performed in 160 patients. MO were defined as organs showing at least one of the following donor attributes in accordance to the guidelines for organ transplantation of the DAEK: donor age over 65 years, sodium over 165mmol/L, BMI over 30, histologic steatosis over 40%, ICU+ventilation over 7d, GOT or GPT 3-fold elevated, bilirubin over 3mg/dl. MO-recipients were compared with a group of non-marginal organ (NMO)-recipients. The primary end-point was one year survival. Secondary end-points were 1-year graft survival, number of retransplantations and acute rejections, biliary complications and liver function after one year.
Results: Ninety-eight patients received a MO and 62 received a NMO. Demographic data and MELD scores were similar in both groups. One year survival was 81% in the MO and 86% in the NMO group revealing no significant differences between groups (p=0.546) and overall survival was 74% for the MO and 77% for the NMO-group (p=0.810) after a median follow up of 993d (371 to 2083d). One year graft survival was MO 75% vs. NMO 81% (p=0.491), acute rejections MO 20% vs. NMO 22% (p=0.918) and proportion of retransplantations between 2003 and 2008 in MO: 13% vs. NMO: 10% (p=0.748) did not reveal significant differences between groups. Biliary complications MO 36% vs. NMO 21% showed a trend towards increased incidence in the MO-group (p=0.066)
Conclusion: MO do not impair one year overall and organ survival but result in an increased number of biliary complications.

P-474 TRANSARTERIAL CHEMOEMBOLIZATION UTILITY AS A BRIDGE TO LIVER TRANSPLANT FOR PATIENTS WITH HEPATOCELLULAR CARCINOMA DURING THE WAITING LIST

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Introduction: Ttransarterial chemoembolization (TACE) increase survival and decrease tumor recurrence after LT for HCC.
Objective: To analyze the relation of TACE with long-term results.
Patients and method: From 1986 to Dec,06 we performed 151 LT in patients with HCC, 46 incidental were excluded; so we studied 105 patients. Only 63 patients (60%) received a TACE before LT.
Results: 63.1% received one TACE, 16p two, 6p three and one patient four. Main chemotherapy agent was adriamycin (80.6%) and Ivalon as embolizant agent (53p). Mean AFP with TACE was 222.96 vs 1693.9;p=ns, with an AFP after TACE of 203.74 ng/ml. Mean waiting time was shorter between TACE (4.8 vs 8.1 months;p=0.008), performing TACE in 44% of the patients with <3 months listed vs 73.3% with >6m listed (p=0.02). 81% (51p) had radiological

response. In the explant, 65.1% had tumor necrosis (34.1% with necrosis of 100%), vs 12% (p=0.0001). The two groups were homogeneus in Milan criteria and vascular invasion. Although there are not differencees in recurrence (22.2% without TACE vs 21.7% with TACE) nor in the recurrence pathway, the recurrence was later with TACE (62.9% >1year vs 25%); and anyone patient received treatment of the recurrence between the patients without TACE and 11/13 with TACE (p=0.027). 65% of the patients with TACE are alive vs 47.2% (p=0.087), and 60% are without recurrence vs 47.2% (0.2). There are not differencees in the 5-y actuarial survival 55.8 vs 64.3%, p=0.38 nor in the disease-free survival, 56.5% vs 62.3%, p=0.7. Tumor recurrence was the main mortality cause between the two groups.
Conclusions: With TACE there is not a decreasin in tumor recurrence nor an increasing in survival or disease survival. Tumor recurrence is later and with more treatment probabilities.

P-475 FIRST CASE OF MALIGNANT TRANSFORMATION IN LIVER ADENOMATOSIS TREATED BY LIVING DONOR LIVER TRANSPLANTATION

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Background/Aims: Liver Adenomatosis (LA) is a rare benign liver disease with unclear pathogenesis, characterized by multiple hepatic adenomas. Patients admitting oral contraceptive or affected by glycogen storage disease type I show a higher risk of developing LA. The management of LA remains controversial. We herein present the first case of LA treated by Living Donor Liver Transplantation (LDLT).
Case: A 48-yo woman came to our attention due to abdominal pain. After radiological examination throughout ultrasound, computed tomography scan and magnetic resonance imaging, multiple liver adenomas were detected. The patient underwent radical surgery with right hepatic resection and segment II nodulectomy. Thirty four months after surgery the patient developed multiple liver nodules with suspicion of Hepatocellular Carcinoma degeneration in two of them. In view of the not-indication for re-resection, the patient underwent LDLT. The definitive histological analysis confirmed a liver parenchyma substituted by multiple adenomas; moreover, two of those nodules (2.5 and 1.9 cm) appeared not capsulated, with infiltrative margins, referable to well differentiated HCC. At 45 months from LDLT, the patient is alive and disease free.
Conclusions: We consider surgical resection as the first line of treatment for nodules at high risk of complications in LA. Close follow-up is mandatory for rapid detection of neoplastic degeneration. LDLT is indicated in cases where resection is not possible and may offer optimal results in view of the absence of portal hypertension and shorter waiting list time. Moreover in this kind of patients with low MELD score and transplant indications debatable at best, LDLT guaranties a fast track transplant without damaging the other patients in the ordinary waiting list for transplantation.

P-476 SMALL DIFFERENCE IN INR MAY YIELD A SIGNIFICANT IMPACT ON PRIORITIES OF PATIENTS LISTED FOR LIVER TRANSPLANTATION

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Priority for liver transplantation is currently based on the Model for Endstage Liver Disease (MELD) score, however it was discovered that different laboratory methods may introduce significant variation in the MELD score. **Aim:** To assess in detail the contribution of INR difference for the MELD score in interlaboratory variability and for the order the complete waiting list.
Methods: The samples of 92 cirrhotic patients were measured on five different systems combining three coagulometers and three thromboplastin products to determine variation in INR and MELD score.
Results: Among the five systems, the range in INR was found 0.90–2.81 and the calculated MELD score varied between 12–24. The INR differences among the first 4 systems varied between 0 and 0.2 resulting in a MELD score difference of 0-2. The MELD scores of the 92 patients varied only among 10 possible integers so that normally 2-10 patients shared the same MELD value respectively. In some cases 1 MELD score difference resulted in even a 10 positions of super positioning on the waiting list. Including one more system (mechanical vs. optical) into our investigations even 5 MELD score difference could be achieved. Supposing an extreme situation where one patient competes with his/her lowest-, all the others with their highest possible score and vise versa the difference may be even 20 positions, overturning the complete waiting list. Same measurements were carried out using ISI values calibrated by plasma of patients with cirrhosis (chirr) (F.Trotter). The instrument and reagent dependence of $INR_{(chirr)}$ and $MELD_{(chirr)}$ were less significant than applying traditional ISI.
Conclusion: The substantial interlaboratory differences in MELD score have profound clinical consequences. The patients may increase their chance of a liver transplantation by selection of a different laboratory.

P-477 MORPHOLOGICAL FEATURES OF ADVANCED HEPATOCELLULAR CARCINOMA AS A PREDICTOR OF SUCCESSFUL DOWNSTAGING AND LIVER TRANSPLANTATION: AN INTENTION-TO-TREAT ANALYSIS

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Loco- regional therapy (LRT) to down stage advanced Hepatocellular carcinoma (HCC) to meet Milan criteria for LT has been shown to achieve good outcome in selected group of patients. However, factors that predict successful treatment have not been clearly identified. In this retrospective cohort study we analyzed our experience with multimodal LRT in down staging advanced HCC prior to LT to determine the factors that predict successful therapy. Thirty two patients with advanced HCC that exceeded the Milan and UCSF criteria for LT were considered for LT and listed upon successful down staging of their tumors. Treatment was successful in 18 (56.2%) patients (group I). However, we were unable to down stage the tumors in 14 patients (group II). There were no intergroup difference in regard to patient's characteristics, and type and number of treatment each group received. However, the mean value of AFP, and number of patients with infiltrative type of tumors were significantly higher in group II compared to group I ($P<0.048$; $P=0.0001$, respectively). The median survival was better in group I compared to group II (42 vs 7 months, respectively $P=0.0001$). Fourteen patients (43.3%) underwent LT. After a median follow-up of 35 months (1.5-50) following LT, 2 patients developed recurrence (14.2%). The Kaplan- Meier survival rate after LT at 1- and 2- years was 92% and 75% respectively. Expanding type of HCC was found to be a significant factor in predicting successful down staging and better outcome in univariate and multivariate analysis regardless of the size and number of tumors. Our study suggests that morphological characteristics of HCC may serve as a surrogate marker for good response, and better outcome following down staging and LT in patients with advanced HCC.

P-478 GRADE AND TYPE OF DECEASED DONOR LIVER STEATOSIS VARIABLY IMPACTS ON GRAFT AND RECIPIENT OUTCOMES

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Purpose: The outcomes of liver transplantation with steatotic donor allografts vary depending on the presence of either macrovesicular (Ma) or microvesicular (Mi) steatosis. This study examines liver transplant outcomes in our unit, versus the type and grade of donor steatosis (S)
Methods: Record review of 297 adult liver transplant procedures 1/2001-12/2007, and donor liver offers. Data obtained included donor information, recipient and graft outcomes. Donor liver biopsies were regraded for steatosis by an experienced histopathologist. Outcome data were analysed based on presence MaS or MiS and grade (mild <30%, moderate 30-59%, severe 60+%). Statistics were by SPPS.
Results: Biopsies were available for 256/297 (86%) of liver allografts, 184/256 (72%) had steatosis of which 114 (62%) had MiS [68 mild; 22 moderate, 24 severe] and 70 (38%) had MaS [59 mild, 7 moderate, 4 severe]. In 65/70 (93%) of allografts with MaS, MiS was present. Donor BMI was higher for mild MaS [p=0.0003] and severe MaS [p=0.0001] allografts versus allografts without steatosis. Primary non function [p=0.002], early renal failure [p=0.040] and retransplantation [p=0.012] were associated with severe MaS. Early biliary complications were associated with moderate MaS [p=0.039]. Graft loss at 3 months (75%) was associated with severe MaS [p=0.005]. Isolated MiS regardless of grade did not impact on early allograft outcomes. During the same period, 12 donor offers (9 interstate), and 41 donor livers (10 interstate)

were declined due to concerns re steatosis. For donor livers declined the mean donor age of 52.5 (27-71) years was greater than for allografts with no steatosis [p=0.0001] or any grade of MiS [p<0.02].
Conclusions: MiS is common in donor liver biopsies and frequently coexists with MaS. The presence of moderate/severe MaS is associated with varying inferior early graft outcomes. These outcomes partly reflect donor liver selection.

P-479 PRE AND INTRA-OPERATIVE PREDICTORS OF THE NEED FOR RENAL REPLACEMENT THERAPY AFTER LIVER TRANSPLANTATION

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Recipients with acute renal failure (ARF) requiring renal replacement therapy (RRT) immediately after liver transplantation (LT) have been reported to have a higher mortality. The objective of this study is to evaluate pre and intra-operative risk factors for ARF early after LT. One hundred four adult LT recipients without pre-transplant renal dysfunction from September 2005 to July 2008 were enrolled in this study. Pre and intra-operative clinical data were retrospectively reviewed. The CRRT group were patients who needed CRRT within 3 days after LT. Among 104 LT recipients, 70 (67.3%) were living donor and 34 (32.7%) were deceased donor LT. There were 79 (76.0%) male and 25 (24.0%) female recipients with a mean age of 51.4±7.7 years. Hepatocellular carcinoma was the most common cause for transplantation (n=44; 44.2%). Seventeen (16.3%) recipients were included in the CRRT group. MELD score >25, intra-operative fluid intake >15 liter, and transfusion >2.5 liter, and hypotensive event (systolic pressure checked less than 80 mmHg in two series by 5 minutes interval) were significant risk factors of post-transplant CRRT (p=0.002, 0.003, 0.045, 0.026, and 0.003 respectively). However, pre-operative high serum creatinine level (≥1.5 mg/dl) didn't show any significance (p=0.095). On multi-variate analysis, the MELD score was an independent risk factor for ARF requiring CRRT (p=0.004, Odd ratio=0.850, 0.760-951 in 95% confidence interval). During the early (within 1 month) period, 8 (7.7%) post-operative mortality cases occurred. The early mortality rate in the CRRT group (5/17, 29.4%) was significantly higher than those of the non-CRRT group (3/87, 3.4%) (p=0.003). To summarize, pre-transplant recipient status that was represented by MELD score, not pre-transplant renal status, is an independent risk factor for developing early ARF requiring CRRT after LT.

P-480 CAN WE APPLY UCSF CRITERIA BY PRE-TRANSPLANT RADIOLOGIC IMAGING AS SELECTION CRITERIA FOR LIVER TRANSPLANTATION IN HEPATOCELLULAR CARCINOMA?

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Despite the high sensitivity of pre-transplantation radiologic study, an adequate correlation between the radiologic and pathologic stage of hepatocellular carcinoma (HCC) has not been obtained. The objective of this study was to verify the clinical validity of a selection criteria by pre-transplant radiologic study. Fifty-one recipients with HCC who underwent liver transplantation from September 2005 to May 2009 were retrospectively reviewed. All recipients underwent a dynamic liver computed tomography (CT) at least 1 month before transplantation and was reviewed by the same radiologist. We compared the pre-transplant radiologic stage with explanted liver pathologic findings. Grouped by pre-transplant criteria of HCC for liver transplantation, 39 recipients (76.5%) met the Milan criteria and 4 recipients (7.8%) were over the UCSF criteria. Eight recipients (15.7%) were grouped as over Milan/below UCSF. Pre-transplant radiologic stage was underestimated in 21/51 (41.2%) and overestimated in 12/51 (23.5%). The accuracy of pre-transplant radiologic stage were compared, 13 among 39 (33.3%) recipients of below Milan group were underestimated, while 6 among 8 (75.5%) recipients of over Milan/below UCSF group were underestimated (p=0.047)(Table). Such disparities between pre-transplant radiologic staging and pathology were mainly caused by increased tumor number (9/39; 23.1%) in the below Milan group, but by vascular invasion (4/8; 50.0%) in the over Milan/below UCSF group. Total tumor necrosis was obtained in 5 recipients by pre-transplant trans-arterial chemoembolization (TACE). However, TACE did not have a significant influence on down-staging the pathologic stage (p=0.535) when compared to the radiologic stage. These findings imply that pre-transplant radiologic staging does not correlate with the pathologic staging in HCCs over the Milan criteria. Therefore, the application of the UCSF criteria in pre-transplant radiologic findings as a patient selection criteria for liver transplantation is not desirable.

		Pathologic staging							Total
		pT0	pT1	pT2	pT3a	pT3b	pT4a	pT4b (vascular invasion)	
Pre-transplant radiologic staging	T1	3	6	5	0	1	0	3	18
	T2	2	6	9	0	0	4	0	21
	T3a*	0	0	1	1	1	1	4	8
	T3b	0	0	0	0	0	1	0	1
	T4a	0	0	0	0	0	2	1	3
	Total	5	12	15	1	2	8	8	51

*UNOS T3 lesion that meets UCSF criteria is temporarily classified as T3a

P-481 DOES VENOUS RECONSTRUCTION OF THE ANTERIOR SECTOR AFFECT ON GRAFT REGENERATION IN LIVING DONOR RIGHT LOBE LIVER TRANSPLANTATION?

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The purpose of this study is to assess the correlation between MHV reconstruction and graft regeneration. From September, 2005 to April, 2008, there were 67 cases of adult LDLT and 63 cases were enrolled in this study. Among them, MHV reconstruction was performed in 47 cases (group R; 74.6%) and

Demographic characteristics

Characteristics	Group R, MHV reconstruction (N=47)	Group EL, Extended right lobe graft (N=13)	Group NR, No reconstruction (N=3)	p-value
Recipient				
Weight (kg)	63.81±8.03	67.31±5.51	54.33±17.21	0.046
BMI (kg/m^2)	23.10±2.22	23.60±2.05	21.79±3.43	0.444
Donor				
Weight (kg)	65.96±8.53	54.62±5.91	58.67±1.16	<0.0001
BMI (kg/m^2)	22.45±2.40	20.69±1.55	21.74±1.04	0.048
GRWR (%)	1.29±0.28	1.06±0.13	1.57±0.62	0.007

MHV, middle hepatic vein; BMI, body mass index; GRWR, graft to recipient weight ratio. Values are mean ± standard deviation.

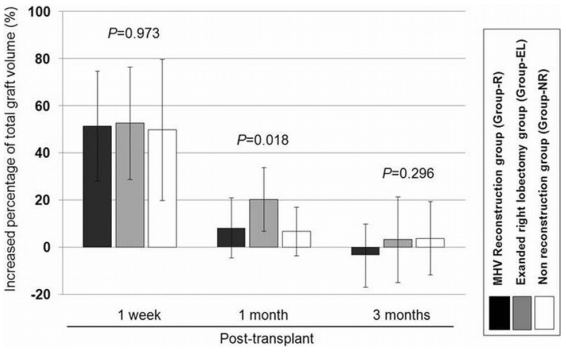

Figure 1. Increased percentage of total graft volume in each group.

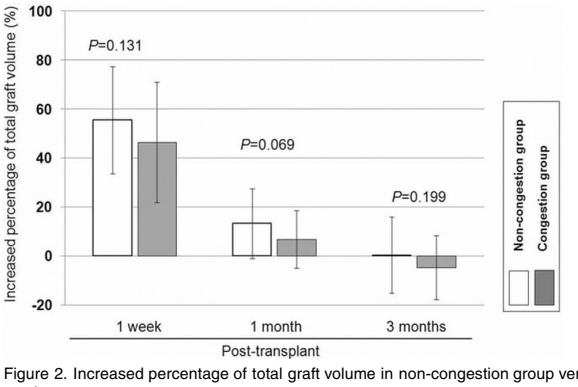

Figure 2. Increased percentage of total graft volume in non-congestion group versus congestion group.

extended donor right lobectomy in 13 cases (group EL; 20.6%). No MHV reconstruction was done in 3 cases (group NR; 4.8%) (table 1). In group R, V5 in 18 cases (28.6%), V8 in 1 case (1.6%) and both in 28 cases (44.4%) were reconstructed. Anterior sector congestion was detected in 22 cases (46.8%) of group R, 2 (15.4%) of group EL and 2 (66.7%) of group NR respectively. There were no significant differences of the graft volume growth rate between each group at post-transplant period (figure 1). Also, there was no significant difference between the congestion group and the non-congestion group (figure 2).
Laboratory findings did not show statistical differences in each group. We concluded that MHV reconstruction may not be mandatory for graft regeneration when the GRWR is large enough.

P-482 THE OUTCOME OF LIVER TRANSPLANT RECIPIENTS WITHOUT RENAL SUPPORT DURING LIVER TRANSPLANTATION

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Purpose: Renal dysfunction is a very common finding in patients undergoing liver transplantation (LT). Recently, intraoperative renal support in the form of continuous renal replacement therapy (CRRT) was employed during LT for patients with renal dysfunction and demonstrated favorable outcomes. The aim of this study is to evaluate outcomes of LT recipients with renal dysfunction without intraoperative renal support.
Method: We performed a retrospective review of adult patients (age $>$18 years) receiving LT between January 1, 1996 and January 11, 2008 at our hospital. Renal dysfunction was defined as an acute rise in serum creatinine to $\geq$1.4 mg/dL. Demographic and perioperative clinical data including renal recovery and survival were collected (Table 1).

Table 1. Demographics and preoperative characteristics

Preoperative feature	n=127
Age	47.81 (8.51)
Male sex (%)	105 (82.7)
Proportion of donor	
Cadaveric donor	30 (23.6)
Living donor	97 (76.4)
Etiology of primary liver disease (%)	
HBV related liver disease	93 (73.2)
Fulminant hepatic failure	13 (10.2)
Alcoholic liver disease	8 (6.3)
HCV related liver disease	6 (4.7)
Others	7 (5.5)
Receiving renal support	10 (7.87)
MELD score*	35 (24-41)
Child-Pugh score	11.89 (1.54)
Child-Pugh class C (%)	90.6
ICU admission (%)	21.3
Mechanical ventilation (%)	11.0
Vasoactive agent (%)	11.8
Bilirubin (mg/dl)*	29.2 (5.6-41.7)
Platelets ($\times 10^3$/dl)*	56 (37-86)
PT (INR)*	2.51 (1.97-3.45)
Hemoglobin (g/dl)	9.61 (1.56)
Sodium (mmol/l)	130.8 (8.7)
Potassium (mmol/l)	4.24 (0.73)
Serum creatinine (mg/dl)*	1.7 (1.32-2.40)
Estimated GFR (ml/min/m^2)*	40.5 (24.7-63.2)
Serum urea (mg/dl)*	4.7 (2.9-7.3)

Data expressed as mean (standard deviation) or *median (interquartile range)

Result: Of 575 LT recipients, 127 patients (22%) had renal dysfunction. CRRT was required in 45 (35.4%) after LT for median (interquartile range; IQR) of 9 (5-16) days. Of these, 17 (37.8%) were transitioned to intermittent hemodialysis for a median (IQR) of 15 (8-31) days. Renal recovery defined as renal support independence occurred in 77% of survivors by 1 month and 97% of survivors by 1 year. The mean (standard deviation) estimated GFR (eGFR) was 66.29 (21.83) ml/minute/m^2, with 40.35% having an eGFR $<$60 ml/minute/m^2 at 1 year. Survival was 90.6% at 1 month and 78% at 1 year.
Conclusion: Intraoperative renal support may be a valuable adjuvant therapy for those with preoperative renal dysfunction; however, it has many complications. Results of our study suggest that the risk and benefit of intraoperative CRRT during LT needs further evaluation.

P-483 RESULTS OF LIVER TRANSPLANTATION (LT) FROM CONTROLLED DONATION AFTER CARDIAC DEATH (DCD) DONORS: A SINGLE CENTER EXPERIENCE

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Introduction: DCD donors have been proposed to partially overcome the organ donor shortage. DCD-LT remains controversial, with reported increased risks of graft failure and ischemic type biliary tract lesions. The authors retrospectively reviewed their experience with DCD-LT in a 6-year period.
Patients and methods: 24 DCD-LT were performed from 2003 to January 2009. All DCD procedures were performed in operative rooms. Mean donor age was 54 years. Most grafts were flushed with HTK solution. Allocation was mostly locally centre-based. Mean DCD warm ischemia was 19.3 min. Mean follow-up was 19 months. Several donors', recipients' and surgical characteristics were correlated with peak transminases (AST) and total bilirubin.
Results: Mean MELD score at LT was 15. Mean cold ischemia was 288 min. Mean peak AST was 2,917 U/L. Mean peak bilirubin was 55.6 mg/dL. One-, 12- and 24-month patient and graft survivals were 100%, 93.7% and 86%, respectively. These results were not different from the results of regular LT performed in the same period. No patient underwent re-LT and there was no PNF. Causes of death were sarcoma (2 cases) and recurrent HCC (1 case). Three patients developed biliary complication: one fistula requiring hepaticojejunostomy, and two successfully managed by endoscopy and/or hepatojejunostomy. No patient developed intrahepatic ischemic bile ducts. There was no correlation between peak AST and the different donor factors, including age. There was a marked trend (p=0.06) between peak AST and length of CI. There was no correlation between peak AST and bilirubin, and length of DCD warm ischemia.
Discussion: In this series, DCD-LT appears to provide interesting results. Short cold ischemia and recipient selection may be the keys to good outcome in DCD-LT, in terms of graft survival and ischemic-type biliary lesions.

P-484 QUICK LINKER DEVICE PROVES EFFECTIVE TO AVOID WARM ISCHEMIA DAMAGE DURING ORTHOTOPIC LIVER TRANSPLANTATION IN RAT

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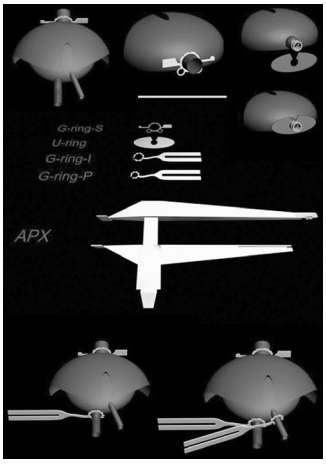
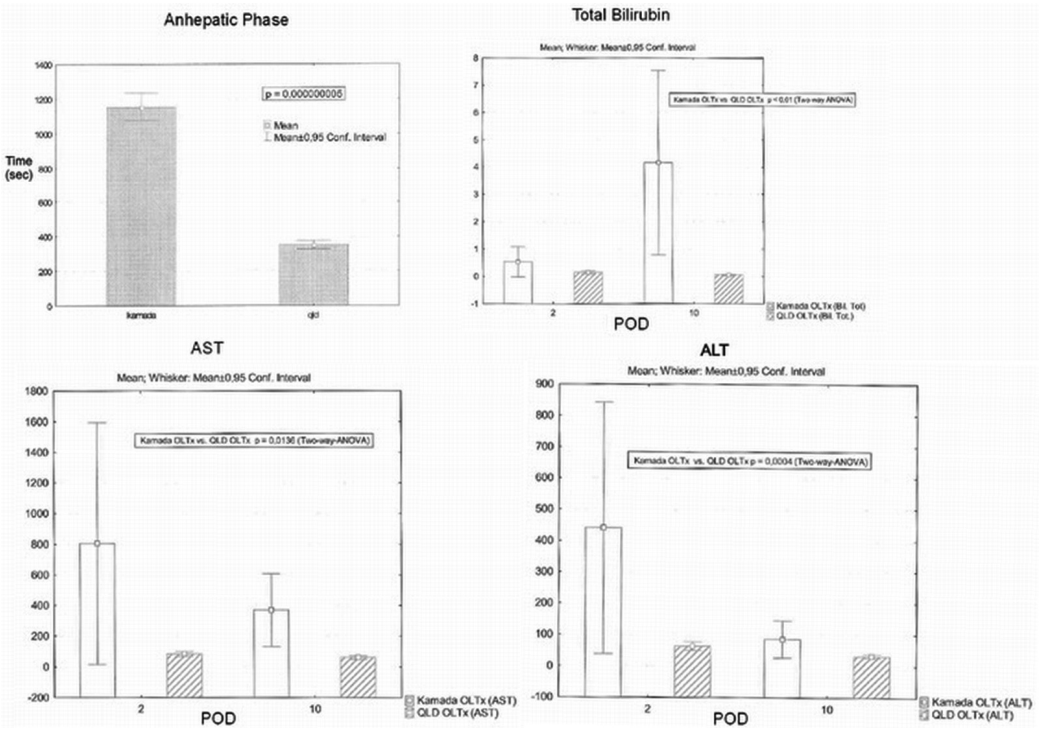
Background: The clinical success of liver transplantation is founded upon years of experimental research. Since Kamada and colleagues developed the "two-cuff" technique, the rat has become the best model for extensive investigations. Although the Kamada technique is technically complex and not easy to master, it is still the mainstay of orthotopic liver transplantation (OLT) in rodents. In 2008 we developed a simpler modified "two-cuff" version of this technique that facilitates anastomosis and markedly reduces implantation time. Furthermore, in this latest work, we investigated on how such improvement can influence warm ischemia damage
Methods: Ten male Lewis rats (group 1, donors n=10, recipients n=10) underwent liver transplantation using the Quick-Linker system (designed and man-





Abstract P-484 – Figure 1

ufactured by our group), while 10 male Lewis rats (group 2) underwent liver transplantation using Kamada technique.
Postoperative survivals, warm ischemia times, ALT, AST and Bilirubin levels were measured for comparison between the groups (on POD 2 and 10)
Results: Survival at posoperative day 14 was 100% for both groups. Warm ischemia times were always inferior to six minutes and superior to 15 minutes for group one and two respectively. Liver function was completely preserved in group one rats only.
Conclusions: The Quick-Linker technique significantly shortens warm ischemia time, completely avoiding graft damage during reimplantation. It can be then considered the most reliable option for microsurgeons looking for quick results, high success rates and instant animal recovery.

P-485 DUAL GRAFT LIVER TRANSPLANTATION USING ABO-COMPATIBLE AND ABO-INCOMPATIBLE GRAFTS COMBINATION TO OVERCOME SMALL-FOR-SIZE GRAFT SYNDROME AND ABO BLOOD BARRIER

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Dual graft liver Transplantation using ABO-Compatible and ABO-Incompatible grafts combination was designed to overcome ABO-blood barrier and graft size mismatch in adult-toadult liver transplantation.
Case 1: The patient was 40-old male and HBV-LC with HCC patient. MELD score was 9. The blood type of recipient was A. First donor was 35-old female and his wife. The blood type was AB. The anti-B antibody titer was 1:16. We used rituximab (375mg/m^2) and performed plasma pheresis once on preoperative 1 day. The estimated volume of right liver of donor was 520cc and the calculated GRWR was 0.54% if we utilize right liver only from his wife. Therefore, we got the lateral section from cadaeveric donor whose blood type was identical and performed dual graft liver transplantation. Actual GRWR was 1.13%. He experienced no episode of humoral rejection and was recovered without any surgical complication. He is doing well now, postoperative 2 months.
Case 2: The patient was 51-old alcoholic-LC male patient. MELD score was 13. The blood type of recipient was O. First donor was 25–old male and his son. The blood type was A. The anti-A antibody titer was 1:64. In this case, we also used rituximab and plasma pheresis. Because anticipated remnant left liver volume of his son was 25.7% of total liver volume, we should select left lobe graft and estimated GRWR was 0.46. Therefore we performed dual graft LDLT by using the additional graft from his daughter whose blood type was identical with recipient. In 2nd donor, we only procured laterl section because ICG R15 was over than 50%. He also experienced no episode of humoral rejection and surgical complication, neither. He is doing well now, postoperative 1 month.

P-486 EARLY PREDICTORS FOR THE DEVELOPMENT OF HEPATITIS-C-ASSOCIATED LIVER GRAFT FIBROSIS

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Background: The inevitable persistence of the hepatitis-c-virus leads to the re-infection of the transplant within a few days. The development of the transplant fibrosis is accelerated and varies among individuals. 20% to 50% of transplanted organs will develop cirrhosis within 5 to 10 years after transplantation. Some predictors for a rapid development of fibrosis e.g. HCV-genotype, donor age, viral load, have been identified. Laboratory findings in the first month after OLT have not been investigated yet.
Method: One-year histological findings of 120 graft recipients were assessed according to inflammation, stage of fibrosis, laboratory results during the first month after transplantation such as transaminases (GOT, GPT, GLDH), alkaline phosphatase, g-glutamyl-transferase, bilirubin, age, donor and recipient gender. These findings were correlated with low and fast fibrosis progression.
Results: A group of 42 patients with fibrosis stage 3 and 4 were compared to a group of 78 patients with stage 1 and 2 fibrosis without fibrosis progression at 3-year biopsy of the liver. We could not identify any correlation between gender incompatibility of the graft recipient and donor, recipients' age and laboratory findings during the first week after transplantation. However GOT measured in the fourth week was significantly ($P<0.05$) increased in the group with early fibrosis and correlated with portal inflammation and stage of fibrosis at one year histological examination. Furthermore we could confirm the importance of donor age in the fast development of fibrosis.
Conclusion: The identification of early laboratory parameters can be important for predicting the severity of fibrosis due to HCV-re-infection after liver transplantation at a very early stage. Furthermore, obviously unapparent laboratory changes could indicate the starting point of HCV-associated inflammation and fibrosis thus influencing antiviral treatment regimen in future.

P-487 SPLIT LIVER TRANSPLANTATION IN ADULT AND PEDIATRIC RECIPIENTS: A 16 YEAR EXPERIENCE IN A SINGLE CENTER

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We present a single-center results of split liver transplantation (SLT) over a 16-year period.
Patients and methods: Since 1991 to 2007, 927 liver transplantations (LT) were performed in 895 patients (799 adults and 128 children). Among these, 121 (13%) transplantations were done by using split liver grafts including 62

right and 17 left livers and 42 left lateral sections in 77 adult and 44 pediatric recipients. Mean recipient ages were 54±9 and 3.3±4 years in adults and children respectively. Since 2000, a SLT program for 2 adults was started by using a full-left liver including the middle hepatic vein and a right liver with only the right hepatic vein.

Results: Adult recipients received 61 right and 16 left livers whereas pediatric recipients had 42 left lateral sections, 1 left and 1 right livers. Seven patients (5.8%) had retransplantation. Adult patient and graft 1, 5 and 10 year survival was 88, 81, 72.5% and 87, 80, 66.4% respectively and 81.4, 75.5, 75.5% and 74.9, 71.5, 71.5% in children respectively. The 1, 5 and 10 year patient survival according to the type of graft was 90.3, 86.3, 72% and 76.6, 59, 59% and 73.7, 70, 70% for the right and left livers and the left lateral section respectively. Early mortality dramatically decreased in the recent past 5 years (10% in 60 patients) particularly for patients having left parts of the liver.

Conclusions: Transplantation of right livers was associated with the best results as compared to those of left livers and left lateral sections. Left livers given to adult patients were associated with initial poor outcomes, nevertheless improved results were observed with better graft selection and allocation.

P-488 IS THERE RELATION BETWEEN THE GRADE OF TUMOR NECROSIS AND THE RADIOLOGICAL RESPONSE AFTER PREOPERATIVE TAC AND THE TUMOR RECURRENCE BETWEEN PATIENTS WITH LIVER TRANSPLANT DUE TO HEPATOCELLULAR CARCINOMA

Baltasar Pérez-Saborido[1], Santos Jiménez de los Galánes-Marchán[1], Juan Carlos Menéu-Díaz[1], Vanessa Barra-Valencia[1], María Donat-Garrido[2], Yillian Fundora-Suárez[1], Alberto Giméno-Calvo[1], Manuel Octavio Salinas[1], Enrique Moreno-González[1]. [1]*General, Digestive and Abdominal Organs Transplant Surgical Department, "12 de Octubre" Hospital, Madrid, Spain;* [2]*Surgical Department, "Infanta Leonor" Hospital, Vallecas, Madrid, Spain*

Introduction: TACE has been postulated as bridge treatment during the waiting list to LT for HCC.

Objective: To analyze is there is relation between the recurrence and the results of the TACE.

Patients and method: From 1986 to Dec,06 performed 151 LT for HCC, 46 incidental were excluded. We performed preoperative TACE in 63 patients (60%).

Results: 65.1% of the patients with TACE had tumor necrosis, of 100% in 14 (34.1%). There are not significative differences between radiological response or not (27.3% vs 20.4%). Between patients without response, 100% of the recurrences were before 1 year vs 10% (p=0.003); more located at liver (100% vs 50%;p=0.11); more die due to recurrence (66.7% vs 33.3%) although there are not differences in survival or disease-free survival. Between the patients with tumor progression recurrence was earlier (50% before one year) and increase liver recurrence (23.1% vs 5.9%). When there are not necrosis 66.7% recurrence befor one year. With 100% of necrosis there are no recurrence, being variable between partial necrosis grades (p=0.004); and there are more patients alive and without recurrence (78.6%). There are not relation between necrosis grade and recurrence pathway, although it is earlier with necrosis <25%. With AFP>200ng/ml postTACE there are more recurrence (57.1%, p=0.04), 50% during the first year, more extrahepatic recurrence (50% vs 33.3%), and less patients alive and without recurrence (14.3%;p=0.d03).

Conclusions: There is no relation of tumor recurrence with radiological response, tumor progression, and no necrosis; although it is earlier. With necrosis of 100% there is no recurrence. With AFP after TACE > 200 ng/ml increase the tumor recurrence.

P-489 TUMOR RECURRENCE AFTER LIVER TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA. RECURRENCE PATHWAYS AND TREATMENT

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Introduction: LT is the choice treatment for patients with HCC. Tumor recurrence short the survival and is the main cause of late mortality.

Objective: Revision of our experience analizying the recurrence rate and the treatment options.

Patients and method: We performed 151 LT for HCC, being known before the LT in 105 patients.

Results: After a mean follow-up of 53.04±45.13 months 23 patients have recurrence (16.8%): 14 hepatic+extrahepatic (10.2%) and 9 only extrahepatic (6.6%); lung in 8 (5.8%) y multiorganic in 10 (7.3%) and 2 adrenal gland. 47.8% of the recurrences are before one year after the LT. 12 patients did not receive treatment (52.25%). 6 patients received surgical treatment, one plus chemoembolization, one plus chemotherapy and another one plus radiotherapy. 5 patients received treatment with Sorafenib. Mean survival after recurrence was 12.87±15.86 months and is larger between the patients that received treatment 6±5.43 vs 21.36±19.95 months (p=0.01) and between the patients with a recurrence one year ago the LT (19.5±19.8 vs 6.72±6.18 months (p=0.05). Patients with liver and extrahepatic recurrence have worse survival 9.35±7.87 vs 19.66±23.06 (p=0.1). Patients with surgical treatment had longer survival after recurrence than those without treatment (p=0.009). Of the 23 patients, 20 died and 18 of them due to recurrence, with a mean survival after recurrence of 14.2±17.39 months. 1-year actuarial survival is shorter with an early *recurrence*: 27.3% vs 72.2%, p=0.015; and without treatmen: 25% vs 79.5%, p=0.0001.

Conclusions: The recurrence rate in our experience is 16%, before one year after the LT in almost 50%. Early recurrence and no treatment is related with shorter mean survival. Patients who received surgical treatment of the recurrence have longer survival.

P-490 LAPAROSCOPIC TREATMENT OF BILIARY PERITONITIS AFTER T TUBE REMOVAL IN PATIENTS UNDERGOING ORTHOTOPIC LIVER TRANSPLANTATION

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Introduction: Biliary complications remain the Achilles heel in the liver transplant. Biliary peritonitis after removal of the biliary T-tube is a serious complication that may require surgery to wash and drain the abdominal cavity. Our purpose is to communicate our experience in laparoscopic surgical treatment of bile peritonitis after removal of the biliary T-tube in liver transplant patients.

Material and methods: From January 2002 to December 2007 we were performed 262 to 246 liver transplant recipients in our hospital. Biliary tract reconstruction was achieved by choledocholedochostomy in 244 patients (125 with T-tube and 119 without T-tube) and by choledochojejunostomy in the remaining 18 patients. Placement of a biliary T-tube was indicated when there was disparity in size between the bile duct of the donor and recipient were not aligned properly or after anastomosis. Kehr tube was removed in all cases between the third and fourth postoperative months after a control cholangiography.

Results: 23/125 (18%) patients have developed bile peritonitis after removal of the biliary T-tube. They have been treated conservatively with rest and analgesia in 12 of the 23 patients (52%). 3 patients have benefited from the puncture radioguided (13%) and 8 patients needed laparoscopic intervention with cleaning and drainage of the peritoneal cavity (35%), placing the laparoscopic ports according to the French school in the laparoscopic cholecystectomy. Mean operative time was 70min. No postoperative deaths, related to the procedure, occurred. There was no need for a laparotomy in any patients with this complication. There was no mortality and mean hospital stay was 9±1.8 days.

Conclusions: Laparoscopic intervention is safe, simple and has solved the problem in all cases of diffuse peritonitis, avoiding major surgery in biliary peritonitis after T-tube removal in liver transplant patients

P-491 EFFECT OF KAMPO MEDICINE "DAI-KENCHU-TO" ON PORTAL BLOOD FLOW IN LIVING DONOR LIVER TRANSPLANT RECIPIENTS

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Background/Aim: Dai-kenchu-to (DKT), known a kampo medicine, has multiple beneficial effects on gastro-intestinal tract including increase effect of gastro-intestinal blood flow. The aim of this study was conducted to investigate the effect of DKT on portal hemo-dynamics in living donor liver transplant (LDLT) recipients.

Patients and methods: Six adult patients who underwent LDLT in our institute were included in this study. Portal venous flows (PVFs) (velocity: cm/sec.,

volume: mL/min.) in each recipient were measured just before and 10, 20, 30, 60 and 120 minutes after 2.5 g of DKT oral administration using the ultrasonic Dopplar ultrasonography. Simultaneously, portal vein pressure (PVP: mmHg) was also measured using an indwelling catheter at each time point.
Results: ABP and HR did not significantly change after DKT oral administration. PVF velocity was immediately increased, and significantly higher within 10 min after DKT oral administration. According to increase of PVF velocity, PVF volume was also significantly increased within 10 min after DKT oral administration. This effect lasted for approximately 60 min. In spite of the increase of PVFs, PVP stayed the same levels through the observation periods.
Conclusion: DKT has an ability to increase PVFs without any PVP elevation in LDLT recipients, which suggests that this drug may have beneficial effects on the stability of liver regeneration and function after LDLTs.

Lung

P-492 ASPIRATION SECONDARY TO GASTRO-OESOPHAGEAL REFLUX BUT NOT DUODENAL REFLUX OCCURS IN THE IMMEDIATE POST LUNG TRANSPLANTATION PERIOD

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Background data: Asymptomatic gastro-oesophageal reflux and aspiration, associated with allograft dysfunction, occurs frequently in lung transplant recipients. Early anti-reflux surgery could improve longterm survival. Indications for surgery include elevated levels of biomarkers of aspiration, including bile salts, in bronchoalveolar lavage fluid (BALF), but measurements have been made more than 3 months post-transplant, potentially after the optimum intervention time. We report a prospective study of reflux/aspiration immediately post-transplantation.
Methods: 18 lung transplant recipients, median age 46years (range 22-59), on daily maintenance PPI, were recruited. Within 3 months post-transplantation, patients completed a Reflux Symptom Index (RSI) questionnaire for extra-oesophageal reflux and underwent manometry and pH/impedance measurements. BALF was assessed for pepsin, bile salts, interleukin-8 and neutrophils.
Results: Manometry was abnormal in 8/18 (44%) patients. 12/17 (70%) had pathological distal reflux and 9/17 had pathological proximal reflux (>15cm above the lower oesophageal sphincter). RSI questionnaire did not significantly predict the presence or absence of proximal reflux. A statistically significant correlation existed between number of proximal reflux events and neutrophilia (Spearman Correlation r=0.52, p=0.03). Pepsin was detected in all BALF samples signifying aspiration, median level 25ng/ml (range 11-43). Bile salts were undetectable, using spectrophotometry and dual mass spectrometry assays [sensitivity 0.1uMol/L].
Conclusion: Reflux/aspiration is prevalent early post-operatively and proximal reflux events correlate with BALF neutrophilia, a predictor of allograft dysfunction and mortality. Pepsin, not bile salts, was detected in BALF, suggesting gastric rather than duodenal aspiration at this time point. Reflux/aspiration can be asymptomatic and validated biomarkers of aspiration may be a useful indicator for the need for therapy, including fundoplication.

P-493 KIDNEY FUNCTION DURING AND AFTER LUNG TRANSPLANTATION SHOULD BE MONITORED BY CYSTATIN C RATHER THAN CREATININE BASED GFR

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The renal disfunction is common complication associated with lung transplantation (LTx) due to ischemia, catecholamines during the procedure and calcineurine inhibitors administration at short/long term follow up. The aim of the study was to compare GFR (glomerulal filtration rate) predicted from serum cystatin C (CysC, GFR-CysC) or serum creatinine (Cr, GFR-Cr) clearance in LTx-patients in various post-transplant periods (early – eTP up to 14 days, post – TP up to 30 days and long – lTP up to two years after LTx).
13 patients were retrospectively included into the trial (3 women and 10 men, mean age 41.2±13.8 yr, BMI 18.7±2.8). In all studied periods mean value GFR-CysC was significantly decreased in compare to GFR-Cr (eTP: 48.7±16.63 vs 78.7±33.59, respectively; $p<0.01$; TP: 59.7±11.54 vs 115.0±102.49, respectively; $p<0.01$; lTP: 68.8±17.84 vs 98.3±41.50, respectively; $p<0.0001$).
CysC and GFR-CysC was different in Sirolimus (Sir) and tacrolimus-administered patients (Tac) at lTP (1.54±0.43 and 1.05±0.15, $p<0.0001$; 42.3±12.71 and 70.1±12.95, $p<0.0001$; respectively). A significant correlation between GFR-CysC and GFR-Cr at TP and lTP in whole studied group was found (r=0.64, p=0.000001 and r=0.76, p=0.000001, respectively). Similarly, the significant correlation between GFR-CysC and GFR-Cr in Sir and Tac groups was observed (r=0.86, $p<0.05$ and r=0.58, respectively; $p<0.05$).
In conclusion, GFR based on cystatin C differs from that based on creatinine and is decreased in all post-transplant periods in lung transplant recipients. GFR based on creatinine in low-BMI-patients seems to be not sensitive enough.

P-494 AGGRESSIVE SKIN CANCERS ASSOCIATED WITH PROLONGED VORICONAZOLE THERAPY IN 4 LUNG TRANSPLANT PATIENTS

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Introduction: Voriconazole is a second-generation azole antifungal agent used for the treatment of severe fungal infections. Adverse cutaneous reactions including photosensitivity reactions are well-known but the development of aggressive skin cancers have been rarely reported in literature. We describe 4 cases of atypical and aggressive cutaneous cancers in lung transplant patients during prolonged treatment with voriconazole.
Case reports: Two patients with a pre-transplant diagnosis of cystic fibrosis, one with a primary pulmonary hypertension and one with emphysema received a prolonged voriconazole therapy (17-60 months) for persistent pulmonary aspergillosis colonization. Our patients received a standard triple immunosuppressive regimen (tacrolimus, corticosteroid and mycophenolate mofetil) and 3 of 4 patients had a bronchial stent for post-transplant airway complication. They developed skin malignancy 30 to 60 months after the onset of voriconazole and, in 3 cases, severe photosensitivity reactions appeared before the emergence of skin carcinomas. Three patients developed invasive squamous cell carcinoma respectively 51, 70 and 78 months after lung transplantation and for two patients, these highly invasive carcinoma involved atypical multifocal lesions of the scalp with several recurrence for one patient, requiring multiple surgeries and at this time radiotherapy and chemotherapy. One other case concerned a rare Merkel cell carcinoma on the left elbow appeared 41 months after lung transplantation treated by large excision.
Discussion: Voriconazole therapy induces severe phototoxic reactions and photoaging-like skin damage. Our cases demonstrate that voriconazole is also probably associated with the development of aggressive cutaneous skin cancers in predisposed patients even if its imputability is difficult to establish in patients with immunosuppressive drugs. Primary prevention and careful monitoring of skin lesions are important in prolonged voriconazole treated patients. Moreover, an alternative antifungal treatment should be considered (for instance with posaconazole) when phototoxicity appears.

P-495 VALGANCICLOVIR (vGCV) PROPHYLAXIS FOR CMV INFECTION IN CARDIAC AND LUNG TRANSPLANT PATIENTS

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Purpose: Cytomegalovirus (CMV) is a current opportunistic infection risk after solid organ transplantation. Intravenous GCV, an hematotoxic drug with renal elimination remains the first-intention treatment for CMV disease, but low bioavailibility GCV was replaced by the oral prodrug valganciclovir (vGCV) for prophylaxis periods. We analyzed retrospectively vGCV efficacy and safety during and for 4 months after withdrawal in heart (HT) and lung-transplant patients with cystic fibrosis (CFLT) or not (LT).
Methods: Selected patients were HT, LT and CFLT, with stable renal function (RF) receiving 900mg vGCV daily during 2005-2007, introduced in the early phase for respectively 3 to 6 months in HT and 12 months in others. Donor (D) and recipient (R) CMV serostatus were collected. GCV therapeutic drug

monitoring (TDM) was realized to document efficient concentrations in the 0.5-1.5mg/L range as plasma GCV trough levels (C0) determined using UV-LC assay. Efficacy was checked by pp65 antigenemia (Ag) detection in peripheral blood leukocytes.
Results: 32 thoracic transplant patients (11 HT, 7 LT, 14 CFLT) were included in the study as 53% D^+/R^-, 25% D^-/R^+ and 22% D^+/R^+. vGCV was maintained during 106±67 days in case of HT versus 270±85 for LT and CFLT. HT, LT and CFLT received respectively 700±225, 915±60 and 820±150 mg/day, resulting in mean GCV C0 0.75±0.5 $mg.L^{-1}$. Lower doses registered in HT were adapted to RF. Safety data recorded only 2/9 neutropenia attributable to vGCV. Three D^+/R^- CFLT presented positive pp65Ag, 1 during prophylaxis and 2 after. Only 2 patients developed CMV disease, well-controlled under curative GCV, resulting in an overall 6% incidence.
Conclusion: 900 mg vGCV daily, adapted to RF appeared effective and safe for long CMV prophylaxis, delivering efficient exposure to GCV in thoracic transplant patients and regular TDM could be unnecessary in case of oral vGCV prophylaxis for stable RF patients.

P-496 LEFLUNOMIDE (A77-1726) AS IMMUNOSUPPRESSIVE (IS) ALTERNATIVE IN THORACIC TRANSPLANTATION

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Purpose: Leflunomide (LFM) is an IS drug approved for the treatment of rheumatoid arthritis expressing an antiviral activity against BK virus (BKV). Oral LFM is entirely converted into its active metabolite teriflunomide (TF) "A77-1726", displaying a particular pharmacokinetic with a long half-life (2 weeks). Therapeutic drug monitoring is recommended for dosage adjustment and because of a teratogen risk. We present the retrospective study of preliminary use of LFM as an IS alternative in heart (HT) and/or lung transplant (LT) patients with cystic fibrosis (CF) or not.
Method: This study included 17 patients (14M/3F) as 8 HT and 9 LT including 7 CF, receiving LFM between 2005 and 2008. TF plasma concentrations were determined by UV-LC assay; therapeutic range referenced as 30-50 mg/L.
Results: The predominant LFM indication was an hematologic intolerance due to mycophenolate mofetil or mTOR inhibitors, one single case of BKV nephropathy. The mean trough TF concentration measured in CF patients (C0= 12.8±5.5 mg/L) was statistically lower than in no-CF (C0= 44.0±24.2 mg/L) ($p<0.05$), despite a ponderal dose in CF (D= 0.32±0.08 mg/kg/d) slightly higher than in no-CF (D= 0.26±0.10 mg/kg/d). LFM steady-state needed 16 to 18 mg/day, achieved within 3 months. Two patients died and LFM was discontinued in 3 patients without strong evidence of LFM relationship. The BKV patient underwent bi-nephrectomy. Hepatic and haematological tolerances were acceptable for an average of 12 months follow-up [1-36]. Initial renal function was maintained in patients with renal failure consistent with a long exposure to calcineurin inhibitors.
Conclusion: We described that LFM could be an alternative in case of intolerance to conventional IS treatment in HT and LT. The outcome was acceptable in complex severe patients who have exhausted IS treatment resources. This have to be evaluated in the long term to be extended to a larger cohort or proposed earlier.

P-497 HOW TO INVESTIGATE THE IMPACT OF DONOR BRAIN DEATH FOR LUNG TRANSPLANTATION? A SYSTEMATIC REVIEW OF EXPERIMENTAL ANIMAL MODELS

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Introduction: Lung transplantation (LTx) suffers from a lack of suitable donors. Brain death (BD) donors remain the primary organ source for LTx. Previous studies suggests that BD may have detrimental consequences on the organ quality and thus on the outcome after transplantation. Experimental research therefore is of great importance to further elucidate the underlying mechanisms of BD in order to improve the quality of the lung itself.
Methods: A systematic review of the literature was conducted to identify the different types of brain death models that have been described. Papers were searched from earliest records to February 2009 using the electronic database PubMed. Non-English languages studies, reviews, letters to the editor, commentaries, and other non-investigational publications were excluded.
Results: The search terms "brain death" or "brain-dead" resulted in 7219 hits, from which 806 were characterized as review articles. The search outline was narrowed by screening for titles using these search terms and by using the limitation "animals". This resulted in 280 hits from which 46 were excluded according to the above lined criteria. Subsequently, manual searching revealed BD models in different species: rat (n=76), pig (n=60), dog (n=58), rabbit (n=18), cat (n=13), baboon (n=8), and sheep (n=1). The heart was the organ most extensively studied (n=96), followed by liver (n=44), kidney (n=27), and finally lung (n=7).
Conclusion: This review indicates that BD research has gained a lot of attention over the past years but focused mainly on cardiac function. Further research is warranted to elucidate the impact of BD on lung graft quality.

P-498 OSTEOPOROSIS AND VERTEBRAL FRACTURES ARE A MAJOR PROBLEM IN CYSTIC FIBROSIS PATIENTS AFTER LUNG TRANSPLANTATION

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Objective: Cystic fibrosis patients (CF) have marked loss of bone mass caused by malnutrition, lower sex hormones, inactivity and chronic inflammation.
In literature the prevalence of osteoporosis in about 30% and compression fractures in 7-35% in adult CF is very high. But no osteologic data exist, when CF are exposed to a high immunosuppressive and glucocorticoid therapy after lung transplantation (CFTX).
Methods and results: We therefore, retrospectively analysed clinical data, bone radiographs and dual-energy X-ray absorptiometries (DXA) of 21 CF (9 m/12 f; age: 28±9 yrs), transplanted between 01/99 and 08/04 at our institution, who survived at least 2.5 years. The mean follow up was 2 yrs (range: 0.1-8.5 yrs).
Only 1 CFTX (4.7%) had normal T-values (mean bone mineral density in young adults), 3 CFTX (14.3%) had osteopenia, 11 CFTX (52.4%) had osteoporosis and 6 CFTX (28.6%) had vertebral fractures in the follow up period.
50% of vertebral fractures were diagnosed within the first year after lung transplantation (LuTX). Bone mineral density was markedly decreased (lumbar vertebral column-mean: 0,97g/cm^2; T score:-2.9 – femur mean: 0.73 g/cm^2, T score: -2.64) and predictive for compression fractures.
Parathyroid hormone (PTH) was elevated in 82%, osteocalcin in 45% and 25-Hydroxyvitamin D was low in 36%. The creatinine clearance in CFTX was 56.4 ml/min in mean. Despite of high physical activity and adequate osteoporosis therapy no significant increase of bone mass could be seen after LuTX.
Conclusion: 1. with progression of pulmonary manifestation all CF should be screened for osteoporosis as early as possible.
2. a biphosponate/calcium/vitD therapy in CF with osteopenia or osteoporosis before LuTX and thereafter, in combination with physical activity and optimal nutrition may reduce the high incidence of osteoporosis and vertebral column fractures within the first year after LuTX.

P-499 CONSENSUS PHARMACOLOGICAL PROTOCOL IN LUNG TRANSPLANTATION

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Purpose: Create therapeutic guidelines for the rational use of drugs in Lung Transplantation (LT).
Methods/Materials: Literature review, meeting with experts, analysis of other LT Centres treatment protocols, observation and training in reference Centres. Authors considered the following therapeutic needs, in face of baseline disease, transplant procedure and potential side effects of immunosuppressive therapy (IT): (1) IT (1a)Prophylaxis (1b) Treatment (2) Antimicrobial therapy (AT) (2a) Prophylaxis (2b) Treatment (3) Other adjunctive therapy.
Results: LT pharmacological protocol: (1) IT (1a) Prophylaxis: Methylprednisolone (MP) intravenous (IV): 500mg on arrival and after implantation; 250mg 8/8h-4 doses; 250-500mg/day-3 days; 100mg/day-1 week. Prednisolone (P): 30mg/day-3 months. Basiliximab: 20mg (days 0 and 4). Cyclosporine (Cyc): 3-5mg/kg/day (divided in 2 doses) or Tacrolimus (FK): 1mg/kg/day (divided in 2 doses). Azatioprina (Aza): 1,5-2mg/kg/day (divided in 2 doses) or Mycophenolate mofetil (MMF): 1g oral twice daily (td) starting in imediate postoperative. (1b) Treatment: MP 500mg td-3 days; 10mg/kg/day-3 days and P 0,5mg/kg/day-1 day. Cyc and Aza replaced by FK and MMF respectively. If acute rejection Antilymphocytes Immunoglobulin 1,5mg/kg/day-7 days. (2) AT (2a) Prophylaxis: Vancomycin: 500mg 8/8h-2 days; Amoxicillin + Clavulanic acid: 1,2g 8/8 h-5 days. Antipseudomonal antibiotics (AP) (double coverage) untill negative cultures. *Cytomegalovirus (CMV):* For high-risk patients (positive donor and negative recipient: D+/R–) Anti CMV imunoglobulin-150mg/kg-72h; 100mg/kg-2,4,6,8 weeks; 50mg/kg-12,16 weeks. Ganciclovir 5mg/kg td (D+/R–). Valganciclovir: 900mg/day-100 days. *Aspergillus:* Inhaled Amphotericin B until hospital discharge; Itraconazole 100mg td. *Candida:* Nystatin-1MIU/ml 5cc, 8/8h. *Pneumocystis carinii:* Cotrimoxazole 960mg td-

3days/week for life. (2b) Treatment: *Cystic fibrosis:* AP-14-21 days; Inhaled tobramycin. *Toxoplasma*: Cotrimoxazole 960mg td or pyrimethamine (D+/R–). *Pulmonar Tuberculosis*: Isoniazid 300mg td if positive Mantoux. (3) Other adjunctive therapy: Ferrous sulfate 525mg td-3 months. Pantoprazol 20mg once daily (od). Pravastatin 20mg od. Calcium 1g od. Sodium alendronate 70mg/week. Enoxaparin 40mg/day. Thiotropium bromide inhalation powder-od.

Conclusion: This protocol was developed considering the opinion of several experts and literature review. Authors believe that it covers the major drug related requirements. However, only protocol implementation will demonstrate its effectiveness and safety.

P-500 COMBINED LUNG LIVER TRANSPLANTATION IN CYSTIC FIBROSIS: THE FRENCH EXPERIENCE

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Purpose: Patients with cystic fibrosis (CF) who have end−stage respiratory failure associated to liver cirrhosis have been considered poor candidates for lung transplantation because of high morbidity and mortality resulting from hepatic insufficiency. We report our exprience about combined lung and liver transplantation in CF patients.

Methods: Heart lung−liver transplantation (n=5) and sequential double lung liver (N=29) transplantation were performed in 34 patients from 1990 to september 2008. We describe surgical techniques and follow up, and survival

Results: Between Jun 1990 and september 2008, 29 patients had sequential double lung liver transplantation (n = 29).

The age ranged from 10 to 30 years. All patients presented cirrhosis associated to portal hypertension.

The transplantation was carried out on two stages: Sequential bilateral lung transplantation followed by liver transplantation. Cardiopulmonary bypass was used in the begining of our experience and after only in patients who develloped hemodynamic dysfunction.

The post operative mortality was 20%. Actuarial survival was 70% at 1 year and 50% at 10 years. The incidence of BOS is 42% for 5 years with 25% of mortality. Significant functional improvement was observed in all survivors.

Conclusions: Combined liver-lung transplantation is an acceptable treatment in selected CF patients with end-stage respiratory and liver disease. The outcome is comparable to the outcome of double lung transplantation, but poorer than the liver transplantation in CF population.

Netherless, the indication of combined heart-lung-liver transplantation must be reserved for patients with cardiac disease.

P-501 RENAL FUNCTION DECLINE BEYOND ONE MONTH AFTER LUNG TRANSPLANTATION DEPENDS ON CNI TYPE

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Background: Renal failure is an important source of co-morbidity after lung transplantation, with calcineurine-inhibitor (CNI) toxicity as a major contributor. The purpose of this study was to determine the extent of renal morbidity and to analyse whether there are differences in renal toxicity between different CNI based treatment regimens.

Methods: We included 121 adult patients who underwent primary lung transplantation between 1990 – 2006, for whom follow-up of at least 24 months was available. Glomerular filtration rate (GFR) was determined by [125I]-lothalamate clearance at baseline (i.e. prior to lung transplantation) and at 1 and 24 months after lung transplantation.

Patients received 3 different CNI based regimens: between 1990-2001 cyclosporine (CsA, n= 65), between 2001-2004 tacrolimus (Tac, n= 19) and between 2004-2007 tacrolimus with lower postoperative target levels (Tac-Low, n= 37).

Results: Mean age at transplantation was 44.4 years (19-66). Mean GFR was 101 (range 43-199) at baseline, 72 (range 19-139) at 1 month and 57 (range 22-174) at 24 months after transplantation.

Table 1. Course of GFR according to the 3 different CNI bases treatment regimens

CNI regimen	CsA (n=65) Mean (SD)	Tac (n=19) Mean (SD)	Tac-Low (n=37) Mean (SD)	P
Baseline GFR	102 (22.2)	98.3 (20.1)	99.8 (29.4)	0.81
% Decline of GFR, 0-1 Months	-22.8 (26.9)	-28.8 (29.4)	-28.4 (24.7)	0.49
% Decline of GFR, 1-24 Months	-24.9 (21.9)	-8.7 (36.2)	-4.8 (32.8)	0.001

Decline in GFR (%) between 0-1 and 1-24 is given in table 1, showing a similar renal function decrease between 0-1 months for the 3 regimens, but a remarkably more stable renal function with the tacrolimus-based regimens from 1-24 months. (p = 0.001) This result did not materially change after adjustment for age, sex and pulmonary diagnosis prior to transplantation.

Conclusion: Renal function declines dramatically after lung transplantation. The initial decline after transplantation is similar for the different CNI regimens, but long-term renal toxicity is lower for tacrolimus based-regimens. Further analysis of risk factors for renal function loss is mandatory.

P-502 LUNG EMBOLISM IN LONG TERM FOLLOW UP AFTER THORACIC ORGAN TRANSPLANTATION – AN UNDERESTIMATED COMPLICATION

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Purpose: Lung embolisms after heart and lung transplantation seamed to by a rare but serious complication.

Methods/Materials: We analysed 138 consecutive patients (HTX n=93, LTX n=40, HLTX n=5) in long term medical attendance (> 6 month) after thoracic organ transplantation from June 2006 to November 2008. All patients were analysed for episodes of lung embolism, clinical presentation, diagnostic, therapy and outcome.

Results: We registered 6 cases (HTX n=3, LTX n=3) with a severe lung embolism (incidence 1,8%). All patients were admitted with dyspnoea (NYHA III n=4, NYHA IV n=2) under suspicion of an acute rejection. In each case acute rejection could ruled out by echocardiography and endomyocardial biopsy in heart transplant or bronchoscopy and lung function in lung transplant recipients. Lung embolism was revealed by CT angiography. All 6 patients received conservative therapy with anticoagulation and recovered form the event (mortality 0%). Noticeable risk factors were not found in transplanted organ, gender, immunosuppressive therapy, heart rhythm or immobilisation.

Conclusion: Our analysis suggests that lung embolism must be considered as an underestimated and important differential diagnosis to acute rejection. The performance of a CT angiography should be considered earlier in the diagnostic process of patients with clinical deterioration long term after thoracic organ transplantation.

P-503 IS THERE AN ASSOCIATION BETWEEN CYCLOSPORINE CONCENTRATION AT 2 HOURS POST-DOSE AND CLINICAL OUTCOMES IN DE NOVO LUNG TRANSPLANT RECIPIENTS?

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Introduction: Although the reliability of cyclosporin A (CsA) concentration at 2 (C2) hours post-dosing has been established for kidney, liver and heart transplant recipients, its use in lung transplantation remains to be tested and validated.

The objective of this study was to investigate the relationship between CsA time point monitoring and clinical outcomes after lung transplantation.

Method: Data from 34 lung transplant recipients (53±10 years) receiving CsA, azathioprin and steroids were followed from 3 to 24 months and included in the study. CsA dosages were based on the trough concentration. CsA concentrations at 0 (C0) and 2 (C2) hours post-dosing were obtained at 1, 2, 3, 6, 9, 12, 15, 18 and 24 post-operative weeks.

Based on average CsA levels of the first 3 post-transplant months (C0: 359±81; C2: 1554±823 ng/ml), different clinical and long-term functional outcome (FEV1, FVC, FEF 25-75, creatinine, systolic and diastolic blood pressure) were evaluated by repeated measurement analysis using generalized estimating equations.

Results: A parallel correlation exists between C0 and FVC (p = 0.033) and systolic BP (p < 0.001) (SBP) but C0 was inversely related to creatinine (p = 0.073). Any correlation was observed between C0 and FEV1 (p = 0.128), FEF 25-75 (p = 0.484) and diastolic blood pressure (DBP) (p = 0.972). Except an inverse but limited relationship between C2 and FEF 25-75 (p = 0.091), there were any correlations of the different clinical parameters and C2 monitorings.

Conclusion: CsA C0 concentrations correlated better with the functional respiratory outcome and the renal dysfunction. This study did not show any clear relationship between CsA C2 monitoring and the long-term clinical outcome.

P-504 SIDE EFFECTS OF A CALCINEURIN-EVEROLIMUS BASED IMMUNOSUPPRESSIVE REGIME IN LUNG TRANSPLANTED RECIPIENTS

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Background: Everolimus, a proliferation inhibitor, is descibed as a safe and well tolerated immunosuppressor in kidney and heart transplanted recipients. But there is less experience in patients after lung transplantation (LUTX).
Methods: 60 patients (29 m/31 f) were switched from a Calcineurininhibitor (CNI), Mycofenolat, Methylprednisolone to a quadruple therapy, in which CNI was reduced to about 50% of baseline levels and Everolimus (EV) added and titrated to an average EV trough level between 5-8 ng/ml. 50 LUTX (83.3%) were switched caused by renal deterioration (median yrs after TX:1.9) and 10 pts (16.7%) because of a postoperative CNI-EV based immunosuppressive study regimen, 3 months after LUTX. Patients were followed for 44±29 months (median: 34 months).
Results: Withdrawal of Everolimus was indicated because of side effects in 9 pts (15.0%)
Reasons for withdrawal were: Quincke edema (1 pt), exanthema (1 pt), mental disorder (1 pt), headache (1 pt), diarrhea/nausea (2 pts), peripheral edemas (1 pt), liver failure (1 pt) and others (1 pt).
The most frequent side effects were leucopenia 13 pts (21.7%), anemia 4 pts (6.7%), thrombocytopenia (10.0%), hypercholesterinemia pts (81.4%), hypertrigyceridemia pts (88.4%) and Quincke edema in combination with an ACE inhibitor therapy in 3 pts (5.0%).
All adverse effects were reversible after EV withdrawal.
Conclusion: A CNI reduced immunosuppressive therapy based on everolimus for preserving renal function is a safe and well tolerated immunosuppressive therapy, associated with less side effects in all lung transplant recipients after anastomoses and wound healing is finished.

Xenotransplantation

P-505 PERITONEAL IMPLANTATION OF CRYOPRESERVED ENCAPSULATED PORCINE HEPATOCYTES IN RATS WITHOUT IMMUNOSUPPRESSION: VIABILITY AND FUNCTION

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Purpose: Encapsulated hepatocyte transplantation is a promising approach to cell transplantation without immunosuppression as an alternative to whole organ liver transplantation.The aim of this study was to assess viability and function of cryopreserved encapsulated porcine hepatocytes implanted intraperitoneally in rats without immunosuppression.
Methods/Materials: Isolated porcine hepatocytes were cryopreserved at -196 degrees Celsius for 1 month. Thereafter they were thawed and encapsulated in hollow fibers (AN69 polymer). Four groups were created: *Group 1 (n=10)*, freshly encapsulated porcine hepatocytes cultured in albumin-free medium for 10 days; *Group 2 (n=10)*, freshly encapsulated porcine hepatocytes implanted in rat peritoneum without immunosuppression for 1 month, and cultured for 10 days after explantation; *Group 3 (n=10)*, cryopreserved encapsulated porcine hepatocytes cultured for 10 days; *Group 4 (n=10)*, cryopreserved encapsulated porcine hepatocytes implanted in rat peritoneum without immunosuppression for 1 month and cultured for 10 days after explantation. Hepatocyte viability, liver enzyme release, urea and albumin production were assessed.
Results: There was no significant difference in urea synthesis between the groups. Albumin synthesis was significantly decreased in group 4 compared to the other groups ($p<0.01$). There was no significant difference in AST, ALT and LDH levels in culture medium ($p>0.05$). Encapsulated cryopreserved porcine hepatocytes explanted from rat peritoneum after 1 month appeared morphologically viable and their ultrastructure was preserved.
Conclusion: Long-term cryopreservation of porcine hepatocytes resulted in retention of their biological activity and in significant viability when transplanted into rat peritoneum without immunosuppression.

P-506 CREATION OF A PREVASCULARIZED SITE FOR PANCREATIC ISLET CELL TRANSPLANTATION USING A V.A.C.®-GranuFoam™ AND HYPERBARIC OXYGENATION IN RATS

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Introduction: Isolated pancreatic islet cells depend on diffusion of oxygen from the surrounding tissue, therefore vascularisation is necessary, when microcapsules are transplanted. After transplantation pancreatic islet cells are likely to become apoptotic due to hypoxia leading to graft dysfunction. The aim of this study was to show to create a prevasularized site using a V.A.C.®-GranuFoam™ and HBO in rats.
Methods: A V.A.C.®-GranuFoam™ were implanted in 40 Sprague-Dawley rats and HBO was administered for different time spans. Blood flow in the V.A.C.®-GranuFoam™ was assessed by szintgraphy and VEGF levels were determined using ELISA. NaCS/PDADMAC microencapsulated HEK 293 cells were transplanted in rats pre-treated with HBO after implantation of the V.A.C.® GranuFoam™. The V.A.C.®-GranuFoam™ was assessed by histology and immunohistochemistry to detect angiogenesis and apoptosis.
Results: The number of vessels per field is significantly higher in all experimental groups except in those treated with HBO alone for 21 days compared to the control group. The area containing the VAC® GranuFoam™ was significantly better perfused in all experimental groups as compared to the same region on the opposite side of the spine. VEGF levels were highest in rats receiving 21 d of HBO treatment. Only a small amount of apoptosis occurs in NaCS/PDADMAC microencapsulated HEK 293 cells after transplantation.
Conclusion: As ischemia damaged pancreatic islet cells are likely to undergo cell death or loose functionality due to hypoxia, the use of the V.A.C.®-GranuFoam™ and HBO might be a promising method to create a prevascularised site to achieve better results in pancreatic islet cells transplantation.

P-507 XENOTRANSPLANTATION OF MICROENCAPSULATED PORCINE ISLET CELLS IN DIABETIC RATS

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Introduction: Xenotransplantation of microencapsulated porcine islet cells might be a possibility to overcome the shortage of human donor organs for pancreas transplantation. Several materials for microencapsulation of cells are described in literature which all show severe disadvantages. NaCS is easy to produce, does not show any cytotoxicity and cell lines survive for a nearly unlimited time-spam after microencapsulation. However, this material has not been tested for microencapsulation and xenotransplantation of porcine islet cells.
Methods: Porcine islet cell isolation and purification was performed according to a newly modified Ricordi method. Porcine islet cells were microencapsulated with NaCS. Diabetes was induced in Sprague Dawley rats by intraperitoneal injection of STZ. Microencapsulated porcine islet cells were transplanted under the kidney capsule of the animals. Blood sugar levels were monitored on a weekly basis, porcine C-Peptide levels and insulin levels were measured using ELISA. Intravenous glucose tolerance testing was performed once a months. After 4 months, the animals were sacrificed, the kidney containing the microencapsulated porcine islet cells was retrieved and processed for histological and immunohistochemical examination.
Results: After xenotransplantation of microencapsulated porcine islet cells diabetes was reversed in rats. Animals stayed normoglycaemic up to four months. Functionality of transplanted porcine islet cells was detected by insulin measurement and detection of C-Peptide. Viability of microencapsulated porcine islet cells after explantation was proven by immunohistochemical viability stains.
Discussion: It is feasible to reverse diabetes in rats by transplanting porcine islet cells microencapsulated in NaCS. Rats stayed normoglycaemic until the end of the study period. NaCS seems to be a promising material for microencapsulation of porcine islet cells in order to treat diabetes. Further studies have to be carried out to show long term survival of transplanted porcine islet cells microencapsulated in NaCS in diabetic rats.

P-508 DEVELOPMENT OF REGENERATED CHIMERIC LIVER GRAFTS AND LONG-TERM EVALUATION OF THEIR POTENTIAL AFTER AUXILIARY TRANSPLANTATION IN MOUSE AND RAT COMBINATION

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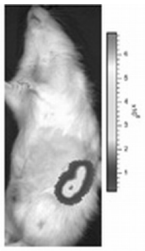
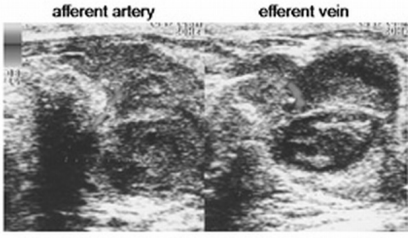
The worldwide shortage of liver grafts causes medical, social and ethical problems. Although this situation requires intensive efforts to develop alternative grafts using regenerative biotechnology, they are still far away from the practical application. Now, we have the strategy to develop regenerative chimeric liver grafts containing human hepatocytes and the scaffold of xenogeneic animals such as transgenic pigs. Using our established rodent model that the chimeric livers with rat hepatocytes and mouse scaffold are transplanted to rat recipients, we evaluated their long-term function after transplantation and outcomes in graft and recipient survivals under immunosuppressive treatments.
We produced chimeric livers in urokinase-type plasminogen activator/severe combined immunodeficiency (uPA/SCID) mouse by cell transplantation with hepatocyte isolated from luciferase transgenic Lewis (LEW) rat (MHC haplotype: $RT1^l$), and transplanted them to wild-type LEW rats ($RT1^l$) and Nagase analbuminemia rats (NAR) ($RT1^a$) in the auxiliary fashion, followed by daily tacrolimus administration. We evaluated the intensity of luminescence derived from the transplanted chimeric liver as a marker of its viability and examined serum rat albumin level in NAR recipients using ELISA. Furthermore, we evaluated blood circulation in chimeric livers using Doppler ultrasonography.
In vivo bioluminescent imaging showed that tacrolimus monotherapy improved graft survivals for four weeks after transplantation, suggesting the controllability of the rejection toward transplanted chimeric livers.
In NAR recipients, chimeric livers produced rat albumin after transplantation, and we could detect it even 170 days after transplantation.
Doppler ultrasonography indicated the arterial inflow and venous outflow in chimeric livers even six months after transplantation.



Luminescence from chimeric liver on day 200 after transplantation



Doppler ultrasonography shows arterial inflow and venous outflow in chimeric liver on day 188 after transplantation

These results suggest that, with appropriate immunosuppression, chimeric livers may work as auxiliary livers for a long-period and our strategy can contribute to solve the critical graft shortage in the world.

P-509 MICROARRAY ANALYSIS OF CHANGES IN PORCINE ORTHOTOPIC CARDIAC GENE EXPRESSION

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Purpose: Xenograft survival is a balance between immunological rejection, and adaptive changes in the graft that can promote accommodation. In this study we identify the changes in gene expression in orthotopic pig-to-primate cardiac xenografts prior to rejection.
Methods: RNA was isolated from two control pig hearts (non-transplanted) and from GT+ (n=3) and GTKO (n=2) orthotopic cardiac xenografts. Gene expression was measured using the Affymetric porcine chip. Annotation of the chip was augmented by BLAST comparison for ortholog mapping to human. Data was processed using GC-RMA background subtraction, fast loess normalization, median polish summarization and the Affymetrix MAS5.0 algorithm.
Results: Recipients survived 57, 40, 34, 22 and 14 days in a healthy condition. Mortality resulted from bowel infarction, pneumonitis, respiratory failure, a surgical bleed, and unknown cause, respectively. Histopathology showed minimal-to-mild rejection in 4 recipients and moderate rejection in the fifth. We detected statistically significant changes in expression of 2,349 probes ($p<0.05$) out of 16,583 expressed transcripts. Signals of 145 probes showed variations of more than 3 standard deviations (SD) compared to control hearts. There were 354 probes and 1143 probes with deviations of more than 2 and 1 SD from mean control values, respectively. Transcripts with the greatest change in expression included over-expression of tissue injury markers, muscle specific genes, extracellular proteases/inhibitors and decreased expression of extracellular matrix components. Metacore pathway analysis using all genes with significant changes in expression (n=1143) identified ten pathways that passed a false discovery rate filter of 0.2.
Conclusion: This is the first assessment of changes in gene expression during pig-to-primate orthotopic cardiac xenograft transplantation. The analysis shows an over representation of transcripts involved in cytoskeletal and extracellular matrix remodeling. These results suggest that there is ongoing process of remodeling in these life-supporting xenografts prior to rejection.

Poster Session 2: Tuesday, 1 September 2009 – Wednesday, 2 September 2009

Ethics, law, psychosocial & public policy

P-510 EDUCATION AND ORGAN SHORTAGE, A PROMISING CHALLENGE

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People plainly accept to donate their organs, however, relatives often refuse to please such will. For a change, it is essential to search for its reasons. Reviews, suggest two groups: A) Public B) Healthcare professionals.
How can organ procurement be improved? The unfair mortality waiting for the "Gift of Life, have encouraged to search for possible solutions. Proposed options were: 1) Legal, 2) Incentives, 3) Expanding donors, 4) Education. The first three aim for rapid results. Nonetheless, their feasibility and ethical acceptance are controversial. Conversely, education seems to be largely accepted.
How should an educational project be organized? Public's lack of knowledge and insufficient medical training are long standing problems which require a proper solution. It should be solved with: State and all Society's participation, and changing the message.
A change of message: People's ambiguous behaviour needs to be transformed. My proposal is to believe that:
1) Organ donation means sharing a chance of life with everybody.
2) Deceased organs are a source of health.
3) Throughout life we are more likely to be organ recipients than donors.
4) Organ donation should be a citizen responsibility.
5) The use of deceased organs should be considered as part of a fair agreement between individuals and society.
Conclusion: Education could be the pathway to improve organ shortage. Prejudism and disinformation must be eradicated. Education should be addressed to all Society, particularly to medical professionals and the youth. Schools should prepare the young ones to be protagonists so as to renovate Society's attitude concerning barriers on transplantation. Experiences performed in Canada and Argentina, showed that children understood this problem and were able to discuss it with their families. Finally, in order to successfully achieve this proposal, it is required: an active participation of the State and Churches, and support of the Transplantation Community.

P-511 NON-ADHERENCE TO IMMUNOSUPPRESSIVE MEDICATION IN RENAL TRANSPLANT RECIPIENTS WITHIN THE SCOPE OF THE INTEGRATIVE MODEL OF BEHAVIOURAL PREDICTION: A CROSS-SECTIONAL STUDY

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Background: Non-adherence to immunosuppressive medication is strongly associated with poor outcomes. Identifying the factors influencing it is a first step in developing adherence interventions. This study's objective was to investigate the prevalence of self-reported and collaterally-reported non-adherence to immunosuppressives, and, based on the Integrative Model of Behavioural Prediction, to explore the association between non-adherence, intention to adhere, attitudes, norms and self-efficacy.
Methods: This cross-sectional study included a convenience sample of 114 renal transplant recipients in follow-up care, one to five years post-transplant. Non-adherence was measured by self-reports and collateral reports. Factors of the Integrative Model of Behavioural Prediction were assessed using a self-report questionnaire.