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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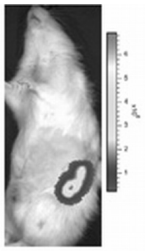
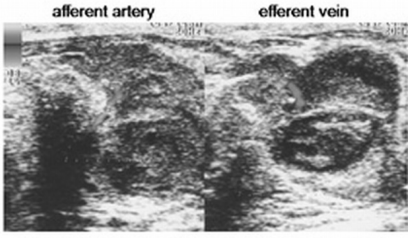
The worldwide shortage of liver grafts causes medical, social and ethical problems. Although this situation requires intensive efforts to develop alternative grafts using regenerative biotechnology, they are still far away from the practical application. Now, we have the strategy to develop regenerative 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.

Results: Self-reports showed non-adherence of 23.7%; collateral reports showed 3.8%; and a combination of the two showed 26.4%. Logistic regression analysis showed that the attitude 'Not all immunosuppressive drugs are necessary to prevent rejection' was less frequent in patients with higher intentions to adhere, with an Odds Ratio of 0.05 (CI 95% 0.01-0.50). The barrier of 'Forgetfulness/Interruption of daily routine' was associated with non-adherence, with an Odds Ratio of 3.74 (CI 95% 1.55-9.03).
Conclusions: Forgetfulness is the most powerful barrier against adherence. Intention to adhere plays a minor role in non-adherence in renal transplant recipients.

P-512 OBSERVATIONAL STUDY ON COMPLIANCE AFTER RENAL TRANSPLANTATION IN PATIENTS WITH ACCESS TO OTIS SOFTWARE (ORGAN TRANSPLANT INFORMATION SYSTEM): INTERIM RESULTS AT 3 MONTHS

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Rationale: Poor compliance concerns 22% of adults and in the field of organ transplantation. Non-compliant patients present a seven-fold higher risk of graft loss than compliant patients. Patient education programs have already been proposed in order to improve the compliance in some chronic diseases. A transplantation information tool, OTIS software (Organ Transplant Information System), has been developed. This tool was therefore proposed to patients during the first 10 days post-transplantation.
Patients and methods: A French, multicentre, prospective observational study was set up to evaluate the treatment compliance of renal transplant recipients based on the use of OTIS software.
Results: Two hundred and twenty five renal transplant recipients were included and 198 were reviewed at 3 months. At M3, the acute rejection rate was 7.1%. 93.1% of patients consulted at least one module of SITO software. 18.8% consulted all of OTIS software. 94% of patients reported that they were satisfied with OTIS software and 95% considered it to be an educational support ensuring a good level of information. At M3, 19.6% of patients were non-compliant. 41.7% of non-compliant patients presented disabling adverse effects versus only 20.4% of compliant patients ($p = 0.02$). Univariate then multivariate analyses demonstrated that the use of anxiolytics (OR = 3.02, $p = 0.04$) as well as a complete consultation of OTIS software (OR = 16.8, $p = 0.01$) were factors associated with good compliance at M3 post-transplantation.
Conclusion: The interim data of this study demonstrated that OTIS software was used just after transplantation by more than 90% of patients with an excellent satisfaction rate. Complete consultation of OTIS software was associated with good early compliance after renal transplantation.

P-513 PSYCHOLOGICAL FACTORS ASSOCIATED WITH NON-COMPLIANCE AFTER KIDNEY TRANSPLANTATION IN DIFFERENT AGE GROUPS OF PATIENTS

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Purpose: Compliance with medication is an inevitable part of the treatment after kidney transplantation (KT) in order to keep a functioning transplanted graft and maintain quality of life. However, only a few studies have considered the psychological factors involved. In this study we explored their role in different age groups.
Methods: 169 patients (64.5% male, 49±11.5 years) were split into 3 age groups (<40 years, 40-55 years, >55 years). They provided us with sociodemographic (family status, education, income) and medical (serum albumin, glomerular filtration, Davies' comorbidity index) data. Patients completed the Eysenck Personality Questionnaire (EPQR-SS), General Health Questionnaire-12 (GHQ-12), End-stage Renal Disease Symptom Checklist (ESRD SCL TM) and Social Support List (SSL). Compliance was assessed as a combination of both the patient's and a nephrologist's evaluation, where only patients with congruent evaluation were taken as compliant. Binary logistic regression was used.
Results: In the youngest age group a model consisting of higher cognitive limitation (ESRD SCL TM) (OR: 12.05; 95%CI 1.19-121.94; $p \leq 0.05$) increased the side effects of corticosteroids (ESRD SCL TM), and anxiety and depression (GHQ-12) explained 51.2% of the variance. In the 40-55 years age group a model consisting of higher psychological distress associated with KT (ESRD SCL TM) (OR: 11.83; 95%CI 3.25-42.99; $p \leq 0.001$) explained 37.8% of the variance. In the oldest age group no significant model was found. Results were controlled for all the mentioned variables.
Conclusions: Psychological factors are associated with non-compliance in KT patients under 55 years old, even when controlled for relevant variables. Different psychological variables play a role in different age groups, a fact that could be relevant for intervention programs aimed at decreasing non-compliance.

P-514 QUALITY OF LIFE (QOL) AFTER LIVER TRANSPLANTATION IN HIV+ SUBJECTS

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Background: The introduction of antiviral therapy has changed the prognosis of AIDS reducing mortality and thereby increasing the risk of developing terminal liver failure as a consequences of chronic co-infection with HCV and HBV. In this context liver transplantation (LT) has became a therapeutic choice.
Aims: Evaluate auto perceived QoL and psychosocial aspects of HIV+ patients subjected to LT.
Material and methods: Case-control qualitative study comparing HIV+ vs HIV- (control group) patients transplanted from 2004 by self-administration of the LEIPAD and BSI tests.
Results: 20 HIV+ vs 25 HIV- negative patients. Median follow-up was 13 months (range 0-22). Gender was male and female respectively in 86% and 14% in HIV+ vs 67% and 33% in HIV- ($p=0.36$). Mean age was 46,7±6,6 vs 56,4±4,9 years, $p=0,006$ for HIV+ and HIV-. Indication for LT, Child a MELD score were not different. The overall (21,1 vs 21,8, $p=0,78$) and single areas LEIPAD scores were similar between the two groups. HIV+ had better, although not statistically significant, results in the area of functional autonomy (3,4±4,4 vs 1,6±1,5 $p=0,20$) and social networks (3,8±1,1 vs 2,7±2,1 $p=0,27$), while HIV- were slightly better in terms of anxiety and depression (2,3±2,1 vs 3,3±4,2 $p=0,59$). Data for BSI were comparable but HIV+ had better scores for somatization (2,4±1,6 vs 3,7±4,0 $p=0,47$), compulsiveness (3,8±3,5 vs 5,6±3,8 $p=0,34$), depression (3,0±1,4 vs 3,6±5,7 $p=0.80$), anxiety (1,2±1,3 vs 1,6±1,5 $p=0.58$), phobic anxiety (2,0±2,4 vs 4,7±6,3 $p=0.31$), hostility (0,5±0,5 vs 1,0±2,0 $p=0.41$) ed paranoid ideation (0,5±0,9 vs 1,9±2,7 $p=0.25$).
Conclusion: Those data show that QoL and psychosocial aspects do not differ between HIV positive and negative patients subjected to LT.

P-515 SELF-RATED HEALTH OF PATIENTS AFTER TRANSPLANTATION IS DEPENDENT ON A CHANGE IN GLOMERULAR FUNCTION

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Purpose: Studies in self-rated health (SRH) in patients after kidney transplantation (KT) are usually focused on cross-sectional analysis of its predictors. Only a few studies have explored the relation between SRH and the graft function. The aim of this study was to analyse the relation between graft function and SRH over time.
Methods: 42 patients (median age 51 years, women 36%) were examined in the third month after KT (T_1) and twelfth month after KT (T_2). Sociodemographic data and data on glomerular function (Cockroft-Gault) were collected. Patients completed the SF-36 questionnaire measuring SRH. Linear regression was used to identify predictors of SRH at T_2. Age, gender, change in glomerular function and SRH at T_1 were set as independent variables.
Results: SRH and glomerular function slightly improved over time. The regression model consisting of age (β=-0.26, 95%CI -1.087;-0.035, $p<0.05$), change in glomerular function between T_2 and T_1 (β=0.31, 95%CI 9.267;63.643, $p<0.01$) and SRH at T_1 (β=0.5, 95%CI 0.247;0,68, $p<0.001$) explained 55% of variance in SRH at T_2.
Conclusions: Although SRH after transplantation is not associated with absolute levels of glomerular function, there is a significant association with a change in glomerular function over time. Improvement of the function of the

transplanted kidney is connected with improvement in self-rated health. This is important to consider when managing a patient, because a positive or negative change in glomerular function may have consequences for the patient's self-rated health.

P-516 "OUT-OF-THE-NORM" EXPERIENCES OF TRANSPLANTED PERSONS IN THE INTENSIVE CARE UNIT: PATHOLOGICAL OR NORMAL REACTIONS?

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The dichotomy between normality and pathology is a confining frame leading health care professionals to interpreting patients' behaviors in a pathologizing perspective, which does not correspond to the experience of the transplanted person. Most professionals feel uneasy when confronted to unusual, and apparently irrational intensive care unit (ICU) psychological reactions. They are usually labeled as psychotic and delirium episodes, or hallucinations.
We propose a theoretical discussion, illustrated with examples out of the analysis of 37 post-transplantation interviews of patients (heart n=12; lung n=14; liver n=11) admitted in the ICU after transplantation.
"Out of the norm" experiences were described. The extra-ordinary situation of transplantation, associated with the ICU threatening environment, psychoactive medication, and pain relievers, provoked in heart, lung and liver transplanted patients (59%) dreams, nightmares, which were so strange and vivid that patients were reluctant to disclose them. Positive (32% of the patients) and negative (49%) experiences were mentioned: the fight for life, mystical or spiritual experiences, feelings of overwhelming love, and near death experiences. Whereas forgetfulness, time were considered the best therapeutic tools by professionals, these experiences remained emotionally present in the mind of our interviewees even after relocation in the continuous care unit, and 24 months after transplantation. Intense emotions and anxiety were durably and intensely experienced.
The meaning associated to these unusual experiences, is not un-reasonable, and they must be contextualized in an interpretative system, of which the transplanted persons hold the key. A non-normative speech space is sought for by the transplanted, a space where emotional and psychological suffering is not considered as pathological. Existential theories allow to integrating these "Out of the norm" as well as the paradoxical situations of transplantation where the limits between life and death are extremely thin.

P-517 THE ETHICAL EQUIPOISE IN LIVING AND DECEASED DONOR LIVER TRANSPLANTATION: TOWARDS DECISION PROCESSES BASED ON MATHEMATICAL MODELS

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Background: The decision process allocating a specific organ from a cadaveric or a living donor to a particular liver transplantation (LT) recipient is strongly influenced by ethical issues.
Aims: A. To effectively represent the potential equipoise achievable between the different ethical principles involved in LT. B. To construct a mathematical decision model able to objectify and quantify these ethical aspects.
Methods: The desirable LT ethical equipoise may be described by a triangle with the transplant benefit (life expectancy with LT minus that without LT) at its superior apex and, the potential harms to the waiting list and to the living donor at inferior apices.

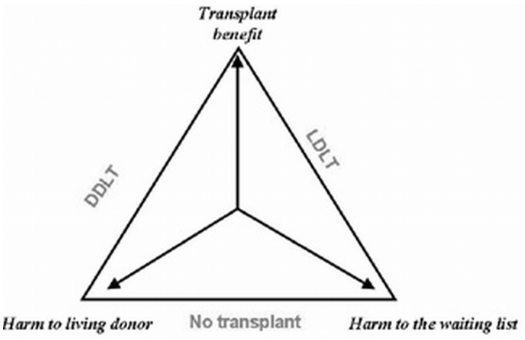

Figure 1. The ethical equipoise in liver transplantation.

We then constructed a Markov model to objectify and quantify the ethical equipoise triangle. The data sources to construct and validate the model were: the online UNOS web-site, and a prospective database from Padua about a new allocation model.
Results: Although our Centre was characterized by a higher proportion of HCC patients in the WL (25% versus 10%) and a lower proportion of high MELD score (>20) non-HCC patients (17% versus 27%) than the average US centre, these proportions were similar among transplanted patients.
By using several simulations of ethically critical scenarios, our model showed that it is possible to objectify, measure, and modulate the clinical-prognostic impact of the following ethical principles: the utilitarianism principles of benefit and of harm to the waiting list, the urgency and fair chances principles, the paternalistic and autonomy principles.

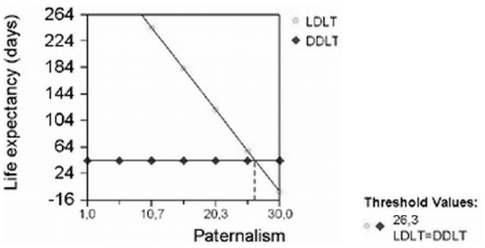

Figure 2. Ethical weight of living donor death.

Conclusion: We constructed and validated the first prognostic – decisional model based on both clinical and ethical variables able to influence the efficacy and safety of liver transplantation.

P-518 ANXIETIES AND DOUBTS ABOUT LIVING KIDNEY DONATION FROM THE RECIPIENT'S VIEWPOINT

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Purpose: In comparison to cadaveric transplantation, living kidney donations have a better outcome, as several studies published in recent years point out. Since there is a shortage of transplant organs in Europe, Germany as well as other European countries endeavour to increase awareness for living organ donation. Usually, the possibility that the donation request is the outcome of a donor-recipient relationship influenced by anxieties and doubts of the recipient is not taken into consideration. Therefore, our study is looking into the question whether recipients' doubts about living organ donation may inhibit a donor's willingness to donate.
Methods: In the context of a catamnestic study of donor-recipient pairs following up donation, in 2006/2007 we conducted an evaluation at the transplantation center of the Friedrich-Schiller-University Jena. Here, we also questioned recipients regarding possible problems connected with the acceptance of the donation request.
Results: We found that 14 out of 49 recipients (16 female, 33 male) did not inform their families about the possibility of a living kidney donation. 22 recipients (45%) had considerable difficulties accepting the donation offer of a close family member. 18 (37%) recipients doubted their decision prior to transplantation and 44 recipients (90%) were worried about the donor's well-being.
Conclusion: Our data suggests that despite terminal kidney insufficiency recipients harbour anxieties and doubts regarding a living kidney donation. Since the potential recipient's attitude may have a considerable influence on the realisation of a donation by a family member, recipients' reservations should be taken into account in the context of informing about living organ donation.

P-519 CORRELATES OF WILLINGNESS TO PAY FOR A KIDNEY TRANSPLANT

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Purpose: Dialysis patients constitute an attractive willingness-to-pay (WTP)

study group because kidney transplant could trigger interest to hypothetically trade wealth for health. Using a Greek sample, this study aimed to identify socio-demographic and clinical correlates of WTP in this patient group.
Methods/Materials: 32 dialysis facilities were randomly selected and 24 agreed to participate. All adult patients (aged 18+) were eligible and chosen by clinical and nursing staff in each facility based on their mental and physical ability to read, comprehend and complete the self-administered survey, which consisted of socio-demographic, clinical and two WTP questions. Overall, 606 dialysis patients were approached (response rate 78.5%). WTP differences were examined (with t-test and ANOVA) as a result of age, gender, education, familial status, employment, comorbidities and previous unsuccessful kidney transplant. Monetary values are reported in € (2004).
Results: The sample (61.6% males, mean age 57.1) was on dialysis for 6.1 years on average. 10% had already been unsuccessfully transplanted and >30% were on the waiting list. 40.5% were unwilling to pay any amount for a kidney transplant, 9.7% would pay up to €15,000, 18.8% exactly €15,000 and 31.0% would pay more. €100,000 was the highest reported amount. Higher WTP was reported by younger patients ($P<0.0005$), males ($P<0.05$), higher education levels ($P<0.01$), single ($P<0.0005$) and employed ($P<0.005$). Patients having experienced an unsuccessful kidney transplant were willing to pay approximately 60% more than those never transplanted ($P<0.05$).
Conclusion: The ethical concern was that patients might be misconceived and think that they would be asked to pay out-of-pocket in an actual transplant situation. Interestingly 75% of "unwilling" patients were not on the transplant list. Contrarily, patients already unsuccessfully transplanted were willing to pay more than others never transplanted, perhaps because they had experienced (sometimes only briefly) the benefits in terms of quality of life.

P-520 DEVELOPMENT OF THE ESSEN COMPLIANCE SCORE – MEASUREMENT OF ADHERENCE IN KIDNEY TRANSPLANT PATIENTS

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The purpose of the project was to develop and validate a new questionnaire and score to measure adherence in transplant patients.
We modified the Morisky-Score to the Essen Compliance Score (ECS). The weakness of the Morisky-Score is its shortness and the categorical answer options. To create a better tool measuring patient adherence, we extended the 4 questions to 24 items and used a Likert-Scale. Clinical data (e.g. creatinine, GFR, GFR slope, CNI levels, etc) and psychological questionnaires were used for validation (End-Stage Renal Disease Symptom Checklist-Transplantation Module (ESRD-SCL-TM), Essen Questionnaire of coping mechanisms of illness (EFK), a short form of the SF-36 health survey questionnaire (SF-8), a questionnaire of social support (F-Sozu-K14)).
Between Dec 2007 and July 2008, 418 kidney transplant patients (57.1±12.8 years, male 56.7%, time since Tx 87.4±80.2 months (range 1-336)) have completed the questionnaire in our outpatients department. 18 of the 24 items were suitable to build the Essen compliance score. A Score of 0 indicates perfect compliance (possible score 0-72). The mean score was 4.89±5.23 (range 0-32). A third of the patients were perfectly compliant. A third of the patients showed low adherence indicated by a score >7. The ECS correlated with acute rejection episodes but missed statistical significance (p=0.06). The ECS showed good correlation with the actual creatinine level ($p<0.01$) and the cyclosporine levels (p=0.04). The score correlated significantly with the ESRD-SCL-TM, the EFK, the SF-8 and the F-Sozu-K14.
In conclusion, the ECS is a reliable and valid instrument for measuring adherence in kidney transplant recipients. The ECS correlates well with clinical and psychological parameters. Compliant and non-compliant patients may be distinguished by the ECS.

P-522 CHARACTERISTICS OF THE REGIONAL TRANSPLANT COORDINATOR IN POLAND

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Objective: The aim of the study was to characterize the job description of the regional transplant coordinators and rates of organ donation per million population (p.m.p) in Poland in the years 2000-2007.
Methods: We analyzed demographic data and Polish legislative acts. The coordination of organs retrieval and transplantation is specified in the Ministry of Health Regulation 2007 as an postgraduate accomplishment in the field of medicine. Furthermore, the requirements regarding education, adequate length of work and experience in the field of organs, tissues and cells retrieval and transplantation for transplant coordinator and senior transplant coordinator are specified by law. However, precise law regulations for coordinators in Poland are lacking.
Results: Transplant centers are present in 11/16 Polish regions. Official duties of the regional transplant coordinators are performed in Poland by 15 professionals (53% females, 47% males, mean age 40) in 10 out of 16 Polish regions. 87% of coordinators have acquired higher education (40% physicians, 53% nurses, 7% other). Mean length of work experience is 11 years. They are employed mostly in kidney transplantation centers as coordinators (60%) and additionally as a part-time workers (86%) in Polish Transplant Coordinating Centre "Poltransplant". Coordinators are responsible for donors detection, organs retrieval and transplant coordination. Mean rate of organ donation in Poland in 2000 – 2007 was 12,83 p.m.p. The highest rate was noticed in Zachodnio-Pomorskie Region (31 p.m.p) and the lowest in Podkarpackie Region (1,1 p.m.p) and Swietokrzyskie Region (0,8 p.m.p).
Conclusions: The rate of organ donation p.m.p in Poland is low. In 6/16 Polish regions there are no official posts of regional transplant coordinators. It is essential to create official posts for local transplant coordinators in Polish hospitals and to implement particular law regulations for transplant coordinators in Poland.

P-525 DONOR'S AND ORGAN REPRESENTATIONS IN LIVER, KIDNEY, HEART AND LUNG TRANSPLANTATION: A QUALITATIVE LONGITUDINAL STUDY

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Purpose: Organ transplantation is a biological and psychological challenge and graft acceptance is an important achievement for patients. Patients' concerns toward the deceased donor and the organ may contribute to this process.
Method: Forty-seven patients involved in heart (N=9), liver (N=8), lung (N=14) and kidney (N=16) transplantation participated in IRB-approved longitudinal semi-structured interviews: (T1) registered on the waiting-list, (T2) six months and (T3) twelve months after transplantation. Qualitative pattern analysis (QUAPA) was carried out on the verbatim transcripts and concerns about the donor and the organ were then analysed.
Results: – Donor's representation:
At T1, patients were reluctant to talk about the donor: 27% expressed culpability and 19% accepted the clause of anonymity.
At T2, intense emotions were associated with the reminiscing about the donor and 45% highlighted the generosity of his/her act. In addition, heart, lung and kidney recipients were concerned about the donor's identity: 42% challenged the clause of anonymity. Liver recipients complained about anonymity, but could nevertheless cope with it.
At T3, 47% of heart, lung and kidney recipients thought daily of the donor and 33% were still looking for information about him/her. Liver recipients rarely have thoughts about the donor.
– Organ representation:
At T1, organ descriptions were biomedical (49% of the interviewees) and more rarely, mainly heart candidates, referred to the symbolic meaning of the organ. After transplantation (T2-T3), function was underlined. Acceptance and organ integration were associated with post-operative outcomes (23%) and psychological well-being (45%). Some patients (32%) inferred the donor's personality from the organ quality and felt privileged having received an organ in such a good state.
Conclusion: Donor's representations should be explored during the transplantation process as they play an important role in the psychological acceptance of the graft.

P-526 ETHICAL CONCERNS SURROUNDING LIVING DONOR LIVER TRANSPLANTATION IN EGYPT

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Since brain-death criteria are not accepted in Egypt, only organs acquired from living donors can be used for transplant. Our objective was to highlight the ethical issues raised by living-donor liver transplant.
Materials and methods: The study was conducted by reviewing publications

from centers performing living-donor liver transplant in Egypt and by consulting with a group of experts in the fields of liver transplantation, clinical ethics, and religious scholarship.
Results: The first successful living-donor liver transplant in Egypt was performed at the National Liver Institute in 1991; however, this programdid not continue because of poor early results. In August 2002, transplants began at Dar-Al-Foaud Hospital; since then, almost 700 cases of living-donor liver transplant have been performed at 9 centers. Although the donor risk is estimated to be low, 2 donors died (0.3%). The ethical principle that best applies to living-donor liver transplant is *primum non nocere* (first, not to harm), as the donor derives emotional benefit fromdonation and the opportunity to save a life. It is important to stress that the alternative to living-donor liver transplant in Egypt is not deceased-donor liver transplant. There are no doubts that this is a beneficial procedure for the recipient with acceptable risks to the donor.
Conclusions: There are significant risks to the living donor, including the risk of death and substantial morbidity, that must be taken into account before patients, physicians, and transplant programs embark on living-donor liver transplant. It is important, therefore, to uphold the highest medical and ethical standards in the programs' transplant practices to obtain maximum benefit for both donor and recipient.

P-527 DONORS/RECIPIENTS REPRESENTATIONS ABOUT LIVING-KIDNEY DONATION

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Living-kidney donation offers an option to patients awaiting renal transplantation. Representations about giving-receiving are explored retrospectively in a qualitative study.
Questionnaires with open questions were sent to thirty donor-recipient dyads. Interviews were also conducted, during which participants were invited to propose an image representing donation.
Thematic analysis was performed on the questionnaires (twenty-nine donors; twenty-five recipients), and on the comments of ten images selected by five donors and five recipients. Percentages are given regarding each part (donors; recipients).
In the questionnaires, life (34.5%; 12%), love (27.6%; 40%), quality of life (27.6%; 8%) and generosity (6.9%; 24%) are common grounds regarding giving-a-kidney. Obviousness, hope, personal benefits or duty are expressed by donors. Recipients explain donation through emphatic sentences, qualify it as a gift or refer to the donor's courage or risk-taking.
Regarding receiving-a-kidney, life (31%; 60%), gift (10.3%; 28%) and debt (3.4%; 4%) are common grounds. Donors refer to generosity or love. Quality of life, donor's risk-taking or emphatic sentences are characteristic of recipients, who highlight that nobody had to die.
Preliminary data on the comments of the images underline that live-donation represents life and love. Mutual help, sharing-act, obviousness and personal benefits are expressed by donors. Recipients use emphatic sentences or refer to quality of life, gift or the difficulty to accept donation.
Life and love are common grounds in live-donation. Improvement in quality of life is underlined by recipients, who stress the donor's courage or risk-taking. Donors describe donation as obvious, sometimes accompanied by personal benefits. Feelings of duty (donors) and of debt (recipients) are less discussed. Representations about giving and receiving differ between donors and recipients. These data show the specificity of each perspective. This analysis provides valuable information in order to adapt individual or dyad psychological support in live-donation.

P-528 FUTURE VISION FOR THE TRANSPLANTS: QUALITY OF CONTEMPORANY LIFE

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Introduction: The potential donor is that with diagnosis of cerebral death, in which have been excluded clinical complications. The objective of the study was to describe and to discuss as the people's lifestyle in the nowadays can interfere in the organ and tissue donors viability for transplants.
Methodology: This is a descriptive observational study. Samples of 385 deaths recorded in the University Hospital-UNICAMP were evaluated by the Commission of the Organ and Tissue Search (COTS), from July to December of 2008. Variables: Gender, Age group: $>$ 12 and $<$70 years old, all notified for cerebral death and cardiorrespiratory arrest. Contraindications: sorologies, juridical and clinical conditions.
Results: Gender: 205 (53%) males and 180 (47%) females. Multiple organ donors: 04 donations, 03 family refusals, 03 clinical contraindications, 01 positive sorology and 15 donors presented cardiorrespiratory arrest. Tissue donors: 06 donated the corneas and 09 family refusals. Contraindications: 13 (4%) sorologies; 9 (3%) juridical; 138 (39%) septicemia and/or shock; 6 (2%) neoplasms and 183 (52%) cardiac, respiratory, renal and gastroenterological diseases.
Conclusion: The health promotion and life quality of the Brazilian population associated to intensive educational actions and efforts of the COTS's can improve the potential donor numbers in the future.

P-529 ANTHROPOLOGY OF THE DONATION: ALTRUISTIC EGOISM AND SUSPENSION OF THE EXCHANGE

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Purpose: The spread of the culture of donation and the management of donors continues demanding for a multidisciplinary approach because of the various forms of donation (blood, haemopoietic stem cells, organ) and because of demographic variables. Thereby, the communication instruments require social-anthropological competences to promoting donation. The aims of the study are a) review of literature regarding the anthropological patterns of the gift; b) the analysis on different kinds of donation
Methods/Materials: A review of literature from the early studies of M.Mauss up to A.Caille' and J.Marion, J.Derrida has been carried out
Results: M.Mauss and A.Caille' argues that the act of donating is based on the fundamental phases of giving-receiving-paying back and that every social system is marked by the gift which becomes a social interaction instrument.The gift, with the reciprocity, is the foundation of personal, family and social interaction and does not exclude the spontaneity and the authenticity of the act itself: it is a paradoxical gift, both interested and disinterested at the same time. On the other hand, Derrida holds the idea of an absolutely free gift which involves the suspension of the exchange: the gift is authentic if it is overflowing, if it exceeds during every gratitude
Conclusion: Among the described anthropological patterns, that of M.Mauss seems to be closer to the blood donation since there is a reciprocity on terms of membership regarding associations and periodical check-ups. The stem cell or organ donor seems to correspond to the model of J.Derrida in which there is a minimum of reciprocity and the gestures exceeds on pay back. The analysis of anthropological patterns may be useful for recognizing the motivations, the sensibility and the ethical background of donors necessary to increase the donor recruitment.

P-530 TRANSPLANT TOURISM FROM THE UK. WHAT IS THE OUTCOME

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Background: An increasing number of patients attending renal transplant assessment clinics ask advice regarding live donor renal transplantation performed outside the UK. There is a lack of data regarding outcome of living related and unrelated renal transplants from patients who travel from the UK to other countries recognised as common destination of transplant tourists.
Material and method: We retrospectively reviewed the database from three different renal transplant units and identified 58 consecutive patients who received a renal transplant abroad. Five had cadaveric transplants and were excluded from the analysis. Fifty-three were from living donors; nine related and 44 unrelated. We used as a control group 40 patients who received a living donor renal transplant in our units and were matched by year of transplant and age of recipient at time of transplantation. We analysed one-year patient and graft survival.
Results: 90% of patients transplanted abroad were Asian. In the control group 70% were Caucasian. Median age was 40 and 39 years.
In the group transplanted abroad there were 9 deaths. One-year patient survival was 83%. Main cause of death was septicaemia. In the same group 9 grafts were lost in the first year. Death censored one-year graft survival was 79.5%. The main cause of graft failure were rejection and technical failure.

In the control group patient survival was 100% and one-year graft survival was 98%.
Conclusion: Transplant tourism is ethically unacceptable and paid donation is illegal.
However a large number of UK resident patients are transplanted abroad. The results of this series are worse than those from our units and national data. Data collection proved to be challenging and some patients may have been missing.
This study may offer a useful tool for counselling patients wishing to travel abroad for a renal transplant.

P-531 INTRODUCTION OF DONOR ACTION PROGRAM IN JAPAN. AN ANALYSIS OF SURVEY RESULTS USING MRR AND HAS DATA

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Purpose: In Japan, in spite of the favorable public attitudes toward organ donation and transplantation, the donation rate remains very low. Opinion polls showed that 43.5% of respondents were willing to donate their organs in case of their deaths, but the donation rate in Japan was 0.86 donors PMP in 2008. Donor Action Program (DAP) was introduced in 2002 to increase the donation from cadaveric donors. As of March, 2009, 47 hospitals in 13 prefectures have introduced DAP.
Methods: We carried out analysis of 1,988 Medical Record Review (MRR) data, and 11,106 Hospital Attitude Survey (HAS) data from 2002 to 2007.
Results: Although 34.1% of MRR cases were considered to be suitable for donation medically, only 3.0% were diagnosed as being brain dead, and family members were contacted for possible donation in 1.1%. HAS showed that most medical staff (79.9%) thought that the life of other people were saved by transplantation, but only 8.2% thought that the grief of the family would be healed by donation.
Conclusion: Our tentative analysis showed that the donation process in participating hospitals in Japan could improve in the areas of donor identification, diagnosis of brain death, and explanation to families about possible donation. HAS results showed that medical staff were likely to underestimate the social needs and positive results of transplantation, to lack experience and feel stressful in being committed to donation, and they wanted education concerning donation and grief care. The intervention consisting of educational program to medical staff would improve organ donation processes is to be evaluated in the future.

P-532 ORGAN TRANSPLANTATION AND KNOWLEDGE TRANSLATION: ETHICAL ISSUES

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The problem: Translation of knowledge in biomedical sciences is usually interpreted as the transfer from bench to bedside ("getting research into practice"), that is the translation of new understandings gained in the laboratory into new methods for the treatment of diseases. Nevertheless, there are two other important "getting research into practice" in research. The first is from clinical studies into clinical practices and policies (*JAMA*, 2008;299(2):211-3). The second follows the opposite direction ("getting research into practice"): it is undeniable that decision-makers have influence on the research agenda and on research priorities (*Bull WHO*, 2007;85(6):424-5).
The framework: From an ethical perspective, translation of knowledge brings opportunities, but also risks. The main risk is to infringe a basic ethical requirement: "getting research into practice" (World Medical Association. Declaration of Helsinki, rev. 2008). The efforts to obtain advances in knowledge and techniques are dutiful, but they should not impair the care for the individual patient. Practically, this means that the efforts to gain knew knowledge and to improve the techniques do not justify exposing patients to disproportionate risks.
Conclusions: The submission of new transplant protocols to ethics committees is highly recommendable. Moreover, members of the ethics committees who are more responsible in evaluating transplantation protocols should be adequately trained. Finally, it would be useful the establishment of a bioethics consultation service (skilled in ethics, law, clinical medicine) in the main transplantation centres.

P-533 ETHICAL CHALLENGES AND DEBATES OF THE ROMANIAN LAW OF TRANSPLANTATION

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The purpose of this study is to explore the ethical dimensions of the current Romanian laws concerning transplantation (Title VI from Law 95/2006). The study examines two particular issues, that are of general interest.
The first one is the legal definition of consent, in light of recent attempts to modify the legislation in a way that would permit the introduction of the "presumed consent". The ethical implications of both positions – the currently accepted one, that of "presumed consent" and the proposed one, that of "presumed consent" are carefully analyzed. The public debate raised by the discussion of the law modification is also documented, with special focus on the ethical limitations of both positions.
The second one concerns the legal prospects of the so-called "presumed consent", i.d., living non-related donors. Currently, Romanian legislation is open to the alternative of altruistic donors; however, some limitations are imposed on them, due to the fact that is illegal to advertise one's condition in search for a transplant. The legal provisions are analyzed in relation to several mediatic cases in which some celebrities publicly admitted looking for organs (and in some cases obtaining them) without being legally sanctioned.
The conclusions of the study summarize the main ethical limitations of the Romanian law of transplantation: the impass concerning the presumed consent, that, if adopted, would raise the number of transplanted organs; and the limitations it imposes on altruistic donors.

P-534 EVALUATION OF THE 3 YEAR POST TRANSPLANT RESULTS OF THORACIC TEAMS IN FRANCE (2000-2004)

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Objective: The Agence de la biomédecine has developed an evaluation of the quality of organ transplantation results in France. The aim was to compare the 3-year graft failure of each transplant centre to the national graft failure rate, after adjusting on the recipient, donor, and transplantation characteristics.
Methods: All recipients transplanted from 2000 to 2004 registered on the national waiting list were included, except living donor transplantations. It represented 1546 heart and 462 lung grafts.
The national database (Cristal) of all patients registered on the waiting list in France and donors was used. The objectives, methodology and univariate analysis results were presented and discussed with medical staff of transplant centres before the final evaluation.
A multivariate Cox regression model was used including all predictive factors of the 3-year graft failure. The adjusted failure rates were estimated for each transplant centre and compared with the 99% confidence interval of the national failure rate using the funnel plot method.
Results: Twenty six centres for 1546 heart transplantations and 12 centres for 462 lung transplantations were included; the national failure rate was respectively 27% and 44%. Thirteen heart and six lung predictive factors were included for adjustment in the multivariate analysis of the 3-year graft failure. One heart centre was significantly upper than the 99% confidence interval of the national failure rate and two heart centres were significantly lower; all lung centres remained in the 99% confidence interval.
Discussion: This work was realised to complete a prior work on the 1-year adjusted graft failure rate using logistic regression model. The results obtained by these two methods were different. Thus, the Agency provides new tools to permit voluntary efforts from transplant centres toward improvement of quality of care.

P-535 INCREASED DEATH FROM CARDIOVASCULAR AND INFECTIOUS CAUSES IN FAR LIVING RENAL TRANSPLANT (RTx) PATIENTS

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We investigated whether patients receiving RTx who live farther from their attending nephrologist are more likely to die than those who live closer. A random sample of 167 patients who undergone RTx between 1996 and 2004 in Egypt was examined. We calculated the distance between each patient's residence location and the practice location of their attending nephrologist. We used Cox proportional hazards models to examine the adjusted relation between distance and clinical outcomes (death from all causes, rejection episodes, infectious causes and cardiovascular complications) over a follow-up period of up to 6 years. During the follow-up period (median 3.3 yr, range 1.0–6.5), (22%)

patients died. Compared with patients who lived within 50 km of their nephrologist, the adjusted hazard ratio of death among those who lived 50.1–150 km away was 1.04, 1.16 for those who lived 150.1–300 km away and 1.19 for those who lived more than 300 km from their nephrologist (p for trend <0.001). The risk of death from infectious causes increased with greater distance from the attending nephrologist (p for trend < 0.001). The risk of developing acute rejection episodes did not increase with distance from the attending nephrologist (p for trend =0.2). The risk of death from cardiovascular causes increased with distance from the attending nephrologist (p for trend <0.05). Compared with patients who lived within 50 km of their nephrologist, the adjusted hazard ratio of death among those who lived >300 km away was 1.75 for infectious causes and 1.39 for cardiovascular causes. We can conclude that mortality and morbidity associated with RTx was greater among patients who lived farther from their attending nephrologist, as compared with those who lived closer.

P-536 EVALUATION OF ACCESSIBILITY AND USE OF WEB BASED INFORMATION TECHNOLOGIES IN PATIENTS ON THE WAITING LIST FOR RENAL TRANSPLANTATION

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Purpose: Websites with medical content are increasingly used by patients with chronic disease. Yet the retrieval of relevant and quality based medical information related to specific topics like renal transplantation remains problematic. This study investigates the usage of web based information technologies among patients on the waiting list for a renal transplantation. It aimed to evaluate the source of information for patients and the barriers of internet search.
Methods: We provided a web portal of quality assessed medical information related to topics of renal transplantation. In order to evaluate accessibility and internet usage a questionnaire was developed including 40 items. It was distributed to 231 dialysis patients on the waiting list for renal transplantation
Results: Results from 117 patients (51%) were subsequently analysed. The internet usage within the group was 70%, with a focus on searching medical information. 82% of the individuals were interested in getting further web based information regarding transplant related topics. However, 35% of the recipients had difficulties within the internet search process. 93% of patients prefer quality assessed information given primarily by their transplant centre or by their physicians (in 73%). The most important topics of interest for patients were information about life after transplantation, the sequels of immunosuppressant therapy and the risks and benefits of the surgical procedure. Yet none of the participants knew established indicators of health information quality assessment
Conclusion: The study highlights the importance of information in this group of patients waiting for renal transplantation. There is still a lack of high quality web based information about renal transplantation. To improve this quality of health information a rigorous input from transplant professionals is necessary.

P-537 ASSESSMENT OF ANXIETY AND/OR DEPRESSION DISORDERS IN A HOSPITAL WARD FOR TRANSPLANT PATIENTS

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Objective: Measurement of depression and anxiety rates in a population of patients hospitalized in a kidney transplant ward.
Material and methods: Nineteen patients hospitalized in a kidney transplant ward (9 men and 10 women), with an average age of 47.05 years and a mean hospitalization of 11.68 days, were assessed on a single day. The following tests were administered: Beck Depression Inventory, Hamilton Anxiety Scale and Closed Interview. All the patients in the ward were assessed, except one with a psychiatric disorder.
Results: Of all the hospitalized patients, 10/19 (53 percent) had depressive symptoms, 2/19 (11 percent) had anxiety symptoms, 2/19 (11 percent) had mixed symptoms (anxiety and depression), and 5/19 (25 percent) had no symptoms whatsoever.
Of all the hospitalized women, 6/10 (60 percent) had depressive symptoms, 2/10 (20 percent) had mixed symptoms, and 2/10 had no symptoms whatsoever.
Of all the hospitalized men, 3/9 (33 percent) had depressive symptoms, 1/9 (11 percent) had anxiety symptoms, and 5/9 (55 percent) had no symptoms whatsoever.
On the first 15 days of hospitalization, 8/19 patients (42 percent) had some kind of symptoms (depression and/or anxiety).
Conclusions: Hospitalization caused anxiety- and/or depression-related symptoms in most patients. The prevalence of symptoms was greater in women than in men. The highest rate of symptoms occurred on the first 15 days of hospitalization.
Anxiety and/or depression may have an influence on the physician-patient relationship, the understanding of information and the expectations for the future.

P-538 LIVE DONOR KIDNEY TRANSPLANTATION (LDKT): ATITUDES OF HEALTHCARE PROFESSIONALS AND PATIENTS TOWARDS ELDERLY AND MARGINAL DONORS

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Purpose: We surveyed the views of medical and nursing staff involved in the care of patients with end-stage renal failure and of patients on dialysis, kidney transplant (deceased or live donor) recipients and live kidney donors regarding the acceptability for LDKT of elderly (>65) and marginal donors with problems such as obesity, hypertension, Type II diabetes or atherosclerosis.
Material & methods: The participants were recruited in a tertiary renal and transplant centre and were invited to complete an anonymous questionnaire. They were then involved into focus groups and semi-structured interviews were conducted.
Results: 464 participants completed the questionnaire (36% healthcare professionals and 64% patients). 64% of participants stated that elderly and 49% that marginal donors should be accepted for LDKT. Healthcare professionals were less keen to accept marginal donors ($p<0.0001$). In the semi-structured interviews participants stated that the risk regarding the effect that nephrectomy will have on the donor's health and quality of life, should be presented not only by the transplant team but also by an independent third party(ies) and that the issue of "how desperate" is the situation of the recipient should also come into the equation. Healthcare professionals stated that no matter how strong is the will of an individual to donate a kidney regardless of his age or health problems and how much he/ she is prepared to take any risk, healthcare professionals should always have the right to say "no" if they believe that performing a certain LDKT is against their professional standards and ethical values.
Conclusions: Elderly and marginal donors were considered as acceptable for LDKT from about half of participants and emphasis was given to the proper calculation and presentation of the risk of such transplant.

P-540 LIVE DONOR KIDNEY TRANSPLANTATION (LDKT): ATTITUDES TOWARDS THE PATHWAY TO SURGERY AND POST-OPERATIVE FOLLOW-UP

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Purpose: We surveyed the views of medical and nursing staff involved in the care of patients with end-stage renal failure and of patients on dialysis, kidney transplant (deceased or live donor) recipients and live kidney donors regarding their attitudes towards the pathway to LDKT and the post-operative follow up.
Material & methods: The participants were recruited in a tertiary renal and transplant centre and were invited to complete an anonymous questionnaire. They were then involved into focus groups and semi-structured interviews were conducted.
Results: 464 participants completed the questionnaire (36% healthcare professionals and 64% patients). Most perceived the risk for the donor as small or very small (63%). 49% stated that a potential donor should be given up to 3 months to re-consider the decision to donate. Participants were almost equally divided whether family consensus of the donor's family is necessary (46%) or not (44%) in LDKT. 71% suggested that patients appreciate more LDKT after even a short period on dialysis. 58% of participants thought that donor and recipient should be next to each other in the post-operative period. 45% believed that the post-operative follow-up for the donor should last up to 1 year and 37% more than a year while 83% believed that the donor follow up should include medical condition and quality of life. In the interviews, participants stated that despite donor's autonomy, family consensus is very important since it makes LDKT a positive experience and ensures long-term family support for donor and recipient.
Conclusions: Participants believed that LDKT is safe for the donor and that the pathway to surgery and the post-operative follow up should be done in a way that ensures lack of coercion, family support and a well rounded post-operative follow up.

P-541 SOCIAL ASPECTS IN KIDNEY TRANSPLANT RECIPIENTS WHO WENT THROUGH TRANSITION FROM PEDIATRIC TO ADULT MEDICAL CARE

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Purpose: Describing social aspects in kidney transplant patients who went through transition from pediatric to adult medical care.
Materials and method: Descriptive study. Period: October-November 2008. Sample: 20 patients transplanted in pediatric centers, currently followed up at the Nephrology and Kidney Transplant Unit of a Public Hospital (adult only) in the C.A.B.A. Disctrict Network. Data Collection Instrument: Structured interview with closed ended questions performed by psycologists.
Results: *Background/demographic information*: Sex: 35% Female, 65% Male. Average Age: 26.
Living situation: 17/20 (85%) live with original family group, 3 young subjects live with relatives.
Education: 16/20 (80%) reached secondary education or further, 9/20 (45%) non-university or university level. As for the impact of disease within formal education period: 5 patients dropped out. In addition, 5/20 (25%) are currently studying and 7 patients plan to continue with their studies.
Employment Status: 11/20 (55%) patients are working. Only 4/11 (36%) of them have retirement funding provisions.
Retirement Status: 9/20 (45%) receive disability pensions, however, the total covered is 14/20 considering allowances collected by parents of children with disability.
Health insurance: 17/20 are covered, the others 3 are covered by Buenos Aires Transplant Program.
Social Benefits: 6/20 (30%) receive social benefits from council from the State.
Conclusions: Importance of the rol played by family in the intellectual-cultural development and high level of instruction reached by the patients is illustrated in this sample. However, only few of them gain access into the benefits deriving from formal employment. Consequently, a high rate of patients keep their disability status to avoid losing social benefits. Social security is still the main support. The social issues of this group shows no substantial differences with groups of patients of others ages.

P-542 COMPARISON OF MEDICAL ECONOMICS ASPECT BETWEEN CADAVER RENAL TRANSPLANTATION AND DIALYSIS IN JAPAN

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Introduction: The number of patients with physical inconvenience was estimated 3,245,000 in Japan. The number of patients with handicap in vision, audio, or language has been leveling off in last several years, however, that with end stage renal disease (ESRD) has increased 36.7% compared to 1996 in Japan (about 10,000 patients increase per year). The increase in this patient load has contributed to the increase in the medical expenses in Japanese society considerably. In this study, the expense of renal transplantation was compared with the dialysis in Japan, and comparison examination of the medical expenses of renal insufficiency medical treatment with Japan and the OECD member nation was carried out.
Materials and methods: The medical expense of the renal transplantation in our institution in these ten years was investigated. The data of the expense for dialysis of other countries and a transplant was investigated and referred to from the health insurance database which can be available.
Results: Average medical expense for dialysis cost 6 million yen ($60,000)/patient/year. Because the number of patients with dialysis is over 280,000 in year 2008, the expense of dialysis reached more than 130 billion yen ($1,300 million) every year. On the other hand, the expense of renal transplantation/patient requires 7 million yen per year ($70,000) in the first year, however, it cost less than 2 million yen ($20,000)/patient/year in second year and afterwards. In addition, there is no calculation to the technology as a transplant specialist in medical treatment fee expense of Japan.
Conclusion: We considered that more kidney transplants should be performed as medical treatment to a renal insufficiency patient in Japan from the predominancy on QOL and medical economy.

P-543 ETHICAL LAW AND PROCUREMENT IN FRANCE: EVALUATION AND COMMENT

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In 1976 the "Cavaillet" law provided, for the first time, a legal framework for organ donation. The principle being based on "Presumed Consent" (PC). Doctors are required to search for the deceased's refusal either in his papers, in the hospital's register or by questioning the relatives. In 1994, the Ethic Law abrogated the previous law and reinforced the fundamental principle. It also gives a more important role to the family. The Doctor is obliged, to gather evidence from the family. Following the first revision of the law in 2004, the non-opposition of the deceased must be sought by his relatives.But what happens in reality? Generally,the experience shows that not only is the law of no help, but in fact is perceived as a hindrance, a rigid framework, in a situation where human factors should take precedence over all other considerations. People are not acquainted with this law and only become aware of it during a difficult and painful situation, and so are in no frame of mind to accept the finality of the law. This law can even give family members the impression of an all powerful medical profession which would be allowed to proceed with procurement in spite of possible opposition from the relatives.To make matters more complicated, when the relatives are not aware of the deceased's wishes, they feel entrusted with a heavy responsibility toward him. So they decide in his place.The next revision planned for 2009/2010, should retain the PC principle. In order to enable the medical profession to apply the law in a more human way, it is a necessity that an information campaign about the content of the law be widely and frequently broadcasted.

P-544 SHIRAZ TRANSPLANT CENTER IS SURPASSING THE LIVING UNRELATED DONORS

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Public education and presumed consent has facilitated the process of obtaining consent in the western countries. The Eastern countries still are in the beginning of the way. Although the number of transplant patients in the Middle East is increasing an it seems that no long waiting list is present but majority of donors are unrelated. For overcome of this problem we started education of the physician and nurses of our area. Shiraz transplant center founded in 1988, the kidney transplantation program continued with living mostly unrelated donor when no cleric Fatwa, no brain death approval no national organization for donation. Fatwa for using deceased donor organs announced in 1989 in Iran. Parliament approved donation from the brain death donors in 2000 and national network for organ transplantation was established in 2002. From 1988 to 2002 our center on the base of cleric Fatwa started education courses of necessity, diagnosis reporting and confirmation of brain death for medical staffs. During this period more than 100 nurses 60 physician participated in the courses. From 1998 to 2002 more than 130 consents were obtained and each years the number was increasing. Transplanted patients in Iran Up to now is 23200 that only 6% is from deceased donor and the rest is from the living mostly unrelated. In our center 25.5% transplanted patients are from deceased donors, 32% from living related and 42.5% for living unrelated donors, while our area population is 1/15 of country's population. In this article we described the detail of the study for increasing number of deceased and living related donors principle.

P-545 RELATIONSHIP BETWEEN SOCIAL AND PSYCHOLOGICAL DIAGNOSES IN ASSESSMENTS FOR INTRATHORACIC TRANSPLANTATION

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Introduction: Both psychological and social evaluations are part of multidisciplinary studies that candidates for intrathoracic transplant usually undergo.
In our experience, we have proved that an isolated evaluation dichotomizes patient's reality, and provides a partial view of the patient's situation.
Objectives: To find out dependence between the psychological and social diagnoses in transplant assessments. To analyze whether social variables condition psychological variables or viceversa.
Materials and methods: Between January 2, 2001 and March 1st, 2005, 331 psychosocial evaluations obtained after both individual and family interviews, social visits and self-administered diagnostic techniques (Zung's depression test and STAI anxiety test) were assessed:
Social categories: Apt; conditionally apt (CA), aspects to be figured out in the short and long term; Social risk (SR). Several variables to be dealt with in the

middle and long term; temporarily non apt (TNA), structural problems calling for a social structural change.
Psychological categories: C1 without contraindication, C2 needs follow up. Neurotic symptoms and reactive anxiety and depression levels, C2HPR, high psychological risk. Severe neurosis, personality disorders, history of psychiatric disorders, addictions; C3: inclusion not recommended. Overt Psychosis. Addictions. Psychopathic personalities.
Results: Diagnoses were as follows: C1: 75 (22.6%); C2: 186 (56%); C2HPR: 50 (15%); C3: 20 (6%); Apt: 191 (57.7%); CA: 99 (29.9%); SR: 29 (8.7%); TNA 2 (3.6%). Variable crossover showed that: *40% (8) of C3 were either RS or NAT; 20% (10) of C2HPR were TNA/SR; 31% (9) of SR were either C2HPR or C3; 75% (9) of TNA were either C2 HPR or C3 ($p<0.001$).*
Conclusions: Dynamic dependence was observed among the psychosocial variables. The psychological variable is more independent than the social variable, since psychological disorders do not necessarily imply the presence of a social issue. Also, marked social difficulties trigger psychological symptoms such as depression, anxiety, distress and stress.

P-546 EULID PROJECT. EUROPEAN LIVING DONATION AND PUBLIC HEALTH

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Purpose: Living donation is, and must be, an altruistic act done in benefit of the health of a third, with no other benefit for the donor than the moral one. This very unique circumstance obligate to do the utmost to protect the donor not only in health but in all life spheres. The EULID's project purpose is to contribute to a European consensus to set standards and recommendations about legal, ethical and living donor (LD) protection practices, to guarantee the LD's health and safety.
Methods: Twelve partner from eleven European Countries work cooperatively. The Project is grant-aided by the Public Health Executive Agency of the EC. http://eulivingdonor.eu/
Partners analize the current European situation and reach a consensus on different topics:legal and ethical aspects, protection practices and LD registry model.
Results: Although LD activities are submitted to authorization in the majority of countries, procedures are very different in aspects like administrative authorization, mandatory national registration, committees and the presence of a LD advocate. Only four countries accept anonymous donation. Each of the pillars of bioethics and categories arises different ethical concerns especially on autonomy and non-maleficency principle. A great heterogeneity also is observed among protection practices. Not only in the establishment of a public medical insurance but also in essential aspects such as sick leave limitation, the possibility of being fired after a sick leave, and systems of reimbursement. Registries are spread but is not a legal requirement in all countries.
Conclusion: The EULID project contributes to a European consensus that could lead to best practices and recommendations that will help to establish a protection framework on LD' health and safety, through laws and regulations in social, medical and psychological fields. The consensus on common registries and the recommendation for their application are important improvements to be implemented.

P-547 EXPERIENCE OF DONATION AND QUALITY OF LIFE IN RELATED AND UNRELATED LIVING DONORS

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Context: Italian guidelines establish that living donation can only be performed by emotionally related donors, whether genetically related or unrelated (spouses for example), who should be evaluated by a Regional Authority's Third Party Commission that assesses their reasons for the donation, their understanding of the potential risks, the existence of a bond of affection and the sincerity of their free and informed consent.
Methods: From 2002 to 2006, the Commission evaluated 201 living donors. A sample of donors were contacted after their surgery to evaluate their living donation experience, the perception of their quality of life and differences between genetically related and unrelated organ donors (spouses). 81 were eligible for the study and 69 responded.
Materials: Donors participating to the research received an anonymous postal questionnaire on the donation experience and a self-rating scale on quality of life (SF-36).
Results: As concerning the SF-36 questionnaire, donors score significantly higher for the quality of life (6 scale of 8) than the normative data for general population, without significative differences between related and unrelated donors. The attitude towards the decision to donate is different: in unrelated donation recipients are more worried about the potential donors' health and the other members of the family show a more neutral attitude. Before donation unrelated donors experiment a little more anxiety and doubts than related donors. After donation there is an improvement in donor-recipient relationship in 55% of unrelated donation vs 36% of related donation, that report more often no changes in the relationship.
Conclusions: Living donation is associated with an improvement in quality of life both for related and unrelated donors. Some differences between the two samples emerge in the attitude towards the decision to donate, in the pre-operative period and in the influence of donation on donor-recipient relationship.

P-548 HUNGARIAN LEGAL ACTIONS ON ORGAN DONATION AND TRANSPLANTATION CONSIDERING OF EUROPEAN UNION RESOLUTION

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Organ transplantation represents the only available life saving treatment for many patients. There are severe discrepancies in organ donation and transplantation activity within and between Member States in the European Union (EU). The different organisational systems in Europe are the result of their origin and history. The Hungarian legal system is based on the civil law model and in the field of organ transplantation the "presumed consent" law is accepted from 1972. The European Commission has adopted important safety and quality measures for organ donation and a 10 point action plan to work with EU Member States on strengthening organ donation and transplantation systems in Europe. The Directive and Action Plan address three key challenges: improving the quality and safety of organs across Europe, increasing organ availability and making transplant systems more efficient and accessible. On 22 April 2008 the European Parliament (EP) adopted a Resolution on organ donation and transplantation. In this study we analysed which legal actions are necessary in the Hungarian National Law system following the EP resolution.

P-549 DETERMINING BRAIN DEATH: ARE THEORY AND PRACTICE IN HARMONY?

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There is a complex relationship between organ transplantation, the definition and determination of death, and decisions to withdraw medical treatment in patients (end-of-life care). Although the 1968 report of the Harvard Committee on 'irreversible coma' has presented the new concept of 'brain death', based on neurological criteria, which is accepted by most medical communities, there are still controversies over the determination of death in different clinical situations (brain dead ventilated patients, non-heart-beating patients). As Capron put it in 2001: "The issue of brain death is well settled and persistently unre-

solved." Critics of the brain death definition point out that the clinical manifestations of death do not correlate sufficiently with the biological and philosophical understanding of death. The question has been raised whether death of the (whole) brain indeed equals the death of the human organism. Another issue is whether cessation of brain function leads to irreversible loss of functional integrity. Others have questioned loss of whole brain function as the crucial element in death, versus loss of function of the cerebral cortex. Fact is, that the practice of organ donation hinges on public trust in the way doctors are making the determination of death and provide end-of-life care to patients who may become organ donors. Non-heart-beating donation (or DCD) that got new impetus since the 1990's, is especially sensitive to good understanding and acceptance of decisions around withdrawal of life-support and confirmation of death. Recently, a report by the US Presidents' Bioethics Commission has surveyed the main criticisms on brain death and DCD, and came up with a reconciliatory approach. This presentation focuses on how a clear explanation, in communication with family and lay people, of the determination of death can be given as part of the process of end-of-life care.

P-550 ADVERSE OUTCOMES IN RECIPIENTS AND DONORS INVOLVED IN COMMERCIAL KIDNEY TRANSPLANTS

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Recently the Declaration of Istanbul has once again emphasized the ethical problems surrounding commercial transplantation, especially when patients resort to organ tourism, and when donors/vendors fall victim to trafficking. There have been alarming reports about the exploitation of vulnerable populations in countries like Pakistan, the Philippines, Iran and China, or closer by in Moldova and Egypt. Several studies based on fieldwork report on the medical, social and psychological problems that these vendors get after donating a kidney. However, a further firm argument against allowing or condoning organ tourism and illegal organ markets is the high incidence of adverse outcomes in the recipients of 'paid for' kidneys. Many transplant centres who have seen some of their patients travel abroad to obtain a kidney, have been confronted with nasty and sometimes fatal complications from surgery, infections or insufficient postoperative care in the returning patient. This presentation gives an overview of the recently reported complications. This information should lead nephrologists and transplant physicians to give more firm warning to their patients not to engage in organ tourism, and should convince these professionals themselves not to facilitate or cooperate in such risky (and unethical) practices.

P-551 PIERDUB PROJECT: INTERNACIONAL PROJECT ON EDUCATION AND RESEARCH IN DONATION AT UNIVERSITY OF BARCELONA: TRAINING UNIVERSITY STUDENTS ABOUT DONATION AND TRANSPLANTATION

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Introduction: Donation and transplantation is an accepted therapeutic option where organ failure or tissue replacement are needed to save or improve quality of life. However, in most medical schools there is no specific training for it.
Objectives: *Knowledge diffusion* about donation to clarify doubts and stimulate positive attitudes toward donation
Training university students in the donation and transplantation process
Research about the previous donation knowledge and the impact in donation indexes
Methodology: Three different phases:
1. Training the UB Health Sciences School students: Train the trainers by giving theoretical and practical educational courses to medical students about donation process. One day of educative campaigns to inform about donation and stimulate positive attitudes. Repeat the same educative and promotional campaigns of one day duration in other Health Sciences Schools.
2. Training the Health Sciences School students in others faculties in Catalonia, Spain and International: Create a faculty's network to apply the same educative model for medical students to develop potential future trainers.
3. Research: Evaluation of the methodology, before and after training. Evaluation of the educational process: Social benefits and impact of the educational activities in the local donation indexes.
Results: Since 2006, we offer yearly Optional Credits to medical students with duration of 45 hours, with 90 participants and 10 trainers. Additionally, one Donation day open to health sciences students has been offered and, since 2007, promotional campaigns in medicine and other health sciences faculties have been carried out. Until now, 650 answered surveys have been collected to evaluate previous knowledge among university students.
Conclusion: Training medical and other health sciences students in the donation process will improve quality of medical education and develop a trainer role for future professionals to help improve donation rates.

Clinical immunosuppression II

P-552 USABILITY OF THE HELPING HAND™: A NEW ELECTRONIC MONITORING TOOL TO ASSESS MEDICATION NON-ADHERENCE

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Purpose: The Helping Hand™ (HH; B&OMedicom) is an electronic monitoring device assessing adherence for medication in blister packages. The HH also includes visual adherence feedback and an acoustic reminder. *Usability* testing, referring to the ease with which people can employ the HH in daily life,is needed. Usability dimensions are *user performance, satisfaction and acceptability.*
Methods/Materials: Using a combination of quantitative and qualitative (mixed method) design (i.e. 2-phase, concurrent triangulation strategy), we included a purposive sample of 11 kidney transplant patients (KTx) and 10 healthy volunteers. At baseline, *performance* was evaluated using thinking aloud methodology and a 10-point Likert scale. After using the HH for 3 weeks, *satisfaction* and *acceptability* were assessed using a semi-structured interview and 5-point Likert scales. Likert scores were expressed as medians for the total and sub groups. Qualitative content analysis was applied to identify the usability dimensions.
Results: *Performance:* All subjects judged the volume of the reminder tone as not being loud enough. Four patients (36%) found that the feedback light signal was too weak. Three patients (27%) and two volunteers (20%) had problems with interpreting the feedback function. Four patients (36%) and seven volunteers (70%) experienced difficulties moving the blister in and out the device. Broad variability in perceived *satisfaction* was observed. Using a 5-point Likert scale, 9% of the patients and 10% of the volunteers scored 'not satisfied at all', while 18% of patients and 20% of volunteers scored 'very satisfied'. *Acceptability:* 4 patients (36%) and 4 volunteers (40%) envision future use of the HH. Half of the patients and volunteers would recommend the device to others.

Figure 1. The Helping Hand™ (B&O Medicom).

Conclusion: Usability testing of the HH showed positive aspects yet problems were identified (i.e.feedback system, weak sound signal and manipulating of blister); elements that need to be the focus of future technical improvements.

P-553 COMPUTER ASSISTED CYCLOSPORINE DOSING IN RENAL TRANSPLANT RECIPIENTS

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Background: Cyclosporine's (CsA) narrow therapeutic window necessitates therapeutic drug monitoring with frequent dose adjustments in order to reach therapeutic target. This may be difficult, time consuming and requires experience specifically if C2 monitoring is performed. This prospective pilot study investigated the applicability of dosing cyclosporine based on a C2 computer model (NONMEM population modeling with age, weight and time after transplantation as co-factors) compared to experienced clinicians.
Methods: Renal transplant recipients on CsA, prednisolone and mycophenolate were included 2 weeks after transplantation, randomized in a 1:1 ratio to either computer dosing (COMP) or control (CONTR) and followed for 8 weeks. CsA was C2 monitored.
Results: 40 patients (COMP 20/CONTR 20, 31 male, 27.5% living donor) between 28 to 80 years were included A total of 631 C2 measurements were performed. There were no difference in overall number of CsA blood concentrations within the therapeutic window between the two arms, 37±17% and

34±18% in the COMP and CONTR arm respectively (P=0.58). The accuracy during the first 5 days was however significantly better in the COMP vs. CONT arm (9±11% vs. 18±20%, P=0.040). There were no difference in CsA dose; 3.55±0.8 vs. 3.90±0.9 mg/kg/day (P=0.19) in respective arm. Biopsy proven acute rejection was seen in 4 and 3 patients in the COMP and CONTR arm, respectively (P=0.50) and the eGFR at the end of the study was 67±24 ml/min in the COMP arm and 66±19 ml/min in the CONTR arm (P=0.86).
Conclusion: The present pilot study showed that the utilization of C2 monitoring and computer assisted dosing of CsA in the early phase after transplantation is applicable and with show some advantages. This tool may for example be helpful for non-experienced clinician or transplant nurses.

P-554 RITUXIMAB USE FOR DESENSITIZATION OF IMMUNOLOGICALLY HIGH-RISKY RENAL TRANSPLANTATION WITHOUT SPLENECTOMY

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Introduction: Recently due to organ shortage, cases of immunologically high-risky transplantation are gradually increasing. Sensitized patients, such as with gross anti-ABO blood type titer or with donor specific antibody (DSA), need to remove the volume of them before transplantation for the decrease of the risk of antibody-mediated rejection onset. Previously we performed several procedures for the antibody removal. Splenectomy was one of them.But it sometimes occurs lifethreatening complication such as much blood loss or leakage of pancreatic juice,and is not preferrable for an infant case. So we have used rituximab (RXM, anti-CD20 antibody) instead of splenectomy in this study.
Methods: We prepared 6 patients for this study. Four recipients were ABO-incompatible and 2 were with DSA. DSA was identified in Flow-PRA test. Five recipients received the graft from living donor and one (with DSA) from cadaveric donor. Four ABO-incompatible and one with DSA recipients have received RXM (100mg/m^2) on the preoperative days -13 and -6, 3 sessions of double filtration plasmapheresis, 1 session of plasma exchange, and mycofenolatic acid (MMF) use from the preoperative days -14. About other cadaveric case 1 session of plasma exchange and single dose of RXM were performed before transplant operation. Just before the operation in ABO-incompatible cases we evaluated anti A/B blood type titer under 1:8,in DSA cases we evaluated the degree of antibody removal in Flow Cytometry Crossmatch test.
Results: All recipients are alive with well-functioned grafts after 7.7 months follow-up in average. We have no episode of antibody-mediated rejection. Associated with the use of RXM, we have no experience of anaphylactoid infusion reaction, late-onset neutropenia, and other adverse events. Some patients have suffered from asymptomatic cytomegaloviral antigenemia, but can be controlled by tapering the dose of MMF. CD19 cells have been decreasing to minimum rapidly after RXM induction.
Conclusion: Our results suggest that RXM is useful and safe for desensitization of immunologically high-risky renal transplantation without splenectomy.

P-555 EVALUATING THE EFFICACY AND SAFETY OF DACLIZUMAB, TACROLIMUS, MYCOPHENOLATE AND CORTICOSTEROIDS IMMUNOSUPPRESSIVE REGIMEN IN COMPARISON TO CURRENT STANDART IMMUNOSUPPRESSION (TACROLIMUS, MYCOPHENOLATE AND CORTICOSTEROIDS) IN RENAL TRANSPLANTATION

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End points: Primary: to determine the biopsy-confirmed acute rejection rate at month 12. Secondary: to determine the renal function, as expressed by serum creatinin and the glomerular filtration rate (assessed by creatinine clearence)over the course of study and at month 12. To determine patient and graft survival rates at month 12.
Study design: *Group A* – daclizumab, tacrolimus, mycophenolate and corticosteroids group. *Group B* – control group tacrolimus, mycophenolate and corticosteroids group.
Number of patients: 40 patients, 20 for each treatment arm. Patients meeting all the selection kriteria were randomized prior to transplantation in 1:1 ratio to one of the two treatment arms of the study.
Results: Acute rejection rate at 12 months - group A one corticosensitive rejection, - group B two corticosensitive rejections – statistically not signifiant. Serum creatinin at month I was: group A 142±44,2 umol/l group B 154±42,7 umol/l and at month 12 group A 133,4±32,2 umol/l, group B148,9±44,3 umol/l (statistically not significant). Glomerular filtration at month I was: group A 1,058±0,385 ml/s group B 0,95±0,280 ml/s and at month 12 group A 1,136±0,389 ml/s group B 1,099±0,256 ml/s (statistically not significant). Patient survival rates at 12 months were 100% in both groups. Graft survival rates at 12 months was: group A 95%, group B 100% (statistically not significant).
Conclusion: The follow up has not documented beneficial effect of daclizumab use to the existing standard regimen. Immunosuppression with tacrolimus in combination with mycophenolate mophetil and corticosteroids is already very efficient regimen and from the long-term perspective brings very good survival and transplanted kidney function results and benefits transplant patients.

P-556 ADVANTAGES OF PSI + LOW-DOSE CNI VS PSI ALONE IN DUAL KIDNEY TRANSPLANTATION (DKT) FROM ELDERLY DONORS

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Immunosuppression in DKT from elderly donors (ED) has to consider that such kidneys result more sensitive to drug-induced nephrotoxicity; in this context, inhibitors of proliferative signal (PSI) have been claimed to be advantageous. In our early DKT experience a PSI-based regimen allowed satisfactory renal function and graft survival, without increasing the risk of acute rejection, but with a very high conversion rate. Aim of this study is to evaluate whether better results might be achieved using PSI in combination with low-dose CNIs in DKT from ED.
Methods: From 12/2008 to 02/2009, 18 patients (Group1) underwent DKT from ED (mean age70.7±4.3). Immunosuppressive protocol included Thymoglobulin induction, low-dose cyclosporine (C2 target400-600 ng/mL), everolimus (trough target6-8ng/mL) and steroids. 6-months results were evaluated and compared to a previous group of DKT recipients (Group2, 78 pts), on a PSI-based protocol receiving thymoglobulin induction, sirolimus (trough target10-15ng/mL), MMF and steroids. The occurrence of conversion to a CNI-based regimen was also evaluated.
Results: Within the first 6 months, neither patient death or graft loss occurred in Group1, 1 death (1.3%) due to heart failure and 2 grafts (2.5%) were lost in Group2 due to renal vein thrombosis and vascular rejection. Incidence of acute rejection was very low in Group1 (5.5% vs 19.0%, p=ns), and S-creatinine at 6 months was satisfactory in both groups (122±36 vs 115±34μmol/L, p=ns). Conversion to full-dose CNI regimen was deemed necessary in 3 pts in Group1 (16.7%) and in 33 cases in Group2 (42.5%), mainly for acute rejection, wound/lymphatic complications, leukopenia.
Conclusions: The association of low-doses of cyclosporine to the PSI allows to obtain optimal results in DKT, with low risk of acute rejection and avoiding the high rate of conversions observed in PSI-alone regimen.

P-557 INTENSIFIED DOSE OF ENTERIC-COATED MYCOPHENOLATE SODIUM (EC-MPS) FOR STEROIDS AVOIDANCE, IN COMBINATION WITH CICLOSPORINE MICRO-EMULSION (CsA-ME): MULTICENTER, RANDOMIZED, OPEN LABEL, COMPARATIVE STUDY IN DE NOVO KIDNEY TRANSPLANTATION (DOMINOS)

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Purpose: Reinforcement of immunosuppression in immediate post transplantation (Tx) with an intensified dose of a non nephrotoxic agent EC-MPS (Myfortic®) could allow steroids avoidance and their complications, in low immunologic risk adults kidney Tx patients.
Methods: 222 recipients of a primary kidney Tx from deceased donors were randomized (14 French centers) in either steroids Avoidance (group A, no

steroids per os, n:112) or Standard steroids (group S, n:110), in combination with EC-MPS (2.16 g/d for 6 weeks and then at 1.44 g/d) and CsA-ME adjusted using C2 monitoring. Both groups received IV steroids peri-operative. Steroids in group S were tapered and eliminated between months 4 – 6 in free BPAR patients. All patients received anti-IL2R antibodies.
Objectives: Primary, is to compare treatment failure (BPAR, graft loss, death or lost to follow up) within 6 months post Tx. Secondary, to compare at 3 and 6 months, renal function, histological features at the 3 month renal biopsy, safety, tolerance.
Results: Baseline demographics were statistically comparable between both groups. 91.9% patients were Caucasians and 65.8% Male. Mean donor and recipient ages were 49.7 (A) and 51.0 (S) years respectively. 14.4% of patients were old for old (D $\geq$60/R $\geq$60 yrs). Mean cold ischemia time (CIT) in both groups was 16.8h (7.7% of patients had CIT $>$24h). CMV D+/R- was 24.3% (A) and 24.5% (S) respectively. 98.6% of patients had panel reactive antibodies=0%. Primary and secondary efficacy and safety results will be available in June 2009.
Conclusions: This study was designed to validate efficacy and safety of steroids avoidance with an intensified dose of EC-MPS, in low immunologic risk adults kidney transplant patients.

P-558 STUDY PROTOCOL: A THERAPEUTIC EXPLORATORY STUDY TO DETERMINE THE EFFICACY AND SAFETY OF CALCINEURIN-INHIBITOR-FREE DE-NOVO IMMUNOSUPPRESSION AFTER LIVER TRANSPLANTATION: CILT

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Purpose: Acute renal dysfunction has been observed in up to 50% of all patients after orthotopic liver transplantation (OLT). More than 90% of patients receive calcineurin inhibitors (CNIs) for immunosuppression after OLT, and nephrotoxicity of CNIs contributes to renal impairement. Early renal dysfunction significantly increases the risk of chronic renal failure und subsequently the risk of premature death.
Multiple trials investigated the effect of delayed CNI and reduced-dose CNI regimens or early withdrawal of CNI in patients with renal dysfunction after OLT. Generally, avoidance of CNIs improves kidney function and does not result in higher rate of rejection when an adequate level of immunosuppression is maintained. Based on the aforementioned data this study protocol was designed to evaluate the efficacy and safety of CNI-free de-novo immunosuppression after liver transplantation.
Methods and design: A prospective therapeutic exploratory, non-placebo controlled, two stage monocenter trial in a total of 29 liver transplant patients was designed to assess the safety and efficacy of de-novo CNI-free immunosuppression with basiliximab, mycophenolate sodium, everolimus, and prednisolone. The primary endpoint is the rate of steroid resistant reject. Secondary endpoints are the incidence of acute rejection, kidney function, liver allograft function (assessed by measurement of AST, ALT, total bilirubine, AP, GGT), treatment failure (reintroduction of CNI), incidence of adverse events, and mortality up to one year after OLT.

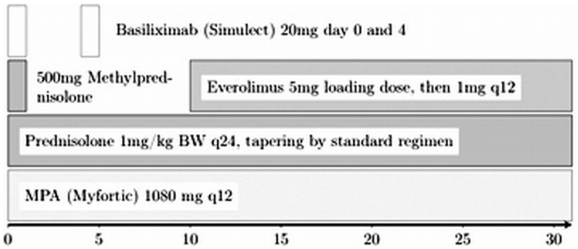

Figure 1

Discussion: The ongoing clinical trial represents an intermediate element of the research chain, along which a scientific hypothesis has to go by, in order to reach the highest level of evidence; a prospective therapeutic exploratory study. If the data of this ongoing research project confirms feasibility of de-novo CNI-free immunosuppression, this should be confirmed in a randomized, prospective, controlled double-blinded clinical trial.

P-559 CONVERSION FROM SIROLIMUS TO EVEROLIMUS IN KIDNEY TRANSPLANT RECIPIENTS

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Purpose: In our institution, renal transplant recipients were converted from sirolimus to everolimus due to our Hospital policy, providing us the opportunity to investigate the safety profile of a conversion protocol.
Materials and methods: Records of renal transplant recipients converted from sirolimus to everolimus were analyzed retrospectively. Study patients had received mycophenolate mofetil, prednisolone and sirolimus therapy. At the time of conversion, patients received everolimus, 1.5 mg/day, 72 hours after sirolimus interruption, onwards. Everolimus trough blood levels of 3-8 ng/mL were considered optimal. Blood samples were taken for quantification of everolimus blood levels using both Seradyn Innofluor® Certican® FPIA and Abbott Architect i System® sirolimus CMIA.
Results: We analyzed data from 53 adult renal transplant recipients (98$\pm$43 months post-transplant). At the time of conversion, sirolimus dose was 2.1$\pm$0.9 mg/day with trough blood levels of 6.9$\pm$2.0 ng/mL. Three months after conversion, everolimus dose was 2.2$\pm$1.0 mg/day with trough blood levels within the target range. Everolimus dose was not statistically different from sirolimus dose (p=0.24) suggesting a conversion factor of 1:1.06. Everolimus trough blood levels obtained using FPIA were 7.41$\pm$2.81 ng/ml and 6.20$\pm$2.29 ng/ml when using CMIA. The analysis of everolimus blood levels showed a linear regression: CMIA = 0.733FPIA + 0.767 (r^2 = 0.804, $p<$ 0.0001). During the first three months post-conversion, no significant changes were observed in serum creatinine (1.56$\pm$0.51 *vs* 1.57$\pm$0.52 mg/dL; p= 0.483), hematocrit level (38.9$\pm$4.8 *vs* 40.3$\pm$4.2%; p= 0.059) or proteinuria (0.45$\pm$0.64 *vs* 0.50$\pm$0.74 mg/g creatinine; p= 0.353). No patient lost his graft or experienced an acute rejection episode.
Conclusions: Conversion from sirolimus to everolimus in renal transplant can be performed safely. Abbott Architect i System® sirolimus CMIA cross-reacted with everolimus. To our knowledge this is the first time a conversion factor between sirolimus and everolimus has been and reported.

P-560 DOSE CONTROL STRATEGY OF MMF EMPLOYING MPA-TDM IN RENAL TRANSPLANTATION

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Purpose: The significance of pharmaco-kinetic (PK) study of MPA in renal transplantation is still controversial. The level of MPA is irregular post transplantation and may cause rejection or adverse effects. We studied clinical outcomes and PK parameters of MPA after renal transplant.
Materials and methods: Thirty one renal transplantation patients were analyzed at several period after graft. Those received four induction immunosuppressives: PSL, CNI (Tac or CsA), MMF and BXM. TDM of MPA was performed at 1, 3$\sim$4 weeks and 2$\sim$3 months after transplantation. In each TDM, at least 4 points of blood sampling for MPA concentration (HPLC) were obtained. As clinical outcomes, we surveyed biopsy proven rejection (BPR) ($\geq$BL, Banff 2003), anemia (Hb$\leq$10g/dl), and CMV infection (positive CMV antigenemia).
Results: From total of 466 points of MPA measurement, PK parameters were as followed; C_0:3.9$\pm$2.4μg/mL, Tmax:1.5$\pm$1.2hr, Cmax:14.5$\pm$8.9μg/mL, $AUC_{0\text{-}12}$:71.0$\pm$35.0μg^{μ}h/mL. Variable coefficient (VC) of C_0 was 80.6% shortly after transplant but, reduced to 35.1% in AUC after 1 year, and intra-individual VC for C_0 and AUC were 38.8% and 34.8% respectively. BPR occurred in 13 patients, CMV infection recognized in 8, anemia in 19. AUC of MPA tended to be smaller in the group with BPR (P=0.083). If AUC was $\leq$40μg^{μ}h/mL, BPR was occurred in 50%, but if $>$120μg^{μ}h/mL all patients had anemia. AUC of MPA did not correlate to CMV infection.
Discussion: The best estimation of AUC of MPA could be obtained by three points sampling (C_0, $C_{0.5}$ and C_4). After one year of transplantation, one point sampling (C_0) was sufficient for MPA-TDM (DC: 0.909). We did not find any difference of estimation and deviation of MPA-TDM between Tac and CsA. From these results, we considered that $AUC_{0\text{-}12}$ of MPA should be controlled in-between 40 and 120μg^{μ}h/mL after renal transplantation.

P-561 THE NUMBER OF HLA MISMATCHES BETWEEN DONOR AND RENAL ALLOGRAFT RECIPIENTS CAN AFFECT THE EXPRESSION OF CD11B AND CD57 WITHIN CD8+CD28- POPULATION

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Some studies suggest that number of HLA mismatches between donor and renal allograft recipient correlates with the function of graft. The function of graft can be also dependent on the level of regulatory lymphocytes including CD8+CD28- cells. This is a heterogonous population contains both suppressor (Ts) and cytotoxic cells (Tc). It is possible that adhesive molecules CD11b and CD57 can be helpful to distinguish between Ts and Tc subpopulations. The aim of this study was to investigate if the number of HLA mismatches influences the phenotype of CD8+CD28- cells in patients after renal transplantation.

Peripheral blood was obtained from patients divided into four groups: CsA-Sta, RAPA-Sta, CsA-CR, RAPA-CR. Sta – stable graft function; CR – chronic graft rejection; CsA – cyclosporine A, azathioprine, prednisone; RAPA – rapamycin, prednisone. HLA genotypes of transplant recipient/donor pairs were determined by PCR using commercially available kits. Peripheral blood mononuclear cells were labeled with mouse anti-human mAbs conjugated with fluorochromes and analyzed by flow cytometry (FACSCalibur).

In CR-CsA group we observed correlations between the level of CD11b+ cells within CD8+CD28- population and the number of HLA mismatches donor/recipient: negative correlation for HLA-A (p=0.057) and positive correlation for HLA-B (p=0.040). The second correlation was more significant for all patients (p=0.009). In CR-CsA group there was also positive correlation between the level of CD57+ cells within CD8+CD28- population and the number of HLA-DR mismatches. Other patients groups had too small variations in the number of HLA mismatches to observe any possible correlations.

The number of HLA mismatches influences the expression of CD11b and CD57 markers within CD8+CD28- population in renal recipients and therefore probably affects the ratio Ts:Tc in this heterogonous population.

P-562 EFFECTS OF MYCOPHENOLIC ACID, CYCLOSPORINE A AND EVEROLIMUS ON CELLULAR AND HUMORAL RESPONSES AFTER VACCINATION

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Guidelines for vaccination in renal transplant recipients (RTR) recommend vaccinations with pneumococcal polysaccharide and tetanus toxoid (TT). However, efficacy of these vaccinations when given in immunocompromised RTR is not fully known. Different immunosuppressive regimens vary in their effects on cellular and humoral responses after vaccination. The effect of everolimus, a new and potent immunosuppressive drug, on vaccine responses has not been studied.

We analysed the capacity of stable RTR to mount cellular and humoral responses after vaccination. 36 RTR using double immunosuppressive maintenance therapy with prednisolone (P) plus either cyclosporine A (CsA), everolimus or mycophenolic acid (MPA) were included. The patients were vaccinated with keyhole limpet hemocyanin (KLH) and TT, which are T-cell dependent antigens, and with pneumovax, which is a T-cell independent antigen. Blood samples were drawn just prior to vaccination and two weeks after. IgG antibody levels were analysed with ELISA. T cell activity was estimated by measuring production of IFN-g, IL-2, IL-4 and IL-17 with Elispot. We compared these data to an age and sex matched group of healthy control individuals (HC).

Antibody titers are represented as a ratio between post and prevaccination levels. Patients on P/CsA, P/everolimus and P/MPA showed median IgG anti-TT ratios of 4.9, 6.8 and 1.3, compared to 5.2 in HC. The median ratios of IgG anti-pneumococcal antibodies in the same groups were 4.2, 2.9 and 1.1 versus 4.9 in HC. Median IgG anti-KLH antibodies ratios were 1.1, 1.4 and 1.0, compared to 2.6 in HC. Elispot assays are currently performed.

Based on these data, we conclude that treatment with P/MPA completely disturbs the primary and secondary humoral response. On the contrary, treatment with P/CsA or P/everolimus inhibits the primary humoral response, but does not affect immunological memory.

P-563 PREVENTION OF CYTOMEGALOVIRUS INFECTION BY VALGANCICLOVIR IN SOLID ORGAN TRANSPLANT RECIPIENTS: INTERIM RESULTS FROM THE ORVAL OBSERVATIONAL STUDY

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Cytomegalovirus (CMV) remains one of the most common pathogens to affect the solid-organ transplant (SOT) recipient. ORVAL, the prospective study of a large cohort of SOT patients in France, is focused on the targeted population receiving VGCV to prevent CMV infection with regard to treatment regimens, both length and dosage as a function of renal function, donor (D) and recipient (R) CMV serological status, and organ transplant type.

Adult patients who received a single or a multiple live or cadaveric organ allograft less than 6 months post-transplantation were included in the study at the time of VGCV treatment initiation. This descriptive analysis includes 201 first patients and their 3 month follow-up, and consists of 133 kidney (66.2%), 28 liver (13.9%), 21 heart (10.4%), 15 lung (7.5%), 4 combined (2%) recipients. Among these recipients 65 are D^+/R^- (32.8%), 71-D^+/R^+ (35.9%), 57-D^-/R^+ (28.8%), 5-D^-/R^- (2.5%). 153 of 201 (76.1%) patients received VGCV prophylaxis, 39 of 201 (19.4%) recipients were initiated on pre-emptive therapy, and 9 of 201 recipients initiated VGCV as the treatment of CMV disease. Patients on prophylaxis comprise of 57 D^+/R^-, 51-D^+/R^+, 38-D^-/R^+ and 4-D^-/R^-. Data available for these patients show that VGCV prophylaxis dosage is based upon the renal function at inclusion in 60 recipients and in 64 – at follow-up visit. 7 patients in risk group receiving prophylaxis experienced CMV infection/disease at follow up visit. VGCV dosage was adjusted to kidney function in 4 of them. Recipients initiated on pre-emptive therapy include 6-D^+/R^-, 15-D^+/R^+, 17-D^-/R^+ and 1-D^-/R^-.

Conclusions: Present data indicate that the majority of SOT recipients were initiated on valganciclovir prophylaxis. Only in half of them VGCV dosage was adjusted to the renal function at the treatment initiation.

P-564 BENIGN SKIN LESIONS AFTER RENAL TRANSPLANTATION

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Background: Progress in immunosuppressive therapy and transplant immunology have significantly increased the lifetime of the recipients after renal transplantation. Together with the increase in survival of the recipients, greater number of skin complications have been observed.

Objective: The objective of the research was to estimate the number and the type of benign skin lesions observed after kidney transplantation.

Methods: Between December 2005 and June 2008, 222 kidney transplant recipients from two transplant centers were enrolled into the study. The average age of patients (95 women and 27 men) was 47, 9 years (18-77 years). Dermatological examination was performed on average of 61 months after transplantation (2 months – 10 yrs). During the examination swabs, skin scrapings and nail clippings were collected from all the changes suspected of bacterial and fungal infection. All the cutaneous lesions were recorded in terms of quality and quantity on the special questionnaire of physical examination.

Results: Benign skin changes have been detected among 220 (99%) renal transplant recipients. 32% of patients were on cyclosporine, prednisone and mofetil mycophenolate. The most frequent iatrogenic skin lesions were: hypertrichosis observed among 61% of patients, purpura among 50% and xerosis cutis among 41% of them. Among chronic immunosuppression lesions, skin infections have been observed the most often: fungal infections among 61% and viral-HSV infections in 30% and CMV in 21% of the patients.

Conclusions: Essential number benign skin lesions develop in the first year after transplantation. Almost 100% of renal transplant recipients have skin lesions. Although skin changes are not dangerous for health and life, they may be a significant aesthetical problem. Returning, resistant to cure infections are also problem from the medical point of view.

P-565 TACROLIMUS DOSING IN THE EARLY POST-TRANSPLANT PERIOD: THE OXFORD EXPERIENCE

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The calcineurin inhibitor tacrolimus (FK506) is a standard component of most current immunosuppressant regimes used for kidney and kidney/pancreas transplantation. As there is considerable variation in tacrolimus dosing practices between units with a tendency toward lower target levels, we analysed tacrolimus dosing, trough levels and graft outcomes in the early post-transplant period in 118 consecutive organ recipients from a single unit. During the period under review, tacrolimus was prescribed at 0.05mg/kg twice daily, half the dose recommended in the British National Formulary at that time.
Methods: A retrospective analysis of patients who received tacrolimus following a kidney or kidney/pancreas transplant between November 2006 and October 2007 at the Oxford Transplant Unit was performed. Data for each patient was collected from the electronic patient record and transplant flow charts. Target trough tacrolimus ranges were 8-12ng/ml for all recipients except those of organs from non-heart beating donors where the initial target was 5-10ng/ml.
Results: 17 (14.4%) of patients received organs from non-heart beating donors, while the remaining 101 patients, received organs from living donors (17.8%) or heart-beating deceased donors (67.8%). 8 episodes of acute rejection were recorded, 5 of which occurred in recipients of organs from living donors. 7 of the 8 patients who had acute rejection had tacrolimus levels below the target range, with significantly lower initial tacrolimus levels recorded (9.86 ng/ml vs 5.63 ng/ml, $p<0.05$).
Conclusions: The trend towards the use of lower doses of tacrolimus following transplantation may be associated with significantly increased risks of graft rejection. This may be particularly important for recipients of organs from living donors, who may benefit from pre-loading in the days prior to transplantation.

P-566 DO WOUND COMPLICATIONS OR LYMPHOCELES OCCUR MORE OFTEN IN PATIENTS RECEIVING mTOR INHIBITORS? A SYSTEMATIC REVIEW

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mTOR inhibitors have often been associated with wound complications and lymphoceles after kidney transplantation. We systematically reviewed the literature to compare these outcomes for solid organ transplant patients receiving mTOR inhibitors versus patients not receiving these drugs. Medline, Embase, Transplant Library and Cochrane's Central Register of Controlled Trials were searched to identify randomized controlled trials (RCTs) in solid organ transplantation comparing mTOR inhibitors with an alternative therapy and reporting on wound complications or lymphoceles. Methodological quality of RCTs was assessed using the Jadad score (0-5) together with allocation concealment and intention to treat (ITT). If there was more than 1 RCT with similar interventions a meta-analysis was performed. Odds ratios (OR) including 95% confidence intervals (CI) were calculated. We identified 21 RCTs in kidney transplantation, 3 RCTs in heart transplantation and 1 RCT in liver transplantation. The Jadad score found 12 (48%) RCTs to be of good quality while in 8 (32%) RCTs there was concealed allocation but most RCTs (92%) analysed data on the basis of ITT. Pooled analyses showed that kidney transplant patients receiving mTOR inhibitors together with calcineurin inhibitors (CNIs) reported more wound complications (10 trials, n=3320; OR 1.83, CI 1.22-2.75) and more lymphoceles (9 trials, n=3424; OR 2.47, CI 1.72-3.54) than patients not receiving mTOR inhibitors. Similarly, kidney transplant patients receiving mTOR inhibitors together with MMF reported more wound complications (9 trials, n=2265; OR 3.63, CI 1.60-8.23) and lymphocele formation (5 trials, n=1963; OR 2.28, CI 1.61-3.23). Heart transplant patients receiving mTOR inhibitors together with CNIs also reported more wound complications (3 trials, n=1104; OR 2.15, CI 1.34-3.45). mTOR inhibitors are associated with a higher incidence of wound complications and lymphoceles after kidney transplantation and more wound complications after heart transplantation.

P-567 MYCOPHENOLATE ACID MAY REDUCE DONOR SPECIFIC HLA ANTIBODY STRENGTH IN KIDNEY TRANSPLANT RECIPIENTS

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Background: The development of donor-specific HLA antibodies (DSA) post-transplant has been associated with chronic rejection and graft failure. We have shown in a longitudinal study that increases in DSA may precede rejection by months, thus allowing time for intervention. We hypothesized that mycophenolic acid (MPA) dose increases may reduce DSA.
Methods: Eleven DSA positive kidney transplant recipients agreed to participate in this protocol. All recipients had a dose increase of mycophenolate mofetil (MMF) 250 mg or enteric coated mycophenolate sodium (EC-MPS) 180 mg bid. The maximum dose given never exceeded the manufacturer's recommended guidelines. Sera were collected at the time of enrollment and at routine clinic visits after MPA dose increase. HLA single antigen beads analyzed in the Luminex instrument were used to establish donor specificity and strength of the antibodies measured as mean fluorescence intensity (MFI). All recipients received anti-lymphocyte induction therapy. Maintenance immunosuppression consisted of a calcineurin inhibitor, prednisone and MPA.
Results: Ten recipients had a reduction in DSA MFI varying from 2.9 to 61.2%. DSA changes appear not to correlate with MPA blood levels.

Patient	Baseline Highest DSA (MFI)	Follow-up Time Post MPA Increase	Last Follow-up Highest DSA (MFI)	Change in DSA MFI (%)
R38	2309	4	896	↓61.2
S49	2314	43	1198	↓48.2
S231	8461	34	4458	↓47.3
S209	701	14	402	↓42.6
R3	5645	45	3527	↓37.5
S205	11269	21	8278	↓26.5
S60	15087	17	12043	↓20.2
S44	12183	39	11654	↓4.3
R15	11338	35	10936	↓3.5
S125	13951	24	13549	↓2.9
S216	4369	21	4486	↑2.7

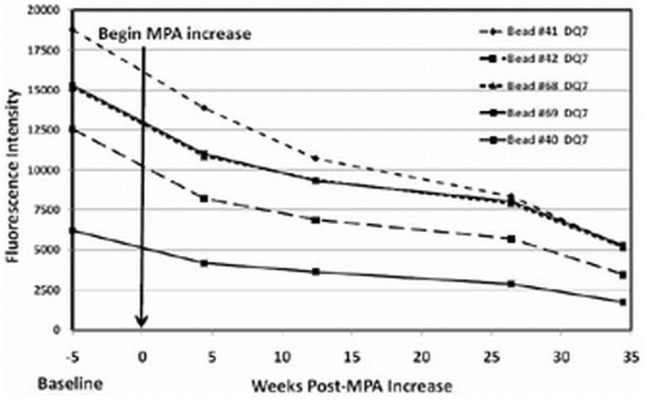

Figure 1. Patient S231 DSA DQ7: Before and after MPA dose increase.

Conclusions: MPA dose increase resulted in DSA reduction in 91% of patients. Patient follow-up for up to one year demonstrated stable serum creatinine and white blood cell counts with no increase in rate of infection. Further follow-up studies are needed to determine if higher doses of MPA can reduce DSA and impact long term graft survival. This pilot study lends strength to the concept that maximum tolerated MPA doses should be used.

P-568 THE EFFECTS OF BISHOSPHONATES TO PREVENT GIOP IN KIDNEY TRANSPLANTATION RECIPIENTS. THE TENTATIVE REPORT OF SINGLE-BLIND RANDOMIZED PROSPECTIVE CLINICAL STUDY

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Purpose: Steriod and immunosuppressants are used as induction and maintenance therapy in kidney transplantation for a long term. Consequently, the risk of GIOP (Glucocorticoid induced osteoporosis) may increase. Comparison examinations of the effect to the bone metabolism of activated vitamin D3 (alfacalcidol) and bishosphonates (alendronate) were carried out. The tentative report is performed this time.
Methods/Materials: Nine patients, who were more than 16 year-old, good renal function (S-Cr 3), and informed consent was provided, were medicated with the activated-vitamin-D3 and bishosphonates at random. The lumbar bone density was measured twice using the DXA method; once after 6 months and the other after 12 months, and urine NTX, serum ALP and serum Ca were measured after 3, 6, and 12-month. Serum Ca increased notably in the activated vitamin D3 group.

Results: As for lumbar bone density, the upward tendency was seen more in the bishosphonates group, and both urine NTX and Serum ALP was intentionally lowered for three months in the bishosphonates group.

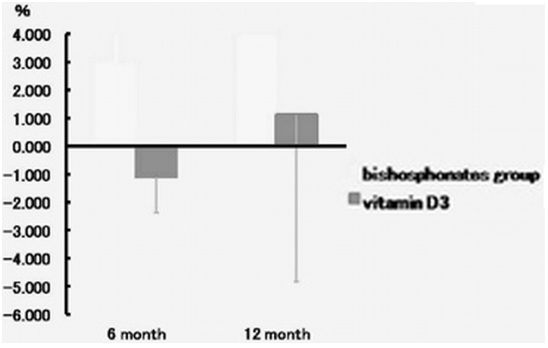

Figure 1. Percent change in BMD.

Conclusion: It seems that bishosphonates is useful as a preventive effect of GIOP in renal transplant recipients. Our goal is to increase the number of cases and to obtain a high-precision result in the near future.

P-569 SWITCHING LONGTERM RENAL TRANSPLANT RECIPIENTS TO mTOR-BASED IMMUNOSUPPRESSION MAY REDUCE DE NOVO SKIN CANCER INCIDENCE

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Background: Skin cancers in longterm transplant recipients (LTR) are a relevant source of morbidity and mortality. The mTOR inhibitors (mTORi), Sirolimus and Everolimus, have been reported to be beneficial in various clinical malignancies. However, unknown is whether the addition of mTORi reduce the incidence of de novo skin cancers in LTRs. This retrospective analysis investigated the effect of adding a mTORi to the immunosuppression (IS) of renal transplant recipients (RTR) with cutaneous squamous cell carcinomas (cSCC).
Method: Chart review of RTRs followed in 2 centers identified patients who a) had mTORi added to the IS at least 3 years posttransplantation, b) remained on mTORi further 2 years, and c) had at least 1 biopsy-proven cSCC in the 2 years prior to switching (mTOR group). In the control group each mTOR patient was matched with a RTR, who a) was transplanted within ±2 years to the index patient, b) not received mTORi during the 4 years and c) had at least 1 cSCC during this period. Primary parameter was the number of cSCC in the 2 years before and after mTOR switch.
Results: All 7 mTOR patients were male, mean age was 69 (range 51-79), mean posttransplantion time was 8 years. 5/7 controls were male, mean age 60 (44-76), mean time posttransplantation was 9 years. Results are shown in Table 1. Thus, the mean number of cSCCs decreased by 41% in mTOR patients but increased approximately 4-fold in controls (p=0.034).

Table 1. mTORi Group

Pt #	Before mTORi		With mTORi	
	Immunsuppr.	No of cSCC	Immunsuppr.	No of cSCC
1	CyA mono	9	Evero/CyA-low	3
2	CyA/Pred	11	Siro/CyA-low/Pred	3
3	CyA/MMF	3	Evero/CyA-low/MMF	10
4	FK mono	4	Evero/FK low	0
5	FK/Aza	1	Siro/FK-low	1
6	FK/MMF	2	Siro/FK-low	2
7	FK/Aza/Pred	2	Siro/FK-low/Pred	0
Mean ± SEM		4.6±1.5		2.7±1.3

Table 2. Control Group

Pt #	Immunosuppr. 4 years	First 24 months No of cSCC	Second 24 months No of cSCC
1a	CyA/MMF	2	6
2a	Aza/Pred	2	0
3a	Cya/MMF	0	3
4a	MMF/Pred	0	4
5a	FK/Aza	0	3
6a	Cya/Aza	1	1
7a	Cya mono	0	3
Mean ± SEM		0.7±0.4	2.9±0.7

CyA = Cyclosporin A; FK = Tacrolimus; CyA-low/FK-low = minimal dose CyA/FK; Pred = prednisone

Conclusions: In LTRs with cSCCs, addition of mTORi appears to decrease the incidence of new cSCCs within 2 years, whereas cSCCs appear with increasing frequency in non-mTOR control patients. Due to the small number of patients and the limited time of followup, the present data will require further validation by more extensive studies.

P-570 CNI-FREE DE NOVO "BOTTOM-UP, ON DEMAND" - IMMUNOSUPPRESSION IN LIVER TRANSPLANT RECIPIENTS WITH PREEXISTING RENAL IMPAIRMENT: AN INITIAL EXPERIENCE

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Background: Patients undergoing liver transplantation with renal dysfunction are prone to further renal impairment under Calcineurin-inhibitor (CNI) therapy
Patients and methods: Thirty patients receiving full-size orthotopic liver transplantation between January 2006 and November 2007 were included into this retrospective case-control study. All patients had preexistent renal impairment prior to liver transplantation. Fifteen patients were treated with a de-novo CNI-reduced immunosuppressive therapy, 15 patients were treated with a CNI-free de novo regimen (basiliximab, MMF, steroids), introducing additional immunosuppressive substances only as "bottom-up", "on-demand"-strategy. Renal function was the primary outcome measure, complications and overall survival secondary outcome measures.
Results: Baseline renal function was similar in both groups: median 2.45mg/dL (1.51 to 4.68mg/dL) in the CNI-free group vs. 1.90mg/dL (1.52 to 4.0mg/dL) in the CNI-containing group [p=0.215]. By month 6 (creatinine [mg/dL] 1.24 (0.41/1.63) vs. 1.35 (0.74/2.41); p=0.046, eGFR [ml/min.] 66 (44/164) vs. 43 (12/85); p=0.05) and 12 (creatinine [mg/dL] 1.23 (0.74/1.53) vs. 1.64 (0.99/3.20); p=0.021, eGFR [ml/min.] 79 (38/116) vs. 40 (22/62); p=0.01) the CNI-free group had significant better creatinine values and eGFR than the CNI-containing group. There was no difference between BPAR, survival and complications but the stay on ICU was significantly shorter in the CNI-free group (9 vs. 21 days; p=0.04)
Conclusion: A CNI-free immunosuppressive approach in liver transplant patients with renal impairment at the time point of transplantation seems to be feasible and may be an innovative approach in immunosuppressive strategies but has to be evidently confirmed in randomized controlled trials.

P-571 OPTIMAL MPA, MPAG LEVELS AT THE EARLY PERIOD AFTER KIDNEY TRANSPLANTATION AS THE KEY CONTRIBUTORS TO IMPROVING LONG-TERM OUTCOMES

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Introduction: Suboptimal MPA, MPAG levels are associated with significant increases in graft loss
Purpose: To assess the influence of MPA, MPAG – Co levels on GFR level and histological changes in the protocol biopsies in kidney allograft recipients
Patients and methods: In a prospective study of 42 low-risk patients receiving MMF, prednisone and a low or normal CsA dose we performed histological assessment according to Banff'97 classification in protocol biopsies before Tx and then at 3, 12, 36 months after Tx, we also assessed GFR at 1, 3, 12, 36 and 60 months after Tx and MPA (ELISA), MPAG (HPLC/UV) Co levels at day 7 and at 1, 3, 12, 36 months after Tx. Statistical analysis was performed with the aid of Generalized Additive Models (SAS System) and Spearman correlation.
Results: We observed significant relationships between MPA, MPAG Co levels and the subclinical rejection episodes (SCR), ci, ct, ah, CAN in the protocol biopsies at 36 month after Tx. In detail: MPA Co level at day 7 after Tx below 1.5 mg/mL was associated with increased risk of SCR (pnl<0.03), ci≥ 2 (pnl<0.05), CAN≥ 2 (pnl<0.04) and with ah≥ 2 (pnl<0.07). MPAG Co level at day 7 after Tx above 100-150 mg/mL was associated with decreased risk of ct≥ 2 (pnl <0.01), ci≥ 2 (pnl<0.04), CAN≥ 2 (pnl<0.04). We also observed significant positive correlations between MPA Co level at 1 month after Tx and negative significant correlations between MPAG Co level at 1 month after Tx and GFR at 1, 3, 12, 36 month after Tx.
Conclusion: Optimal MPA exposure in the early post-transplant period may improve renal graft outcomes.

P-572 IMPACT OF EVEROLIMUS MONOTHERAPY VERSUS CYCLOSPORINE AFTER LIVER TRANSPLANTATION IN HCV PATIENTS: RESULTS OF A PROSPECTIVE, RANDOMIZED TRIAL

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Background and aim: HCV recurrence after LT is a frequent complication that may worsen patient survival and lead to liver graft failure.
There are not any studies evaluating safety and efficacy of an immunosuppressive regimen based on the m-TOR inhibitor everolimus (Evr) in HCV positive patients undergoing LT.
Purpose of the present study is to evaluate patient survival, graft loss and HCV-recurrence rates in de novo LT recipients receiving an immunosuppressive regimen based on Evr monotherapy compared to patients receiving cyclosporine (CsA) monotheraphy.
Materials and methods: From November 2006 to August 2008 we enrolled in our prospective, single-centre, randomized study 45 patients in the Evr group (20 (44.4%) of them HCV-positive) and 24 patients in the CsA group (8 (33.3%) of them HCV-positive). HCV viral load was dosed before and 1, 3, 6, 9 and 12 months after LT. If not previously clinically required, a liver biopsy has been performed in all patients 6 months after LT.
Results: HCV viral load resulted similar 1, 3, 6, 9 and 12 months after LT between the two groups (p=NS). In Evr group 10 (50%) patients out of 20 and 4 (50%) patients out of 8 in CsA group experienced a biopsy-proven HCV-recurrence on average 4.3±2.5 and 3.74±2.21 months after LT respectively (p=NS).
One-year patient survival was 85.9% and 80% for Evr and CsA group respectively (p=NS).
One-year HCV-recurrence free-survival was 44.0% and 37.5% for Evr and CsA group respectively (p=NS).
In Evr group 4 patients (20%) died, 2 of them due to hepatic failure HCV-related, 1 patient (12.5%) in the CsA group due to pulmonary aspergillosis.
Discussion: Evr monotherapy in de novo HCV-positive recipients provides a similar patient survival and a higher, although not statistically significant, HCV-recurrence free-survival than CsA.

P-573 LONG TERM RESULTS IN A COHORT OF LOW RISK RENAL TRANSPLANT RECIPIENTS INDUCED WITH BASILIXIMAB

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Systematic antibody induction in renal transplantation might improve long-term results by decreasing ischemia reperfusion damage, retarding anticalcineurinic initiation, or creating immunological tolerance. We analyzed retrospectively a cohort of patients induced with Basiliximab (BSX) in order to determine long-term graft survival, rejection incidence, and HLA sensitization. The clinical records of fifty-three renal transplants without delayed graft function (DGF) treated in a single center between 1999 and 2006 were examined. Proportion deceased vs live donor was 36/17, mean HLA mismatch was 3,3. Patients received minimal maintenance steroid doses, one antiproliferative (Azathioprine, Inosin monophosphate dehydrogenase or mTOR inhibitors) and calcineurin inhibitors (Neoral 36 cases, Tacrolimus 14 recipients and none 3 cases). Eight year patient and graft survival were 94% and 83% respectively. Seven recipient graft-loss was due to non-immunological related events. Nine patients (16.9%) had biopsy-proven acute rejection, 4 were antibody-mediated rejection (AMR); one recipient did not recover graft function despite steroid therapy, plasmapheresis, rituximab. In 9 patients anti HLA antibodies were determined showing an increase from 0 in pre transplant studies to a mean 2% for Class I and 13% (range 0 to 56) for Class II at a mean 6,5 years following transplant; of these recipients 3 became sensitized. Mean peripheral blood FOXP3 percentage in 8 patients was 4,2%, similar to normal controls. In conclusion, low risk patients BSX induced have good long-term patient and graft survival. Late AMR low incidence did not impact significantly the prognosis: only one patient lost the kidney due to immunological cause. The absence of FOXP3 increase, the anti HLA Class II formation in 1/3 of cases favor the maintaining effective immunosuppressive therapy even in late post- transplant periods in order to avoid rejection.

P-574 PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY IN A KIDNEY TRANSPLANT RECIPIENT – CASE REPORT

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Background: Most of reported cases of multifocal progressive leukoencephalopathy (PML) were of patients subject to AIDS or neoplasma of heamatopoetic system, their clinical outcome has been reported unfavorable. More recent reports state cases of PML occurring in transplant recipients or in autoaggressive diseases.
Material: We present a case of a 58 year old female recipient of unrelated living kidney, who possibly developed PML on an immunosuppressive regimen consisting of ATG in induction, MMF, tacrolimus and prednizolone. At 47th month after transplantation the patient presented with abrupt onset of diplopia, vertigo and paraesthesia of the right side. Brain neuroimaging revealed widespread lesions to the white matter without mass effect or apparent contrast enhancement. Analysis of CSF revealed marked hyperproteinemia, hypergammaglobulinemia, higher pleocytosis with 78% being lymphocytes. Results of cytological examination and immunofenotypization of CSF were not conclusive for immunoproliferative disease. CSF was not tested for JCV. Brain biopsy was not performed due to neurosurgical dissuasion. Two months after onset of neurological symptoms, the patient was bedridden, disorientated, somnolent, nauseous, demonstrating urine and faeces incontinence. Neurological examination disclosed nystagmus and decreased muscular strength. Consequent observation revealed apathy, mood swings, memory impairment. Due to suspicion of PML dosage of MMF and tacrolimus was considerably reduced. 12 months after onset of previously described neurological symptoms the patient complains of occasional headaches. Neuroimaging discloses resolution of white matter lesions. Graft function has markedly worsened over the period and biopsy revealed chronic graft glomerulopathy. The suspicion of PML in this kidney-recipient was brought from retrospect and based upon clinical manifestation and outcome.
Conclusions: 1. PML should be considered in differential diagnosis of psychiatric and neurological symptoms in transplant recipients. 2. Minimizing of immunosuppressant may lead to regression of this potentially fatal disease.

P-575 META-ANALYSIS OF THE SAFETY AND EFFICACY OF CALCINEURIN INHIBITORS FOR DE-NOVO IMMUNOSUPPRESSION AFTER LIVER TRANSPLANTATION

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Purpose: After liver transplantation more than 90% of the patients receive an immunosuppressive regimen based on calcineurin inhibitors. Aim of this study was to establish estimators of the safety and efficacy of calcineurin inhibitors for de-novo immunosuppression after liver transplantation. These may then be used as reference in therapeutic exploratory studies of calcineurin inhibitor free de-novo immunosuppression.
Methods: A systematic review of studies comparing the safety and efficacy of tacrolimus and cyclosporine has been published. But the overall common effects of calcineurin inhibitors have not been reported. The data of 16 controlled clinical trials was used as source data for the meta-analysis. Several methods to estimate the overall common effects and their appropriate confidence interval were evaluated: weighted average with exact confidence interval, a fixed and random effects model with logit transformed rates, estimation of the marginal mean proportion as described by Fleiss, and weighted average with a confidence interval obtained by bootstrap. In a simulation with 10 studies, with variable true common rate, variable sample size, and variable between study variance weighted average with a confidence interval obtained by bootstrap was the most robust method to infer the common true rate and its confidence interval.
Results: The following estimates were obtained by weighted average with 95% bootstrap confidence interval: mortality 14.58% [11.52; 17.12], graft loss 18.25% [14.3; 21.57], acute rejection 42.38% [29.56; 52.1], steroid resistant rejection 12.61% [6.36; 18.65], post transplant de-novo dialysis 2.06% [0.25; 6.95], post transplant de-novo diabetes 18% [5.72; 37.2], and post transplant lymphoproliferative disease 1.08% [0.35; 2.56].
Conclusion: A robust estimation of the overall common effects of calcineurin inhibitors in liver transplant patients has been obtained by weighted average with a bootstrap confidence interval.

P-576 IMPACT OF FOXP3$^+$CD4$^+$CD25$^+$T CELLS IN THE RECIPIENTS ACQUIRING ALMOST TOLERANCE AFTER LIVING DONOR LIVER TRANSPLANTATION WITH INTRA-PORTAL DONOR SPECIFIC ANTIGEN TRANSFUSION

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An immunological tolerance is a goal for all transplant surgeons. We have reported that repeated donor specific antigen transfusion (DST) via portal vein allow rapid reduction of immunosuppressants with decreased acute cellular rejection in living donor liver transplantation (LDLT). Moreover we demonstrated that intraportal DST induces macrochimerism of donor type CD56$^+$ T cells in the graft liver. In this study, it was examined about the impact of FoxP3$^+$CD4$^+$CD25$^+$ T cells in the recipients acquiring almost tolerance after LDLT with intra-portal DST.
Materials and methods: We defined the amount of immunosuppressant below one time per week as an almost tolerance after LRLD. The recipients acquiring almost tolerance was 14.6% in the patients with DST after adult to adult LDLT. One patient have gotten none of any immunosuppressants more than 6 months after LDLD 4 year ago. It was examined that the impact of FoxP3$^+$CD4$^+$CD25$^+$ T cells both in the recipients with almost daily immunosuppressants and the recipients acquiring almost tolerance.
Results: The proportion of FoxP3$^+$/CD4$^+$CD25$^+$ T cells in the almost tolerance group was significantly higher than that in the almost daily immunosuppressants group ($p<0.01$). The increase of proportion of FoxP3$^+$/CD4$^+$CD25$^+$ T cells is significantly correlated with a time after LRLD ($y = 0.0931x + 41.799$, $R^2=0.8888$).
Conclusion: Repeating intra-portal DST might be good tool for inducing immunological tolerance after LDLT. FoxP3$^+$ CD4$^+$CD25$^+$ T cells might act as important regulatory cell for tolerance. The period after LDLT is important for acquiring immunological tolerance.

P-577 A PHASE III, RANDOMIZED, OPEN-LABEL, COMPARATIVE, MULTI-CENTER STUDY TO ASSESS THE SAFETY AND EFFICACY OF PROGRAF (TACROLIMUS) AND MODIFIED RELEASE TACROLIMUS (MR4) IN DE NOVO LIVER LIVING DONOR LIVER TRANSPLANTATION

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Purpose: To assess the safety and efficacy of modified release tacrolimus (MR4) once daily in de novo living donor liver transplantation (LDLT).
Patients and methods: Total 82 LDLT recipients of 4 centers were enrolled and randomized into 2 treatment arms receiving once daily MR4 (MR4 group) or tacrolimus twice a day (Tac group). Among them, 74 patients (MR4:37/Tac:37) have been analyzed, who finished 6-month follow up. Primary endpoint of this study was the event rate of patients with biopsy-proven acute rejection (AR) within 24 weeks after LDLT. And secondary endpoints were the incidence of and time interval to first AR within 12 weeks, severity of AR and patient- and graft- survival rates within 12 weeks and 24 weeks after LDLT. And we analyzed all adverse events to evaluate the safety of MR4 once daily regimen.
Result: There were no statistical differences in biopsy-proven AR rate within 24 weeks. Incidence of and time to first AR within 12 and 24 weeks were not significantly different. Severity of AR was also similar. Patient and graft survival rates within 12 weeks and 24 weeks were similar. The safety profiles including incidence of adverse events, hypertension, hyperlipidemia, new onset DM and infectious complications were similar. Trough levels of both groups were not different after postoperative 2 weeks and 6 month after transplantation, but requiring dose of MR4 to maintain target trough level was higher.
Conclusion: The results of this study support MR4 once daily dose regimen is the safe and effective alternatives to tacrolimus twice daily regimen in de novo LDLT. However, further pharmacokinetic study to clarify dosing amount according to AUC should be ensued.

P-578 AN OPTIMAL SETTING OF PLASMAPHERESIS FOR REMOVAL OF PREEXISTING ANTIBODY BEFORE RENAL TRANSPLANTATION

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Objectives: Removal of preexisting antibodies against donor antigen is important before ABO incompatible or positive crossmatch renal transplantation. The goal of this study was to obtain an optimal setting of plasmapheresis to remove such antibodies effectively.
Methods: Plasmapheresis was performed before ABO incompatible or positive crossmatch renal transplantation. Ninety-three sessions of double filtration plasmapheresis (DFPP) was performed using polysulfone membrane as a primary plasma separator and ethylene vinyl alcohol polymer membrane with pore size of 100Å as a secondary separator. Ratio of plasma pump speed to drain pump speed was kept at 5 to 1. Serum levels of total IgG and IgM were measured before and after DFPP. Titers of anti-blood type antibody (IgG and IgM) were also measured. Removal rates of both total and anti-blood type IgG and IgM were estimated. Volume (ml) of albumin replacement fluid per kg body weight (Ex/BW) was compared with IgG and IgM removal rate.
Results: Removal rates of total IgG and IgM ranged from 34.9 to 89.1% and 41.2 to 93.8%. Removal rates of total IgG or IgM correlated to that of anti-blood type IgG or IgM ($r^2=0.149$, $p<0.01$, $r^2=0.168$, $p<0.01$). Logarithm of Ex/BW strongly correlated with total IgG ($r^2=0.689$, $p<0.01$) and total IgM ($r^2=0.585$, $p<0.01$). A formula for IgG removal rate was obtained: IgG removal rate = $-1.425 + 22.466 \times \log(\text{Ex/BW})$.
Conclusions: Removal of total IgG can be estimated from the volume of replacement fluid per body weight. Therefore, the optimal volume of replacement fluid for each setting can be calculated according as the target removal of antibody titers.

P-579 HCV AND LIVER TRANSPLANTATION: THE ROLE OF MINIMAL IMMUNOSUPRESSION ON PATIENT, GRAFT AND HISTOLOGICAL OUTCOME

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Aim: Compare the evolution of HCV patients and allograft histological recurrence after LT study the influence of induction IS and (modality of) steroid use.
Methods and methods: During the period 2000-2005 35 HCV positive patients were included in a prospective, randomized, double-blind, placebo-controlled study comparing TAC-Placebo (PLAC) (n=14) vs. TAC-short-term (3mo) low-dose steroid (STER) (n=21) use. All patients received identical perioperative care. HCV recurrence was classified following Ludwig score.
Results: One-, 3- and 5- year patient survival rates were 93; 85 and 75% in TAC-PLAC group and 91; 71 and 66% in TAC-STER group (p 0.38). One-, 3- and 5- year graft survival rates were 93%; 86% and 69% in the TAC-PLAC group and 91%;61% and 61% in the TAC-STER group (p 0.46). During the first post-LT year no TAC-PLAC patient developed S3-4 stage nor lethal cholestatic hepatitis, whereas one (4.8%) and two (9.5%) TAC-STER patients did (p 0.26). Two TAC-PLAC patients died due to HCV cirrhosis at 54 and 72 months. Seven TAC-STER group patients died due to HCV recurrent disease: two patients died at 5.8 and 9 months due to cholestatic hepatitis and five died due to HCV cirrhosis at 18, 22, 34, 73 and 79 months. In total two (14.3%) of 14 TAC-PLAC patients and seven (38.1%) of 21 TAC-STER patients died of HCV recurrence during the study period (p 0.26). The composite HCV endpoint including S4 fibrosis, Retransplantation and death due to HCV recurrence showed a significant advantage in favour of the TAC-PLAC group (2/14 vs. 10/21; p: 0.04)
Conclusion: Steroid-free, low dose TAC IS has a favourable impact on long-term outcome of liver transplantation in HCV patients when taking into consideration a composite endpoint (S4 fibrosis, Retransplantation and related HCV death).

P-580 EARLY RESULTS FROM A TRIAL COMPARING SIROLIMUS WITH TACROLIMUS AS PRIMARY IMMUNOSUPPRESSION FOR RECIPIENTS OF NON HEART BEATING DONOR (NHBD) KIDNEYS AFTER ANTI-IL2 MONOCLONAL ANTIBODY

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Introduction: NHBD kidneys are subjected to significant ischaemia/reperfusion injury. An immunosuppressive regime with minimal nephrotoxicity is paramount to optimising long term function. This study aimed to determine whether sirolimus used in combination with MMF and prednisolone is one such regime.
Methods: In this prospective, open, paired study, recipients of kidneys from each NHBD were randomised to receive either sirolimus or tacrolimus. Both groups received daclizumab induction, MMF (2g/day) and prednisolone (20mg/day). Once renal function improved (creatinine <350 micromol/L) MMF was reduced to 1g/day and recipients were randomised to start either sirolimus (target trough 5-10mcg/L) or tacrolimus (target trough 5-10mcg/L).
The primary endpoint was eGFR at 1year (Cockroft-Gault) and secondary endpoints were biopsy proven acute rejection (BPAR), patient and graft survival and safety.
Results: Of the 31 consecutive donors, recipient pairs from 19 donors were recruited (other recipient pairs excluded for various reasons e.g. consent, graft thrombosis etc).

Groups	N (ITT)	eGFR (median) ml/min/1.73m^2			BPAR 3m/1y N (%)	1y Graft survival (%)	1y Patient survival (%)
		3m (N=19)	6m (N=17)	1y (N=13)			
Sirol	19	56.7	67.3	56.1	4 (21)/4 (21)	100	95
Tac	19	58.0	55.5	58.8	2 (11)/2 (11)	100	100

The intention to treat (ITT) analysis showed that patient and graft survival and eGFR's at all time points were similar. Ten of the sirolimus group had to be switched to tacrolimus for either BPAR or sirolimus complications. When these 10 were censored out, the eGFRs were higher in sirolimus recipients in 8/14 pairs at 3 months (3m), 6/11 pairs at 6m and 3/7 pairs at 1y (median eGFRs similar at each time point).
Conclusion and discussion: Sirolimus instead of tacrolimus as primary immunosuppression combined with MMF and prednisolone apparently does not improve long term graft function. Better outcomes may be achieved if an alternative induction agent (e.g. ATG) is used or if tacrolimus is only replaced by sirolimus at 3 months post transplant.

P-581 DACLIZUMAB VERSUS ANTI-THYMOCYTE GLOBULIN-FRESENIUS (ATG-F) AS INDUCTION THERAPY IN LOW RISK KIDNEY TRANSPLANT PATIENTS

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Purpose: The efficacy and safety of 2 types of induction therapy were studied in 98 kidney transplantation (KT) performed in our center between March 2000 and January 2008.
Material/Methods: Group I (55 patients) receiving daclizumab as induction therapy was compared to Group II (43 patients) induced with a single intraoperative bolus therapy of ATG-F. All patients were immunologically at low risk. The recipient and donor demographics and the immunosuppression regimen used were comparable in both groups.
Results: Drug safety as studied by the occurrence of side effects was almost comparable in the 2 groups except for more thrombocytopenia and anemia in Group II (p value < 0.016). Acute rejection rate and severity as well as post-operative infection rates were not significantly different in both groups. Moreover, the patient's hospital stay, the rate of delayed graft function as well as the 1 year patient and graft survival were similar in both groups. However, the mean serum creatinine levels upon discharge, at 1, 6 and 12 months were: 1.29±0.55, 1.24±0.38, 1.22±0.33 and 1.18±0.33 in Group I and 2.12±2.03, 1.5±0.4, 1.41±0.4 and 1.37±0.3 in Group II respectively ($p < 0.026$).
Conclusion: Both daclizumab and ATG-F were effective and safe as induction therapy in KT. However, we noticed lower serum creatinine levels without any effect on the 1 year graft survival in patients receiving daclizumab.

P-582 THE IMPACT OF EVEROLIMUS ON RENAL FUNCTION IN MAINTENANCE LIVER TRANSPLANTATION

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We investigated retrospectively the impact of conversion from calcineurin inhibitors (CNI) to everolimus (EVL) monotherapy on renal function (RF) in liver transplant (LT) recipients. Between January 2006 and July 2007, 70 recipients (51 M, 19 F; mean age 55.9±11 years) from a deceased donor were enrolled into a program of conversion to EVL monotherapy at a mean interval of 45±35.9 months from transplantation (range 7-192). Indications for conversion were deteriorating RF in 63 (90%). Efficacy failure was defined as persistence of CNI, EVL discontinuation, death, graft loss, loss to follow-up and need for dialysis at 12 months. Twelve months after switching, 53 patients (75.7%) were on EVL monotherapy and the mean change of creatinine clearance (CrCl) from baseline (-day 1 before EVL introduction) to endpoint (12 months) was 5.8±13.1 mL/min. On univariate and multivariate analyses the clinical variable correlated with the greatest probability of improvement was the baseline CrCl ($p<0.0001$). Conversion from CNI to EVL monotherapy is successful in 75.7% of cases and the improvement in RF is correlated with baseline CrCl. These data support pre-emptive minimization of CNI in the post-transplant course in order to delay the decline in renal function.

P-583 LOW DOSE CYCLOSPORINE AND SIROLIMUS REGIMEN IN RENAL TRANSPLANT PATIENTS – SINGLE CENTER EXPERIENCE

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Purpose: Sirolimus (SRL) is often used as an alternative to calcineurine inhibitors (CNI). In some cases, the use of a combination of low-dose CNI and SRL is an efficient, better controlled therapy, with fewer side effects.
Material & methods: This study retrospectively evaluated the safety and efficacy of conversion from tacrolimus (Tac) to a combined SRL and low-dose cyclosporine (CsA) regimen. Between January 2002-July 2008, 532 renal transplants were performed in our institution. 56 patients presented during the first 6 months posttranplant a great variability of Tac blood levels which could not be controlled by uptake. SRL was introduced in doses of 3-4 mg/day (target level 8-12 ng/ml), Tac was replaced with low doses of CsA (Co 50-75 ng/ml, C2 400 ng/ml). The dose of MMF was reduced to 1.5g/d, steroids were maintained at the usual doses. The patients were assessed regarding their renal function, the incidence of acute rejection and the occurrence of adverse events over 6 months of follow up.
Results: Patient and graft survival were 98.21%, 96.42%, respectively. At 6 months, creatinine clearance was significantly raised to a mean value of 48 ml/min vs 36 ml/min ($p<0.05$). Acute rejection rate was 17.85% (10 patients). Two patients lost the graft (one hemolytic uremic syndrome, and one rejection). There was no significant differences in serum lipid levels after the conversion. Of the 13 patients with Tac induced diabetes, 5 patients stopped and 4 reduced the antidiabetic drugs after conversion.
Conclusion: Following this study, in selected renal transplants with great variability of tacrolimus blood levels exposing them to a high risk of acute rejection or toxicity, conversion to combined low-dose cyclosporine and sirolimus regimen is a useful, efficient and easy to monitor option.

P-584 SINGLE PRETRANSPLANT PEAK LEVEL OF TACROLIMUS PREDICTS POST TRANSPLANT TACROLIMUS DOSE IN RENAL TRANSPLANTAT PATIENTS

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Introduction: Tacrolimus shows great inter-individual variability in dose requirement. The present study evaluated whether a single pretransplant peak tacrolimus blood level ($C2_{Tacrolimus}$) could predict the trough level ($C0_{Tacrolimus}$) obtained after transplant and post transplant dosing.
Methods: This was an open label, nonrandomized, single arm, single centre, pilot study conducted in 20 renal allograft recipients. All patients received a single dose of Tacrolimus (Tacrograf, Biocon, India) at 0.1mg/kg/dose and 2 hr post dose blood level (C2 level) was estimated 4-7 days before transplantation. All patients were started on 0.2mg/kg/day of tacrolimus one day before transplant. Trough levels were measured on 2/5/10/15/30 days posttransplant. Correlation was done between the pretransplant $C2_{Tacrolimus}$ with mean post-transplant $C0_{Tacrolimus}$ and the dose requirement.
Results: 20 patients were included in the study. Mean age 35.2±8.9 yrs,

M:F: 16:4, Mean body weight 55.4±10.2kg. The mean $C2_{Tacrolimus}$ in the pretransplant period was 24.6±17.4 ng/ml. The mean first $C0_{Tacrolimus}$ obtained 48 hours after transplant was 11.0±5.9ng/ml. There was a strong positive correlation [r=0.62] between the pretransplant $C2_{Tacrolimus}$ and posttransplant $C0_{Tacrolimus}$. There was a large variation in dose requirement at the end of two weeks in these patients [0.05-0.42 mg/kg/day] with a mean of 0.26±0.11mg/kg/day. There was a good negative correlation between pretransplant $C2_{Tacrolimus}$ and dose requirement at the end of second week [r= -0.57]. A peak level >30 ng/ml could identify 80% (4/5) patients who achieved trough levels more than the desired range and all patients (4/4) with a peak level of less than 10ng/ml had subtherapeutic levels in the first post-transplant week.

Conclusions: A strong correlation was observed between pretransplant $C2_{Tacrolimus}$ with posttransplant $C0_{Tacrolimus}$ and dose requirement which can optimize tacrolimus dosing in renal transplant recipients.

P-585 MEASURING ADHERENCE IN ADULT LIVER TRANSPLANT PATIENTS: RESULT OF THE EAST STUDY

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There is increasing awareness that nonadherence (NA) to the therapeutic regimen after transplantation is an important risk factor for poor graft and patient survival. We report the results of a single-center, cross-sectional study on the prevalence and determinants of NA among adult, maintenance liver transplant (LT) recipients. NA was measured in a composite way by means of a structured questionnaire and collateral reports of transplant physicians. Self report methods included the Basel Assessment of Compliance with Immunosuppressive Medication Scale (BAASIS), the Visual Analog Scale (VAS BAASIS), and the Immunosuppressive Therapy Adherence Instrument (ITAS). Patients' attitudes, intentions and normative beliefs towards immunosuppression (IS) were measured by an instrument consisting of health beliefs proved to be related to NA in previous adherence research in transplantation. Self-efficacy expectations were measured by an adapted version of the Long-Term Medication Behavior Self-Efficacy Scale (LTMBSES). Environmental and personal constraints were measured by an instrument consisting of twenty items, derived from research on barriers to medication taking in HIV patients. Out of 368 eligible candidates, 311 were contacted. Two hundred sixty-eight of them (86.1%) responded to the questionnaires and were available for the current analysis (male-to-female ratio 207:61; mean age 54.4±8.9 years). Altogether, 89 patients (33.2%) recalled an episode of NA over the previous 4 weeks, either as skipping one dose of IS, not taking IS exactly as prescribed, or lowering the dose of IS irrespective of their physician's advice. Nonadherers showed statistically significant weaker intention (p =0.003) with no difference in terms of attitudes and/or normative beliefs. Prevalence of NA among adult, maintenance LT recipients is high even in the setting of a National-Health-System-based setting and we suggest multifactorial patient profiling pre and post-transplantation period to allow for continued improvement of clinical results.

P-586 SYMPTOMS PREVALENCE AND BELIEFS IN MAINTENANCE LIVER TRANSPLANT PATIENTS

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Exploring the prevalence of symptoms in liver transplant (LT) recipients in view of tailoring immunosuppression (IS) is a crucial area of research. We report the results of a single-center, cross-sectional study on symptoms prevalence and beliefs among adult, maintenance (≥6 months) LT recipients. The assumption was that prevalent symptoms that patients believe are correlated with IS may lead to nonadherence with medication taking thus requiring closer monitoring. The prevalence of symptoms over the last 4 weeks was investigated with a structured questionnaire consisting of 15 items that were identified in previous qualitative research as relevant to solid organ transplantation. Patients were invited to express their beliefs whether the symptoms they experienced were related to IS. Out of 368 eligible candidates, 311 satisfied the inclusion criteria and were contacted. Two hundred sixty-eight of them (86.1%) responded to the questionnaires and were available for the current analysis (male-to-female ratio 207:61; mean age 54.4±8.9 years). Symptom prevalence and beliefs are illustrated in Table 1.

The five most prevalent symptoms were fatigue (48.5%), back pain (43.3%), joint pain (39.9%), sleep disturbance (36.5%), and weight gain (33.9%). On the opposite, the symptoms most frequently thought to be correlated with IS were tremors (75.8%), increased hair growth (77.3%), loss of muscular strength (67.4%), blurred vision (65.4%), and fatigue (65.4%). On average, symptoms were believed to be correlated with IS by 56.7% of patients. A remarkable exception was weight gain, reported by 33.9% of LT recipients, but thought to be correlated with IS by only 37.3% of affected patients. As much as half of patients believe that their symptoms are related to IS. These data underscore the need for constant education and close monitoring to reduce the risk for nonadherence to IS.

Table 1

Symptom	Prevalence (%)	Patients who believe symptom to be related with IS (%)
Unusual tremor/shakes	58 (21.6)	44/58 (75.8)
Increase hair growth	66 (24.6)	51/66 (77.3)
Change in appearance	35 (13)	14/35 (40)
Stomach or bowel upsets	77 (28.7)	48/77 (62.3)
Skin that bruises or tears easily	35 (13)	22/35 (62.8)
Loss of muscle strength	86 (32.1)	58/86 (67.4)
Weight gain	91 (33.9)	34/91 (37.3)
Difficulty in concentrating	87 (32.4)	56/87 (64.3)
Swelling of hands or feet	51 (19)	26/51 (50.9)
Back pain	116 (43.3)	39/116 (33.6)
Lost sex drive	73 (27.2)	44/73 (60.3)
Joint pain	107 (39.9)	59/107 (55.1)
Blurred vision	73 (27.2)	40/73 (54.8)
Fatigue	130 (48.5)	85/130 (65.4)
Sleep disturbance	98 (36.5)	43/98 (43.8)
Mean	29.4%	56.7%

P-587 MINIMIZATION OF IMMUNOSUPPRESSION IN PRIMARY ADULT LIVER TRANSPLANTATION WITH STEROID-FREE REGIMEN USING LOW DOSE OF TACROLIMUS WITH MYCOPHENOLATE MOFETIL AFTER DACLIZUMAB INDUCTION

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In the aim to minimize side-effects of steroids and calcineurin inhibitors in liver transplant (LT) patients, we conducted a pilot study comprising a steroid-free regimen using low dose of tacrolimus (Tac) with mycophenolate mofetil (MMF) after daclizumab induction.

Patients and methods: From september 2005 to december 2007, 64 primary LT adult patients were enrolled in this prospective one-year pilot study. Two doses of daclizumab were given at post-operative day (POD) 0 and 7, a 500 mg intra-operative bolus of solumedrol was administrated and thereafter stopped. Tac was started at POD 1 in order to reach trough levels below 8ng/mL and 2 g per day of MMF were given according to white blood cell count. All alive patients were followed for one year.

Results: Mean Tac trough levels at POD 7, 3 months and 1 year were 7.5, 6.7 and 5.9nl/ml respectively. Mean serum creatinine levels prior LT, at 3 months and 1 year were 81, 102 and 94 mol/L respectively. Ten (15.6%) patients were withdrawn from MMF secondary to side effects. Acute rejection was histologically diagnosed in 18 (28%) patients. Six were mild and observed on the one-year protocol biopsy with normal LTs, 10 were moderate and 1 severe. All rejection episodes resolved with no treatment (n=5), increased tacrolimus dose (n=11) and solumedrol boluses (n=2). In univariate analysis, risk factors for rejection were initial MMF doses and donor BMI. Twelve patients were switched to everolimus or cyclosporine and 6 (10%) patients developed de novo diabetes. One year patient and graft survival was 96.8%.

Conclusions: The one-year results of this dual immunosuppressive steroid-free regimen comprising Tac low dose and MMF suggest that side-effects can be minimized without jeopardizing efficacy.

P-588 THE IMPACT OF SIROLIMUS ON WEIGHT CHANGE IN LIVER TRANSPLANTATION: A CLINICAL PICTURE OF A COMPLEX INTERACTION

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Introduction: The mammalian target of rapamycin (mTOR) dichotomously regulates body metabolism across a complex pathway, both stimulating adipogenesis peripherally while suppressing appetite centrally in the hypothalamus. Sirolimus, an mTOR inhibitor, may have varied effects on weight but its impact post liver transplant (OLT) is not established. We review the largest experience of OLT patients with initial sirolimus immunosuppression to determine the clinical impact of sirolimus immunosuppression on post OLT weight changes.

Materials and method: All 1554 OLT patients from 1998 – 2007 were reviewed identifying those using sirolimus as initial immunosuppression. The control group included the remaining patients where no sirolimus was given. Weight was recorded at specific post-op intervals. The baseline weight was established at 4 weeks post-transplant and both the change in actual weight and percent change over 5 years were calculated.
Results: Sirolimus was used as initial immunosuppression in 210/1554 OLT patients, 567 patients had sirolimus added later, leaving a control group of 777 OLT patients having never received sirolimus. The recipients in the sirolimus group were slightly older (54 yrs vs 50 yrs, p=0.0001) with no sex difference. There were more HCV patients in the sirolimus group (51.9% vs 44.1%). The ratio of cyclosporin/tacrolimus skewed strongly to cyclosporin use in the sirolimus group (81.5%/15.9% vs 2.7%/86.2%) compared to tacrolimus use in controls with no difference in steroids. Initial pre-transplant weight (82.30 kg vs 82.25 kg) and post-transplant weight (83.70 kg vs 83.90 kg) were similar in both the sirolimus and control group.

Table 1. Post-transplant weight change at defined intervals in sirolimus patients vs non-sirolimus controls

Time Interval	SRL Group	Control	p value
3 Month	–1.55 kg	+0.70 kg	0.004
1 Year	+1.90 kg	+5.80 kg	0.004
2 Year	+0.65 kg	+8.20 kg	0.0006
5 Year	+8.95 kg	+11.40 kg	NS

Table 2. Percent weight change at defined intervals in sirolimus patients vs non-sirolimus controls

Time Interval	SRL Group	Control	p value
3 Month	–1.93%	+0.91%	0.004
1 Year	+2.41%	+7.74%	0.004
2 Year	+0.59%	+11.62%	0.0006
5 Year	+8.95%	+14.78%	NS

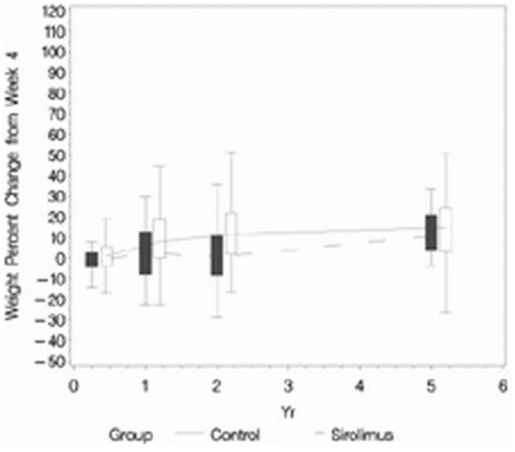

Figure 1. Precent weight change post OLT in SRL pts vs non-SRL control pts at defined time intervals.

Conclusion: Sirolimus use in OLT patients results in significantly less weight gain, with essentially unchanged weight the first 2 years, even when used with the known weight gain promoter cyclosporin. Limiting post-transplant weight gain with sirolimus might potentially limit future weight related comorbidities.

P-589 A PROSPECTIVE CLINICAL TRIAL COMPARING TACROLIMUS-MMF TO CYCLOSPORINE-EVEROLIMUS IN DE NOVO RENAL TRANSPLANT RECIPIENTS: 2 YEARS RESULTS

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Aim of this prospective clinical trial in renal tx was to evaluate the renal function in a CNI based immunosuppressive regimen (tacrolimus-MMF, TAC) compared to a CNI-sparing regimen (everolimus-cyclosporine, EVE).
Materials and methods: 60 sequential deceased donor renal tx recipients were assigned to TAC (30 pts) or EVE (30 pts) and followed up for 2 years. All patients received induction with basiliximab and corticosteroids in the maintenance post-tx phase. After tx, pts were maintained on low dose TAC (C0 5-8 ng/mL) or low dose CsA and EVE (CsA C2 150-300 ng/mL, EVE C0 3-8 ng/mL).
Results: Demographic characteristics were similar in the two groups of pts. After 2 years follow-up, patient and graft survival were not different (PTS: TAC 100% vs EVE 100%; *p=ns; GS:* TAC 96.7% vs EVE 93.3%; *p=ns*). Mean serum creatinine and mean creatinine clearance were also not significantly different (creatinine, mg/dl: TAC 1.41±0.60 vs EVE 1.46±0.5, *p=ns*; creatinine clearance, ml/min: TAC 67.4±21.3 vs EVE 62.3±16.5, *p=ns*). Patients in the EVE group showed more acute rejection episodes (TAC 4/30 13.3% vs EVE: 6/30 20%; *p=ns*), but this was not statistically significant. Patients in the EVE group showed significantly more dislipidemia (serum cholesterol, mg/dL TAC 207±36 vs EVE 235±45, *p*=0.022; serum triglycerides mg/dL TAC 142±105 vs EVE 238±119, *p*=0.006; statines use TAC 25% vs EVE 80%; $p<0.05$). Patients on hypertensive medications and patients diagnosed with PTDM were similar in the two groups.
Conclusions: Our data show that 2 years after renal tx the combination of low dose TAC-MMF produces similar renal function, acute rejection rates, graft and survival compared to the Eve-CsA association, but has better cardiovascular profile.

P-590 CLINICAL OUTCOME IN TWO GROUPS OF KIDNEY RECIPIENTS TREATED WITH DIFFERENT CYCLOSPORINE FORMULATIONS

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Purpose: Cyclosporine microemulsion Neoral (Novartis) was introduced to organ transplantation more than 20 years ago and it's efficacy and side effects are well known. Since 2002 a new formulation of cyclosporine Equoral (Teva) with similar pharmacokinetic profile is available. We conduct study to compare clinical effect of both formulations.
Methods and materials: There were 37 (14 women, 23 men, mean age 45 years) consecutive recipients of first cadaveric kidney graft receiving Equoral in our center in the study group. The control group consisted of 48 (23 women, 25 men, mean age 47 years) consecutive graft recipients received Neoral. In multivariate analysis there were no differences between groups in: donors and recipients age, time on dialysis, HLA mismatch, total ischemic time, panel reactive antibodies and incidence of delayed graft function.
Results: 1-year and 3 years graft survivals were similar in both groups: in Equoral group 95,8% and 93,3% and in Neoral group 97,3% and 96,6% respectively. There was no significant difference in mean serum creatinine concentration in the groups.

Mean serum creatinine concentration [mg/dl]

	3 months	6 months	1 year	2 years	3 tears
Equoral	1,9	1,7	1,5	1,6	1,8
Neoral	1,9	1,7	1,6	1,7	1,7
p value	ns	ns	ns	ns	ns

There were 12 biopsy proven acute rejection in study and 14 in control group. Equoral was discontinued in 2 cases due to nephrotoxicity and in 3 cases switched to tacrolimus due to biopsy proven acute rejection. Neoral was change to sirolimus in 1 case (trombotic microangiopathy) and to tacrolimus in 6 cases (4 acute rejection and 2 nephrotoxicity). Steroids dose at 6 months were: 10 mg in study and 12,5 mg in control group. Number of hypotension drugs used and incident of postransplant diabetes mellitus did not differ significantly in both group.
Conclusion: New formulation of cyclosporine (Equoral, Teva) has comparably efficacy and safety clinical profile as widespread use cyclosporine microemulsion (Neoral, Novartis). Both drugs can be equivalently use in kidney transplant recipients.

P-591 A NOVEL RISK ASSESSMENT TOOL FOR REJECTION AND INFECTION TO INDIVIDUALLY TAILOR IMMUNOSUPPRESSION IN RENAL TRANSPLANTATION

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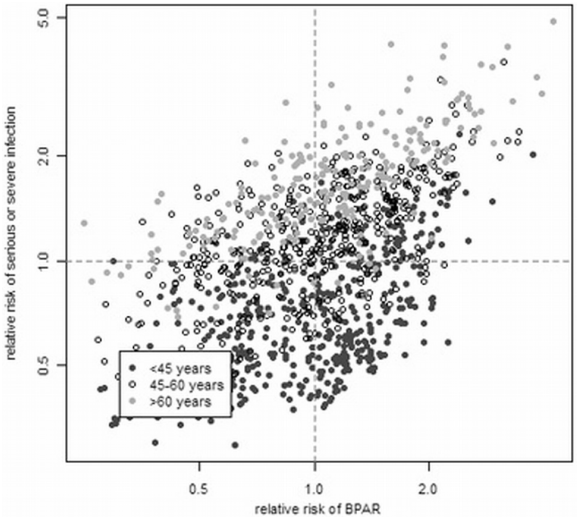
Purpose: Infection represents a major threat to patients in the first year after kidney transplantation, but risk profiling for infectious events is not routinely used to select the immunosuppression protocols. Here we develop a risk profiling system for infection and acute rejection.
Methods: From Symphony, a recent large de-novo study assessing four current immunosuppression regimens, we evaluated patients receiving mycophe-

nolate mofetil (2 g/day), steroids plus either cyclosporin (standard dose without induction or low-dose with daclizumab induction) or tacrolimus (with induction). Using Cox regression we assessed the risk profile of patients with respect to infection and biopsy-proven acute rejection (BPAR) in the first year based on donor and recipient information at transplantation. More specifically, we contrasted the relative risk of serious or severe infection or of death against the relative risk of BPAR or graft loss. The reference was a virtual patient with average covariates. Another recent large study employing similar regimens, FDCC, was used for validation.

Results: In Kaplan-Meier estimates 40% of patients experienced an infectious complication or BPAR in the first year. The relative risk for the two endpoints covered a wide range of values over more than one order of magnitude (Figure).



The main explanatory variables with a significant and relevant impact on the endpoints were recipient age and CMV constellation (mainly affecting infection), donor type (affecting both) and HLA mismatches and treatment type (mainly affecting BPAR). External validation with FDCC data supported these findings.

Conclusion: The risk profile for acute rejection and for serious infection varies considerably among individual patients currently receiving the same post-transplant treatment. Stratification for both types of risks at transplantation may be useful to individualize the immunosuppressive and antiinfective regimes. This approach will be tested in a prospective clinical trial.

P-592 INITIAL EXPERIENCE WITH ADVAGRAF IN RENAL TRANSPLANTATION

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Introduction: Advagraf is the new modified release version of tacrolimus (tac) which requires once daily dosing as compared to the traditional Prograf twice daily dosing.

We report the largest single centre UK experience using Advagraf in renal transplantation.

Methods: During the 13 month period to 31/10/2008, 134 renal transplants were carried out at our institution, of which 64 (48%) received Advagraf immunosuppression, together with anti-CD25 induction, an anti-proliferative (azathioprine or MMF) and corticosteroids.

Results: Dose adjustment based on blood levels takes longer (36 hours) than with Prograf (12 hours) and a learning experience on optimal dosing occurred. Advagraf was discontinued in 12 (19%) of the 64 patients and discontinuation occurred mostly (9/12 patients) during the first 4 months of our experience with the drug. This was mostly in patients with delayed graft function (6/9 of the patients) where our standard practice is to halve the dose of calcineurin inhibitor and we were not sufficiently confident during our early experience to adjust the dose of Advagraf. Advagraf was also discontinued because of failure to swallow tablets (one patient), failure to absorb the drug due to severe diabetic gastroparesis (one patient) and neurological side-effects (two patients). Two patients developed graft dysfunction attributed to calcineurin inhibitor toxicity on biopsy and had Advagraf stopped.

Of the remaining 52 patients receiving Advagraf, three had the Advagraf treatment temporarily stopped but then recommenced.

Thirteen (25%) of the 52 patients had 17 episodes of rejection (15 biopsy proven) within the first 6 months. Currently graft survival is 98%.

Conclusion: Our experience with Advagraf is generally favourable. It has the advantage of once daily dosing and provides a satisfactory alternative to Prograf.

P-593 PHARMACODYNAMIC MONITORING IN KIDNEY ALLOGRAFT RECIPIENTS WITH AND WITHOUT CALCINEURIN INHIBITORS

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Pharmacodynamic monitoring may establish risk factors of clinical and subclinical rejection, arteriolar hyalinization and CAN.

Purpose: Monitoring of the selected immunological parameters in the peripheral blood in kidney allograft recipients with and without CyA

Patients and methods: In a prospective study 42 low-risk patients were randomized to either a reduced CyA dose followed by its complete withdrawal at 10 month and daclizumab (group A, n=21) or to a normal CyA dose without daclizumab (group B, n=21). In both groups we assessed the number of CD3+ cells and CD3+/CD4+, CD3+/CD8+, CD3+/CD28+, CD3+/CD152+, CD3+/CD11a+, CD3+/CD49d+, CD3+/CD25+, CD3+/CD69+ cells before Tx and then at 1 day and 1, 3, 12, 36 months after Tx. Protocol biopsies and GFR were assessed at 1, 3, 12, 36 months after Tx.

Results: The number of CD3+/CD25+ cells was lower in group A ($p<0.03$), but the number of CD3+/CD28+ cells was higher in group A ($p<0.02$). The number of cells with expression of remaining examined molecules did not differ between groups. The number of cells with all examined CD molecules significantly decreased at 1 day after Tx and then quickly returned to a normal level at 1 month after Tx (time effect $p<0.001$), with exception for the number of CD3+/CD25+ cells in group A – the lower expression was present till month 3 (time*group effect $p<0.0001$). The number of CD3+, CD3+/CD4+, CD3+/CD8+, CD3+/CD49+, CD3+/CD11a+ cells at month 3 was a risk factor for subclinical rejection in both groups. GFR was significantly lower in group A than in group B during all the study.

Conclusion: Pharmacodynamic monitoring may help in identification of risk factors of subclinical acute rejection episodes and in assessment of effectiveness of immunosuppressive treatment with and without calcineurin inhibitors.

P-594 PERFORATED SIGMOID DIVERTICULITIS AFTER ORGAN TRANSPLANTATION IS A RARE, BUT LIFE-THREATENING EVENT

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Background: Complicated diverticulitis is a serious condition in transplant recipients, because immunosuppressed patients show an increased incidence of colonic perforation with high morbidity and mortality. Symptoms and clinical presentation can range from non-specific signs of abdominal discomfort with delayed diagnosis of perforation to life-threatening abdominal sepsis. The standard surgical management is still controversial: both Hartmann procedure and creation of a primary anastomosis are associated with high morbidity and mortality.

Material and methods: Between 2000 and 2008 four out of 2286 patients (0,17%) after solid organ transplantation (lung x 2, kidney x 1, liver x 1) were admitted to the department of surgery for acute sigmoid diverticulitis with free perforation (4 male patients; median age 65, range 35 to 87) requiring emergency laparotomy. Two patients underwent a Hartmann procedure, two patients had a primary anastomosis.

Results: The time interval between transplantation and perforation ranged between 7 months and 12 years with two patients having a history of diverticulitis. A wound dehiscence after laparotomy and an anastomotic leakage required reoperation in two patients. Postoperative morbidity included acute rejection, pneumonia and acute renal failure. Two patients died with MODS following pneumonia and acute rejection (bilateral lung transplantation x 2, primary anastomosis with anastomotic leakage x 1, Hartmann procedure x 1).

Conclusion: Sigmoid perforation in transplant recipients is a rare, but life-threatening event. Hartmann procedure as well as primary anastomosis are associated with high mortality. Thus, elective surgical interventions should be considered in patients with a history of diverticulitis and a high risk of perforation (steroids, heart and lung transplantation).

P-595 PHA STIMULATION OF PERIPHERAL BLOOD MONONUCLEAR CELLS FROM KIDNEY TRANSPLANT RECIPIENTS PRODUCES LESS ATP THAN FROM NORMAL CONTROL

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Background: The methods currently available to measure immune function are expensive, time consuming or require radioactive material. Peripheral blood mononuclear cells (PBMC) contains T lymphocytes that are known to be stimulated and to proliferate in response to a lectin: phytohemagglutinin (PHA).
Aim: To measure ATP response of PBMC from patients on various immunosuppressive agents and controls following PHA stimulation.
Methods: PBMC were separated from patients on cyclosporine, tacrolimus or sirolimus based regimen and control blood samples by means of density gradient centrifugation. Fifty thousand PBMC per well were incubated overnight (15-18 hours) in triplicate with or without PHA. The Promega Cell Titre-Glo Luminescent Cell Viability assay which signals the presence of intracellular ATP by means of the luciferin/luciferase enzyme reaction and the Turner Biosystem luminometer were used to measure ATP in relative lights units (RLU) and converted to ng/ml. Chi-square test was employed to assess the statistical significance of differences.
Results: PBMC's response to the PHA challenge in vitro demonstrated statistically significant differences between the control population (34% ATP increase) and each of the groups of patients on cyclosporine, tacrolimus and rapamune (10%, 16%, 11% ATP increase respectively) ($p<0.001$). The majority of patients who were diagnosed with infections or were clinically stable had immune responses characterised as low (ATP <200ng/ml) or moderate (ATP<201-501ng/ml). Of interest, the only patient who was diagnosed with rejection was found to have a strong immune response (ATP>501ng/ml).
Conclusion: These preliminary results demonstrate that in-vitro PHA stimulation of PBMC of kidney transplant recipients produces 2 to 3 times less ATP than normal controls. This test may help in the clinical monitoring of transplant patients.

P-596 USE OF MYCOPHENOLATE MOFETIL IN LIVER TRANSPLANT PATIENTS. ANDALUSIAN LIVER REGISTRY

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Aim: -To evaluate the efficacy and safety of different immunosuppressant regimes with mycophenolate mofetil (MMF) from induction.
Patients and methods: A prospective, observational, multicentre study of 226 liver transplants performed in 2005-2006 with 24-month follow-up.
The variables studied were indicators of kidney, liver and blood function, intercurrent infections, cardiovascular risk, acute-chronic rejection, recurrence of hepatitis C virus, de novo tumours and survival.
The patients were classified in 4 groups, according to treatment: (A) No MMF (n=91), (B) MMF from induction (n=83), (C) Late introduction of MMF (n=30), (D) MMF at induction with early withdrawal (n= 22).
Results: The biodemographic characteristics were similar in all groups. The patients with MMF were higher risk, had worse MELD and Child-Pugh scores and worse pre-transplant blood and kidney values.
Significant differences were observed between the creatinine levels: between groups B and C 0.45 mg/dl at month 1 ($p<0.01$), 0.27 mg/dl at month 3 ($p<0.01$) and 0.3 mg/dl at month 6 ($p<0.05$); on the other hand, a difference of 0.34 mg/dl ($p<0.01$) was observed in the first month between groups A and C, and there were differences in the 3rd month between groups A and B of 0.17 mg/dl ($p<0.05$).
No differences were observed in white blood cells, acute rejection (19%) and chronic rejection (5%), graft transplant (80%) and HCV recurrence rate (75%) between the four groups.
For B-D, the infection rate at three months was 34.5% versus 17.9% in A-C ($p<0.05$).
Conclusions: The use of MMF at induction and the introduction in the first three months post-transplant helps to preserve and restore creatinine levels (in case of worsened kidney function) and to keep them stable, without increasing the risk of rejection and optimising the dose of anticalcineurins.

P-597 LONG TERM FOLLOW-UP OF DE NOVO MALIGNANCIES AFTER 1300 LIVER TRANSPLANTATION: A CASE-CONTROL STUDY

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Long-term survival data on de novo malignancy are limited following orthotopic liver transplantation (OLT) when compared with controls without malignancies.
Methods: Over a 23 yr period at our institution, 62 of 1300 patients (4.7%) who underwent OLT were identified to have 62 de novo malignancies. The clinical characteristics and survival of these patients were retrospectively reviewed and compared with a control cohort of 62 OLT recipients without malignancy matched with the incidence cases by age, year of OLT, sex, and type of liver disease.
Results: Chronic hepatitis C (48%), alcohol (10%) and chronic hepatitis B (20%) were the three leading causes of liver disease. Skin cancer was the most common malignancy (26%) including 5 cases of skin Kaposi's syndrome, followed by gastroenterologic cancers (23%), hematologic malignancies (13%), eye and rhinomaxillary malignancies (11%), genitourinary cancers (7.7%), lung cancers (6.2%), breast cancers (6.2%).
The cases and controls were not significantly different in the main immunosuppressive regimen (Neoral vs Prograf, p=NS) and the number of rejection episodes (15 vs 16, p = NS). The median age of cadaveric liver donor is similar in cases and controls, respectively (52 vs 47, p=NS). The five- and 10-year Kaplan–Meier survival rates for the cases were 82% and 63%, respectively, vs. 79% and 72%, respectively, for the controls (p=NS by log-rank test). Patients with skin cancers had 10-year survival similar to the controls (88% vs 72%, p=NS), but significantly better that non-skin cancers (88% vs 56%, p=0.01). The prognosis for patients with gastrointestinal tumors was poor, with a median survival of 8.6 months after the diagnosis.
Conclusion: In this study, de novo malignancies after OLT were uncommon. Due to the poor prognosis of gastrointestinal tumors, is mandatory a yearly surveillance protocol to treat eventually this kind of tumors at an early stage.

P-598 MYCOPHENOLATE MOFETIL AND LOW DOSES OF CALCINEURIN INHIBITORS IN PATIENTS WITH RENAL DYSFUCTION AFTER LIVER TRANSPLANTATION. A TEN YEAR SINGLE-CENTER PROSPECTIC STUDY

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Background: Renal dysfunction (RD) after liver transplantation (LTx) is a relatively common event in the MELD era.
Methods: This is a prospective single-center study started on Jan 1999 and completed on Dec 2008. After written consent, 100 pts were enrolled. Mycophenolate mofetil (MMF) was associated with low doses of calcineurin inhibitors (LDCI). Inclusion criteria: age >18; stage 3 chronic kidney disease (glomerular filtration ratio, GFR 30-59 ml/min/1.73m^2). Exclusion criteria: previous steroid resistant acute rejection, WBC count <2000/mm^3. GFR was calculated according to Levey formula. Median age was 52.7 years (23-71). Median time from LTx to enrolment was 16.6 months (0.2-4.6). Median follow up was 43.1 months (2-125). Pts were stratified in groups according to the starting time of the MMF-LDCI association. There were: Early Renal Dysfunction group (ERDg, before 30th pod, N=24) and Late Renal Dysfunction group (LRDg, after the 30th pod, N=53). In a third group (control group, N=23) the MMF-LDCI association was adopted soon after LTx in absence of RD. At the enrolment, 69% of pts were on CsA and 31% on TAC.
Results: After the introduction of MMF, renal function was stable in the 3 groups. LRDg presented the lowest GFR ($p<0.05$). Prevalence of renal failure (continuous dialisis need) was equal to 4% (N=1) in the ERDg and to 11% (N=6) in the LRDg (^{2}, $p<.05$). Prevalence of acute rejection (AR) was 6% (N=3) in the LRDg and 33% (N=8) in the ERDg (^{2}, $p<0.05$).
Discussion: Use of MMF as a renal-sparing agent is safe and efficacious in ERDg and LRDg. LRDg showed an higher prevalence of renal failure and a lower AR rate. We suggest the MMF-LDCI association in LTx pts with RD

P-599 CNI AVOIDANCE AND STEROID WITHDRAWAL IN RENAL TRANSPLANTATION. RESULTS AT THREE YEARS OF A PROSPECTIVE MULTICENTER RANDOMIZED TRIAL COMPARING SIROLIMUS (SRL) AND CYCLOSPORINE (CsA): THE SPIESSER STUDY

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Introduction: CNI avoidance with de novo introduction of SRL demonstrated a benefic impact on renal function at one year in the Spiesser study. A 3- year follow-up study investigates the intermediate term impact of this strategy.
Methods: We evaluated the renal function and safety of an immunosuppressive regimen with SRL (group A) or CsA (group B) at M 24 and M 36. The 133 patients who completed the one year core study (64 in group A, 69 in group B) were included (ITT population). eGFR was calculated according to normalized Cockcroft and Gault formula.
Results: Preliminary results were reported in 123 patients (61 in group A, 62 in group B). eGFR was better in group A throughout the study: 61±18 vs 57±16 at M12 (NS), 64±21 vs 56±18 at M24 ($p<0.03$), 62±23 vs 56±19 at M36 (NS), particularly in patients who received at M 12 their treatment according to the protocol (50 in group A, 55 in group B) (per protocol population): 63±18 vs 56±15 at M12 ($p<0.03$) 66±21 vs 56±17 at M 24 ($p<0.01$) 65±22 vs 55±18 at M 36 ($p<0.02$).
2 deaths and 1 graft loss were observed in group A, 1 graft loss in group B. Occurrence of cancer tended to be lower in group A (2 patients) than in group B (6 patients). Complete efficacy and safety results will be available and presented.
Conclusion: The improvement in renal function observed at 12 months with SRL was maintained at 36 months.

P-600 EVOLUTION OF PROTEINURIA UNDER SIROLIMUS IN 62 MAINTENANCE KIDNEY TRANSPLANT PATIENTS A SINGLE CENTER ANALYSIS

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Sirolimus (SRL), is an alternative treatment option for kidney transplant recipients, that were on Calcineurin-inhibitors (CNI) and showing CNI-related nephrotoxicity. Observations suggest that a subgroup of patients (pts), converted to SRL develop proteinuria, which might be a negative predictor for long-term graft function. In a retrospective, single-center study we followed 62 long-term kidney transplant recipients over at least one year after withdrawal of CNI and conversion to SRL.
Pts were converted either due to chronic allograft dysfunction (n=50) or malignancies (n=12). Our aim was to evaluate occurring proteinuria and renal function over the study period. SRL was started after a meantime of 7,2 (±5,3) years post transplantation. Proteinuria increased significant from 483 (98-3083) mg/day to 1063 (112-8133) mg/day (n=57; p=0,0001) during the first 3 months after conversion, with stable proteinuria of 1160 (89-6099) mg/day (n=50) one year after conversion. Remarkably, over the first year 23% of pts showed significant proteinuria (1,5g/day). In 24 pts SRL was stopped due to side effects or noticeable proteinuria with a mean of 2071 (275-7014) mg/day (p=0,02), after an average treatment time of 100 days. Notably, this group offered elevated baseline proteinuria of 1237 (50-5767) mg/day at the time of SRL conversion. After cessation of SRL, proteinuria declined within three months to 1618 (116-9800) mg/day
Renal function was stable over observation period, GFR=41,9 ml/min (±22,4ml/min).
Within 3 months after conversion to SRL a substantial number of pts will develop significant proteinuria (1,5g/day). Pts with elevated baseline proteinuria have a higher probability for aggravation of proteinuria. The effect of SRL on proteinuria was partly reversible after withdrawal. At the time point of SRL introduction baseline proteinuria is an important aspect for the decision to convert maintenance pts from CNI to SRL.

P-601 DO PATIENTS KNOW WHAT DOCTORS TOLD THEM TO DO?

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Background: Transplant patients are prescribed a variety of medications with multiple dosing schemes at different time points.
Methods: In this cohort-study a self-designed not validated self-reporting questionnaire were applied in our out patient clinic for renal transplant recipients to obtain information on demographics, actual therapeutic scheme, compliance with respect to missing, timing, dosing related to different retrospective time scales. In parallel we extracted actual clinical data (prescriptions, renal function, drug level) from the electronically database.
Results: Questionnaires were completed by 173 patients, matching with clinical data were possible for 162 pts. Most common kind of self-reported non-compliance (srNC) was a deviation in timing (57.8%), followed by a skipped dose (42% at least one dose/month) whereas only 21.4% reported incorrect amount of dosing. Most of the patients did not recall the exact number of actual prescribed drugs. If this unintentional non-adherence was combined with self-reported skipping only 22/163 pts (%) reached optimal scoring. These patients had a trend or better renal function compared to pts with intermediate and low scoring (71.3±20.7, n=22; 63.4±29.6, n=96; 60.6±23.4, n=44). Self-reported skipping is not associated with the actual renal function (63.3 vs. 63.6), whereas correct recall of number of drugs was associated with better renal function (71.1±22.3, n=43 vs. 61.1±28.1, n=119, $p<0.05$). No further differences were observed in both groups except a higher median for the number of prescribed drugs (10 vs. 7, $p<0.001$) and a trend for higher systolic blood pressure (135 vs. 129, p=0.052) with ui-NA.
Conclusions: In our cohort unintentional non-adherence as estimated by the incorrect recall of the number of the prescribed medications increases with the number of different drugs per day and seems to be more important for the clinical outcome than the self-reported compliance.

Immunobiology & basic science

P-602 RENAL TRANSPLANTATION IN PATIENTS WITH NEGATIVE CDC CROSSMATCHES: VALUE OF DONOR SPECIFIC ANTIBODIES DETECTION ON FIRST GRAFT

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Objectives: The clinical significance of the presence of pre-transplant donor specific anti-HLA antibodies (DSA), despite negative cytotoxicity crossmatches, is still unclear. We tried to test the impact of detection of anti-HLA antibodies on the outcome of renal transplantation.
Material and methods: Our study included 153 live donor kidney transplant recipients whose pretransplant sera were available. All of them had negative complement dependant cytotoxic (CDC) crossmatch and they were retrospectively evaluated for the presence of anti-HLA antibodies and their donor specificities with the use of Luminex technology. All recipients follow up data were reviewed.
Results: Anti-HLA antibodies were detected in 49 patients (32%), 33 patients had donor non specific anti-HLA antibodies and 16 patients had donor specific Anti-HLA antibodies. Although, there was a trend for more acute rejection in those patients with Anti-HLA antibodies (22%) in comparison to those without anti-HLA antibodies (17%) but this difference did not attain any statistical significance (p 0.378%). Patients with donor specific anti-HLA antibodies had a significant higher incidence of acute cellular rejection (19% Vs 6%) and vascular rejection (25% Vs 6%) in comparison to those patients with donor non specific anti-HLA antibodies [p 0.04].
Conclusions: Although, our study was carried out on a relatively small number of patients we could identify that the presence of donor specific antibodies as detected by Luminex carries higher risk of humoral rejection in the early post transplant period without a significant impact on patients or graft survival.

P-603 SEROEPIDEMIOLOGY OF INFECTION WITH EPSTEIN- BARR VIRUS AMONG ASYMPTOMATIC STUDENTS ATTENDING ISLAMIC AZAD UNIVERSITY OF KAZEROUN, SOUTHWEST OF IRAN

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Purpose: EBV is a herpesvirus which establishes a persistent life-long infection in over 95% of adults world-wide. Infection is usually asymptomatic but the virus is associated with a variety of diseases, including nasopharyngeal carci-

noma, Burkitt's lymphoma and EBV-associated B lymphoproliferative disease in the immunocompromised host, particularly organ transplant recipients. Our study focuses on seroepidemiology of EBV infection in asymptomatic healthy students.
Materials and methods: In our study, the study group comprised 90 students. These included 49 males and 41 females healthy volunteers. All of them was at the age of 20-25 (average 22.8). At first, demographic data were recorded. For serological studies 5 ml of blood sample was collected and the serum was isolated. Serological assays including ELISA and hemagglutination monospot test were used for determination of IgG and IgM antibodies titer to the EBV capsid antigen (VCA) and IgG titer to the EB unclear antigen (EBNA) and early antigen (EA). Finally the results were analysed by statistical methods.
Results: Overall, EBV antibody was positive in 80 persons (88.9%) out of 90 subjects and they had a previous infection. VCA, EBNA and EA IgG antibodies were detected in 79 (87.8%), 80 (88.9%) and in 2 (2.2%) samples out of 90 subjects respectively. VCA IgM antibody was determined only in one (1.1%) sample and monospot test was positive in 4 (4.4%) sample out of 90 sera. EBV antibody was not identified in 10 (11.1%) subjects. Also we didn't find any significant relationship between students with different sexuality, field of study and their residence ($p>0.05$).
Conclusion: The overall incidence of EBV infection in this study was 88.9% which is close to the observations in the other works with healthy individuals specially in underdeveloped countries.

P-604 (+1057) G/A POLYMORPHISM OF THE CD86 GENE IN ACUTE RENAL ALLOGRAFT REJECTION

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Allograft rejection is an immune response directed against alloantigens present on the surface of the graft cells. As T-cells activation requires co-stimulatory signals, we focused on one of the numerous molecules involved in this pathway: CD86. The binding of CD86 to CD28, a T lymphocytes receptor, stimulates T-cell activation, whereas, when CD86 is fixed to CTLA-4, the counter receptor of CD28, T lymphocytes proliferation is down-regulated.
In this study, we examined, by direct sequencing, the (+1057) G/A polymorphism of CD86 gene, in 102 healthy subjects and 169 kidney allograft recipients. Patients were classified into two groups according to the HLA haplotype similarity between graft donor and graft recipient: Group I included 31 HLA-identical haplotype allograft recipients and Group II included 138 recipients showing one or more mismatches in the HLA haplotype. 45 patients: 8 (26%) in G1 and 37 (27%) in G2, developed at least one acute rejection episode (AR).
No differences were found between genotypic distributions in the two groups of patients and controls. Our results revealed that the A/A genotype and the A allele frequencies were lower in patients without acute rejection than in those with acute rejection episode (2,22% and 0,233 vs 9,68% and 0,282). However, these differences are not statistically significant. Furthermore, the graft mean survival rate, after 10 years of follow-up, was higher in A/A carrying recipients (92,30%) than in G/A (84,61%) or G/G (84,61%) ones. The graft mean survival time was 9,84 years in AA genotype bearing patients while it was 7,61 in G/A and 8,21 in G/G patients.
In Tunisian recipients, the (+1057) A/A genotype of CD86 gene could have a protective effect against renal allograft loss. These results should be confirmed by further study concerning a larger cohort of patients.

P-605 FORENSIC MEDICINE METHODS ALLOW TO DETECT DONOR DNA IN RECIPIENT BLOOD FOR YEARS AFTER KIDNEY TRANSPLANTATION

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After organ transplantation DNA from passenger cells and cellular debris from ischemia and rejection damaged cells is disseminated in the recipient. The question is whether this DNA may be incorporated into recipient cell genome in the process of the so called "illegitimate DNA incorporation" a frequent phenomenon in nature.
Aim: To search for donor DNA in recipient tissues and cells after allogeneic transplantation and immunosuppression.
Materials: Recipient's blood samples were collected before and after kidney transplantation 1, 14, 28, 90, 180, 360 and 720 days and genomic DNA was isolated. Short tandem repeats analysis (STR) was applied. The investigated loci were: phospholipase A2- *HUMPLA2A1(AAT)n*, cytochrome P450 *HUMCYARO(AAAT)n* and *D1S80*.
Results: Donor cytochrome P450 or HUMPLA2 or D1S80 genes were detected in recipient blood cells up to 2 years after kidney transplantation. Positive results were observed 24hr after grafting in 3 out of 3pts and in 4 out of 4 pts after 14 days, in 28 out of 28 after 28, in 2 out of 2after 90, in 3 after 180, in 1 after 1 and in 2 out of 2 after 2 years.
Conclusions: Donor DNA can be detected in recipient blood cells 2 years after kidney transplantation. The question as to whether the detected donor DNA was contained in the surviving donor cells or in a form of apoptotic or necrotic bodies in recipient phagocytes or was incorporated into recipient cell genome remains to be answered. Recent study documents presence of donor DNA in nuclei of recipient APCs.

P-606 IS DONOR DNA INCORPORATED INTO RECIPIENT LYMPHOID CELLS?

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Introduction: Processing and incorporation of fragments of DNA and oligonucleotides by mammalian and bacterial cells is a continuing physiological process. It is strongly intensified in inflammation, cancer and after tissue and organ transplantation. The outcome of DNA transfer between mammalian cells remains not well understood. It has been suggested that donor DNA may play a role in rejection or creating partial tolerance.
Aim: To study whether donor DNA may be identified in recipient immune cells and if so, whether it locates in cytoplasm or penetrates into nucleus.
Methods: In sex- mismatched combination male rat DNA was injected i.v. into 10 female rats. Recipient blood (PBM), lymph node (LN) and spleen (SPL) mononuclear cells were examined 24 hr later for the presence of SRY gene characteristic for Y-chromosome. SRY was detected using polymerase chain reaction (PCR) method and real-time PCR. The PCR products was analyzed by electrophoresis in12,5% polyacrylamide gel (PAGE; Phast System, Amersham Pharmacia Biotech) and silver stained (Silver Staining Kit; Amersham Pharmacia Biotech).
Results: SRY gene was detected in female PBM, LN and SPL cell cytoplasm in 2 out of 10 rats. Moreover, it was detected in PBM nuclei in 4 out of 10 rats and in LN cell nuclei also in 4 out of 10 rats.
Conclusion: Detection of donor male DNA in nuclei isolated from female cells suggests its spontaneous transport into recipients cells and their nuclei. The question remains open whether this finding may have any relevance to the rejection or tolerance process.

P-607 NON-INVASIVE BIOMARKERS FOR ACUTE REJECTION IN RENAL TRANSPLANTATION USING 1H-NMR SPECTROMETRY

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Aims: Acute rejection (AR) can effect up to 30% of renal transplants. Earlier diagnosis leads to improved outcomes. The current gold standard for diagnosis is invasive biopsy, which has associated morbidity and is not normally performed before day seven. We aim to identify a non-invasive plasma biomarker capable of diagnosing AR earlier using 1H-nuclear magnetic resonance (NMR) spectroscopy and chemometrics.
Methods: 12 renal transplant patients, 7 with no rejection and 5 with AR had nine blood samples taken at separate time points. The blood was centrifuged and plasma separated and frozen until required. Subsequently the plasma was analysed Each spectrum was divided into regions of uniform separation and the areas in these regions measured. These data were then subjected to principal component analysis.
Results: Clear differentiation between AR and no rejection was seen in principal components 1 and 2 from day 1 post operation. The cause of the separation is the biomarkers which appear in the region 3.24-3.4ppm of the spectrum. The nature of the biomarkers remains to be confirmed.
Conclusions: These preliminary studies support the suggestion that 1H-NMR based metabolic profiling can provide an early non-invasive test for detection of acute rejection in renal transplantation.

P-608 POST-TRANSPLANT PROTEINURIA ASSOCIATED WITH EVEROLIMUS. DEFINITION OF MAIN FEATURES BASED ON AN INTEGRATED PROTEOMIC APPROACH

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Aim of this study was to characterize the everolimus induced proteinuria and to verify whether proteinuria was linked to apoptosis of renal cells.
We report clinical, pathology and laboratory features of 27 recipients of renal transplant who were treated with everolimus as first line drug and were followed for at least 6 months. Urinary proteins were characterized by an integrated proteomics approach (quantitative assays, two-dimensional electrophoresis, MALDI-TOF, Western Blot). Detection of renal cell apoptosis was performed by analysis of renal biopsies with caspase 3 antibodies.
Proteinuria developed in all but 2 patients, in concomitance with the recovery of renal function and persisted over time. After 6 months renal function was normal in all. During the study 3 patients developed heavy proteinuria (>3 g/24 hours), 9 presented intermediate levels (between 1 and 3 g/24 hours) and 16 had proteinuria between 0.2 and 1 g/24 hours.Most patients developed proteinuria within 30 days from transplant. A mixed tubular-glomerular pattern of proteinuria was found in all proteinuric patients with presence of albumin, IgG, β1-microglobulin, α1 microglobulin and free λ chains. All urines were also characterized by the presence of anti-protease inhibitors such as α1-antitrypsin and α1-chimotrypsin and by products of tubular degradation never identified in other tubular diseases. Finally nephrotic urines did not contain fragments of albumin and α1-antitrypsin, that are normal urine components in other nephrotic states. Renal biopsies showed variable degrees of tubular apoptosis.Glomerular staining was limited to cases with highest proteinuria.
At our knowledge this is the first description of everolimus induced proteinuria, based on a proteomics approach. Composition of urinary proteins of tubular and glomerular origin reflects structural changes characterized by diffuse apoptosis of tubular epithelia and, more limited, of podocytes.

P-609 VALIDATION OF TCR Vβ SPECTRATYPING FOR MONITORING T-CELL RECEPTOR COMPLEXITY

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A diverse T-cell receptor (TCR) repertoire is important for immunocompetent individuals to be able to respond to numerous antigenic challenges. T-cell immunity is greatly affected in individuals that are immunocompromised, leaving them open to opportunistic infections. TCR Vβ spectratyping enables qualitative monitoring of the TCR Vβ repertoire of an individual and can be combined with quantitative TCRVβ antibody monitoring to give an overview of the TCR repertoire.
Currently there is little published data on the lower normal limit (LNL) of TCR Vβ spectratype complexity for $CD3^+$, $CD4^+$ or $CD8^+$ T-cell populations or the minimum number of cell required to achieve a reproducible result. The aim of this study was to validate TCR Vβ spectratyping for $CD3^+$, $CD4^+$ and $CD8^+$ T-cells.
$CD3^+$, $CD4^+$ and $CD8^+$ T cells were isolated by magnetic separation. Following RNA extraction and reverse transcription, samples were amplified with 24 individual TCR Vβ primers and a constant region specific primer, using methodology adapted from Pannetier *et al.* The TCR Vβ complexity scores were calculated from the sum total of the amplified peaks for all 24 TCR Vβ families.
This study has successfully defined the lower normal limit of TCR Vβ complexity as 143 for $CD3^+$, 154 for $CD4^+$ and 132 for $CD8^+$ T-cells populations, using 10 normal controls. The $CD3^+$ T-cell data confirms that previously published by Wu *et al.* The minimum number of T-cells required to yield a reproducible TCR Vβ complexity score was determined as $1.5\text{-}2.0 \times 10^6$ cells for all T-cell subsets and has not been previously published. Such methodology can be applied to cohorts of patients post bone marrow transplantation, acute rejection episodes in renal transplantation and immunodeficient individuals, to assess their TCR repertoire and therefore aid their clinical management.

P-610 A NOVEL METHOD TO ASSESS THE LEVEL OF IN VIVO IMMUNOSUPPRESSION IN TRANSPLANT PATIENTS USING AMNIS IMAGESTREAM TECHNOLOGY

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Contemporary immunosuppressive protocols rely on drug dosing guidelines learned from large clinical trials, but the effect of this therapy in a transplant recipient remains difficult to predict. To assess the level of immunosuppression in each patient, we measured the degree of NFkB translocation in peripheral T cells by Amnis ImageStream technology. Upon activation, NFkB inhibitors are degraded, releasing NFkB to translocate to the nucleus. The abundance of NFkB in the nucleus vs. the cytosol reflects the activation state of a particular cell type. Peripheral blood cells were isolated from 17 subjects, stimulated in culture for 24 hours with PMA and ionomycin and stained for T cell surface markers and the major intracellular isoform of NFkB, RelA or p65. We compared nuclear NFkB in resting and activated CD3, CD4 and CD8 T cell subsets. Compared to normal controls (n=8), transplant recipients on tacrolimus, MPA and prednisone showed reduced translocation of NFkB to the nucleus. Patients with stable allograft function (n=5) had a 36-75% reduction in nuclear NFkB translocation in all 3 T cell subsets. In contrast, patients with acute rejection (n=2) had an increase in ability to translocate NFkB in CD3 and CD8 cells and only a 9% suppression in CD4 cells. Patients with viral infections (n=2) had severely compromised NFkB translocation with 100% suppression in CD3 and CD4 subsets and 92% suppression in CD8 T cells. NFkB inhibition strongly correlates with overall immunosuppression and clinical outcomes. The novel Amnis Imagestream assay may be a useful guide to individualizing immune therapy or directing minimization strategies.

P-611 ROLE OF THE INTEGRATED STRESS RESPONSE IN EPITHELIAL PHENOTYPIC CHANGES INDUCED BY ISCHEMIA

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Ischemia is characterized by the association of hypoxia and nutrient deprivation. Whereas the cellular response to hypoxia is well understood, the consequences of a nutritionnal stress remain to be determined. Nutrient deprivation, including glucose and amino-acid starvation, activates the Integrated Stress Response (ISR) that regulates translation in response to glucose and aminoacids deprivation. The ISR induces a global translation inhibition mediated by the activation of the kinase PERK and the phosphorylation of the translation initiator eIF2a. However, some mRNA are specifically and selectively traduced during this response.
The aim of this study is to decipher the biological response of human renal tubular cells in culture to glucose deprivation with a particular focus on the role of the ISR on epithelial phenotypic changes.
Primary cultured renal epithelial cells cultured in glucose-deprived medium display phenotypic changes suggestive of epithelial to mesenchymal transition, including E cadherin down regulation, fibronectin expression, beta-catenin nuclear translocation and morphological changes suggestive of a fibroblastic shape. CTGF, lysil-oxydase and bFGF transcripts are also up regulated, suggesting that tubular cell display fibrogenic properties. In parallel, glucose starvation activates ISR in tubular cells. Interestingly, Snail, a transcriptional factor that play a central role in epithelial-to-mesenchymal transition, is significantly expressed at the protein level during glucose starvation but not at the mRNA level, suggesting that its expression post transcriptionnally regulated. Genome wide analysis using DNA microarrays of the mRNAs that are selectively translated during glucose starvation is ongoing.
In conclusion, this study demonstrates for the first time that glucose starvation induces tubular phenotypic changes and stimulates the expression of fibrogenic transcripts. Our results suggest that the Integrated Stress Response may lead to the selective traduction of mRNAs including Snail, that control epithelial-to-mesenchymal transition and fibrotic process.

P-612 HIGH EXPRESSION OF CD16 BY GAMMA DELTA T CELLS DURING CYTOMEGALOVIRUS INFECTION IN KIDNEY TRANSPLANT RECIPIENTS: IMPLICATION IN THEIR ANTI-VIRAL AND ANTI-TUMOR FUNCTION

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Background: A few years ago, we have observed a expansion of circulating gamma delta (gd) T cells following cytomegalovirus (CMV) infection in kidney transplant recipients (KTR). These unconventional T cells display TCR dependent cytotoxicity against both CMV-infected cells and carcinoma cells. In the present study, we investigated the role of CD16 overexpressed by these gd T cells.
Methods: Flow cytometry was used to phenotype gd T cells. CD16+ gd T cell lines were generated from CMV-infected KTR and were activated with CMV immune complexes, CMV-infected fibroblasts and tumor cell lines.

Results: An extensive phenotyping of gd T cells from KTR lymphocytes allowed us to demonstrate that 71.9±15.9% of gd T cells from CMV-infected KTR expressed the CD16 (a NK-marker usually absent on conventional T-cells), when compared with only 19.8±16.7% in non CMV-infected KTR. These CD16+ gd T cells were able to produce IFN-γ (a potent anti-viral cytokine) in a CD16-dependent manner when activated by CMV/Ig immune complexes. This production was greatly enhanced by IL-12 and IFN-alpha, two cytokines produced during CMV infection. The CD16 molecule is known to mediate antibody-dependant cellular cytotoxicity (ADCC), especially in NK cells. In keeping with this property, we demonstrated that these CMV-induced CD16+ effector gd T cells could make ADCC against lymphoma cell lines and skin carcinoma cell lines preincubated either with rituximab or cetuximab, respectively.
Conclusion: These *in vitro* data reveal a new CD16-dependent anti-CMV function of gd T cell through recognition of immune complexes. Moreover, this CMV-induced subset of T lymphocyte could be involved *in vivo* in the anti-tumor ADCC.

P-613 LIPOCALIN-2 FORMS A COMPLEX WITH MATRIX METALLOPROTEINASE 9 AND PROTECTS IT FROM DEGRADATION DURING ISCHEMIA AND REPERFUSION OF THE TRANSPLANTED HEART

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Purpose: Matrix Metalloproteinase 9 (MMP-9) is known to be involved in cell migration, tissue repair and remodelling. Lipocalin-2 (NGAL/Lcn-2) forms a complex with MMP-9 preventing it from degradation. Retrieved from previous data about the role of NGAL/Lcn-2 during ischemia and reperfusion (IR) following murine heart transplantation, this study focuses on the interaction between MMP-9 and NGAL/Lcn-2 in analogous settings.
Material and methods: Male inbred C57BL/6 and the Lcn-2-/- mouse were used for heterotopic heart transplantations. RT-PCR, Western blot, gelatine zymography and immunohistochemistry were performed to visualize MMP-9 and NGAL/Lcn-2 expression in the graft at different time points (0, 2, 12, 24 and 48h). Polymorphonuclear cells (PMN) isolated from wildtype and Lcn-2-/- mice were used for in vitro experiments.
Results: MMP-9 expression was upregulated 8 fold and peaked at 48h compared to NGAL/Lcn-2 expression which peaked at 24h. Similar expression patterns were observed in the different experimental settings (Lcn-2-/- donor Lcn-2-/- recipient, wildtype donor and recipient and mixed wildtype/Lcn-2-/- transplantations). However, MMP-9 protein levels were significantly lower in Lcn-2-/- grafts corresponding to a reduced infiltration of PMN in Lcn-2-/- recipients. In vitro PMN retrieved from Lcn-2-/- mice showed lower levels of MMP-9 than from wildtype mice. Stimulation of PMN with recombinant NGAL/Lcn-2 did not increase MMP-9 expression.
Conclusion: Our data demonstrate an interaction between MMP-9 and NGAL/Lcn-2 expression during IR in heart transplantation. Reduced MMP-9 expression in Lcn-2-/- grafts is directly related to the simultaneously decreased infiltration of PMN described previously, thus suggesting a chemotactic function of the MMP-9/Lcn-2 complex during IR of the transplanted heart.

P-614 TCR-INDEPENDENT EXPANSION OF FOXP3$^+$CD4$^+$ REGULATORY T CELLS BY CD137 STIMULATION

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Purpose: We want to examine the role of CD137, a member of TNF receptor superfamily, in regulatory T cells.
Methods/Materials: The C57BL/6 unirradiated or irradiated (C57BL/6 x DBA/2)F1 (BDF1) acute GVHD was used as an experimental system.
Results: We found that administration of anti-CD137 mAb (3H3) completely prevented the development of acute GVHD in the C57BL/6 unirradiated BDF1 GVHD model. This occurred because anti-CD137 mAb induced activation-induced cell death of donor CD4$^+$ T cells and CD8$^+$ T cells. Interestingly, there was no GVHD when GVHD had been re-introduced in the 3H3-treated mice by donor T cells. This result suggests that 3H3 can form a tolerogenic environment in the host. We identified host Foxp3$^+$CD4$^+$ regulatory T cells as the factor that was responsible for the tolerogenic environment induced by 3H3; administration of 3H3 resulted in a marked expansion of host Foxp3$^+$CD4$^+$ regulatory T cells in the presence of donor T cells, and depletion of Foxp3$^+$CD4$^+$ regulatory T cells abrogated the effect of 3H3 on forming the tolerogenic environment. Curiously, administration of 3E1, another clone of anti-CD137, induced no GVHD but complete donor cell engraftment in BDF1 recipients that received sublethal irradiation (400 rad), unlikely 3H3 that resulted in lethal GVHD under the same conditioning. It seems that the inhibitory effect of 3E1 was also due to a marked expansion of host Foxp3$^+$CD4$^+$ regulatory T cells. Finally, we found that anti-CD137 mAb induced an expansion of Foxp3$^+$CD4$^+$ regulatory T cells in naïve mice.
Conclusion: Our results indicate that CD137 stimulation induces TCR-independent expansion of Foxp3$^+$CD4$^+$ regulatory T cells. Anti-CD137 mAb may be used as precondition to block allograft rejection or to prevent GVHD.

P-615 PROCALCITONIN AND C-REACTIVE PROTEIN SERUM LEVELS FOLLOWING HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Objective: Hematopoietic cell transplantation (HCT) is a curative therapy for several malignant and nonmalignant disorders. The purpose of this study was to investigate any association of serum levels of high sensitive-CRP (hS-CRP) and procalcitonin (PCT) concentration with complications such as acute GVHD (aGVHD), veno-occlusive disease (VOD) or infection occurrence after HSCT.
Methods: Serum hS-CRP and PCT levels were sequentially measured by enzyme-linked immunosorbent assay and semi-quantitative immunochromatografic assay respectively in 35 patients who had undergone HSCT
Results: hs-CRP serum level was increased in patients with aGVHD. It was also was increased in sepsis. Increased PCT levels were only associated with bacterial infection. Only PCT values discriminated between exclusive infection and other single TRC. VOD did not alter CRP and PCT levels.
Conclusion: These results support the idea that that hs-CRP and PCT serum levels are a helpful biomarker for transplant related complications such as GVHD and infection and the PCT can differentiate infection from GVHD.

P-616 IS THE EFFECT OF HYPERBARIC OXYGEN THERAPY ON P-SELECTIN EXPRESSION DURING COLD ORGAN PRESERVATION TISSUE DEPENDENT?

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Introduction: P-Selectins represent glycoproteins expressed on endothelial cells and platelets responsible for capture and transient adhesion of leucocytes and activated platelets to vascular endothelium during Ischemic-Reperfusion Injury (IRI). Hyperbaric oxygen (HBO) treatment affects many of the components in IRI, but to a variable degree. This study aimed to compare the effect of HBO therapy on P-selectin expression
Methods: Thirty kidneys and sixty livers were procured from male Lewis rats and submerged in cold (4°c) University of Wisconsin (UW) solution. Specimens were stored for periods of 4, 12, 16, 20, and 24 hours. Group 1 (n=15) kidneys and group 3 (n=30) livers were stored in room air, while group 2 (n=15) kidneys and group 4 (n=30) were treated with 2.5 atmosphere absolute HBO. At the end of each time interval the organs underwent preparation and levels of P-Selectin expression in the tissues were measured using western blotting and readings quantified with a densitometer.
Results: Down-regulation of P-Selectin expression was observed in cold stored kidneys for 4, 12, 20 and 24 hours under HBO conditions as compared to room air. In contrast, the level of P-Selectin expression tended to be greater in cold stored liver tissues under HBO conditions, at time points 4, 12 and 16 hours.
Discussions: The study demonstrates that the effect of HBO treatment on P-Selectin expression in kidney tissues may not parallel that in liver. HBO treatment has also been shown to affect IRI, including lipid peroxidation, NO production, and microvascular blood flow. Hence, further studies are needed to characterize the overall influence or the predominant effect of HBO therapy on specific tissues.

P-617 THE INTERLEUKIN-6 AND VASCULAR ENDOTHELIAL GROWTH FACTOR IN HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Objective: This study investigated whether or not there is a correlation between the changes in the serum levels of vascular endothelial growth factor (VEGF) and Interleukin-6 (IL-6) with complications such as acute GVHD (aGVHD), veno-occlusive disease (VOD) or infection occurrence after hematopoietic cell transplantation (HCT).
Methods: Serum VEGF and IL-6 levels were sequentially measured by enzyme-linked immunosorbant assay (ELISA) in 35 patients who had undergone HSCT
Results: Serum levels of IL6 in patients with aGVHD were increased in comparison to patients without aGVHD but it is not statistically significant. Serum level of VEGF was only increased in patients with aGVHD during early days after transplantation. No altered levels were observed for of IL-6 and VEGF in patients with VOD or sepsis condition.
Conclusion: These results supported that that VEGF and IL-6 may be a good biomarker for transplant related complications especially GVHD, because the rising levels were only detected in a GVHD rather than other TRC.

P-618 INVARIANT NKT CELLS ARE ESSENTIAL IN LIVER SINUSOIDAL ENDOTHELIAL CELL-INDUCED IMMUNOSUPPRESSION OF T CELLS WITH INDIRECT ALLOSPECIFICITY

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We have reported that liver sinusoidal endothelial cells (LSECs) endocytose portally injected allogeneic splenocytes and can negatively regulate T cells with indirect allospecificity via the Fas/FasL pathway. As a result of *in vitro* transmigration across the LSECs from BALB/c mice treated with a portal injection (PI) of B6 MHC class II-deficient (C2D) splenocytes, the naive BALB/c $CD4^+$ T cells lost their responsiveness to the stimulus of BALB/c splenic antigen presenting cells that endocytosed the donor-type alloantigens. In the present study, we examined whether invariant NKT (iNKT) cells influence the ability of LSECs to endocytose irradiated allogeneic cells. BALB/c wild-type (WT) mice or BALB/c CD1d-deficient (*CD1d*$^{-/-}$) mice that lacked iNKT cells were portally injected with irradiated B6 C2D splenocytes labeled with PKH-26. Only 4.44±1.16% LSECs endocytosed the labeled splenocytes in the BALB/c *CD1d*$^{-/-}$ mice at 12 h after PI, whereas 18.30±2.61% LSECs endocytosed the labeled splenocytes in the WT control mice ($P < 0.001$). The liver mononuclear cells (LMNCs)isolated from either BALB/c *CD1d*$^{-/-}$ or WT mice were adoptively transferred via the tail vein into the BALB/c *CD1d*$^{-/-}$ mice. Only WT LMNCs that contained iNKT cells resulted in a significant increase in the proportion of LSECs that had endocytosed PKH26-labeled splenocytes. Adoptive transfer of the LSECs from BALB/c WT mice treated with a PI of irradiated B6 C2D splenocytes prolonged the survival of subsequently transplanted B6 C2D hearts, but a similar effect was not observed when the LSECs from BALB/c *CD1d*$^{-/-}$ mice treated with a PI of irradiated B6 C2D splenocytes were transferred into BALB/c WT mice. These findings strongly suggest that iNKT cells play a crucial role in the endocytotic activity of LSECs.

P-619 CALCULATED WITHDRAWAL OF LOW-DOSE IMMUNOSUPPRESSION BASED ON A DETAILED IMMUNOLOGICAL MONITORING AFTER KIDNEY TRANSPLANTATION BETWEEN MONOCYGOTIC TWINS

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Purpose: Pretransplant screening in living donor kidney transplantation includes human leukocyte antigen matching, and panel reactive antibodies analysis, whereas T cell mediated anti-donor reactivity is not assessed. We investigated T cell reactivity after living related kidney transplantation between two monocygotic twins and in consequence correlated the withdrawal of individual immunosuppressive medication with immunological findings.
Methods: Immunosuppression consisted of mycofenolate mofetil; a single shot of steroids – to prevent an ischemic/reperfusion injury – and induction therapy with rabbit antithymocyte immunoglobulin was given once prior to transplantation.
Results: Flowcytometric analyses of recipient peripheral blood cells revealed unchanged frequencies of cells from the innate immune system before and after transplantation. Although we detected antigen presenting cells in the patient's blood from the 5th until the 90th postoperative day, lack of clinical signs of transplant rejection suggest a failure in the activation of transplant-specific T cells. Indeed, T cell numbers in the patient's blood were comparable before and after transplantation, moreover, the majority of CD4 and CD8 T cells was in an inactivate state.
Analyzing T cell alloreactivity, a mixed lymphocyte reaction before and after transplantation revealed no donor-specific T cell activity. IFN-γ (detecting the Th1 subtype) and IL-10 (detecting Th2 cells) protein levels in supernatants of recipient cells cocultivated with donor cells supported the lack of T cell activation and effector cell differentiation.
Conclusion: Based on immunological findings on day 5 and day 20 MMF-therapy was reduced (1g daily) and stopped on day 25 post transplantation. Immunological monitoring on day 90 confirmed the absence of immune reactions against donor tissue. Our study illustrates that analyzing T cell alloreactivity in living donor recipients allows the identification of high or low risk transplant candidates and subsequent individualized immunotherapy.

P-620 SKEWED INTRAGRAFT T_H17/REGULATORY T CELL RESPONSES DURING REJECTION IN TRANSPLANT PATIENTS

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IL-17, produced by T_H17 cells, is a cytokine with multiple proinflammatory functions. T_H17 cells might be involved in alloreactivity leading to acute rejection, while FOXP3+ regulatory T cells have anti-inflammatory properties and control the anti-donor response. Differentiation into either T_H17 or regulatory phenotypes is mutually exclusive and depends on the local cytokine milieu. Here, we determined the gene expression of IL-17A, IL-17F, and FOXP3 both in biopsies from heart transplant patients and in vitro after stimulation in the MLR. In vitro alloactivated T cells produced large amounts of IL-17A, IL-17F and FOXP3 mRNA. Addition of calcineurin inhibitors (CNI) inhibited the IL-17A, IL-17F and FOXP3 mRNA levels significantly (> 90%). In biopsy samples from CNI treated patients IL-17 was hardly detectable, irrespective of the rejection grade. IL-17A was present in only 8 and IL-17F in 10 out of 56 biopsies. In contrast, FOXP3 mRNA expression was measurable in all samples and positively associated with acute rejection ($p<0,01$). Cytokines that stimulate IL-17 production (IL-6, IL-23) as well as those that inhibit IL-17 (IL-2, IL-27) and IL-35 important for FOXP3 regulatory T cells were present in the biopsies. IL-6 and IL-23 gene expression were not associated with IL-17 transcription and rejection, while IL-2, IL-27 and IL-35 genes were highly expressed during rejection (all $p<0,05$) and correlated with FOXP3 levels (all $p<0,0001$). Importantly, isolated graft lymphocytes exhibited strong and donor-specific regulatory activities during rejection.
In conclusion, we found no evidence for a prominent role of T_H17 cells in rejection processes in immunosuppressed transplant patients, while at the graft site regulatory T cells are involved in damage control rather than prevent rejection.

P-621 MURINE STROMAL CELL LINE, AFT024 ENHANCED IN VIVO ENGRAFTMENT POTENTIAL THROUGH EPIGENETIC MODIFICATION

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Purpose and methods: To address the mechanism that AFT024 cell line governs enhancement of *in vivo* engraftment potential as primitive hematopoietic progenitor cells (HPCs) *ex vivo*, we employed co-culture using high pore density insert, coated outside the bottom with irradiated AFT024 cell line. The cultured cells were analyzed phenotype of primitive HPCs by flow cytometry, LTC-IC and Western blot for histone modification.
Materials/Results/Conclusion: Human umbilical cord blood (UCB)-derived

$CD34^+CD38^-$ cells were cultured in the co-culture system in serum free media with cytokines. Increment of frequency of CD34+Lin- cells in the co-cultured was 30 fold, but 6 fold in control. Total colonies from LTC-IC were increased 1.5 fold in co-cultured, compared to control. To address our co-culture system maintains HPCs as primitive state through epigenetic modification, we employed Western blot analysis for histone modification. Cells from co-cultured, showed more primitive state as open chromatin structure, highly methylated in Me-H3K4, under-methylated Di-Me-H3K9 and more acetylated H4, compared to control. Taken together, our results demonstrate that AFT024 cell line maintains HPCs as the primitive state through epigenetic modification.

P-622 APE1/Ref-1 GENE OVER-EXPRESSION IN HUMAN HCC IS ASSOCIATED TO CANCER ETHIOLOGY

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Alteration of cellular redox plays an important role in HCC development. The immunohistochemical detection of APE1/Ref-1, a master regulator of cellular response to oxidative stress, is more frequent in HCC than in surrounding liver cirrhosis (SLC) and its cytoplasmic localization correlates with poor prognosis. Since no data are available about APE1/Ref-1 gene expression in HCC, the aim of the study was to assess APE1/Ref-1 transcript levels in HCC and SLC compared to distal liver cirrhosis (DLC). Samples of HCC, SLC and DLC were collected and snap frozen from 30 patients (30% HCV, 30% HBV, 40% alcohol) subjected to liver transplantation. Histological diagnosis and APE1/Ref-1 localization was assessed by immunohistochemistry. Ape1/Ref-1 protein levels were assessed by Western Blot (WB). RT Real-time PCR was performed to determine APE1/Ref-1 mRNA expression. APE1/Ref-1 immunostaining was detectable in all cases in cirrhosis and HCC tissue. APE1/Ref-1 reactivity was mainly observed in the hepatocytes. APE1/Ref-1 mRNA expression levels were 2-folds higher in HCC ($p=0.001$) and 1.5-folds in SLC ($p=0.011$) than in DLC data confirmed at the protein level by WB. APE1/Ref-1 was up-regulated in HCC in 90% of the patients, while increased levels were seen in only 66% of the cases in SLC. APE1/Ref-1 transcript levels in HCC were higher in HCV-related cancers than in alcohol and HBV ($p<0.05$). APE1/Ref-1 over-expression was not related to the HCC grading or Child-Pugh score. APE1/Ref-1 was over-expressed in HCC and the up-regulation increases moving from DLC to SLC and HCC. APE1/Ref-1 mRNA content was higher in the HCV related cancers. These data demonstrate that APE1/Ref-1 transcript levels are 1) significantly increased in HCC 2) more elevated in SLC than in DLC 3) associated with HCV infection, suggesting a possible link between HCV viral infection and APE1/Ref-1 over-expression.

P-623 DONOR PRE-TREATMENT WITH SIMVASTATIN REDUCES GRAFT IMMUNOGENICITY FOLLOWING PROLONGED COLD ISCHEMIA IN THE LONG-TERM

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The protective effects of 3-Hydroxy-3-methylglutaryl coenzyme A reductase inhibitors (HMG-CoARIs, statins) have been widely demonstrated in numerous models. Based on their anti-inflammatory properties, we investigated the potential effect of donor pretreatment with statins on ischemia/reperfusion injury in a rat model of kidney transplantation (Tx). F-344 donor rats were pretreated with Simvastatin for 3 days prior to transplantation (10 mg/kg/day) and kidneys were grafted into Lewis recipients following a prolonged cold ischemia of 24h. Frequencies of cell populations were analyzed by flow cytometry and the mRNA expression of relevant candidate genes. By analyzing allografts after 24h and 14 days post Tx we detected reduced numbers of $CD3^-CD4^+$ monocytes in spleens of recipients following donor pretreatment with Simvastatin (Simvastatin vs. control, 24h: $6.8\pm2.1\%$ vs. $12.1\pm2.6\%$, $p=0.007$; d14: 20.3 ± 2.9 vs. $25.0\pm1.0\%$, $p=0.018$), whereas the number of $CD3^+CD4^+$ T cells was comparable in both groups. At both time points the chemokine receptor CCR7 was markedly reduced in the spleen as well as its ligands CCL19 and CCL21. Interestingly, by analyzing renal allografts after 6 months this observation was even more amplified. Spleens derived from recipients receiving an allograft derived from Simvastatin pretreated donors displayed a significant reduction of markers associated with graft immunogenicity such as MHC class II ($p<0.006$), CCL19 ($p<0.012$), and CCL21 ($p<0.0061$). Moreover we detected decreased mRNA levels of immunoproteasome subunits including PSMB8 ($p<0.0061$), PSMB9 ($p<0.0061$) and PSMB10 ($p<0.042$) which have been recently illustrated to be highly induced as a consequence of prolonged cold ischemia (Kotsch et al. 2007). Our data suggest that pretreatment with Simvastatin following prolonged cold ischemia reduces graft immunogenicity by modulating potential antigen presenting cells and their homing to lymphoid organs and may therefore represent an attractive tool to preserve renal function after ischemia/reperfusion injury.

P-624 FGF2 AND TGFb PLAY DISTINCTIVE ROLES IN MYOFIBROBLAST DIFFERENTIATION FROM $CD45^+$ BONE MARROW FIBROBLAST-LIKE CELLS

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Background: Recent evidence shows that a CD45+ population of fibroblast-like cells (FLC) isolated from the bone marrow can become aSMA-expressing myofibroblast. Such CD45+ FLC are also found in experimental cardiac allografts undergoing chronic rejection. The current work studies the cytokine regulation of the $CD5^+$ FLC in myofibroblast differentiation.
Methods: Dish-adherent stromal cells isolated from the bone marrow of F344 rats were fractionated through FACS into $CD45^+$ and $CD45^-$ subpopulations. Both fractions of cells were subjected to differentiation cultures with different stimuli, including TGFb, FGF2, and intragraft fibroblast-derived conditioned-medium (CM).
Results: Conditioned medium prepared from intragraft fibroblastic cell cultures (1:1 in volume) supported a vigorous myofibroblast differentiation of $CD45^+$ BMSC while conventional DMEM failed to do so. Surprisingly, addition of fibrogenic growth factor TGFb1 (1-10ng/ml) in DMEM did not promote proliferation of $CD45^+$ BMSC, resulting in a decrease in cell numbers after 7-8 days in culture. In contrast, the cells stimulated by recombinant FGF2 (1-20ng/ml) exhibited morphological changes from oval-shaped cells into dendritic, then to large polygonal cells. The majority of the newly developed polygonal cells stimulated by FGF2 did not express aSMA stress filament until the cells are exposed to TGFb. Quantitative PCR showed that $CD45^+$ BMSC expressed high levels of mRNA coding for FGFr1, and low levels of FGFr2c and FGFr3.
Conclusion: The data suggest that FGF2 act at the early stage of fibroblast differentiation by morphological conversion of $CD45^+$ to $CD45^-$ fibroblast-like cells while TGFb act at the later stage of myofibroblast end-differentiation by promoting stress aSMA expression. Therapeutic intervention of FGF2 and TGFb signaling may serve a strategy to prevent allograft fibrosis by blocking the pathway of myofibroblast differentiation.

P-625 NATRIURETIC PEPTIDE B PRE-OPERATORY LEVELS IN LIVER TRANSPLANT RECIPIENTS

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Purpose: To study plasma pre-operatory levels of natriuretic B peptide precursor (pro-BNP) in patients with hepatic cirrhosis from different etiologies in active waiting list for liver transplantation.
Patients and methods: Study developed in 51 liver transplant recipients from Liver Transplant Unit of Virgen de las Nieves University Hospital. Written informed consent was obtained from the patientsor their relatives and the study protocol was approved by the local Clinical Research (Ethics) Committee. Patients were distributed in 2 groups of study: 1) Group of patients with alcoholic hepatic cirrhosis (n=26). 2) Group of patients with virus C hepatitis cirrhosis (n=25). A group of healthy volunteers collaborate to establish normal (basal) values of pro-BNP (n=13).

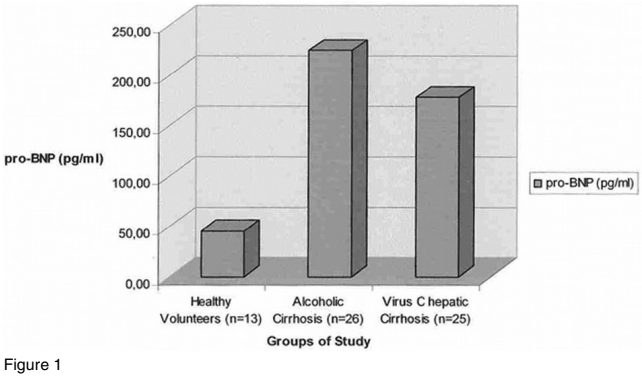

Figure 1

Pro-BNP values were determined in plasma blood samples by an electrochemiluminiscence immunoassay using an ELECSYS equipment (Roche Diagnostics, Barcelona, Spain).
Results: Pro-BNP plasma levels were 5 times much higher in patients with alcoholic hepatic cirrosis than in healthy volunteers, whereas in patients with virus C hepatitis cirrhosis, pro-BNP values were 4 times much higher than in healthy volunteers, such as is noted in figure 1.
Conclusion: The detected enhancement of pro-BNP plasma levels are an indication of advanced hepatic degradation, and would be related to cardiac dysfunction in progressive cirrhosis. It must be taking into account that pro-BNP is an indicator of cirrhosis progression and cardiac dysfunction, but not of hyperdinamic blood circulation.

P-626 MICROARRAY STUDY OF GENE EXPRESSION PROFILE IN STEATOTIC HEPATOCYTES

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Purpose: To evaluate gene expression profile in steatotic hepatocytes obtained from liver tissue removed via surgical resection as a possible model of 'bridge' transplantation of isolated liver cells as a less invasive alternative to whole organ for patients who are awaiting a donor liver.
Methods: Study developed in non-steatotic and steatotic hepatocyte cells kindly provided by Cytonet GmbH (Germany). Cells were obtained from liver tissue removed via surgical resection. Written informed consent for research purposes was obtained from the patient, being the study protocol approved by the local Clinical Research (Ethics) Committee. RNA from non-steatotic and steatotic hepatocyte cells was extracted and purified, just RNA samples with 28S/18S ratios above 1.5 were selected to obtain the cDNA and cRNA. cRNAs were used for hybridization of the genes included in Human Whole Genome CodeLink arrays (Applied Microarrays). Arrays from each cell type were done in triplicate, loading 2 μg of cRNA for each array. Arrays were read with a laser scanner and quantified and normalized with CodeLink Software 4.2 (Applied Microarrays).
Results: The expression of 84 genes increased in steatotic hepatocytes when compared to non-steatotic hepatocytes, being identified: Interleukin-6; ANKH which controls pyrophosphate levels; TPCN2, major voltage-gated Ca^{2+} channel across plasma membrane; CHUK, part of the IKK complex in NF-kappa-B activation; ALDH2, enzyme of the major oxidative pathway of alcohol metabolism; SOCS3, a cytokine-inducible negative regulator of cytokine signaling. ($>$20-fold, $p<0.05$). Other over-expressed genes were GADD45G, which mediates p38/JNK pathway activation via MTK1/MEKK4 kinase; ADH6, an alcohol dehydrogenase expressed in liver; NOSIP, which negatively regulates nitric oxide production.
Conclusion: Gene expression profiling data in steatotic hepatocytes identifies genes related to inflammation pathways, as well as alcohol metabolism. The entire microarray data set is important as it gives clues to the molecular mechanisms involved in disease processes.

P-627 PLASMA INDOLEAMINE 2,3-DIOXYGENASE ACTIVITY IN RENAL TRANSPLANT RECIPIENTS PREDICTS ACUTE REJECTION

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Indoleamine 2,3-dioxygenase (IDO) catalyses the degradation of tryptophan (Trp) leading to generation of kynurenine (Kyn). Recently, IDO has been described as an immunoregulatory component which plays a role in maternal tolerance against the allogeneic foetus. Based on these observations one would expect that high IDO activities in graft recipients protect the transplanted organ from rejection. We conducted this study to examine whether pre-transplant plasma IDO activity has a predictive value for allogeneic kidney graft rejection.
Patients and method: High Kyn and low Trp values denote increased IDO activity. The concentrations of Trp and Kyn were measured by reverse phase-high performance liquid chromatography (RP-HPLC) in pre-transplant (pre-Tx) plasma of 215 first deceased renal recipients and compared with those of 30 healthy controls.
Results: Plasma Kyn levels were significantly higher in pre-Tx plasma of allograft recipients ($p<0.001$) than in healthy controls. Significantly higher levels were found in patients who developed an acute rejection (AR) (n=63) as compared to those who did not (n=152) ($p<0.001$), indicating an increased IDO activity. Trp concentrations were generally decreased in patients as compared to healthy controls ($p<0.001$) probably due to increased IDO activity. The association of increased Kyn levels with rejection is unexpected because Kyn suppresses the immune response and should protect from rejection. Because this is a statistical study, functional interpretations of findings, however, remain a matter of speculation.
Conclusion: Contrary to expectations, our results demonstrate that patients with high pre-Tx Kyn plasma levels are at risk of AR. Kyn might be a useful measure for evaluating the risk of AR at the time of transplantation.

P-628 EFFECTS OF *TACROLIMUS* ON SYNAPTIC TRANSMISSION BETWEEN PARALLEL FIBRES AND PYRAMIDAL CELLS IN THE DORSAL COCHLEAR NUCLEUS OF THE RAT

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There is a growing body of evidence that *tacrolimus* has different effects on the central nervous system. Besides its protective effect in hearing deficiencies, it is also considered to be able to cause tinnitus. In the present work we tried to specify its effects on a characteristic synapse of the auditory system which may be involved in the pathogenesis of tinnitus. The specific aim of the present study was to investigate the effects of *tacrolimus* on the excitatory synaptic transmission occurring between the parallel fibres and the pyramidal cells in the rat dorsal cochlear nucleus.
200 μm thick slices of the dorsal cochlear nucleus were prepared from 9–14-day-old Wistar rats. In response to the stimulation targeting the superficial layer of the dorsal cochlear nucleus, excitatory postsynaptic currents developing on the cell bodies of the pyramidal neurones were recorded using whole-cell voltage-clamp. Short-term plasticity was investigated using high frequency stimulation (50 Hz). *Tacrolimus* was applied extracellularly, in a concentration of 1 μM.
The short-term synaptic plasticity of the parallel fibre–pyramidal cell synapse was investigated. *Tacrolimus* effectively and reversibly inhibited glutamatergic neurotransmission in this synapse (from -145 ± 26 pA to -55 ± 15 pA; n=7). The inhibitory effect was evoked by increasing the failure number of the synaptic transmission and by changing the coefficient of variation (CV^{-2} changed from 0.029 ± 0.014 to 0.006 ± 0.003; n=7). These data suggest a presynaptic inhibition.
Tacrolimus affected short term synaptic plasticity in the rat dorsal cochlear nucleus, and it was also capable of inhibiting the glutamaterg neurotransmission. These effects suggest that *tacrolimus* may have a neuroprotective effect in this structure, and it may not be particularly potent in causing hyperexcitability of the pyramidal cells of the cochlear nucleus.
This work was supported by OTKA 72812.

P-629 EFFECT OF ENDOGENOUS AND VECTOR DELIVERED A20 ON ENDOTHELIAL CELL ACTIVATION AND APOPTOSIS

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Endothelial cell (EC) damage is implicated in the pathogenesis of chronic rejection (CR). EC respond to insults and stimuli by both activation and apoptosis, two overlapping phenotypes associated with CR. We studied the role of the endogenous A20 in EC responses to tumour necrosis factor alpha (TNF) and to conditions modelling ischaemia reperfusion injury (IRI). We tried to protect EC from activation and apoptotic cell death (ACD) by overexpression of A20 using a lentiviral vector (LV).
A20 was expressed in human umbilical cord endothelial cells (HUVEC) after transduction using LV based on HIV-1, confirmed by Western. EC activation was assessed by chemokine/cytokine array assay. ACD was assessed using caspase 3 activity and Annexin V/PI staining analysed by FACS.
TNF-mediated activation of EC upregulated ICAM-1 expression and increased endogenous A20, as well as upregulating expression of a wide range of chemokines/cytokines, but ACD was not increased above background (Figure 1). LV-mediated A20 overexpression significantly inhibited TNF-induced ICAM-1 and upregulated selected chemokines/cytokines.
IRI failed to upregulate ICAM-1 and endogenous A20, but rendered EC susceptible to ACD in the presence of TNF, possibly because of impaired A20 upregulation. Like TNF alone, IRI also upregulated chemokine/cytokine expres-

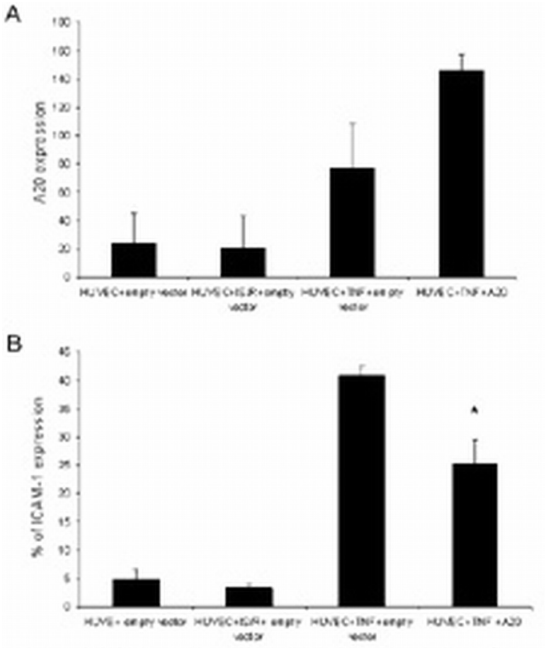

Figure 1 A: A20 expression in HUVEC. B: Effect of transduced A20 on TNFα induced ICAM-1 expression in HUVEC. Data are mean ± SE from three experiments. * significantly different from transduced with empty vector ($p<0.05$)

sion. Overexpression of A20 partially protected EC from ACD and this correlated with inhibition of upregulation of G-CSF, GM-CSF, sICAM-1 and MCP-1. When EC were treated with cycloheximide to prevent protein synthesis, TNF induced EC apoptosis (66%) which was partially reversed by overexpressing A20 (Figure 2).

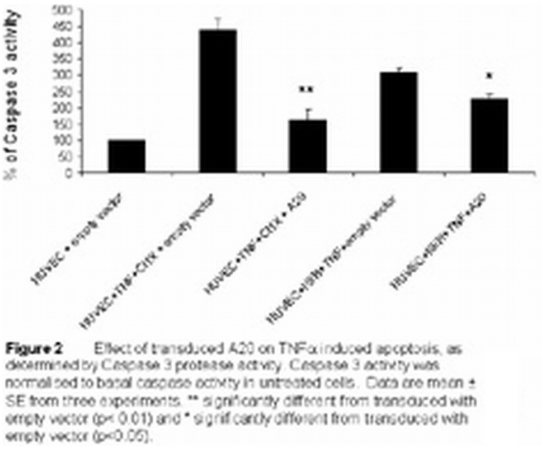

Figure 2 Effect of transduced A20 on TNFα induced apoptosis, as determined by Caspase 3 protease activity. Caspase 3 activity was normalised to basal caspase activity in untreated cells. Data are mean ± SE from three experiments. ** significantly different from transduced with empty vector ($p<0.01$) and * significantly different from transduced with empty vector ($p<0.05$).

Together these findings suggest that endogenous A20 upregulation, which accompanies EC activation, is sufficient to protect EC from ACD under normal conditions. LV mediated-A20 overexpression is required to protect EC from the more damaging IRI and inhibit EC activation, this may have an important role in protection against triggers of CR

P-630 INCREASED EXPRESSION OF TRANSGLUTAMINASE TYPE 2, A PROTEIN CROSS-LINKING ENZYME, IN THE FISHER-TO-LEWIS RAT MODEL OF CHRONIC ALLOGRAFT NEPHROPATHY

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Introduction: Chronic allograft nephropathy (CAN) involves expansion of the extracellular matrix (ECM). Transglutaminase type 2 (TG2), a protein cross-linking enzyme, acts through the formation of ε(γ-glutamyl)-lysine dipeptide bonds resulting in ECM deposition. This study has investigated the activity and the distribution of TG2 and ε(γ-glutamyl)-lysine in the Fisher-to-Lewis rat model of CAN.

Methods: Donor kidneys obtained from either Fisher rats (allograft) or Lewis rats (isograft) were transplanted into Lewis rats. Renal function and systemic blood pressure were monitored over a 12 month period. TG2 activity was measured using the [^{14}C] putrescine incorporation assay. TG2 protein and its cross-linked product ε(γ-glutamyl)-lysine were detected by immunofluoresence (FITC) and quantified by computerised image analysis. Results were expressed as a ratio of the areas of FITC positive stain to nuclear stain (DAPI).
Results: The allografts (n=7) were hypertensive (94±5 vs. 121±6 mmHg, $p<0.05$) and proteinuric (37±17 vs. 303±80 mg/24h, $p<0.05$) with raised serum creatinine (60±5 vs. 194±48 μmol/l, $p<0.05$) than the isografts (n=5). Histology and electron microscopy confirmed CAN. The allograft kidney showed higher TG2 activity (0.41±0.03 vs. 1.09±0.13 nmol/h/mg protein, $p<0.05$), a marked increase in the ratios for both TG2 protein (glomeruli: 2.11±0.17 vs. 64.55±17.61 $p<0.001$; interstitium: 3.19±0.44 vs. 13.72±1.62, $p<0.001$) and ε(γ-glutamyl)-lysine (glomeruli: 1.98±0.37 vs. 21.74±2.71, $p<0.01$; interstitium: 0.42±0.11 vs. 37.96±17.06, $p<0.05$) compared to the isograft.
Conclusions: An increased expression of TG2 and ε(γ-glutamyl)-lysine was observed in b glomerular and interstitial compartments in the allografts. This may be a suitable model to examine the effect of TG2 inhibitors on the progression of CAN.

P-631 AMELIORATION OF TRANSPLANT ASSOCIATED INJURY BY THE NOVEL HEME OXYGENASE-1 INDUCER HEME ARGINATE

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Purpose: Ischaemia reperfusion injury (IRI) is an important cause of delayed graft function which adversely affects renal allograft survival. Endothelial cells are highly susceptible to IRI. Promoting their survival is likely to be beneficial by maintaining organ perfusion. Hemeoxygenase-1 (HO-1) improves outcomes in animal transplantation models. We evaluated the novel HO-1 inducer Hemearginate (HA) in models of IRI and murine renal transplantation
Methods: Murine cardiac endothelial cells (MCECs) were pretreated with HA, and exposed to hypoxia + hypercarbia (HCR) (0.5% O2, 11.5% CO2) for 24h followed by 24h recovery. Viable cells per high-powered field (hpf) were counted. In Vivo IRI was induced by 20min clamping of the left renal pedicle with right nephrectomy in FVB/n mice. Animals received 30mg/kg iv HA or PBS control. Renal function was determined by serum Creatinine (SCr). Acute tubular necrosis (ATN) was determined by quantifying necrotic tubules in the outer medulla. Preliminary studies looked at the effect of donor mouse HA pretreatment in a model of renal transplantation
Results: HCR caused increased MCEC death compared to normoxic cells (9.2±5.9 vs 30.1±3.9 viable cells/hpf, p 0.05). HA protected from HCR compared to untreated cells (22.7±3.5 vs 9.2±5.9 viable/hpf, $p<0.05$). A specific inhibitor of HO-1 (Zinc Protoporphyrin) reversed this protection. In renal IRI, HA therapy offered significant structural (69.6±10.2 vs 36.5±3.5% ATN control vs HA; $p<0.05$) and functional protection (sCr 132±44.4 vs 78±24.3mol/l control vs HA; $p<0.05$). HA therapy tended to preserve the microvasculature (% medulla CD31+ve 8.7±1.3 vs 13.1±2.0 p=0.096). Initial results in HA treated isografts showed encouraging protection of both CD31+ microvasculature and medullary tubular integrity compared to controls.
Conclusion: Our data show that HO-1 upregulation protects renal structure and function post IRI. HO-1 Induction by HA is a novel and feasible intervention for this key component of post-transplant injury.

P-632 DETERMINATION OF DENDRITIC CELLS EXPRESSING INHIBITORY RECEPTORS ILT3 AND ILT4 IN KIDNEY TRANSPLANTED PATIENTS WITH DIFFERENT OUTCOMES AND HEALTHY CONTROLS

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Purpose: The long-term allograft survival has been attributed to the development of operational tolerance due different mechanisms as clonal deletion, anergy and immune regulation by regulatory and suppressor T cells. In vitro experiments have demonstrated that the direct interaction between dendritic and suppressor T cells results in upregulation of the inhibitory receptors ILT3 and ILT4 on dendritic cells, allowing them to get tolerogenic capacities to anergize alloreactive CD4+ T cells. The aim of the current study was to determine the percentage of circulating dendritic cells expressing ILT3 and ILT4 from kidney transplanted patients with different outcomes and healthy controls.
Methods: Using whole blood, we determined, by flow cytometry, the percentage of circulating dendritic cells (Lin-HLA.DR+) and in this population we determine the expression of ILT3 and ILT4 in 10 patients with long-term renal allograft survival (≥10 years, LTS patients), 10 transplanted patients with short

term allograft survival (STS), 9 with chronic rejection (ChrRx) and 10 healthy controls (HC).
Results: LTS patients had a similar percentage of circulating dendritic cell expressing ILT3 as compared with healthy controls, interestingly, it was decreased in ChrRx and STS patients as compared with LTS patients ($p<0.05$ in both). The same tendency was observed in circulating dendritic cells expressing ILT4.
Conclusion: Results show that the percentage of circulating dendritic cells expressing ILT3 and ILT4 was normal in LTS patients and diminished in ChrRx patient, suggesting that rejection may partly be the result of a lack of some regulatory properties. Results suggest that normal percentage of circulating dendritic cells expressing ILT3 and ILT4 in patients with long-term allograft survival are possible indicators of a regulatory process that contributes to get a longer periods of allograft survival and absence of rejection.

P-633 TRANSPLANT VASCULOPATHY: A PROPHYLAXIC ROLE FOR RAPAMYCIN?

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Introduction: Transplant vasculopathy is an important predictor of graft failure. It is caracterized by intimal hyperplasia caused by accumulation of smooth muscle cells and myofibroblasts. Apoptosis of endothelial cells plays a major role by releasing mediators that provoke resistance of fibroblasts to apoptosis and their differenciation into myofibroblasts. Our hypothesis was that rapamycin could block this differenciation by it's inhibitory effect on mTORC2.
Method: Fibroblasts were incubated in medium containing various concentrations of rapamycin. Myofibroblasts were also treated with rapamycin to determine if their phenotype could be reversed. Fibroblasts from *SIN* knock-out mice were analysed. For each manipulation, the protein alpha-smooth muscle actin, a marker of fibroblast differenciation, was dosed by Western blot.
Results: Rapamycin inhibited fibroblast differenciation at a minimal effective concentration of 10*n*M. When rapamycin was administered to myofibroblasts, not only they did not dedifferenciate into fibroblasts, but the differenciation was increased. Fibroblasts from *SIN* knock-out mice maintained the capacity to differenciate into myofibroblasts.
Conclusion: Our results show that rapamycin can inhibit fibroblast differenciation *in vitro*; this effect does not seem to be mediated by mTORC2, but by mTORC1. These observations suggest that rapamycin could potentially prevent transplant vasculopathy, but not treat it.

P-634 CONJOINT IMMUNOSUPPRESSION AND ANTIBIOSIS IMPROVE SURVIVAL OF POLYMICROBIAL ABDOMINAL SEPSIS

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Purpose: Growing numbers of patients under immunosuppression entail an increasing incidence of threatening infections and complications of surgical therapies. The modified response of the attenuated immune system is matter of intense research but is still poorly understood. The aim of this study was to investigate the effects of immunosuppressants on the progression of abdominal sepsis due to anastomotic leakage in an experimental mouse model.
Methods: C57/BL6 mice were treated with different immunosuppressants starting seven days before septic peritonitis was induced by Colon Ascendens Stent Peritonitis (CASP). The survival was monitored and in vitro measurements of cytokines in serum and peritoneal lavage fluid, FACS-analysis of peritoneal macrophages and granulocytes, and bacteria counts of peritoneal lavage and liver parenchyma were performed.
Results: We clearly revealed that simultaneous application of tacrolimus (Tacr), mycophenolate-mofetil (MMF), and methylprednisolone (Mpred) lead to fatal outcome of abdominal sepsis. Combining immunosuppressants with antibiotic therapy (Sultamicillin), however, survival increased significantly to 95%. Furthermore, we could show that the application of MMF and Mpred is both necessary and sufficient to raise survival of abdominal sepsis in the presence of antibiosis.
In contrast to solitary antibiotic therapy, the combination of immunosuppressive *and* antibiotic therapy, lead to decreased bacterial load in peritoneal lavage fluid and liver. Whereas cytokine levels in plasma and peritoneal lavage fluid were not affected by immunosuppressive therapy, significantly increased expression of activation markers and production of reactive oxygen metabolites by peritoneal neutrophils were detected.
Conclusions: Notably, combined immunosuppressive and antibiotic therapy may enhance survival and bacterial clearance during abdominal sepsis by mechanisms that involve improved activation and efficiency of neutrophil granulocytes.

Survival after 18G CASP dependent on immunosuppressive/antibiotic treatment

Treatment		n	Survival
Immunosuppression (d^{-7} – d^{5})	Antibiosis (d^{0} – d^{5})		[%]
Placebo	Placebo	12	33
Placebo	Sultamicillin	30	53
Tacr/MMF/Mpred	Placebo	10	0
Tacr	Sultamicillin	10	30
MMF	Sultamicillin	14	64
Mpred	Sultamicillin	15	60
MMF/Mpred	Sultamicillin	28	82
Tacr/MMF/Mpred	Sultamicillin	20	95

Tacr = Tacrolimus, MMF = Mycofenolate-mofetil, Mpred = Methylprednisolone

P-635 EVALUATION OF CMV SPECIFIC T-CELL RESPONSE IN HEART TRANSPLANT RECIPIENTS

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The restoration of human Cytomegalovirus (CMV) specific T cell response is one of the most desirable achievements in heart transplantation. We investigated in a cross section study the CMV specific T cell response in a cohort of 60 heart transplant recipients. We evaluated the T cell specific response using IFN-g ELISPOT method at 0, 30, 60, 90, 180, 360 days after transplantation. CMV viremia was analyzed using CMV DNAemia method. CMV seropositive recipients (R+) patients were treated using pre-emptive therapy while CMV seronegative recipients (R-) of a CMV seropositive donor (D+) were treated with CMV prophylaxis. Pre-emptive CMV DNAemia threshold for antiviral therapy inception was established at 1000 CMV DNA copies/ml whole blood.
The study shows that in R+ recipients the minimum CMV specific T cell response occurred at day 30 after transplantation. A slow process of immune reconstitution begun at day 90 until day 360 after transplantation, however a substantial high number of patients displayed an inefficient antiviral immune reconstitution at day 180 and 360 after transplantation. None of the R-/D+ patients developed a substantial immune reconstitution during prophylaxis therapy. A small number of R-/D+ patients developed a protective immune reconstitution (150 IFN-g spot forming colonies/200000 PBMCs) after an intermediate CMV DNAemia event (10000 copy number/ml whole blood).
We conclude that: 1) T cell monitoring of CMV specific T cell reconstitution is a valid tool to predict subsequent CMV infection/disease. 2) T cell immune monitoring is a valid tool to determine patients with inefficient CMV specific T cell reconstitution at risk of late CMV disease. 3) In CMV D-/R+ patients CMV antiviral prophylaxis does not promote antiviral immune reconstitution. 4) In CMV D-/R+ patients a modest CMV DNAemia event is sufficient to prime an efficient antiviral T cell response.

P-636 P-GLYCOPROTEIN AS A POTENTIAL NOVEL THERAPEUTIC TARGET IN ALLOTRANSPLANTATION. ROLE ON DENDRITIC CELL MATURATION AND LYMPHOCYTE PROLIFERATION

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Introduction: P-glycoprotein (Pgp, MDR1 gene product) has been defined as a novel role in differentiation switch in DC maturation and resultant alloimmune Th1 responses. Dendritic cells (DCs) participate in innate and adaptive immune responses. The goal of this study was to analyse the effect of specific P-glycoprotein inhibition in DCs maturation induced by LPS or alloreactive T cells.
The effect of ABC transporters on DC maturation was evaluated by using specific inhibitors (MK571 and Probenecid) for MRPs and PSC833 for MDR1. The functional capacity of DCs depending on their maturation status to elicit T cell alloresponse was studied in 6 days MLR (CFSE-labelled).
Methodology: Peripheral blood monocytes were transformed into DCs by IL-4/GM-CSF. Maturation of DCs after LPS or allo-T cells stimulation was evaluated by assessing the expression of CD40, CD83, CD86 and HLADR by flow cytometry, in the presence or absence of PSC833. The functional capacity of DCs depending on their maturation status to elicit T-cell alloresponses was studied in 6 days MLR between DCs and allo-Tcells (CFSE-labelled T cell).

Results: 1) The up-regulation of maturation markers in stimulated cells was strongly abrogated when MDR1 inhibitor was added in alloreactivity and LPS stimulis.

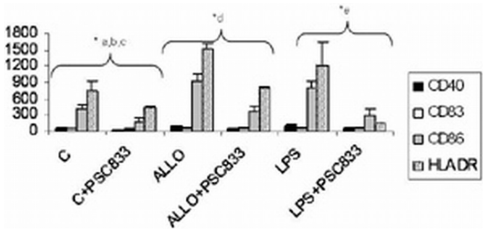

Figure 1. Mean fluorescence intenstity. $p<0.05$ in: *a C vs Allo, *b C vs LPS, *c C vs C + PSC, *d ALO vs ALO + PSC and *e LPS vs LPS + PSC.

3) Functional study showed that mature DCs stimulated with both conditions induced higher T-cell proliferation than non stimulated DCs (C). DCs matured by alloreactive T cells or LPS with Pgp inhibitor showed significantly lower allo T-cell proliferation (approximately 33% and 25% respectively) compared with mature DCs without inhibitors.
Conclusions: Our study suggests that Pgp could be a potential novel therapeutic target to induce immunomodulation.

P-637 A RAPID DECELLULARIZATION TECHNIQUE FOR ORGAN STORAGE AND RECELLULARIZATION

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Purpose: Given that current donor organ transplant procedures highlight the paucity of available tissue, we proposed a rapid decellularization technique for a variety of organs including kidney, intestine and pancreas, which leaves an intact extracellular matrix and can be applied to enhanced recellularization.
Materials/Methods: Porcine organs were obtained following euthanization procedures in accordance with ACUC guidelines. Following isolation and cannulation of the vasculature of the kidney, intestine and pancreas, organs were perfused with dH2O for 24 hrs (wash step). Organs were decellularized with 1% Triton-X/0.1% Ammonium hydroxide in ddH2O solution at 10-60 ml per hour for 4-24 hrs until translucent, followed by an overnight blocking step with 1% FBS to quench endogenous degradation enzymes and a final wash step in dH2O for 24 hrs. Organs were split into 0.5-inch pieces and either embedded in OCT for cryosectioning and histological analysis, processed for DNA content, or lyophilized for scanning electron microscopy (SEM) analysis.
Results: Porcine organs provided a model size and weight for human organs, with a timeframe for collection to complete recellularization of approximately 48 hrs. Perfusion of the decellularization solution resulted in complete lysis and removal of cellular content, as demonstrated histologically by negative haematoxylin staining. Morphological analysis with SEM confirmed the absence for cellular content, revealing an intact stratified matrix structure, and quantification of DNA content resulted in a 99% reduction in comparison to non-decellularized tissue controls. Importantly, perfusion of FITC-labeled dextran beads confirmed the maintenance and patency of the main vessels of the vascular tree.
Conclusions: These studies demonstrate the preparation of rapidly decellularized whole organs which may be critical for future organ tissue engineering for organ transplantation. These findings therefore provide a significant platform for the investigation of re-cellularization protocols for application to organ transplantation and regenerative medicine studies.

P-638 THE ROLE OF ISCHEMIA REPERFUSION INJURY IN ALLOGRAFT VASCULOPATHY

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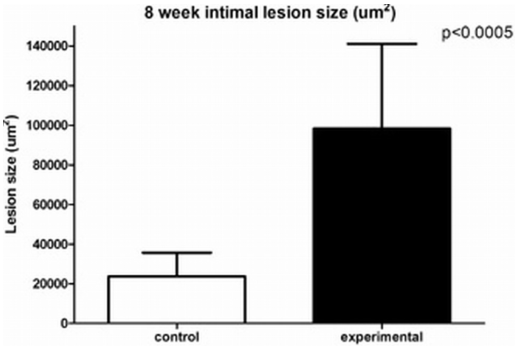
Purpose: Many (50%) cardiac transplants fail within 10 yrs, primarily due to allograft vasculopathy (AV). AV is characterized by vascular remodeling of the transplant coronary arteries resulting in an occlusive neointimal lesion. We have shown that prolonged cold ischemia exacerbates AV in the presence of immunosuppressive therapy in an allogeneic transplant model. We hypothesize that this exacerbation of AV is due to increased innate immunity which enhances adaptive immunity.
Methods/Materials: Aortic grafts from C3H/HeJ mice were transplanted into C57BL/6 mice. Control grafts were subjected to 20 min of cold ischemia versus 60 min for experimental grafts. Cyclosporin A (50mg/kg/d) SQ was administered to ablate acute rejection. Grafts were harvested early (1-5d) and late (5-8wk). Apoptosis in the grafts was measured using TUNEL (Chemicon International). Infiltrating neutrophils and macrophages were identified via immunohistochemistry using the monoclonal antibodies anti-neutrophil (Cederlane) and anti-F4/80 (Abcam) respectively. Lesion size was assessed at 8 wk using digital image analysis.
Results: Lesions in grafts exposed to prolonged ischemia were significantly ($p<0.0005$) larger than the control group.



There was a significant ($p<0.05$) increase influx of neutrophils in the media at 1 d. Macrophages were not present in either group at 1 d but present in both groups at 2 d and 5 d. There was a significant ($p<0.01$) increase in apoptotic cells at later time points.
Conclusions: Using our clinically relevant model, a three-fold increase in the duration of cold ischemia had a significant impact on neutrophil influx and lesion size. Macrophages and apoptotic cells were present in increased numbers over time in our prolonged cold ischemia group. These data are consistent with our hypothesis that prolonged cold ischemia exacerbates innate immune responses which subsequently enhances the adaptive immune response.

P-639 THE RELATIONSHIP BETWEEN RECIPIENT CYTOKINE TNF-α AND IL-10 GENE POLYMORPHISM AND ACUTE BIOLOGICAL REJECTION AFTER LIVER TRANSPLANTATION

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Objective: To determine if the acute biological rejection is related to the presence of these genetic polymorphisms in tumor necrosis factor (TNF)-α, Interleukin (IL)-10 (either alone or in combination) within recipients.
Methods: 2 ml peripheral venous blood anticoagulated with 400ml 5% EDTA from 63 recipients and 60 volunteers was collected for DNA extraction using QIAamp DNA Blood Midi Kit. Cytokine polymorphism were performed using polymerase chain reaction sequence-specific primers (PCR-SSP) technique with commercially available kits (One Lambda Inc., USA).
Results: We found that the age, gender, Child score, surgical procedure, primary liver disease and blood compatibility were not associated with acute biological rejection in liver transplantation. The ratio of high tumor necrosis factor (TNF)-α profiles to low tumor necrosis factor (TNF)-α profiles of recipient in the rejection group was significantly higher than that in the non-rejection group (10/15 vs 5/33,p=0.016). The high recipient tumor necrosis factor (TNF)-α profiles/low IL-10 profiles were mainly seen in the rejection group (9/16) compared to the non-rejection group (5/33, p=0.033).
Conclusions: The results show that the recipient cytokine combination in high tumor necrosis factor (TNF)-α profiles/low IL-10 profiles were related to acute biological rejection.

P-640 TRANSCRIPTIONAL PATHWAYS ACTIVATED IN THE DONOR HEART DURING BRAIN DEATH INDUCTION

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Brain death (*bd*) in the donor should be regarded as a major risk factor affecting graft survival. The aim of the study was to analyze systematically the transcriptional pathways activated in the heart of *bd* rats using the RT^2 PCR transcriptional *pathway* finder (SABioscience, USA).
Methods: Brain death induction in DA rats was performed as described by Pratschke. 30,120 and 360 min after *bd* animals were sacrificed and compared to sham operated animals. The Rat Signal Transduction Pathway Finder Array profiles the expression of 84 key genes representative of 20 different signal transduction pathways.
Mitogenic-, Wnt-, Hedgehog-, TGF-β-, Survival-, PI3 Kinase/AKT-, Jak/Src-,

NFκB-, p53-, Stress-, NFAT-, CREB-, Jak-Stat-, Estrogen-, Androgen-, Calcium and Protein Kinase C-, Phospholipase C-, Insulin-, LDL- and the retinoic Acid pathway were screened.
Data were analysed using the DDCt Method and are expressed as differences in fold up or down regulation. P-value <0.05 (p*)was considered to be significant.
Results: Estrogen-, androgen- and Jak/Srs pathway related genes were only marginal upregulated after 360 min of brain death (1.5 to 2.1 fold upregulation compared with sham).
Insulinpathway was first down- (p*) but after 360 min upregulated (p*).
Wnt-, Crebb-, mitogenic-, stress-, p53 and pospholipase C pathways started upregulation within 30 min (p*) and reached max. of fold different upregulation after 360 min. PI3/AKT patway started with the significant downregulation of PTEN at 30 min, that reached max. of 70 fold downregulation at 360 min (p*).
NF*k*B-, Jak-Stat-, TGFβ-, LDL-, Cacium/PKC, hedghoge-, retinoid-acid-, LDL- and NFAT-pathway related gene reached significant fold upregulation at 360 min of brain death (p*).
Conclusion: BD induces the upregulation of differnt pathways which contribute to the immunological activation of the graft, thus leading to chronic rejection and graft dysfunction after transplantation.

P-641 INCIDENCE OF HEPATITIS B VIRUS REINFECTION AFTER LIVER TRANSPLANTATION

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Objective: To explore the cause of hepatitis B virus reinfection after liver transplantation.
Method: 128 liver transplantation recipients with HBV-related end-stage liver diseases were analyzed retrospectively, include of these chronic fulminant hepatitis B, end-stage liver cirrhosis and liver carcinoma were given lamivudine pre-transplantation to prevent hepatitis B virus reinfection; post-transplantation medicines of Lamivudine was administered in 3 cases; lamivudine and hepatitis Bimmunoglobulin (HBIG) in 125 cases. Adefovir dipivoxil (ADV) was administered to the patients of HBV reinfection. All of patients were followed-up 3∼48 months.
Results: Two of the three cases who taken lamivudine developed reinfection, the little time is 6 months following liver transplantation. There are five of 125 cases taken lamicudine and HBIG (small dosage) developed reinfection. Five HBV reinfection patients were given ADV treatment and HBV-DNA negative conversion was observed in 3 patients after three months of treatment.
Conclusions: Lamivudine and low dose of HBIG post-transplantation offer effective prevention against hepatitis B virus reinfection. ADV is effective for patients with reinfection of HBV by suppressing HBV variant replication. **Key word:** Liver transplantation; Hepatitis B virus (HBV); Reinfection

P-642 GRAFT TREATMENT WITH BILIRUBIN AMELIORATES ISCHEMIA REPERFUSION INJURY

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Introduction: Purpose of the study was to find out the best way of administration of bilirubin by either treating the donor, the recipient or applying bilirubin locally to the graft via a rinse prior to anastomosis by assessing early mitogen activated protein kinase (MAPK) activation, graft function and apoptosis.
Methods: C57Bl/6 mouse hearts were transplanted heterotopically into C57Bl/6 recipients after 12 hours of cold ischemia. Grafts were rinsed with Ringer's lactate solution, unconjugated bilirubin (UCB) or conjugated bilirubin ditaurate dissolved in Ringer's lactate solution at 125μM. Further, UCB (17,5mg/kg) was administered i.p. to the donor and/or the recipient. Hearts were harvested at 15min, 12h and 24h after reperfusion and probed for total and phosphorylated forms of MAPKs as well as BIM and caspase 9. Western blots were quantified using ImageJ. Serum creatin kinase MB (CK-MB) was assessed at 12h after reperfusion. Graft function was monitored by palpation.
Results: In control hearts, 15 minutes after reperfusion a significant increase in MAPK activation and 24h after reperfusion an increase in caspase 9 cleavage and BIM was seen. Triple therapy (donor, graft, recipient) with UCB significantly inhibited MAPK activation. When only the graft was treated with UCB, MAPK activation was equally suppressed, what was not seen when bilirubin ditaurate was used. Treatment of the donor, but not the recipient, less pronounced ($p<0,05$) suppressed MAPK activation. 12h after reperfusion CK-MB levels were lower and functional score was better in the UCB rinsed grafts when compared to the control ($p<0,05$). Further, UCB rinse resulted in a significant decrease of caspase 9 cleavage and proapototic BIM.
Conclusion: Rinsing mouse heart grafts prior to anastomosis with UCB, but not conjugated bilirubin, prevents MAPK activation after reperfusion, improves outcome and may be considered as a simple method to minimize ischemia reperfusion injury.

P-643 ANTI-IL-2α CHAIN RECEPTOR ANTIBODY SIGNIFICANTLY DOWN-REGULATES THE EXPRESSION OF TLR-4 PRIMED BY LPS

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We have previously reported that kidney transplants treated with anti-IL-2-αchain receptor antibody (IL-2RαAb) have a significant down-regulation of TLR-4 expression in transplant biopsies. TLR is one of the candidates for linking innate and adaptive immunity in alloresponse. We test if this modulation was a direct consequence of this monoclonal antibody.
Methods: 5×10^3 PBMC/150μL from healthy donors were incubated in RPMI 1640 medium containing 10% heat-inactivated FCS. Then group I received no further treatment (n=6); II, an incubation with 10μg/mL of LPS (Sigma) for 4 hours (n=8); III, an incubation with LPS equal to II plus 50μg/mL of IL-2RαAb (n=5); IV, a pre-incubation for 48h with 50μg/mL of IL-2RαAb followed by a second one with LPS as in II (n=7). Cells were recovered at each of incubation period. Immunohistochemical staining procedure of slide samples were done by avidin-biotin complex (ABC) methodology using the Ultravision Detection System Anti-mouse, HRP/DAB from LabVision and the TLR4 monoclonal antibody (40μg/mL, Santa Cruz Biotechnology). Statistics by Mann-Whitney.
Results: For groups the means and SD for positive cells were: I, 6±6.1; II, 26.7±10.6; III, 3.8±0.8; IV, 11.1±4.1. When comparing I vs II, p=0.004, II vs III, p=0.012 and II vs IV, p=0.004.
Conclusion: In this in vitro model we document that IL-2RαAb directly inhibits LPS-induced up-regulation of TLR-4 and that this effect is stronger when both factors, LPS and IL-2RαAb are simultaneously present than when following a preconditioning with IL-2RαAb we let LPS action to run alone. This direct IL-2RαAb effect was not reported before and is probably connected to the benefits of its use in human transplants. We plan to test if IL-2RαAb is able to modulate other pathways of TLR-4 activation of relevance in human transplants and of other TLR.

P-644 The CD52 GENE POLYMORPHISM AND ITS POTENTIAL SIGNIFICANCE FOR RESPONSE TO ALEMTUZUMAB IN RENAL TRANSPLANT RECIPIENTS

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CD52 antigen is an important target for alemtuzumab aiming on leukocyte depletion in hematological malignancies and after organ transplantations. Recently two variants of CD52 were reported – rs1071849 (A119G; Asn40Ser) and rs17645 (A123G; Ile41Met). In this study we provide a first data on the distribution of both alleles in population of kidney graft recipients and control group. Also, based on the results of bioinformatic analysis we conclude that in fact this polymorphism may affect the efficiency of formation of GPI anchor, what may indirectly alter the response of anti-CD52 therapeutics.
Genomic DNA of 108 kidney graft recipients as well as controls (200 consecutive newborns) was extracted from the EDTA treated whole blood using QIAamp®DNA Mini Kit (Qiagen). The genotypes of rs1071849 and rs17645 (CD52 A119G and A123G respectively) were determined by PCR-RFLP technique,
Results: Both rs1071849 (A119G) and rs17645 (A123G) CD52 genotype distribution conformed to the expected Hardy-Weinberg equilibrium in renal transplant recipients and in control group. No significant differences in frequencies of rs1071849 and rs17645 genotypes or alleles were detected between group of renal transplant recipients and control group. There was a strong linkage disequlibrium between A119G and A123G loci in renal transplant recipients ($D'=0.971$, $p<0.001$), and in control group ($D'=0.986$, $p<0.001$).
We conclude that the analyzed variants of CD52 (N40S, I41M) do not influence the antigenic properties of the target for alemtuzumab. Since CD52 is one of the most abundant leukocyte antigens, we believe that even reduced number of accessible antigen due to less efficient post-translational modification will not significantly decrease total activity of this monoclonal antibody. Further functional studies of biological effects of alemtuzumab activity are needed to assess the impact of these polymorphisms in clinic.

P-645 EPITHELIAL-MESENCHYMAL TRANSITION (EMT) AND FIBROSIS ARE RAPIDLY INDUCED DURING ACUTE REJECTION (AR) OF HUMAN RENAL ALLOGRAFTS

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AR is a major cause of chronic renal allograft damage characterised by fibrosis, and EMT is a potential pathogenic mechanism. TGFβ1 promotes EMT and the tubular cell specific αVβ6 integrin is involved in local TGFβ1 activation. EMT results from the imbalance between pro- and anti-EMT cytokines.
We measured intragraft levels of mRNA for pro-EMT genes (β6 integrin, TGFβ1, FGF2, CTGF), anti-EMT genes (HGF, BMP7), tubular cell markers (E-cadherin, NKCC2, USAG1), fibroblastic markers (vimentin, FSP1, α-smooth muscle actin), and genes involved in fibrogenesis (fibronectin1, collagen1, TIMP1, PAI1) in 31 allograft biopsies from kidney transplant recipients: 12 with graft dysfunction and biopsy-confirmed AR and 19 with stable allograft function and normal (protocol) allograft biopsy. Total RNA were isolated from the biopsy, reversed transcribed, and mRNA levels measured by real time quantitative PCR assays using gene specific primers and probes. mRNAs levels were normalized by 18S rRNA copies. The median values of 18S normalized copies/ug total RNA are shown in the table.

mRNA	Acute Rejection (n=12)	Normal Biopsy (n=19)	P-Value (Mann Whitney)
Pro-EMT transcripts			
β6 integrin	5198	1357	0.02
TGFβ1	3508	2407	0.23
FGF2	121	178	0.71
CTGF	2647	2769	0.58
Anti-EMT transcripts			
HGF	646	1211	0.70
BMP7	53	387	0.003
Tubular cell markers			
E-cadherin	2111	6435	0.17
NKCC2	10750	40490	0.01
USAG1	2055	12518	0.002
Fibroblastic markers			
Vimentin	247219	146786	0.64
FSP1	19497	16069	0.15
α-SMA	41926	81745	0.17
Fibrogenesis markers			
Fibronectin1	23722	15832	0.34
Collagen1	100199	26943	0.13
TIMP1	1005000	71142	0.001
PAI1	10.7	0.4	0.0003

β6 integrin and PAI1 were significantly higher during AR, suggesting the activation of the TGFβ1 pathway, whereas BMP7 and the tubular cell markers NKCC2 and USAG1 were significantly lower in AR. The TGFβ1 to BMP7 ratio was drastically reduced during AR (median: 75.0 vs 4.3, $P<0.0001$). This imbalance between pro- and anti-EMT transcripts during AR provides an explanation for the triggering of EMT and fibrosis by the allo-immune injury. Moreover, the upregulation of TIMP1 during AR may facilitate extracellular matrix accumulation by impairing matrix turnover.

P-646 REDUCED EXPRESSION OF THE ACTIVATING RECEPTOR NKG2D IN NK CELLS FROM END-STAGE RENAL DISEASE PATIENTS

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To characterize the immune defect of patients with end-stage renal disease (ESRD) on the waiting list, we performed NK cell subset analysis in 66 patients with ESRD treated by hemodialysis (n=59) or peritoneal dialysis (n=7). Compared to healthy blood donors, patients with ESRD showed a profound decrease in NKG2D-positive cells within both the CD8-positive T cell (58% vs. 67%, p=0.03) and NK cell (39% vs. 56%, p=0.002) populations. CD56dim cells, which comprise the majority of NK cells in the periphery, were more affected in this regard than CD56bright cells. Uremic serum could decrease NKG2D expression on NK cells from healthy donors. Among factors which could contribute to the decrease in NKG2D expression in ESRD patients, reactive oxygen species (ROS) play a major role. We found that catalase could reverse the effects of uremic serum on NKG2D expression ($p<0.001$) and that ROS down-regulated NKG2D at the mRNA level and at the NK cell surface. In addition, ESRD patients had both increased soluble MICA (203 pg/ml vs. 110 pg/ml; $p<0.001$) and increased membrane-bound MICA on monocytes (p=0.04). ROS could increase in vitro the expression of the NKG2D ligand MICA on the renal epithelial cell line HK2. Together, these studies suggest for the first time that both low NKG2D expression and upregulation of its ligand MICA is related to ROS production and may participate to immune defects in ESRD patients.

P-647 EFFECT OF ISCHEMIA-REPERFUSION AND ANTI-THYMOCYTE GLOBULIN ON THE PERIOPERATIVE CYTOKINE PROFILE IN CLINICAL RENAL TRANSPLANTATION

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Background: Cytokines are the main mediators of Ischemia reperfusion injury in solid organ transplants. Cytokine levels can be affected by administration of immunosuppressive antibodies such as Anti-Thymocyte Globulin (ATG). In this study we assessed the effect of reperfusion and the first dose ATG on cytokine levels during perioperative period.
Materials and methods: Peripheral blood from 20 adult renal transplant recipients was collected at four time-points; i.e: at induction of anaesthesia, just before reperfusion, 1 hour after reperfusion and 24 hours after reperfusion. 27 different cytokines were measured in those serum samples by Luminex based Bioplex suspension array method. Patients were divided into 3 groups according to the source of the graft: Live Donor (LD) (n=4), Deceased Donor (DD) (n=8) and Donor following Cardiac Death (DCD) graft group (n=8). DCD recipients received an initial dose of 1.25 mg/kg of ATG in intravenous infusion over 4 hours, following induction of anaesthesia.
Results and discussion: In LD and DD groups, there were no major increases in cytokine concentrations at any time point. In DCD group, there were increased levels of cytokines 1 hour after initiation of ATG infusion, before reperfusion of the graft. Pro-inflammatory cytokines such as IL-1, IL-6, IL-8, TNF-α and IFN-γ were elevated (p=0.02, 0.06, 0.05, 0.05 and 0.02 respectively) as compared to their induction sample. Interestingly the anti inflammatory cytokine-IL-10 was also elevated (p=0.02). Raised levels of cytokines were observed without an obvious physiological effect on intra-operative vital parameters.
Conclusion: We conclude that the first dose ATG infusion is associated with significant elevation of both pro and anti inflammatory cytokines without any obvious immediate physiological changes. Reperfusion by itself had no apparent impact on the cytokine profile as shown by the LD and DD groups.

P-648 DETERMINATION OF CYTOTOXIC T LYMPHOCYTE ACTIVITY AGAINST DONOR SPLEEN CELLS AND ESTIMATION OF MICROCHIMERISM FOR TOLERANCE MEASUREMENT

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There is a urgent need for quantification of transplant specific tolerance that cannot be achieved directly in patients. So, aim was to establish mixed lymphocytes culture cytotoxicity assay with donor derrived spleen cells and a very sensitive assay for microchimerism.
The spleen cells and PBMC from different patients were stimulated with Con-A up to 6 days. Spleen cells were labelled with Dio18(3). The MLC were established by culturing different ratios of unstained PBMC (effectors lymphocytes) with irradiated spleens cells. After different time intervals, the cells suspension were harvested and by adding PI to samples, FACS analysis was carried out on. Cytospin preparations of Bw4/Bw6-different donor-recipient combinations were stained with the corresponding antibody.
Maximum stimulation of spleen cells was observed with 2 μg Con-A after 24 h. Whereas, the stimulation of peripheral blood lymphocytes (PBMC) was also with 2 μg Con-A, but after 8 days of activation of PBMC from different patients, generated markedly higher levels of cytotoxicity against targets cells. Maximum reduction of spleen cells (2-3%) in the MLC was observed after 6 days of incubation. The degree of decrease of spleen cells was 95% using PBMCs from healthy persons and from third-party immunosuppressed patient 20%. With PBMC from the recipient no decrease was observed.
In conclusion, the Dio18(3) assay is a quantitative methods for the detection of cell- mediated cytotoxicity and providing a greater insight into the mechanisms of cell-mediated cytolysis by different effector populations. Cytospin preparations provide reproducible results in mircochimerism rates even below 1%.
A clinical study using both methods on liver transplant recipients is on the way with the aim to correlate the findings to the clincal data.

P-649 INJECTION OF DONOR-DERIVED OX62+-SPLENIC DENDRITIC CELLS AND ANTI-CD4 MONOCLONAL ANTIBODY INTO A FISCHER TO LEWIS RAT COMBINATION INDUCES INDEFINITE SKIN GRAFT SURVIVAL VIA THE GENERATION OF DONOR-SPECIFIC CD4+CD25+FOXP3+ T CELLS AND INHIBITS DONOR-SPECIFIC ALLOANTIBODIES PRODUCTION

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Purpose: Previous studies have shown that association of donor-derived dendritic cells (DCs) and non-depleting anti-CD4 monoclonal antibody (MoAb) inhibits alloresponse *in vitro* in rodent models. This study tests the ability of a protocol using donor-derived DCs and anti-CD4 MoAb (1) to prolong skin graft survival (2) to generate donor-specific CD4+CD25+FoxP3+ regulatory T cells (Treg) and (3) to abrogate the production of donor-specific antibodies (DSA).
Material and methods: At first, OX62+-splenic (non-plasmocytoid) DCs were isolated from Fischer rats with magnetic beads (Miltenyi-Biotec) and injected (2.10^6) into Lewis recipients with or without 2mg/rat of a non depleting anti-CD4 MoAb (W3/25) at d-28 (n=4) or d-1 (n=4) before skin grafts. Injection of anti-CD4 MoAb alone was used as control. Secondly, CD4+CD25+FoxP3 T cells were harvested with magnetic beads from "conditioned" Lewis rats and injected (1.10^6) into naive Lewis recipients at day-1 before skin grafts from Fischer (n=4) or third-party (Brown Norway, n=4) donors. DSA were detected in recipients using flow cytometric cross-matches.
Results: Recipients of splenic-donor OX62+DCs and anti-CD4 MoAb at d-28 accepted skin grafts from Fischer rats indefinitely (>100 days), whereas recipients at d-1, as recipients of anti-CD4 MoAb alone, did not. CD4+CD25+FoxP3+ Treg alone, isolated from conditioned Lewis, prolong indefinitely the survival of skin grafts from Fischer to naive Lewis (>100days), but not from a third party. DSA were not detected in all but one recipients of the tolerant groups.
Conclusion: These data show that donor-derived splenic OX62+ DCs+non depleting anti-CD4-MoAb prolong indefinitely skin graft survival when injected 4 weeks before grafting. This protocol induce donor-specific Treg that indefinitely prolong allogenic skin grafts survival. The production of DSA is inhibited

P-650 A NOVEL ENDOGENOUS MURINE ADULT CARDIAC STEM CELL POPULATION AND ITS FLUX AFTER ISCHAEMIC INJURY

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Purpose: It is now well established that cardiac stem cell-like populations exist in adult mammalian hearts, defined by cell surface markers. However the relationship between populations defined by these markers is unknown and few studies have formally surveyed cardiac progenitor populations using multiple markers or relative to stem cell characteristics other than marker expression and multipotency in vitro. We have explored sub-fractions of the murine adult cardiac interstitium for colony forming ability in a colony forming unit fibroblast (CFU-F) assay and for lineage potentiality in vitro, and have also examined the flux of these cells after ischaemic injury.
Methods: Pdgfra-GFP knock in mice were used between 8-12 weeks of age. Sham operated mice were compared with mice which had surgical ligation of the left coronary artery, Flow cytometry in addition to immunohistochemistry was used to quantify changes in interstitial subfractions prior to plating for CFU-F assay.
Results: In sham operated animals only the $Sca1^+/Pecam^-/Pdgfra^{HIGH}$ fraction had CFU-F activity and colony cells were shown to be able to differentiate into cardiomyocytes, endothelial cells, smooth muscle, adipocytes, chondrocytes and osteocytes in vitro. Post infarct, there was an increase (p=0.002) in a novel $Sca1^+/Pecam^-/Pdgfra^{MEDIUM}$ population which had reduced CFU-F activity. Colonies from the $Pdgfra^{MEDIUM}$ population did not have ability however for serial passage in culture, a feature of most colonies from the $Pdgfra^{HIGH}$ cells.
Conclusions: A population of $Pdgfra^{HIGH}$ cardiac interstitial cells has been identified which have a propensity for forming colonies which contain stem-like cells, showing long-term proliferation and the ability to self-renew. The $Pdgfra^{MEDIUM}$ cells may be a derivative of the $Pdgfra^{HIGH}$ cells and appear to contain cells that form progenitor-like although not stem cell colonies. We continue to study these populations and their flux in disease and pro-regenerative models.

P-651 CHARACTERISATION OF EPITHELIAL AND MESENCHYMAL STEM CELLS IN ADULT HUMAN LIVER

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Background and aim: The human liver is a complex organ mainly composed of epithelial and mesenchymal elements. It is currently accepted that adult tissue may maintain their own stem cell pools, which may represent ideal canditates to be used for liver cell therapy. We therefore identified and characterized the intrahepatic epithelial and mesenchymal stem and progenitors cells.
Methods: Liver samples from 20 patients with chronic liver disease and 10 multi-organ donors were dissociated by a three-steps collagenase perfusion method. Single-mononuclear cell suspensions obtained after enzymatic digestion were examined by six-color flow cytometry, analyzing at least 10^6 cells per sample. Moreover, specific culture systems were implemented to confirm the identity and differentiation potential of stem cell lineages.
Results: More than 70% of total intrahepatic stem and progenitors cells are committed towards the epithelial lineage (EpCAM+/CD49f+/CD29+/CD45-), while mesenchymal stem cells, identified by the tipical phenotype CD105+/CD73+/CD90+/CD45- and their adipogenic and ostegenic differentiation potential, represent about 15% of the total hepatic stem cell compartment. Intrahepatic MSC showed several cultural and immunophenotypic peculiarities when compared to their extrahepatic counterparts. The morphology of the epithelial progenitors gradually changed during in vitro culture: they became larger and flatter with several binuclear cells, expressing the P450 cytochromes in 70% of the cells at the fifth passage.
Conclusions: Our data confirmed that adult human liver contains stem cells and progenitors of mesenchymal and epithelial origins. The isolation and expansion of these cells lead to propose them as an attractive cell source for stem cell therapy in human liver diseases.

P-652 $CD4^+CD25^+FOXP3^+$ REGULATORY T-CELLS IN THE PERIPHERY OF STABLE RENAL TRANSPLANT RECIPIENTS RECEIVING DIFFERENT COMBINATIONS OF IMMUNOSUPPRESSIVE DRUGS

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Recent studies indicate that regulatory T-cells (Tregs) play an important role in transplant tolerance. We studied thymus-derived Treg levels ($CD4^+CD25^{high}$ $Foxp3^+$) in 39 stable renal transplant recipients (19 patients with good graft function and 20 patients with chronic allograft nephropathy) by flow cytometry. All patients received induction therapy (basiliximab) and were on triple immunosuppressive regimens with calcineurin inhibitors (cyclosporine n=17 or tacrolimus n=22), mycophenolate mofetil (MMF, n=24) or everolimus (n=15) and steroids (n=39). Blood samples drawn from 20 healthy subjects served as controls. Renal transplant recipients had significantly reduced absolute numbers and percentages of $CD4^+CD25^+Foxp3^+$ Tregs compared to controls. Phenotypic analysis of the T-cell populations and subtypes thereof carried out in parallel, showed that the immunosuppressive drugs administered to protect the allograft from alloimmune reactions diminish specifically the T helper effector and thymic Treg populations. Renal allograft function did not correlate with Treg levels. Statistically significant correlations between $Foxp3^+$ Tregs and tacrolimus levels (r=0.63, $p<0.003$) were detected. Patients receiving MMF had higher $Foxp3^+$ Tregs (5.7 ± 5.2) compared to patients on everolimus (2.2 ± 1.2, p=0.01) who were also receiving lower doses of calcineurin inhibitors. Overall, immunosuppression lowers $Foxp3^+$Treg levels significantly in the periphery in renal transplant recipients. In addition, different immunosuppressive regimens have different impact on $Foxp3^+$ Tregs, a fact that may influence long-term allograft survival.

P-653 PLASMA FROM KIDNEY TRANSPLANT RECIPIENTS HAS A LESSER INHIBITORY EFFECT ON T CELL ACTIVATION THAN PLASMA FROM HEALTHY CONTROLS

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Reduction of lymphocyte proliferation by human plasma has been previously

reported. Several causes including alpha globulin, lipoproteins have been proposed. Reduced activation of lymphocytes of patients on immunosuppressive drugs is well documented. We have investigated the properties of plasma from transplant recipients and compared with plasma for healthy controls.
Methods: Peripheral blood mononuclear cells (PBMC) were separated from the blood samples of healthy controls and kidney transplant patients on cyclosporine, rapamune, and tacrolimus based regimens by density gradient centrifugation, cells were counted and incubated overnight with and without phytohemagglutinin (PHA). The luciferin-luciferase enzyme reaction which induces bioluminescence and the Turner Biosystem luminometer were used to measure intracellular ATP levels in relative light units (RLU) and converted to ng/ml using an ATP standard curve. Chi-square test using Instat 3 program (Graphpad^R)was used to compare results.
Results: PHA stimulation of PBMC from healthy individuals produced a 47% increase ATP production. The ATP increase is reduced to 14% when normal plasma was added ($p<0.05$). However when normal plasma was replaced by patient plasma, the ATP increase improved to 31%. Similar difference between patient and control plasma was recorded when using PBMC from transplant patients.

Table 1. ATP production (ng/ml) in PBMC according to stimulation

	Unstimulated PBMC	PBMC + PHA	PBMC + PHA + control plasma	PBMC + PHA + patient plasma
Control	2988±216	4235±236	3313±200	3716±196
Cyclosporine	2406±175	2649±178	1915±150	2510±208
Sirolimus	2250±242	2505±255	1834±151	2336±230
Tacrolimus	2325±470	2691±501	1252±64	2149±101

Conclusion: It appears that plasma isolated from patients on immunosuppressant drugs and more so plasma from healthy controls contains factors which suppress the response of lymphocytes to PHA stimulation.

P-654 ROLE OF IMMUNOSUPPRESSION IN DEVELOPMENT OF COLON ADENOCARCINOMA. A COMPARATIVE IMMUNOHISTOCHEMICAL STUDY OF RENAL TRANSPLANT PATIENTS AND GENERAL POPULATION

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Introduction: Immunosuppressive treatment (IST) causes an increased frequency and aggressiveness of colon adenocarcinoma (ADK) in renal transplant patients (RTP) compared with control patients without IST (CP). Our aim is analyze the effect of the IST on different pro-oncogenic signals in colon ADK
Material and methods: Epidemiological and clinical data of RTP and CP with colon ADK were recorded (Jan/1992-Dec/2007). Tumour expression of PTEN, PI3KCA, AKT, mTOR, phospho-mTOR (Ser 2448), p70S6K, phospho-p70S6K (Thr389), VEGF and TGF- were evaluated by conventional immunohistochemistry. Antibodies expression as 0%(-), 1-10%(+), 11-50%(++) and >50%(+++) and staining intensity as absent (0), weak (1), moderate (2), and strong (3). Proportion comparison by Chi- square and means comparison by independent-samples T-test were statistical analysis
Results: 23 colon ADK in RTP (12 with available tissue sections).13 colon ADK in CP. RTP were younger (61,54;63,76 years). Males (61,9%;69,2%). Colon and sigma sites (RTP: 42,9%/28,6%; CP: 46,2%/38,5%). DUKE states more aggressive (C2 23,8% vs B2 30,8%), same relapse index, and higher metastasis rate (19%; 15,4%) in RTP. Non statistical significance (SS) proportion relation found between RTP and CP. Means comparison analysis showed higher SS expression of phospho mTOR (*p=0.049*) and p70S6K(*p=0.033*) in CP, and higher non-SS expression of PTEN and mTOR and intensity of PTEN, PI3KCA, phospho-mTOR and VEGF in RTP. Sample size makes other antibodies could be expressed in relation to immunosuppression or IST
Conclusions: Colon ADK has more aggressive behaviour in RTP with significant differences in important markers of tumour biology that could be useful in identification of new therapeutic targets. Increased expression of mTOR and intensity of phospho mTOR and VEGF in RTP support the strategy of introduction of mTOR inhibitors in RTP affected by or at risk of colon ADK

P-655 A NOVEL ASSAY TO QUANTIFY DIRECT PATHWAY ALLOREACTIVE T-CELLS LONGITUDINALLY AFTER LIVER TRANSPLANTATION

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Current assays for quantification of allo-reactive T-cells are relatively insensitive. Therefore, contributions of the direct and indirect pathways of allorecognition in liver graft acceptance are poorly defined. We present a novel assay using CD40-activated B-cells as stimulators, and established the dynamics of post-transplant T-cells with direct pathway donor-specificity after liver transplantation (LTx).
Allo-reactive T-cell frequencies were determined in 8 LTx-patients before, and 1 week, 1 month, 3 months and 1 year after LTx. B-cells were expanded from donor splenocytes or patient PBMC using CD40L-transfected fibroblasts, IL-4 and Cyclosporin A. CFSE-labelled recipient PBMC were stimulated with irradiated donor-derived, 3rd party or autologous CD40-B-cells, and frequencies of responding T-cells were calculated from CFSE-dilution patterns. Numbers of HLA-mismatches between donors and 3rd parties were similar, and donors and 3rd parties differed in 1.7 major HLA-A, 1.0 HLA-B and 0.8 HLA-DR alleles. Donor-specific responses (RR) were calculated as the ratio of anti-donor to anti-3rd party reactivity.
CD40-B-cell stimulation compared to stimulation with splenocytes resulted in 3-fold higher alloreactive T-cell frequencies ($p\leq0.01$). Median allogeneic CD4+ and CD8+ precursor frequencies were 3.6% and 8.0%, respectively, while only 0.6% and 1.6% reacted upon stimulation with autologous CD40-B-cells. Donor-specific CD4+ and CD8+ responses significantly increased 1 week after LTX compared to pre-LTX (RR CD4+ 1.3±0.5 versus 1.0±0.4; p= 0.016, and RR CD8+ 1.4±0.5 versus 0.8±0.3; p= 0.031), followed by a decrease to pre-LTx values at later time-points up to 1 year.
Conclusions: Stimulation with CD40-B-cells results in detection of high frequencies of allo-reactive T-cells. Donor-specific CD4+ and CD8+ T-cell responses peak 1 week after LTx followed by a decrease to pre-LTx values thereafter. No donor-specific hyporesponsiveness was observed, suggesting that T-cells with direct allospecificity may contribute to rejections late after transplantation.

Kidney II

P-656 HYPOTHERMIC MACHINE PERFUSION OF DCD KIDNEYS: THE ROLE OF OXYGEN IN RECOVERY FROM IR-INJURY

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Purpose: Deceased after cardiac death donors (DCD) represent a valuable source of organs to face the growing waiting lists. However they present additional ischemia reperfusion lesions due to a period of warm ischemia prior to cold preservation, hence hypothermic preservation using machine perfusion (MP) is recommended. This technique demonstrated improved early graft function and long term beneficial effects which however proved not as significant as expected. We therefore aim to optimize hypothermic machine perfusion, adding oxygen to the preservation solution to overcome (warm-)ischemia reperfusion injury.
Methods: Kidney function after warm ischemia (30 minutes), cold preservation (4°C, 20 hours) and transplantation was studied in an autotransplant model using Large White pigs (±40 kg). Cold preservation was performed by conventional non-oxygenated MP (MP-group, n=3) or oxygenated MP (MPO_2-group, n=3).
Results: We determined that MPO_2 grafts displayed a lower serum creatinine peak (714.7±249.1 versus 1440.7±73.6 μmol/L in MP at 5days, $p<0.05$) and a faster return to normal levels (151.7±11.5 versus 284.0±14.7 μmol/L at day 11, $p<0.01$).
Preliminary RT-PCR analysis of kidney biopsies performed 10 min after unclamping revealed upregulation of EPO, a major growth factor (18.8±5.6 vs. 1.07±0.2 folds to control in MP) as well as decreases in inflammation markers MCP-1 (3.9±0.4 vs. 8.5±3.5 folds in MP) and IL-6 (2.9±0.2 vs. 4.4±1.6 folds in MP).
Conclusion: Our preliminary data suggests that this new machine perfusion system is efficent to preserve DCD kidneys, indeed oxygenation of the graft

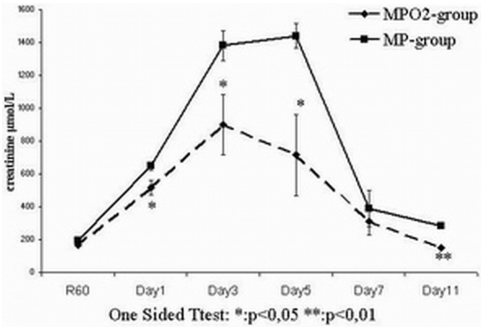

Figure 1. Serum creatinine.

during machine perfusion greatly enhances the capacity of the graft to withstand preservation stress and enables the organ to recover its functional capabilities in a shorter delay. We also observed an increase of function, as stabilized serum creatinine for MPO_2-grafts is significantly lower than for grafts preserved with MP alone.

P-657 THE OUTCOMES OF ABO-INCOMPATIBLE LIVING UNRELATED KIDNEY TRANSPLANTATION

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Background: ABO-incompatible living unrelated kidney transplantation is a high- risk immunological procedure. Few reports regarding the outcomes of ABO-incompatible living unrelated donor kidney transplantation have been documented.
Patients and methods: We analyzed 12 kidney transplants using ABO incompatible living unrelated donors between August 1999 and December 2007, focusing on immunosuppressive protocol, complications and graft survival.
Immunosuppressive protocol: To remove anti-A/B antibodies, patients underwent four to ten sessions of double-filtration plasmapheresis (DFPP) and/or plasma exchange (PE) prior to kidney transplantation until anti-A/B titers were more than 1:16. Splenectomy was performed at the time of kidney transplantation in 5 patients. Four patients without splenectomy received two doses of rituximab 150 mg/m^2 2 weeks prior to and on the day of transplantation. Three patients with high anti-A/B antibodies titer (more than 1:512) received both splenectomy and administration of rituximab.
Results: We recorded 100% patient and graft survival rates in our recipients. However, one patient experienced antibody mediated rejection and intractable acute cellular rejection, one had antibody mediated rejection and one had acute cellular rejection. By the intensive immunosuppressive treatment their grafts survived. Three episodes of late-onset neutropenia grade 3 were detected after administration of rituximab.
After administration of granulocyte colony stimulating factor, neutropenia improved. There were no severe complications among the all recipients.

Table 1. Outcomes and complications

Patient	Acute cellular rejection	Antibody-mediated rejection	Graft survival	Follow-up (months)	Current S-Cr level (mg/dl)	CMV antigenemia	Other complications
1	+	–	Yes	112	2.59	+	–
2	–	–	Yes	58	1.22	+	–
3	–	–	Yes	55	1.12	+	–
4	–	–	Yes	54	1.10	–	–
5	–	–	Yes	33	0.75	–	–
6	–	+	Yes	32	0.96	–	–
7	–	–	Yes	31	0.89	–	LON
8	–	–	Yes	24	1.15	+	–
9	–	–	Yes	23	0.84	–	LON
10	–	–	Yes	23	1.49	–	–
11	+	+	Yes	12	1.55	–	LON
12	–	–	Yes	6	1.48	–	Subcutaneous abcess

S-Cr, serum creatinine; CMV, cytomegalovirus; LON, late onset neutropenia.

Conclusions: Severe rejection may occur due to ABO-incompatibility and poor histo-compatibility. Therefore, appropriate desensitization and immunosuppression are needed for a successful outcome. Our results have become significantly improved due to the advance of immunosuppression and desensitization therapies.

P-658 CA19.9 IS A DIAGNOSTIC MARKER FOR HEPATIC CYST INFECTION IN ADPKD KIDNEY TRANSPLANT PATIENTS

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Purpose: Hepatic cyst infection is a serious complication in autosomal dominant polycystic kidney disease (ADPKD) patients. Its diagnosis is difficult. We hypothesized that Carbohydrate antigen 19.9 (CA19.9), secreted by the biliary epithelium lining the cysts, is overproduced in case of cyst infection.
Methods: CA19.9 was measured in the serum of four kidney transplant ADPKD patients who presented with hepatic cyst infection, and in the cystic fluid of 3 of them. CA19.9 was also measured in the serum of 19 consecutive ADPKD and 22 non-ADPKD renal transplant recipients. CA19.9 immunostaining was done in 5 polycystic livers of ADPKD patients and compared with control normal livers.
Results: Four ADPKD patients with hepatic cyst infection had markedly elevated serum CA19.9 levels (963, 2975, 601 and 7960 U/ml respectively; N < 35 U/ml). Three patients required cystic fluid drainage. CA19.9 level was extremely elevated in the cystic fluid. A striking decrease in serum CA19.9 level was observed upon clinical improvement in all patients. Serum CA19.9 from 19 consecutive asymptomatic ADPKD patients with liver cysts was significantly higher than in controls (median: 29.55 vs. 10.3 U/ml, $p < 0.001$). Bilirubin level was normal in all patients of both groups. Immunostaining for CA19.9 revealed strong staining in biliary tree epithelia and cysts of human polycystic livers, significantly more intense than in normal livers.
Conclusions: CA19.9 is synthesized by the biliary cystic epithelium and can be elevated in ADPKD patients with liver cysts. A marked increase in serum CA19.9 level is observed with liver cyst infection. Thus, serum level of CA19.9 can be a diagnostic tool for hepatic cyst infection, contributing to early diagnosis and appropriate management. Measurement of baseline serum CA19.9 level in ADPKD patients could serve as a reference value.

P-659 TACROLIMUS ONCE-DAILY PROLONGED RELEASE (ADVAGRAF®) IN KIDNEY, LIVER AND HEART RECIPIENTS: 4-YEAR RESULTS

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Purpose: To assess long-term efficacy and safety of Advagraf® in kidney, liver and heart transplant recipients.
Methods: Adult transplant patients completing European Advagraf Phase II *de novo* (kidney and liver) or conversion studies (kidney and heart; Prograf twice daily to Advagraf) were entered into a follow-up open study. Patients remained on their original immunosuppressive regimen unless medical needs necessitated otherwise. Biopsy was performed if rejection was suspected. Primary endpoints were patient and graft survival. Secondary endpoints included incidence of BPAR episodes and incidence of adverse events (AEs).
Results: 179/240 (74.6%) patients completed the 4-year follow up: 31/47 *de novo* liver, 33/47 *de novo* kidney, 55/67 kidney conversion and 60/79 heart conversion. Mean daily tacrolimus dose and mean blood trough level (C_{min}) decreased over time (Table 1). Mean total daily doses at 46–48 months were 4.0, 5.4, 5.3, 4.5 mg/day. At 4 years 81%, 6%, 46% and 7% of patients were on Advagraf monotherapy.
13/240 (5.4%) patients died during the 4-year follow-up: 4 *de novo* liver, 4 kidney conversion and 5 heart conversion patients. 48/240 (20.0%) patients

Table 1. Advagraf dose and C_{min}

Months of follow up	Liver *de novo*		Kidney *de novo*		Kidney conversion		Heart conversion	
	mg/kg	ng/mL	mg/kg	ng/mL	mg/kg	ng/mL	mg/kg	ng/mL
10–12	0.09	8.7	0.10	8.9	0.07	6.7	0.07	8.7
22–24	0.07	7.7	0.09	7.8	0.07	6.5	0.07	8.1
34–36	0.06	6.6	0.08	7.7	0.07	6.4	0.06	7.7
46–48	0.05	6.5	0.08	7.2	0.07	6.1	0.06	8.1

Table 2. Outcomes after a further 4 years' follow-up following initial Phase II study

	Liver *de novo* (n=47)	Kidney *de novo* (n=47)	Kidney conversion (n=67)	Heart conversion (n=79)
Kaplan-Meier patient survival (%)	90.9	100	93.6	92.5
Kaplan-Meier graft survival (%)	90.9	100	92.2	92.5
BPAR	3 (6.4%)	5 (10.6%)	0	9 (11.4%)
Corticosteroid-resistant episodes	0	1	0	1
Mean serum creatinine (µmol/L)*	96.0	145.1	142.5	117.8
Mean creatinine clearance (mL/min)*	94.3	63.7	70.9	80.6

*Completers only.

were withdrawn – mostly due to AEs (5.8%) or withdrawal of consent (3.8%). Table 2 presents efficacy and renal function at 4 years. Most rejections were mild/moderate except in 1 *de novo* liver patient (severe) and 2 heart conversion patients (both severe). Most commonly reported AEs (all groups) were diabetes mellitus (insulin and non-insulin dependent), hyperglycaemia, headache, tremor, renal insufficiency and hypertension. Reported serious AEs were low. AEs were consistent with the known safety profile of tacrolimus.
Conclusions: Patient and graft survival estimates exceeded 90% at 4 years' follow-up in liver, kidney and heart transplant recipients on a simplified tacrolimus once-daily regimen (Advagraf). Rejection was infrequent and renal function well maintained.

P-660 LONG TERM OUTCOME OF THE EARLY STEROID WITHDRAWAL AND SUBSEQUENT STEROID FREE MAINTENANCE THERAPY IN THE KIDNEY TRANSPLANTATION

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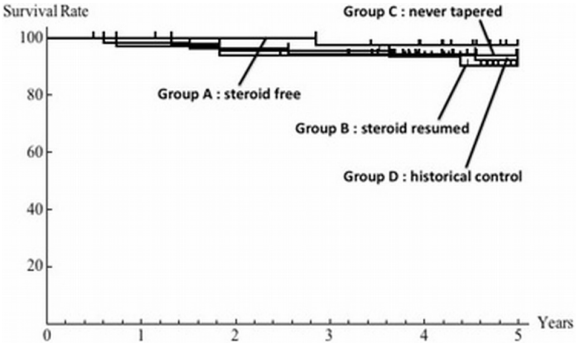
Purpose: In 2002 we started the early steroid withdrawal regimen in kidney transplantation. In this prospective study we report the long term outcome of the subsequent steroid free maintenance therapy.
Method/Materials: We performed 116 live kidney transplantations between 2002.5 and 2004.12. CNI, MMF and MP with basiliximab as an induction were used. MP was tapered off on 14 POD if possible. This observation group separated into steroid freed group (Group A), steroid resumed group (Group B) and never-tapered group (Group C) because of early rejection or steroid demanding diseases like SLE. On the other arm, 52 live renal grafts with CNI, MMF and MP between 2000.1 and 2002.4 were followed as a historical control (Group D). Steroid free ratio, graft survival rate and serum creatinine values were investigated.
Result: In the observation group, 83 followed the regimen and the remaining 33 comprised Group C. Five years later, out of 83 cases, 35 (42.2% Group A) kept steroid free, 37 (44.6% Group B) resumed steroid and 11 (13.3%) lost grafts or died. Five years graft survival rates of Group A, B, C and D were 97.2%, 90.4%, 93.9% and 92.3%, respectively without any significant difference between them.



Mean creatinine values of Group A, B, C and D for five years were 1.30±0.11mg/dl, 1.71±0.16mg/dl, 1.69±0.21mg/dl and 1.41±0.15mg/dl, respectively with significant differences between any two of them
Conclusion: Steroid free ratio at five years was 42.2% with graft survival rate comparable to steroid continual groups and excellent graft function. It shows that substantial part of renal transplant recipients could go steroid free if they pass uneventfully right after operation in the era of basiliximab and MMF.

P-661 SERUM NGAL IS SUPERIOR TO URINE NGAL AS A PREDICTOR OF DGF IN DECEASED DONOR KIDNEY TRANSPLANTATIONS

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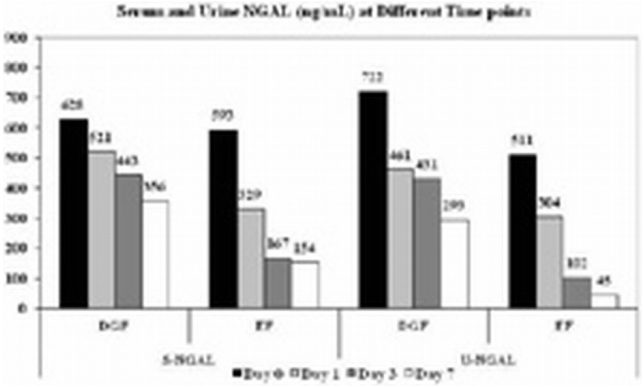
Expression of neutrophil gelatinase-associated lipocalin (NGAL) is proposed to indicate kidney tubular injury. It can be detected in serum and urine. We tested whether serum and urine NGAL measured early after kidney transplantation could be used for distinguishing delayed graft function (DGF) from early function (EF).
We recruited 100 dialysis dependent adult deceased donor kidney recipients. Serum and urine samples were collected immediately before transplantation (day 0) and on days 1, 3 and 7 after transplantation. The samples were analyzed for NGAL using a commercial ELISA kit. Serum and urine NGAL concentrations are expressed as ng/mL.
On the day 0, the mean serum NGAL was 605ng/mL (range 309-877) and the mean urine NGAL was 571ng/mL (range 14-2392). DGF was seen in 34% of the transplantations. Mean cold ischemia time was longer in the DGF group compared to the EF group (22.7 vs 21.1 hours, p=0.04) but no significant differences in age, gender, underlying kidney disease or mode of dialysis were noted. After transplantation, both serum and urine mean NGAL levels decreased from day 0 levels, however, the decrease was more pronounced in the EF group.



The predictive power of serum and urine day 1 NGAL was studied in a ROC analysis. Serum NGAL produced an AUC of 0.81 (CI 0.26-0.90) and urine NGAL an AUC of 0.64 (CI 0.51-0.77). At a cut-off point of 383ng/mL serum NGAL predicted DGF with a sensitivity of 0.85 and specificity of 0.70, whereas, at the cut-off point of 259ng/mL, urine NGAL had a sensitivity of 0.75 and specificity of 0.56.
In conclusion, serum NGAL outranged urine NGAL in early prediction of delayed graft function after kidney transplantation.

P-662 A PROSPECTIVE STUDY FOR PREVENTION OF POST TRANSPLANTATION BONE LOSS IN RENAL TRANSPLANT RECIPIENTS

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Purpose: We aimed to investigate treatment with alendronate plus alphacalcidol for the prevention of bone loss post-renal transplantation.
Methods/Materials: Twenty adult renal transplant recipients were enrolled into the study. Patients were randomized into 2 groups: group I (9patients, 7males, mean age 36±8years) received oral alendronate 70mg/week plus alphacalcidol (0.25μg every other day) and group II (11patients, 8males, mean age 38±14years) was considered a control group. iPTH, calcium, phosphate, $TmPO_4$/GFR, 25(OH)VitD and $1,25(OH)_2$VitD were measured before and 12 months post-transplantation. Sex hormones were also measured. Bone mineral density (BMD) was measured by DEXA at lumber spine (LS) and femoral neck (FN) at baseline and at 12 and 24 months.
Results: Mean BMD at baseline was below normal (T-score -1.11 at LS and -1.79 at FN). At 12 months, BMD decreased at LS by 4.42% and 2.76% in groups I and II respectively (p=NS). At 24 months, BMD was increased in group I by 2.18% from baseline (p=NS), but decreased by 5.61% in control group ($p<0.05$). At FN, BMD decreased in group I by 1.45% (p=NS) and was increased in group II by 3.74% (p=NS) at 12 months, and was increased in both groups by 6.32% and 11.57% (p=0.119 and $p<0.05$ respectively) at 24 months. iPTH levels decreased significantly in both groups (232±169 vs 70±63, $p<0.05$ and 167±14 vs 92±51, $p<0.05$ respectively). Phosphate levels and $TmPO_4$/GFR were lower in group I (3.1±0.6 vs 3.6±0.5, p=0.069 and 2.3±0.6 vs 3.2±0.4, $p<0.05$ respectively). In the whole population, LS BMD at 24 months correlated with age (r=0.534, p=0.04), weight (r=0.900, $p<0.001$), $1,25(OH)_2$VitD (r=0.755, p=0.005) and testosterone (r=0.758, p=0.011) and FN BMD with 25(OH)VitD (r=0.745, p=0.008).
Conclusion: Our study indicates that treatment with alendronate plus alphacalcidol prevents bone loss at LS that occurs after renal transplantation.

P-663 OCCLUSION OF ACCESSORY VESSELS IN MULTIPLE RENAL ARTERY ALLOGRAFTS MAY PRESENT AS GRAFT DYSFUNCTION

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Introduction: As back-bench arterial reconstruction techniques have evolved, the use of multiple renal artery allografts with complex vascular anatomy has increased in recent years. Occlusion of accessory vessels in such grafts may lead to graft dysfunction which may be difficult to distinguish clinically from an acute rejection episode. In this pilot study, we sought to establish the prevalence of graft dysfunction attributable to late occlusion of accessory vessels.
Methods: We identified all recipients of renal allografts with complex arterial anatomy transplanted between Jan 2006 and Jan 2008. Data on number of vessels, vascular damage and reconstruction technique was obtained from operative records. Graft function, peri-operative hypotension episodes, use of antiplatelet agents, proteinuria and history of procoagulant tendency or thrombotic events was also recorded. To detect vascular occlusion, recipients with graft dysfunction were imaged by DMSA SPECT scan to delineate perfusion defects. Patients with a positive DMSA scan were further imaged by angiography.
Results: 92 patients were identified with complex vascular anatomy. To date, 16 patients have undergone screening by DMSA scan for investigation of declining graft function. 8/16 grafts (50%) show areas of hypoperfusion or discrete cortical defects on DMSA scanning. 4/16 (25%) have clearly defined inflection points on their log creatinine slopes which likely correlate with acute occlusion of an accessory vessel.
Conclusion: Patients receiving allografts with complex vascular anatomy are at increased risk of late thrombotic events. Loss of accessory vessels may cause acute graft dysfunction and this should be considered in the differential diagnosis in any such patient with otherwise unexplained deterioration in graft function.

P-664 AN INCREMENTAL INCREASE IN CHRONIC ALLOGRAFT DAMAGE DETECTED ON PROTOCOL BIOPSIES DURING THE FIRST YEAR POST-TRANSPLANTATION

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Introduction: Chronic allograft nephropathy (CAN) remains the leading cause of late renal allograft failure. We conducted a 12 month prospective study to investigate the accumulation of graft damage in newly transplanted patients.
Method: All patients transplanted consecutively from September 2006 underwent protocol biopsies at 0 (post-perfusion), 2 and 12 months. Immunosuppression comprised Tacrolimus, Mycophenolate mofetil with early steroid withdrawal for the majority. Specimens were anonymised and assigned an index of chronic damage (ICD) by a single histopathologist. ICD is a morphometric assessment of interstitial fibrosis (IF) and tubular atrophy (TA) expressed as a percentage of cortical cross-sectional area. The trends in ICD over the 12 month period were noted for each recipient. Additional data was also compiled; biochemistry, donor age, cold/warm ischaemic times.
Results: A total 168 biopsy specimens from 62 patients were analysed between Sept 2006 and Dec 2008. 44 patients (132 specimens) had biopsies at 0, 2 and 12 months respectively. 41% of graft were from non-heart beating deceased donors (NHBD). The mean ICD for live donor grafts were 4% (T0), 6.4% (2 mths) and 14.8% (12mths). The mean ICD for heart-beating deceased donor grafts were 5.2%, 8% and 18.8% respectively. The mean ICD for NHBD grafts was 7.1%, 11% and 21% respectively. The increase in ICD during the first year was statistically significant.
Conclusions: Chronic graft damage develops as early as 2 months post-transplantation and is progressive. We saw a threefold rise in ICD during the first year alone. Protocol biopsies facilitate early detection of such graft damage. Measures aimed at preventing CAN must be targeted in the early period.

P-665 BASILIXIMAB INDUCTION NOT ONLY REDUCES REJECTION RATES IN THE FIRST YEAR POST RENAL TRANSPLANTATION BUT ALSO REDUCES THE DECLINE IN eGFR OVER TWO YEARS: A SINGLE CENTRE RETROSPECTIVE ANALYSIS OF BIOPSY RESULTS AND RENAL FUNCTION

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Aims: To assess the impact on the rates of biopsy proven acute rejection (BPAR) between patients transplanted in three different immunosupressive eras: TAP (Tacrolimus, Azathioprine and Prednisolone), TMP (Tacrolimus, Cellcept and Prednisolone) and TMPS (Basiliximab induction, Tacrolimus, Cellcept and Prednisolone).
Methods: 456 patients received kidneys from heartbeating or live donor sources in our centre between 01/01/1998 and 01/08/2007. Patients were labelled as belonging to the TAP, TMP or TMPS era using pharmacy protocol dates.

Frequency Distribution of Donor Sources

ERA	Donor Source	n	ERA	Donor Source	n
TAP	HBD	10	TMPS	HBD	62
TAP	LRD	42	TMPS	LRD	61
TAP	LunRD	6	TMPS	LunRD	28
TMP	HBD	77			
TMP	LRD	56			
TMP	LunRD	16			

TAP: Tacrolimus, Azathioprine, Prednisolone. TMP Tacrolimus, Cellcept and Prednisolone. TMPS, TAcrolimus, Cellcept, Prednisolone and Simulect. HBD, Heart beating donor. LRD, Live related donor. LunRD, Live unrelated donor.

The above table demonstrates the frequency distribution of donor sources. Patient specific eGFR and histology results were extracted and collated using a MS Access database.
Results: There were no differences in recipient age or HLA MM. The TMPS cohort had significantly worse initial eGFRs in both the cadaveric and live donor subgroup analysis.

ERA (Mean eGFR)	Diff in Mean eGFR	95% CI
TAP (53 ml/min) vs TMP (55 mls/min) LD	-2.2	-5.5 vs 1.1
TAP (53 mls/min) vs TMPS (47 ml/min) LD	5.7	2.4 to 8.9
TMP (55 mls/min) vs TMPS (47 ml/min)	7.8	5.4 to 10.3
TAP (45 ml/min) vs TMP (55 mls/min) CAD	-10.2	-13 to -6.9
TAP (45 mls/min) vs TMPS (46 ml/min) CAD	-3.9	1.9
TMP (55 ml/min) vs TMPS (46 mls/min) CAD	5.6	12.8

There was a statically significant reduction in the 3month culmalative BPAR rates between the three ERAs (TAP (55%) vs TMP (21%) and the TAP Vs TMPS (9%) both pValues$<$ 0.001).
There was no improvement in number of rejections between 4 and 12 months post transplant between any of the groups (Fishers exact test).
Despite having a lower mean eGFR at baseline the eGFR in the TMPS's group was unchanged (0.3mls/min) between 12 and 24 months compared to

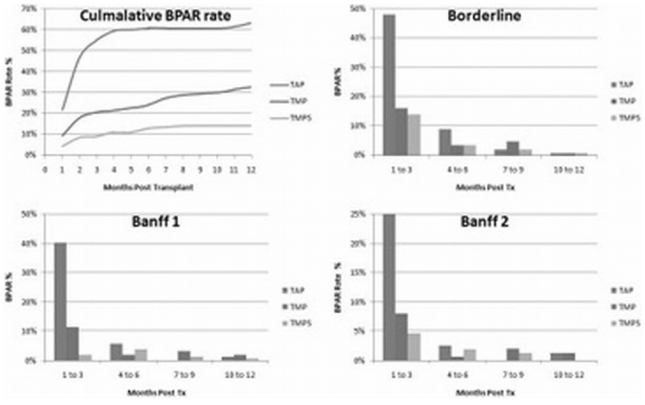

Figure 1. Rejection rates.

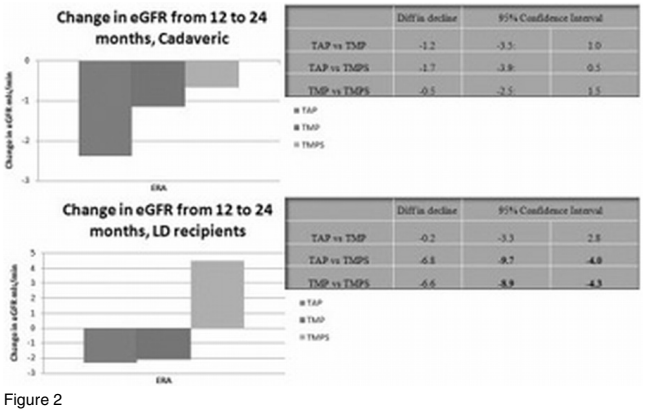

Figure 2

a significantly different decline the TAP (4.1mls/min,pValue 0.004) and TMP (4.2mls/min, pValue 0.014) groups. Sub group analysis reveled that the siginficant difference between the mean eGFR persisted in the live donor patients.
Conclusion: Quadruple immunosupression significantly reduces early BPAR rates and the decline in eGFR between months 12 and 24 post transplantation. However no impact has been made on late rejections.

P-666 A MATCHED COMPARISON OF CHRONIC KIDNEY DISEASE (CKD) COMPLICATIONS BETWEEN NON-TRANSPLANT AND TRANSPLANT PATIENTS

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Purpose: It has been suggested that patients with advanced CKD (stage 5) following renal transplantation fall below targets established for non-transplant patients. The purpose of this study was to compare CKD parameters and targets, across the entire spectrum of CKD, in transplant recipients with a matched group of non-transplant patients.
Methods/Materials: Adult (≥18 years) renal transplant recipients (n=216), who underwent transplantation between 2003-2006 were studied. Prevalent detailed demographic, clinical and laboratory data were recorded over a 2 month study period (March 2008–May 2008). The variables of interest were those complications with guideline targets set by either the UK RA or the US NKF-KDOQI. In addition, the same variables were collected from an age, sex, ethnicity and CKD stage matched cohort of non-transplant CKD patients. Significant differences in CKD parameters and target attainments between the groups were identified.
Results: Of all CKD stages, transplanted patients within CKD stage 3 (n=82) demonstrated the most striking difference with the non-transplanted population, and fewer transplant patients achieved guideline targets. Transplanted patients had significantly higher systolic and diastolic blood pressures (146 vs 134 and 81 vs 74 mmHg respectively, $p<0.001$ for both), lower serum albumin (41 vs 43 g/L, $p<0.001$), lower serum bicarbonate (25 vs 27 mmol/L, $p\leq0.001$) and higher serum corrected calcium (2.4 vs 2.2 mmol/L, $p<0.001$). Conversely, transplant recipients had lower serum phosphate levels (0.97 vs 1.09 mmol/L, $p<0.001$) and markedly lower urinary albumin creatinine ratios (9.8 vs 66.9 mg/mmol, $p<0.001$), despite higher blood pressures.
Conclusion: This report demonstrates the disparity between CKD parameters post transplantation compared with the non-transplant CKD population. It highlights the need for attention to be given to complications of CKD at earlier stages than previously reported, when there is a propensity to focus solely on transplant specific management, if guidelines are to be achieved.

P-667 SERUM PHOSPHATE AND CALCIUM CONCENTRATIONS ARE ASSOCIATED WITH REDUCED PATIENT SURVIVAL FOLLOWING KIDNEY TRANSPLANTATION

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Purpose: The long-term impact of chronic kidney disease related mineral and bone disorder (CKD-MBD) and arterial stiffness following kidney transplantation has not been defined. We studied the association of serum phosphate and calcium levels, and surrogate measures of arterial stiffness, determined by both arterial augmentation index (AIx) and the timing of the return of the reflected arterial wave (Tr), with long term kidney transplant recipient and allograft survival.
Methods/Materials: 270 prevalent adult (≥18 years) renal transplant recipients (mean 81±69 months post transplantation) were prospectively studied, with a subsequent median follow up of 88 months. Detailed demographic, clinical and laboratory data, in addition to both peripheral and central non-invasive pressure measurements were recorded. Cox regression and Kaplan-Meier survival analysis were used to determine the association of candidate variables with patient and graft survival.
Results: Higher serum phosphate and calcium concentrations were associated with reduced patient survival following adjustment for other covariates ($p<0.001$ and $p=0.04$ respectively). Every 0.1 mmol/L increase in serum phosphate and serum calcium resulted in a 21% and 22% increase in the risk of death respectively. Serum phosphate and calcium were associated with death-censored graft loss on univariable ($p<0.001$ and $p=0.02$ respectively), but not multivariable analysis. AIx and Tr were not associated with either mortality or graft loss.
Conclusion: This is the first report to demonstrate that higher serum phosphate levels are associated with increased mortality in kidney transplant recipients. It highlights the need for randomised trials assessing current interventions available for improving phosphate control following renal transplantation.

P-668 A COMPARISON OF TRANSPLANT OUTCOMES IN PERITONEAL AND HEMODIALYSIS PATIENTS- A PAIRED KIDNEY ANALYSIS

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Background: Studies examining the effect of pre-transplant dialysis modality on graft and patient survival have given conflicting results. Therefore, we studied the effects of pre-transplant dialysis modality on transplantation outcome. To minimize the donor variability and bias, a paired kidney analysis was used.
Methods: From December 1994 to December 2005, 69 peritoneal dialysis (PD) (31 m, 48 f) patients received transplantation. PD constituted 12% of all kidney transplantations performed in our centre at that time. 50/69 PD patients (27 m, 23 f) aged from 14 to 64 (mean 39.9±12.4) years had their hemodialysis (HD) pair (34 m, 16 f) aged from 16 to 69 (mean 42.6±11.5) years.
Results: Studied groups (PD *vs* HD) differed significantly with respect to duration of RRT before transplantation (19.7±20.4 *vs* 35.5±50.7; $p<0.05$) months. The groups (PD *vs* HD) did not differ significantly with respect to: number of mismatches, type of immunosuppressive protocol, one year patient survival (96% *vs* 100%), and one-year graft survival (86% *vs* 86%). PD *vs* HD had lower incidence of delayed graft function (18% *vs* 46%; $p< 0.05$) and acute rejection (22% *vs* 30%), graft thrombosis was more commonly listed as a cause of graft failure in PD group, also all types of infections occurred more frequently in PD patients (44% *vs* 32%). Graft function estimated one year after transplantation applying creatinine concentration was similar in PD *vs* HD group (1.57 mg/dl vs 1.61 mg/dl).
Conclusions: The outcome of RT is similar in patients coming from either PD or HD. Delayed graft was less common in PD patients by this potential benefit appears to be counterbalanced by other factors with are associated with graft loss.

P-669 PULSATILE PERFUSION KIDNEY MACHINE IMPROVES KIDNEY PRESERVATION AND PROVIDES INFORMATION ABOUT ORGAN VIABILITY IN KIDNEYS FROM EXPANDED CRITERIA DONORS

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Introduction: Careful evaluation of the organs that are to be transplanted is essential, specially in kidneys from expanded criteria donors (ECD) Continuous pulsatile perfusion (PP) improves kidney preservation and provides us with useful information in order to determine which organs will be viable after transplantation.
Material & methods: Since July 2004 and December 2008, 384 kidneys from ECD were evaluated: 223 from brain death (BD) donors and 161 from Non heart beating donors (NHBD). From each donor, one kidney was connected to a pulsatile perfusion machine and the contralateral was preserved in cold storage at 4C (CS). Kidneys were discarded if their renal resistance index (RR) was higher than 0,4 or the biopsy score was unacceptable. We also compared hospital length of stay, creatinine level outcome, delayed graft function, acute tubular necrosis and cold ischemia time between PP kidneys and controls (differentiating BD and NHBD)
Results: The percentage of kidneys discarded for transplantation was similar in both groups. Initial RR (1.05 vs. 1.97), final RR (0.28 vs. 0.61) and final arterial flux (78.2 vs. 56.5) were different between accepted and discarded groups, all being statistically significant ($p<0,05$).
When comparing PP kidneys with controls in the BD group, cold ischemia time was shorter in the first group. When analyzing the NHBD group, hospital length of stay was shorter too. As regards to primary non-function allograft, no PP kidney presented this complication.
Conclusions: PP is a non invasive method that provides very useful information about organ viability. As PP kidneys had a significant longer cold ischemia period and renal function showed no statistical difference, we think that PP improves kidney preservation. In NHBD, hospital length of stay was much shorter.

P-670 MAXIMISING THE UTILISATION OF EXPANDED CRITERIA DONOR (ECD) KIDNEYS: AVOIDING BIOPSY RESULTS IN ACCEPTABLE OUTCOMES

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Demand for donated kidneys has led to increased use of extended criteria donors (ECD) defined as donor aged ≥ 60 years and donor 50-59 years with two of the following: history of hypertension, CVA as cause of death, terminal serum creatinine >132.5μmol/L *(Sung et al. 2008).*Outside these criteria donors were classified as non-ECD donors.
US Registry data found that 41% of ECD organs were not transplanted based on biopsy or machine perfusion parameters.
Analysis of accepted ECD organs in a large single centre between Jan'00 to Jan'08 was performed. All accepted ECD (n=170) and non-ECD (n=444) kidneys were compared with exclusion of Non Heart beating donors.
Recipient age was significantly higher in the ECD group (Mean Age ECD vs non ECD= 51.3 vs 45.7years $p<0.05$) but other parameters were comparable. Machine perfusion was not performed on any of these kidneys. Over this period <1% kidneys were biopsied. None were discarded based on non neoplastic biopsy findings.
Despite a very low discard rate the actuarial graft loss was not significantly different in either group (graft loss n=22 vs 47 for ECD vs non ECD; p=0.43) with graft survival being 87.1% in the ECD group and 89% in the non ECD group (Kaplan Meier). Equally delayed graft function (DGF) was not significantly higher (ECD 44.7% vs non ECD 38.3%1; p=0.17).
Functionally serum creatinine (mean ± SD micomol/L) was higher in ECD then non ECD 199.7±126.8 vs 156.2±98.7 ($p<0.01$) and 206.5±137.7 vs 171.2±130.7 ($p<0.01$) at 3 months and 1 year respectively.
The low discard rate of ECD donors may reflect differing practice with discard based on clinical pre-acceptance criteria. However these results do support low discard rates with acceptable clinical outcomes if pre-implantation biopsies are not used.

P-671 THE STORY OF POLYETHYLENE GLYCOL PART 1: PEG DURING COLD PRESERVATION PRESERVES GRAFT FUNCTION

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Purpose: Ischemia reperfusion injury remains the main cause of early graft loss. To adress this, several conservation solutions have been created. Polyethylene glycol (PEG) is believed to bring general homeostasis benefits, and provide immune camouflage during reperfusion. To date however, no study exists on its role during organ preservation.
Method: We used a Large White pig model of autotransplantation. The kidney is preserved at 4°C for 24h in either UW as a gold standard or SCOT® (Krebs like solution with an extracellular ionic composition) containing either 15 and 20 g/L PEG20kDa as colloid.
Results: Graft preservation with SCOT® 15 improved early graft function (graph), allowing a return to stable serum creatinine levels by 7days posttransplant (150.8±19.7 versus 871.8±79.4μmol/L in UW, $p<0.001$). 20g/L PEG allowed a more modest amelioration, with stable creatinine reached by 11days (254.8±31.6 versus 694.5±66.3μmol/L in UW, $p<0.001$).
RT-PCR analysis during cold preservation showed that SCOT® 15g/L grafts upregulated hypoxia resistance marker HIF1α and stress proteins Hsp27, 70 and 90. These grafts also showed downregulation of VEGF and its receptor Flk. Grafts preserved with SCOT 20g/L showed downregulation of VEGF as well as Hsp90. UW grafts upregulated Hsp70 during preservation.

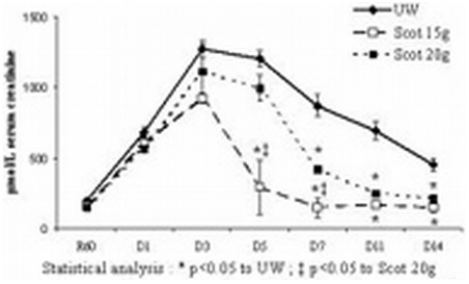

Figure 1. Serum creatinine in transplanted grafts preserved for 24 h.

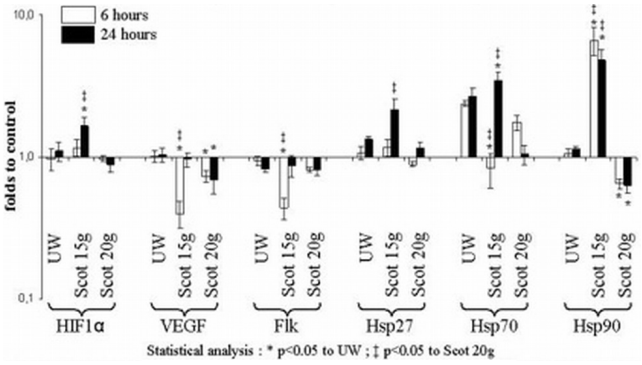

Figure 2. Real time gene expression analysis during cold preservation.

Summary: 15g/L PEG in SCOT® allowed activation of hypoxia and stress resistance pathways during cold preservation, permitting an efficient resuming of function. 20g/L PEG confirmed the positive influence of VEGF downregulation during preservation. Heat Shock proteins interactions are complex: while upregulations of Hsp27, 70 and 90 was found in grafts with the best early function, Hsp70 induction alone was noted in the worst functionning grafts.
Conclusions: Hypoxia and stress resistance pathways can be activated during cold preservation, and impact the early behavior of the kidney graft. 15g/L of PEG20kDa in SCOT® solution is associated with excellent recovery of function.

P-672 THE STORY OF POLYETHYLENE GLYCOL PART 2: PEG DURING COLD PRESERVATION PROTECTS AGAINST CHRONIC GRAFT FIBROSIS

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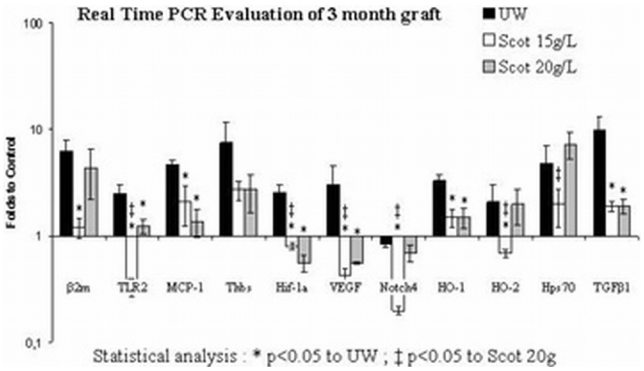
Purpose: Ischemia reperfusion injury (IRI) is strongly associated with chronic graft outcome. Several conservation solutions have been created to reduce IRI severity, some including polyethylene glycol (PEG), which brings general homeostasis benefits and provides immunocamouflage. However, PEG influence on chronic graft outcome remains to be determined.
Method: In a Large White pig model of autotransplantation, kidneys were preserved at 4°C for 24h in either UW as a gold standard or SCOT® (Krebs like solution with an extracellular ionic composition) containing either 15 and 20 g/L PEG20kDa as colloid. Kidneys were evaluated 3 month posttransplant.
Results: Use of either dose of PEG in SCOT® solution improved long-term creatinine as well as interstitial fibrosis compared to UW ($p<0.05$, see Table). Furthermore, 15g/L of PEG allowed for improvement of proteinuria compared to UW or SCOT® 20g/L ($p<0.05$).
Quantitative PCR analysis demonstrated that 20g/L PEG lowered the expression of innate immunity markers TLR2 and MCP-1, as well as hypoxia marker HIF1α and angiogenic marker VEGF. Protection against hypoxia was

Renal function and fibrosis at 3 months

	UW	SCOT 15g/L PEG	SCOT 20g/L PEG
Serum creatinine (μmol/L)	230.8±3.6	150.2±11.3*	169.2±7.2*
Proteinuria (g/24h)	0.7±0.1	0.2±0.18*‡	0.7±0.2*
Fibrosis score	16.0±1.5	4.6±0.2*	5.0±0.1*

Statistical test: *$p<0.05$ to UW; ‡$p<0.05$ to SCOT 20g/L.



confirmed by reduction of HO-1 expression. Lastly, expression of pro-fibrosis TGFβ1 was downregulated.
SCOT® with 15g/L PEG provided broader protection, as downregulations of the same markers was showed, to which was added downregulation of CMH-I formation protein β2-microglobulin, pro-injury marker Notch4, oxidative stress marker HO-2 and stress protein Hsp70.
Conclusions: Combination of 20kDa PEG with SCOT® preservation solution protected kidney grafts against long term lesions. A dose of 15g/L was best able to maintain graft function and integrity, through downregulation of lesional pathways such as inflammation, hypoxia and cellular stress.

P-673 MOLECULAR EXPRESSION OF mTOR PATHWAY IN SKIN KAPOSI'S SARCOMA AFTER RENAL TRANSPLANTATION

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Introduction: The HHV-8 infection and the immunosupresion state are thought to be the main risk factors known for the development of Kaposis Sarcoma (KS) in transplant population. Studies based on animal models describe the AKT/mTOR/p-70S6K pathway activation by the viral G Protein coupled receptor. Clinical regression of KS using mTOR inhibitors supports the critical role of this pathway in the development of this neoplasm. In spite of this data, the expression of mTOR pathway and TGF-b as a mediator of calcineurinic inhibitors (CI) have not been extensively studied on human skin KS specimens.
Objective: Assess the expression of HHV-8, Phospho p-70S6K, VEGF, PTEN and TGF-b in skin KS biopsies of kidney transplant recipients (KTR).
Methodology: KS biopsies specimens of 12 KTR were submitted to immunohistochemical analysis of these proteins. Extension of positivity was categorized as absence, low and high expression with 0%, <25%, >25% of tumoral cells, respectively.
Results: 11/12 KTR were on CI at the KS onset. Histological stages and cases: patch (4), plaque (5) nodule (3).
All cases exhibited nuclear HHV-8 expression. Phospho p70S6K and VEGF were positive in all cases with a high expression in 50% and 100% of the cases, respectively. Low PTEN immunostaining was seen in 8 cases and in 3 cases was negative.
TGF-b showed a endoluminal pattern in 11 cases with a low expression in the majority of the cases (8).
Conclusion: The expression of p-70S6k and VEGF is a marker of the mTOR pathway activation in skin KS. The low PTEN expression confirms the disregulation of this pathway like in other tumors. TGF-b expression could be a marker of the protumoral effects of the use of CI. These proteins could be usefull as a markers of the mTOR inhibitors response in this tumor.

P-674 DONOR-GIFTED RENAL STONE DISEASE AND THE ROLE OF URETEROSCOPY AT LIVE DONOR NEPHRECTOMY

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Purpose: A report on the management of incidental asymptomatic urolithiasis found in potential kidney living donors, investigating the role of ex-vivo ureteroscopy to remove donor stones at the time of transplant.
Methods: We performed a retrospective analysis of all living donors identified with renal calculi on pre-operative computed tomography between 2004 and 2008.
Results: 6 (3.9%) of the 158 living donors were found to have incidental renal calculi. In two cases the stone-bearing kidney was left in the donor. One of these donors subsequently experienced obstructive uropathy in their remaining native kidney two years post-operatively. In the remaining four cases the stone-bearing kidney was transplanted, with no subsequent history of urolithiasis in recipient or donor. Ureteroscopy was performed in three cases, with an embedded stone left in situ in one case, no stone found in the next case, and a small stone successfully removed in the most recent case.
Conclusion: The donor is the most important in the live donor/recipient combination and therefore the choice of kidney should reflect this, leaving the donor with the healthiest kidney. In order to do this strategies should be evolved to manage the stone in the transplanted kidney. One such strategy is to utilise ureteroscopy and possibly stone removal during the ex vivo stage

P-675 eGFR EVOLUTION BETWEEN 6 AND 24 MONTH PREDICTS LONG-TERM KIDNEY TRANSPLANT SURVIVAL IN PATIENTS WITH INFERIOR GRAFT FUNCTION

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One-year serum creatinine and other clinical and immunological factors remain uncertain predictors of long-term kidney allograft outcome.
The aim of our study was to assess the prognostic significance of eGFR (MDRD) monitoring in patients with suboptimal kidney allograft function. This retrospective analysis looked at the eGFR at 6 posttransplant month and every 6 m. thereafter in 323 patients who received kidney transplant between 1995 and 2007; follow-up 7.5 yr (range 1.8 to 12).
Based on eGFR at 6 m. patients were divided into 3 groups.We identified patients with significant eGFR improvement as judged by >20% increase between 6 and 24 m. Demographics and characteristics including time on dialysis, HLA matching, CIT, DGF, AGR, hypertension, hyperlipidemia, %change in body weight were similar across groups. Significant kidney function improvement occurred in 32% pts. They did not experience AGR (72 pts) or had early episode (31 pts). An excellent graft survival was noticed in patients with eGFR improvement between 6 and 24 m; at the end of follow up 95% patients had functioning grafts.

eGFR ml/min/1.73m²	Patients N=323	103 pts with GFR impairment			220 pts without GFR impairment		
		6 month eGFR	24 month eGFR	5 y graft survival	6 month eGFR	24 month eGFR	5 y graft survival
≥50	189	56	71	100%	62	49.5	93%
40-49	71	46	61	100%	45	44	92%
≤40	63	37	45	94%	36	32	68%

Conclusion: eGFR periodic assessement is a valuable biomarker for long-term kidney transplant outcome in patients with inferior function. Tendency to increase GFR in the first 2 posttransplant years is advantageous for graft survival and may indicate a state of immunological quiescence

P-676 THE EFFECT OF MYCOPHENOLATE MOFETIL ON LONG-TERM GRAFT SURVIVAL IN RENAL TRANSPLANTATION: A SINGLE-CENTER RETROSPECTIVE ANALYSIS

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Background: Mycophenolate mofetil (MMF) is known to reduce the incidence of acute rejection and improve short-term graft survival in renal transplantation. However, its effect on long-term graft survival is not well known. This study aims to evaluate the effect of MMF on long-term graft survival in renal transplantation.
Methods: We analyzed graft survival in 1615 renal allograft recipients who received the graft between June 1971 and December 2007 at our center. A total of 107 patients were treated with steroids and AZ or MZ (non-CNI group); 823 patients, with CNI, steroid, and AZ or MZ (CNI group); and 685 patients, with CNI, steroid, and MMF (MMF group). The 10-year graft survival rate was calculated by Kaplan-Meier estimation.
Results: A significant difference in the 10-year graft survival rate was observed among the 3 groups. The rate was 51%, 66%, and 84% in the non-CNI, CNI, and MMF groups, respectively ($p<0.01$; Fig. 1). There was no difference in the graft survival rate between the non-CNI and CNI groups after excluding patients with graft loss within 1 year; however, the graft survival rate in the

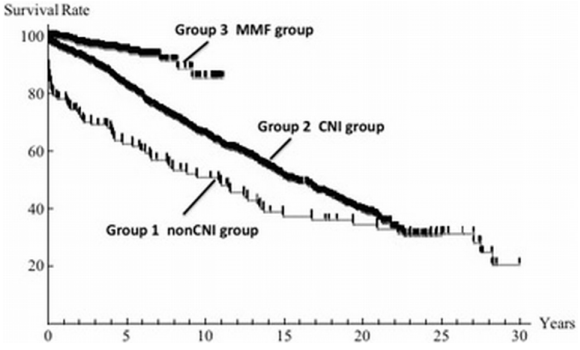

Figure 1. Comparison of graft survival.

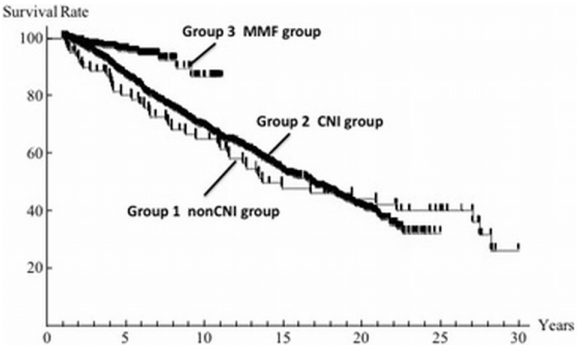

Figure 2. Comparison of graft survival (excluding patients with graft loss within 1 year).

MMF group was significantly better than that in the non-CNI or CNI group (Fig. 2).
Conclusion: Our results suggest that CNI is effective in reducing the incidence of acute rejection and improving short-term graft survival. On the other hand, MMF is effective in not only evading acute-phase graft insufficiency but also improving long-term graft survival in renal transplantation.

P-677 PRETRANSPLANT PBMC IDO ACTIVITY IS LOWER IN RENAL TRANSPLANT RECIPIENTS THAN IN HEALTHY CONTROLS AND IS NOT PREDICTIVE OF ACUTE GRAFT REJECTION

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Subject: IDO is an IFN-gamma-inducible, intracellular enzyme that catalyzes the initial and rate-limiting step in the degradation of tryptophan (TRP) leading to generation of kynurenine (KYN), 3-OH anthranililc acid (3-OHAA), and other downstream metabolites. IDO suppresses the immune response mainly through the cytotoxic effect of TRP metabolites on lymphocytes. The role of IDO in solid organ transplantation is controversial. The aim of this study was to determine whether pretransplant activity of IDO in PBMC of renal transplant recipients is predictive of acute rejection (AR). If IDO produced by peripheral PBMCs has an immunosuppressive function, one would expect that high IDO activity protects from graft rejection.
Methods: The IDO activity of PBMCs before transplantation (Tx) was analyzed in cultures with and without induction by IFN-g. IDO activity was defined by decrease of TRP and increase of KYN/3-OHAA concentrations in supernatants of cultured PBMCs. Transplant recipients with (n=30) and without subsequent AR (n=55) and 24 healthy controls were analyzed.
Results: Transplant recipients had lower Kyn ($p=0.014$ and $p=0.001$, respectively) and 3-OHAA ($p=0.017$ and $p<0.001$, respectively) concentrations, and lower KYN/TRP ratios ($p=0.006$ and $p<0.001$) than healthy controls, both before and after IFN-g stimulation of their PBMCs. This indicates suppressed IDO activity in PBMCs of dialysis patients with end stage renal disease. Allograft recipients with or without AR had similar pretransplant KYN, TRP, 3-OHAA, and KYN/TRP with and without IFN-g stimulation. Measurement by relative qRT-PCR showed that PBMCs of transplant recipients have the potential to upregulate their IDO-expression following stimulation with IFN-g.
Conclusion: Our results demonstrate that pretransplant PBMC IDO activity is lower in potential transplant recipients than in healthy controls, and that it is not predictive of acute rejection.

P-678 LYMPHOCYTES FROM STABLE RENAL TRANSPLANT PATIENTS WHO HAVE HAD CMV VIRAEMIA SHOW A DIFFERENT IL-2 RESPONSE TO CALCINEURIN INHIBITORS COMPARED TO PATIENTS WITHOUT INFECTION

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Calcineurin inhibitor (CNI) immunosuppression in renal transplantation puts patients at increased risk of infection, malignancy and allograft nephropathy. Therefore, an objective measure of CNI sensitivity to allow safe dose reduction would be useful in reducing these complications. Patients with cytomegalovirus (CMV) infection tend to have worse graft function long-term.
Method: Peripheral blood mononuclear cells were prepared from 67 stable renal transplant patients at least one year post-transplantation at time equivalent to trough levels. These were plated with varying concentrations of CNI in ELISpot plates, and stimulated with phorbol myristic acetate (PMA) and ionomycin. Interleukin-2 (IL-2) production was measured and dose-response curves plotted. The concentration of CNI needed to reduce spot number by 50%(IC50) was interpolated from the curves.
Results: The mean IC50 for tacrolimus for patients who had had CMV viraemia requiring treatment, was greater than for those who had not had CMV infection (1.49ng/ml for patients with previous CMV vs. 0.78ng/ml for those who had not had infection. $p=0.029$) Similar results were obtained with ciclosporin, but were not statistically significant (mean IC50 was 109.6ng/ml for patients with previous CMV cf. 66.63ng/ml for those without infection ($p=0.421$)). There were equal numbers of CMV seropositive and seronegative patients in the group developing infection post-transplant.

Mean IC50s in presence of tacrolimus and ciclosporin

	Mean IC50 tacrolimus (ng/ml) n=32	Mean IC50 for patients with cyclospoirn (ng/ml) n=35
CMV infection	1.49	109.6
No CMV infection	0.785	66.63
p value	0.0298	0.421

Conclusions: CMV infection results in prolonged changes to lymphoctye response. The IL-2 response may be a factor in development of subclinical rejection and worse long-term graft function in patients who have had CMV infection.

P-679 PULSATILE PERFUSION PRESERVATION OF EXPANDED-CRITERIA DONORS KIDNEYS: A FRENCH ACADEMIC HOSPITAL EXPERIENCE ON GRAFT FUNCTION

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Purpose: Expanded-criteria donors (ECD) kidneys are a potential solution to organ shortage. Kidneys from ECD exhibit more delayed graft function and worse long-term function. Pulsatile Perfusion Preservation (PPP) has been proposed to decrease injury in this type of kidneys. We present our initial experience in this field.
Methods: Kidneys were considered for PPP whenever they fulfilled at least one of these criteria: 1/ ECD definition (any brain-dead donor aged $>$ 60 years or aged 50-60 years with at least 2 of the following: – history of hypertension – terminal serum creatinin level $\geq$ 1.5 mg/dL (132.6 μM) – death resulting from a cerebrovascular accident), 2/ Donor prolonged circulatory arrest ($>$ 20 mn), 3/ previsible cold ischemia time (CIT) longer than 24 hours.
Results: From February 2007 to January 2009, 14 kidneys from ECDs were preserved by pulsatile perfusion before transplantation in our center. Donor age was 60 (23-77) years. Cerebrovascular accident was the main cause of death (70%). Terminal serum creatinin of the donor was 120 (54-199) μM. CIT was 19 (12-41) hrs. Indications for PPP were: ECD in 8 cases, circulatory arrest with acute renal failure in 4 cases, and prolonged CIT in 2 cases. Recipients were 61 (38-80) years old. M/F ratio was 8/6. Delayed graft function was seen in only 2 of the 14 recipients (14%), with a progressive decline in serum creatinin after 7 days (need for 3 dialysis). At one month after transplantation, serum creatinin was 136 (65-204) μM, corresponding to an estimated GFR (MDRD formula) of 50 (29-114) ml/min/1.73m^2.
Conclusion: Pulsatile perfusion preservation of kidneys from ECD produced promising results for initial graft function, while long term outcome needs further evaluation.

P-683 COMPARISON OF PANCREATIC ISLETS PRESERVATION CONDITIONS IN A MODEL OF MOUSE PANCREAS DONOR AFTER CARDIAC ARREST

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Purpose: In the current organ shortage, the use of organs from donors after cardiac arrest increases, enhancing interest in improving graft preservation, particularly through optimization of organ conservation solutions. We designed a new preservation solution – SCOT 15® ("Solution de Conservation des Organes et des Tissus", Macopharma, France) – of extracellular ionic composition containing 15g/L of PEG 20 kDa as a colloid.
Methods: We compared several conservation solutions, UW® (Viaspan®, Bristol-Meyer-Squibb, France), Celsior® (Genzyme, France), IGL-1® (IGL, France), CMRL-1066® (VWR, France) and SCOT 15® on pancreatic islets harvested from mice subjected to warm ischemia (WI, duration equivalent to 30 min in humans) (n=3 islet isolation experiments for each group). Endpoints were, islet yield (IEQ), cell viability (MTT) and insulin secretion after glucose stimulation, 1h and 20h after islet culture at 37° C + 5% CO_2. In addition, islets

Abstract P-683 – Table 1. Islet evaluation

	Time after islet isolation	UW®	Celsior®	IGL-1®	CMRL®	SCOT 15®
Islet yield (IEQ/pancreas)	1 h	109¶	115¶	178*¶	256*¶	360*
Viability (% to UW)	*1 h*	*100*¶	*152**	*103*¶	*139**	*164**
	20 h	*100*¶	*117*	*146**	*68*¶	*131**
Insulin secretion after stimulation (ng/mL)	1 h	2.726	2.578	2.199	0.816¶	3.352*
	20 h	12.106	10.142	1.826*	2.085*	10.897
Fibrosis (histological scoring)	90 days post-transplant	++	++	++	+	+
Mitochondria alteration (histological scoring)	90 days post-transplant	50%	60%	50%	30%	30%
Lymphocyte infiltration (histological scoring)	90 days post-transplant	+	++	+	++	+

ANOVA and T test *$p<0.05$ vs UW® and ¶$p<0.05$ vs SCOT 15®.

were grafted in healthy mice and harvested 90 days post-transplant for histological evaluations: cellular structures, fibrosis and lymphocyte infiltration.
Results: Compared to other solutions, SCOT 15® resulted in significantly better IEQ islets yield ($p<0.05$). SCOT 15®-islets showed superior viability after 1h and 20h of culture at 37°C (test MTT). These islets also displayed excellent insulin secretion function after 10 mM arginine stimulation at 1h to 20h. Compared to other solutions, 90 days post-transplant, SCOT 15® grafts showed lesser fibrosis, better cellular structures (mitochondrial alterations <30%) and fewer CD3 T cells infiltration (CD3 immunostaining).
Conclusion: In summary, SCOT 15® improved islet yield, a critical goal as the current donor/recipient ratio for islet transplantation is 2/1. Moreover, SCOT 15® improved islets metabolism and long-term *graft histology* as compared to the standard solution UW®.

P-684 MULTIVARIATE ANALYSIS OF RISK FACTORS FOR LEFT VENTRICULAR HYPERTROPHY PERSISTENCE AFTER SUCCESSFUL RENAL TRANSPLANTATION

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Purpose: Left ventricular hypertrophy (LVH) is an indipendent risk factor for cardiac complications in both the general population and chronic kidney disease patients,including renal transplant recipients (RTR).LVH is the main feature found in chronic uremia,being present in 75% of dialysis patients.In general,correction of uremic state by renal transplantation (RTx) leads to reduction of left ventricular mass (LVM),but in many RTR LVH persists.Actually relatively little is known about the factors which may contribuite to perpetuate this complication after RTx.
The aim of this study was to determine the changes in LVM after successful RTx in a cohort of uremic patients affected by pre-RTx LVH and to evaluate the importance of some clinical,laboratory,and echocardiographic variables on LVH persistence in these patients.
Methods: In 25 non diabetic dialysis patients we prospectively evaluated LVM index (LVMI) by echocardiography before and 2 years after RTx.
LVH was defined as a LVMI value greater than 134 and 110 g/m^2 for men and women,respectively.
All these patients showed LVH before RTx. Potential covariates were analysed with respect to LVH persistence after RTx in an univariate and multivariate regression model.
Results: After 24 months of follow-up,all RTR had good renal function (serum creatinine<1.8mg/dL).At 2 years after RTx, we observed a reduction of LVMI (172.3±46.5 vs 133.1±25.6 g/m^2, $p<0.007$)but in 13 RTR LVH persisted.In the multivariate regression model, time on dialysis ($p<0.004$), the post-RTx % BMI increase ($p<.004$),and 24- hr systolic blood pressure load ($p<0.002$) were found to be indipendent positive predictive factors of LVH persistence.
Conclusions: Successful RTx reduces LVM but the prevalence of LVH persists high in RTR. Indipendent risk factors for LVH persistence are a long dialysis time and an insufficient control of weight and blood pressure after RTx.

P-685 TREATMENT OF CHRONIC HEPATITIS C IN RENAL TRANSPLANT RECIPIENTS WITH ULTRALOW-DOSE PEGINTERFERON-ALFA2B PLUS RIBAVIRIN

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Purpose: Hepatitis C virus (HCV) infection is relatively common in renal transplant recipients and can be life-threatening in a small number of patients. The treatment of HCV infection with interferon in renal transplant recipients, however, remains controversial due to the potential risk of interferon-induced graft dysfunction. The treatment of HCV infection in general population with peginterferon-alfa2b and ribavirin has reached a sustained virological response rate of 48% and 90% in genotype 1b and 2a, respectively. We determined whether a lower dose of peginterferon-alfa2b and ribavirin is effective and does not lead to acute rejection.
Patients and methods: Eleven renal transplant recipients (7 men, 4 women, aged 57±9 years, genotype 1b in 9 patients and genotype 2a in 2 patients, respectively) with HCV RNA-positive were enrolled in this study and the mean level of eGFR was from 44 ml/min/1.73m^2. The mean difference time between transplantation and study entry was 14.6 years (range, 1.8-27.9 years). Immunosuppressive treatment was based on cyclosporine or tacrolimus. We treated 11 patients with injection of ultralow-dose peginterferon-alfa2b (0.25 μg/kg body weight for initial four weeks and 0.5 μg/kg subsequently) subcutaneously once a week and oral ribavirin 200 mg/day for 72-96 weeks.
Results: (1) Four of 11 cases cleared HCV RNA and 9 of 11 cases demonstrated a normalization of serum ALT level at the end of treatment. Two of 2 cases with genotype 2a cleared HCV RNA and demonstrated a normalization of serum ALT. (2) All patients with substitution of amino acid 70 in the HCV RNA core region of genotype 1b showed interferon resistance. (3) Two cases terminated the therapy prematurely because of the elevated serum creatinine level.
Conclusion: This regimen is relatively safe and moderately effective.

P-686 DELAYED CALCINEURINE INHIBITOR INDUCTION CAN SHORTEN DELAYED GRAFT FUNCTION PERIOD OF KIDNEY ALLOGRAFTS FROM EXTENDED CRITERIA DONORS

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Introduction: An allograft from a non-heart beating donor (NHBD) is vulnerable to calcineurine inhibitors drug toxicity upon hypoxic stress during agonal stage. In Japan, immunosuppressants instead of CNI are still limited. We used delayed CNI induction protocol for NHBD graft and herein discussed the outcome and applicability.
Materials and methods: Twenty-four kidney allografts from 12 NHBDs available for the comparison with each counterpart were included in this study. Twelve recipients were treated with delayed CNI regimen comprising MMF, corticosteroid (from Day0), basiliximab (Day0 and 4) and delayed CNI (10 TAC, 2 CSA) (initiated if sCr was less than 3.0 mg/dl) (DR). In contrast 12 counterparts accepted standard CNI (11 TAC, 1 CSA)-base quadruple regimen (SR). Outcomes, adverse events and pathological change of tubular damage were compared between two groups.
Results: Patients backgrounds (age, sex, dialysis period, HLA mismatch number and TIT) were similar and all the recipients are alive. DR initiated CNI on Day 8.3 in contrast SR did on Day 0.5 (mean) ($p=0.0001$). DGF period were significantly shorter in DR (mean 5.5 vs. 15.5 d) ($p=0.0328$). However, this effect on the best sCr (1.15 mg/dl in DR, 1.39 mg/dl in SR) was not significant. The frequency of acute rejection and opportunistic infection were comparable (one acute T cell mediated rejection in each group from a same donor). Eleven in DR and 10 in SR showed pathological ATN on 1Hr. graft biopsy specimens and all except for 1 in DR (mild) were free from ATN change on discharge-biopsy specimens.
Conclusions: Without substitute immunosuppressive agents for CNIs, just delayed initiation could shorten DGF period of a kidney allograft from NHBDs. This regimen is safe, applicable for kidney recipients of the graft with supposed tubular damage.

P-687 TESTICULAR PAIN AND SWELLING FOLLOWING LAPAROSCOPIC DONOR NEPHRECTOMY (LDN) FOR LIVING DONOR RENAL TRANSPLANT

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Introduction: Laparoscopic donor nephrectomy (LDN) is now a well-established method for the procurement of kidneys from living donors. Since the introduction of LDN in our centre in February 2005, approximately one-third of all nephrectomies have been performed using this approach. At present in our centre, LDN is only offered to donors suitable for left nephrectomy. Our aim was to investigate the incidence of testicular pain and swelling following LDN.
Methods: 54 left-sided LDNs were performed in our centre between February 2005 and December 2008, 25 of which were in men. A transperitoneal totally laparoscopic approach was used in all cases. An equal number of consecutive male donors who received left-sided open donor nephrectomy (ODN) were identified as a control cohort. A retrospective structured interview was conducted and data collected on testicular pain, swelling and numbness, as well as urinary symptoms and sexual dysfunction.
Results: Data was acquired from 25 of 25 (100%) LDN and 25 of 25 (100%) ODN patients. Of 25 LDN patients, 11 (44%) experienced testicular pain and/or swelling. In most instances pain was of immediate onset, mild to moderate in severity, lasted for a few days to several weeks and was associated with testicular swelling (10 of 11). One donor had testicular swelling alone. Testicular pain or swelling was not apparent in those who had received ODN, with only 2 of 25 (8%) experiencing mild testicular pain, one with swelling. Testicular pain and swelling following LDN was not associated with any urinary symptoms or sexual dysfunction.
Conclusion: Testicular pain and swelling following laparoscopic living donor nephrectomy appears to be a common problem but is under-reported in the literature. Further investigation is required into the causation of these symptoms. Division of gonadal vein at mid-ureter, injuries to testicular innervation and disruption of lymphatic drainage during mobilization of left colon, and retraction of ureteric pedicle during dissection may contribute.

P-688 THE VALUE OF CXCR3 AND CXCR4 AS TOOLS FOR MONITORING HUMAN KIDNEY TRANSPLANTS

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Chemokines are non redundant players in the alloimmune response and we showed that Mig and IP-10 are different when comparing stable with acutely rejecting kidney transplants (Ktx), both in graft infiltrating cells and in blood. CXCR3 and CXCR4 are MIG and IP-10 receptors and we studied its expression in fine-needle aspiration biopsies (AB).
From fifty cadavers Ktx, 40 remained stable for at least one year (I) and 10 developed acute rejection (II) between day 6 and 1400, confirmed by a classical biopsy. All Ktx received triple therapy and two re-Ktx ATG. AB was done on day 7 in I and on the 1st day of rejection in II. AB samples were studied by ABC methodology (Ultravision Detection System Anti-mouse, HRP/DAB, LabVision) and using CXCR3 and CXCR4 monoclonals from R&D. A ratio for renal cells over positive cells (+/R) and for mononuclear cells over positive ones (+/M) were found.
No significant differences were observed for demographic data of donor-recipient, CNI levels and serum creatinine between I and II. For CXCR3, I/II: positive cells- 3.5±46/43±73 (p=0.0034); +/R – 0.007±15.7/0.225±0.3 (p=0.003); +/M – 0.007±0.08/0.20±0.14 (p=0.000). For CXCR4: positive cells – 15±22/80±62 (p=0.001); +/R – 0.056±0.12/0.22±0.22 (p=0.000); +/M-0.076±0.12/0.2±0.13 (p=0.001). We establish +/R cut-off for rejection of CXCR3 $\geq$0.15 and CXCR4 $\geq$0.12. For CXCR3 PPV was 60%, NPV 97.4% while for CXCR4 PPV was 66.6% and NPV was 97.2%.
Those IFN associated chemokines receptors confirm the utility of evaluating the afferent arm of the alloimmune response. While the PPV values were low the NPV were very high, surmising the non dispensable presence of these factors for rejection mounting. Following a larger group of chemokines and their receptors an accurate and timely diagnosis of acute rejection can be made.

P-689 ADULT PRE-EMPTIVE KIDNEY TRANSPLANTATION: A PAIRED KIDNEY ANALYSIS

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Background: The present study compares the outcome of 43 adults transplanted without prior dialysis i.e. preemptive transplantation (PET) and their kidney pairs transplanted after variable duration of dialysis i.e. pretransplantation dialysis (PTD). We look for potential advantages of PET.
Material and methods: From November 2003 to December 2008, some 43 patients (30m, 13f) received PET (4 living and 39 cadaver donors). PET constituted 10.6% of all kidney transplantations performed in our centre at that time. 36/43 PET patients (24m, 22f) mean age 40,4 years had their PTD kidney pair (26m, 10f) mean age 44,6 years. PTD patients remained on dialysis for 3.5 to 180 (mean 38) months before transplantation.
Results: Transplantation waiting mean time was 3.3 *vs* 23 months ($p<0,05$) and the mean Charlson co-morbidity index was 2.4 *vs* 2.8 in PET and PTD group (NS). Studied groups (PET *vs* PTD) did not differ significantly with respect to: number of mismatches, one year patient survival (97.2% *vs* 97.2%), one-year graft survival (88.9% *vs* 88.9%), one-year death censored graft survival (91.7% *vs* 91.7%) and the incidences of acute rejection (28% *vs* 33%). 4 (11%) PET patients and 10 (28%) PTD patients experienced delayed graft function ($p<0.05$). Estimated GFR (MDRD and Cocroft Gault formulas) during one year after transplantation was similar in both groups but the comparison of the creatinine concentration (measured at the discharge from hospital, after 3 months, after 12 months and during last ambulatory control – 1 month to 60 months) – revealed that it was significantly lower in PET group and stable during observation. ($p<0.05$). More PTD patients had professional activity both before and after transplantation ($p<0.05$).
Conclusions: Our single-centre results confirm that PET is an optimal mode of renal replacement therapy for both medical and socioeconomic reasons.

P-690 LOW PRETRANSPLANT ADIPONECTIN LEVELS INDEPENDENTLY PREDICT RENAL TRANSPLANTATION OUTCOMES

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Background: Adiponectin has anti-inflammatory and anti-atherogenic properties and circulates in different multimers. In this regard the high-molecular weight (HMW) isoform selectively attenuates endothelial inflammation. In kidney transplant recipients, endothelial dysfunction is almost universal, representing a risk factor for allograft failure. The aim of this study was to evaluate the predictive value of pretransplant total- and HMW adiponectin levels for kidney transplantation outcomes.
Methods: We measured total- and HMW adiponectin levels (by ELISA/Western blot) in pretransplant serum from 206 renal transplant recipients. Follow up was conducted for 2 years and renal function after transplantation was estimated by measurement of serum creatinine and by rejection diagnosis.
Results: Pretransplant total- and HMW adiponectin levels were significantly associated with the incidence of death-censored graft loss (r=-0.226, r=-0.216, both $p<0.005$). In multivariable Cox proportional hazard regression models (adjusted for traditional risk factors for graft loss) patients in the lowest total- and HMW adiponectin quartile showed an significant increased risk: Hazard ratio [95%CI]: 4.25 [1.27-14.24; p=0.019], and 3.35 [1.04-10.76; p=0.042], respectively. This difference was almost entirely explained by cellular rejection-associated graft loss (lowest vs. highest quartile: adiponectin=9.0 *vs.* 0%; HMW=10.5 *vs.* 0.5%; both $p<0.05$). Rejections, confirmed by renal biopsy, were observed in 43 patients (31 cellular and 12 humoral rejections). Multivariable logistic regression analysis showed the patients with lower pretransplant total- and HMW adiponectin concentrations to be those at greater risk of developing cellular rejection episodes: Odds ratio [95%CI] highest vs. lowest quartile: 4.40 [1.33-14.56; p=0.015], and 3.60 [1.19-10.89; p=0.023], respectively.
Conclusion: Low pretransplant total- and HMW adiponectin concentrations are associated with development of cellular rejection episodes and independently predict allograft loss in kidney-transplanted patients. Our results indicate that low pretransplant adiponectin levels may promote an accelerated inflammatory endothelial milieu associated with adverse allograft outcomes after kidney transplantation.

P-691 HYDROGEN SULFIDE (H_2S) INDUCED HYPOMETABOLISM IS PROTECTIVE DURING HEPATIC ISCHEMIA/REPERFUSION

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H_2S has historically been regarded as a foul smelling and highly toxic molecule. It has been recently established that H_2S can reversibly induce a hypometabolic state mimicking hibernation. Recently we showed the highly protective effects of H_2S in a model of renal ischemia/reperfusion. Here, we investigated whether H_2S-induced hypometabolism could protect livers from ischemia/reperfusion injury (IRI).

Male C57BL/6 mice were subjected to hepatic ischemia-reperfusion by clamping of the blood supply to the left lobe of the liver for 60 min. Animals received 0 (Control) or 80 ppm H_2S in the inhalation air for 30 minutes prior to ischemia until 5 min pre-reperfusion. Core body temperature was maintained at 37°C. Animals were sacrificed after 1, 6 or 24 hours (n=5 per group). Blood and liver tissue was collected.

Animals treated with H_2S had a reduced production of CO_2 during exposure, indicating a state of hypometabolism Hepatic ischemia caused extensive hepatic damage in the Control animals which was reflected by increase of enzyme levels at all time points. Animals treated with H_2S showed massively decreased enzyme levels (AST: 566 vs. 180 U/L at t=1h 722 vs. 177 U/L at t=24 ($p<0.05$), ALT: 403 vs. 197 U/L at t=1h, 1493 vs. 186 U/L at t=24h ($p<0.05$ for all). At t=6 hours enzyme levels were elevated to the same extent in both control and H_2S treated animals indicating either a toxic effect of H2S or a delayed release of hepatic enzymes due to the metabolic depression of the animals. Microscopic evaluation indicated reduced necrotic lesions in livers of the H_2S treated animals

In hepatic ischemia/reperfusion H_2S treatment is protective possibly by reducing the demand for O_2 during ischemia. Treatment with H_2S is therefore a very promising strategy for reducing liver surgery related IRI including liver transplantation.

P-692 DESENSITIZATION PROTOCOL FOR ABO-INCOMPATIBLE HIGH-TITER KIDNEY TRANSPLANTATION

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Background: The field of ABO-incompatible kidney transplantation has achieved remarkable clinical success in Japan. The 5-yr graft survival rates of the ABO-compatible and ABO-incompatible kidney transplantations were comparable. However, previous reports have shown worse outcomes in patients with high pretreatment anti-A/B antibody titers. The immunosuppressive protocol for ABO-incompatible high-titer kidney transplantation has not been established yet.

Methods: A total of 5 blood type-incompatible patients with high anti-A/B antibody titers ($\geq$1: 512) were enrolled in this study. Our immunosuppressive protocol was initiated 4 weeks prior to surgery and included mycophenolate mofetil (1 g/day) and low dose steroid (8 mg/day). Two doses of rituximab (150 mg/m^2) were administered 2 weeks before and on the day of transplantation. We performed antibody removal using plasmapheresis (double filtration plasmapheresis or plasma exchange) before transplantation. The frequency of plasmapheresis was determined by the baseline antibody blood group antibody titer, and the goal of plasmapheresis was to achieve a titer of $\leq$1:16 at the time of the transplant. If antibody titer remained above 1: 512 after eight sessions of plasmapheresis, kidney transplantation was postponed. Splenectomy was also performed on the day of transplantation. Postoperative immunosuppression followed the same regimen as ABO-compatible cases.

Results: Of the 5 patients, 4 subsequently underwent successful kidney transplantation. One patient had an antibody blood group titer that was greater than 1: 512 in spite of the pretransplant antibody removal with the 8 sessions of plasmapheresis. At 12 months, the mean serum creatinine level was 1.33 mg/dl, and graft survival rate was 100%. Acute cellular rejection and acute antibody mediated rejection episodes occurred in 1 of the 4 who received transplants.

Conclusions: These findings suggest that our immunosuppressive regimen may prove effective as a desensitization protocol for blood type-incompatible patients with high anti-A/B antibody titers.

P-693 INFLUENCE OF THE AGE ON GLUCOSE TOLERANCE IN RENAL TRANSPLANT RECIPIENTS

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Background: Previous reports have shown one of the risk factors in new onset diabetes mellitus after transplantation (NODAT) was the age levels of recipients at the time of transplant. The older recipients may have abnormal glucose metabolism without prior diagnosis of NODAT. The present study was designed to evaluate the relationship between patients' ages and glucose tolerance in renal transplant recipients.

Methods: A total of 33 renal transplant recipients without prior evidence of diabetes were enrolled in this study. Patients were divided into two groups by age at the time of transplant; group A (age 55 years and over, n=9) and group B (under age 55, n=24). Two years after renal transplantation, insulin resistance and insulin secretion were determined after 75 g oral glucose tolerance tests (OGTT) and compared between the two groups. Categories of glucose tolerance were defined according to World Health Organization criteria.

Results: Glucose intolerance [impaired glucose tolerance (IGT; 140mg/dl $<$2 h plasma glucose $<$200mg/dl), impaired fasting glucose (IFG; 110mg/dl $<$fasting plasma glucose $<$126mg/dl), diabetes mellitus (DM; fasting glucose $>$126mg/dl or 2h plasma glucose $>$200mg/dl)] was detected in 6 patients (66.7%) of the A group, while 4 patients (20%) had glucose intolerance in the B group. Insulinogenic index was lower in the A group than in the B group. There were no significant differences between the two groups in the homeostasis model assessment of insulin resistance (HOMA-R), the homeostasis model assessment of β-cell (HOMA-β), gender, body mass index, type of calcineurin inhibitors, and serum creatinine levels.

Insulin resistance and insulin secretion

	Group A (n=9)	Group B (n=24)
HOMA-R (mIU mmol l^{-2})	1.55±0.43	1.55±0.90
HOMA-β (mIU/mmol)	57.0±22.6	77.8±37.8
Insulinogenic index (μU 10/mg)	0.52±0.27*	1.77±2.00

HOMA-R, the homeostasis model assessment of insulin resistance; HOMA-β, the homeostasis model assessment of β-cells. *$p<0.05$.

Conclusions: The frequency of glucose intolerance was significantly higher and early insulin response was lower in older renal transplant recipients than in younger recipients. Beta-cell dysfunction may contribute to glucose intolerance in the older renal transplant recipients.

P-694 ARA290 PROTECTS AGAINST RENAL ISCHEMIA/REPERFUSION INJURY IN PIGS

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Cytoprotective action of erythropoietin (EPO) involves binding to a heteromeric receptor complex (EPOR-βcR) consisting of an EPO-receptor (EPOR) and a β-common receptor (βcR). Binding of EPO to this receptor complex induces activation of the JAK_2-pathway. EPO treatment increases the risk of cardiovascular events by stimulating erythropoiesis. ARA290 is a small synthetic peptide derived from the binding site of EPO to the EPOR-βcR complex and does not bind to the classical EPO-receptor. In an earlier study we demonstrated that ARA290 was renoprotective in rats. In this study we investigated the cytoprotective capacities of ARA290 in a large animal model.

Methods: Eight female Dutch Landrace pigs (50-70 kg) were exposed to unilateral ischemia for 45 minutes, with simultaneous canulation of the urether of the ischemic kidney. After removal of the clamp, ARA290 or saline was administered by an intravenous injection at 0, 2, 4 and 6 hours post-reperfusion. At t= -47 (2 min prior to ischemia), t=-2 (2 min prior to reperfusion, and t=15 min (15 min post reperfusion) biopsies were taken.

During 7 days, daily blood samples were withdrawn and urine was collected. Animals were sacrificed after 7 days and kidneys were collected. Clinical parameters were measured and rt-PCR analysis for IL-6, TNF-α, NGAL, EPO, and TGF-B was performed.

Results: The oligurea observed in control animals was largely reduced by ARA290 treatment. Accordingly, GFR was better in ARA290 treated animals. EPO expression was increased after ischemia in the control group but not in the ARA treated group (t=-2). MCP-1 and IL-6 expression was decreased in ARA290 treated animals immediately post-operative (t=15). Expression TGF-Beta was increased in ischemic control kidneys but not in ARA290 treated pigs after 7 days.

Conclusion: ARA290 is a candidate drug for protection against ischemic injury following transplantation.

P-695 LOW-GRADE ALBUMINURIA REDUCTION WITH ANGIOTENSIN II TYPE 1 RECEPTOR ANTAGONIST IN RENAL TRANSPLANT RECIPIENTS

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Background: Microalbuminuria, defined as urine albumin to urine creatinine ratio of 30 to <300 mg/g, is an established risk factor for cardiovascular diseases. Low-grade albuminuria (<30 mg/g) is considered a marker for subclinical vascular damage that predisposes to future cardiovascular diseases and death. Although it has been reported that treatment with angiotensin II type 1 receptor antagonist (ARB) can reduce microalbuminuria in renal transplant recipients, there is no evidence regarding the effect of ARB on low-grade albuminuria.
Patients and methods: This 6-months prospective observation study used a randomized control design. We examined the effects of ARB (valsartan) on blood pressure (BP), urinary albumin excretion, and estimated glomerular filtration rate (eGFR) in normotensive recipients with allograft of more than 1 year previously. A total of 35 renal transplant recipients were enrolled in this study. Patients were assigned randomly to two groups; ARB group (n=18), receiving 8 mg valsartan daily for 6 months and the control group (n=17). Changes in BP, urine albumin to urine creatinine ratio, and eGFR from baseline to 6 months were compared.
Results: In the ARB group, both systolic BPand diastolic BP significantly decreased from 118.6±7.2 mmHg to 112.0±6.5 mmHg, and from 74.0±7.2 mmHg to 67.0±6.0 mmHg, at 6 months after administration, respectively. Urine albumin to urine creatinine ratio was significantly reduced from 25.9±19.1 mg/g to 12.0±9.6 mg/g at 6 months after administration. eGFR decreased slightly at 6 months after administration. However, no patients undergoing treatment for adverse effects required discontinuation of ARB.
Conclusions: This present study reveals that ARB reduces low-grade albuminuria in normotensive renal transplant recipients. Thus, early treatment of ARB in recipients with low-grade albuminuria may prevent cardiovascular disease after renal transplantation.

P-696 DOUBLE-J VERSUS EXTERNAL URETERAL STENTS IN KIDNEY TRANSPLANTATION: A RETROSPECTIVE ANALYSIS

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Introduction: The use of ureteral stents in kidney transplantation is almost undisputed. In literature internal uretero-vesical (double-J) stents are most common used. In our institution uretero-vesico-cutaneous (external) stents have been consistently used for years. Advantages of this method are to estimate the graft's renal function, the simple radiological examination of the ureteroneocystostomy. However, the extended stay of double J-stents may prevent ureteral complications more sufficiently.
Method: A retrospective analysis was performed of all renal transplants done at our institution in 2007. In this period external and double-J stents were used in parallel by three experienced transplant surgeons. Hospital stay and stent associated complications was evaluated. The statistical testing was done by the Fisher-test ($p<0.05$).
Results: In 76 kidney transplants 33 double-J (Group 1) and 43 external stents (Group 2) were used. No demographic differences between the two groups were observed. There was no evidence of a significant difference in the number of urinary tract infections, ureteric stenosis or necrosis. The overall mean length of hospital stay was comparable in both groups. (19.3 days in Group 1, 20.7 days in Group 2, p =0.533). Whereas the hospital stay of patients without immunological complications was significant reduced using double-J stents (10.8 days in Group 1, 12.9 days in Group 2, p =0.018). An ureteroneocystostomy leakage occurred in 6 of the 43 patients in Group 2. No case of insufficient anastomosis was observed in Group 1 (p=0.035). Macrohematuria was monitored in 13 of the 43 patients in Group 2, compared with 3 cases in the 33 patients in Group1 (p=0.045).
Conclusion: This non-randomised comparison of stent types in kidney transplantation supports the use of prophylactic double-J stents – in terms of decreased ureteric complications and reduced hospitalization.

P-697 END THE WAIT! OFFERS COMPREHENSIVE SOLUTION TO KIDNEY TRANSPLANT WAITING LIST IN THE U.S.

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Purpose: END THE WAIT! is a new initiative focused on solving an old problem: how to end the wait for a kidney transplant in the United States. Working in collaboration with other donation/transplant organizations and U.S. Congress, the National Kidney Foundation (NKF) believes that the wait for a kidney transplant can be eliminated within 10 years.
Methods: END THE WAIT! is comprehensive approach, using tested strategies that are proven to be successful:
1. Improve transplant outcomes, reducing the need for second transplants. Immunosuppressive medication must be provided for the duration of the transplant. Chronic Kidney Disease Stage 4 patients should be evaluated for transplant prior to the initiation of dialysis, and education about treatment options, including living donation, is critical to ensure best outcomes.
2. Increase deceased donation by continuously improving the care of potential donor families, ensuring that all donation-related costs are always covered, minimizing discard and utilizing Extended Criteria Donors and Donation after Cardiac Death donors.
3. Increase living donation by guaranteeing coverage for all donation-related expenses, including lost wages during recovery and expenses for potential donors who are ultimately unable to donate for any reason. Donation must be cost-neutral and living donors should have guaranteed health, life and disability coverage for any donation-related complications. Laparoscopic nephrectomy can be made more widely available. Transplantation of incompatible donor/recipient pairs can be maximized through the development of a nationwide system of matched donation.
4. Improve the system and increase efficiency and equity with regard to rates of consent, living donation, early transplantation and access to transplantation.
Results/Conclusion: NKF believes that by working collaboratively using methods that are already successful, the wait for a kidney transplant can be eliminated in the U.S. A complete list of the END THE WAIT! recommendations are available at www.kidney.org.

P-698 SPONTANEOUS REGRESSION OF ASYMPTOMATIC TRANSPLANT RENAL ARTERY STENOSIS DIAGNOSED BY SERIAL DOPPLER ULTRASOUND

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Background: Transplant renal artery stenosis (TRAS) may cause hypertension and/or deterioration of graft function, both non-specific findings after transplantation. The incidence, clinical implication and spontaneous course of TRAS detected by Doppler ultrasound (US) after transplantation is unknown.
Method: A Doppler US examination of the transplant artery was performed 2 months after transplantation in consecutive patients. Blood pressure (BP), number of antihypertensive drugs, serum creatinine and living/deceased donor were recorded. Patients with an elevated peak systolic velocity (PSV≥1.8m/s) were reexamined 18 months later with Doppler US and clinical assessment.
Results: A total of 98 consecutive stable renal transplant recipients were included. Fifteen patients (group A) had an elevated PSV of 2.5 (1.8-3.6) m/s and 83 patients (group B) had a normal PSV of 1.3 (0.7-1.7) m/s at the initial examination ($p< 0,01$). However, there was no statistical significant difference in clinical parameters between group A and B; mean age (51 vs 55 years), gender distribution (75% vs 61% males), living donor recipients (69 vs 42%), systolic BP (137 vs 144 mmHg), diastolic BP (80 vs 83 mmHg), number of antihypertensive drugs (1.8 vs 1.7 pr patient), creatinine (117 vs 132 μmol/L). One patient lost his graft due to non-compliance in the group A. In the remaining 14 patients in group A the second Doppler US at 20 months showed a mean reduction in PSV of 0.5 (-0.7-1.2) m/s from 2.4 (1.8-3.4) m/s to 1.9 (1.2-3.1) m/s (p= 0.02). PSV was reduced in 12 patients, and in seven of these PSV had normalized.
Conclusion: The isolated finding of an elevated PSV early after transplantation has no clinical implication and spontaneous regression is frequently observed. Routine Doppler US to detect TRAS early after transplantation should not be endorsed.

P-699 KIDNEY TRANSPLANTATION WITH A VIRTUAL CROSSMATCH

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Background: Waiting pretransplant crossmatch (FXM) may delay the transplant, prolonging cold ischemia time (CIT), increasing risk of delayed graft function (DGF), rejection (AR), causing worse outcome. We reviewed our experience to define situations where FXM could be avoided
Materials: Between August 2008 and November 2008 we performed 31 kidney transplant from deceased donors.12 (38,7%) had always negative HLA antibodies screening by CDC and Luminex: six male, six female, median age 51. Five black (41,6%), 4 Caucasian (33,3%) and 3 Asian (25%). 9 on haemodial-

ysis (75%), 3 on peritoneal dialysis (25%). Median dialysis length was 3 years. On admission, median serum creatinine (sCr) was 783. Donors were 6 heart beating (HBD)and 6 non heart beating (NHBD).
Methods: Recipients, screened for anti-HLA antibodies by CDC and Luminex every two months, resulting always negative, having sample within three months from transplantation, no intercurrent sensitising events, received a transplant without the FXM. A retrospective XM was performed postransplant by CDC and flow-cytometry.
Results: Median CIT for recipient from HBD and NHBD was 11 and 14,5 hrs. In 2007, when FXM was always performed CIT, for recipients from HBD and NHBD, were 18,5 and 20 hours. Eight patients (66,6%) had DGF (median length 12,7days), 3 (33,3%) immediate function. Median sCr at 7 days postransplant was 651. 75% of the patients underwent renal biopsy. There was 1 border-line AR treated with Methylprednisolone. Median length of hospital stay was 16 days. One month postransplant the median sCr was 160. All retrospective-XM were negative with no episodes of hyperacute rejections
Discussion: In defined group of kidney recipients, careful antibody screening allows proceeding to transplantation without a FXM, reducing the CIT, length and percentage of DGF and length of hospital stay. Retrospective XM confirmed its safety: no cases of positive XM nor hyperacute rejections

P-700 COMPARATIVE ANALYSIS OF IGL1 AND MPS IN MACHINE PERFUSION, A WATERS RM3 STUDY

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Purpose: To face the growing demand for organ replacement, transplantation centers use a growing number of extended criteria grafts. These grafts are particularly sensitive to ischemia reperfusion injury (IRI). Deceased after cardiac arrest donors (DCD) grafts represent an untapped source for organs, thus it becomes critical to determine the optimal preservation strategy for these graft.
Methods: We used a Large White pig model of DCD autotransplantation to test the performance of kidney machine perfusion with two different preservation solutions: MPS, of largely extracellular composition, and IGL-1, which include intracellular components as well as a low concentration of polyethylene glycol. Kidneys undergo 60 min of warm ischemia before being stored 24h at 4°C either in cold storage (CS) or machine perfusion (MP) in a Waters RM3 machine.
Results: After 3 month, we determined that MPS MP organs, as well as IGL-1 grafts (CS or MP alike) displayed lower serum creatinine, although without reaching significance. Evaluation of proteinuria revealed that MP with MPS ameliorated graft function, an effect reproduced with IGL-1, regardless of MP or CS.
Quantitative PCR determined that MP of the graft using MPS ameliorated graft inflammation (Complement C3 and IL-17) as well as oxidative stress (NADPH oxidase element p47Phox). IGL-1 used in CS was able to reproduce that effect regarding both p47Phox and IL-17 expression. Finally, use of IGL-1 in the RM3 machine showed the most positive gene expression, with downregulation of inflammation markers TNFα, C3 and IL-17, oxidative stress marker p47Phox, and endothelial activation marker Thrombospondin.

Table 1. Graft evaluation 3 months post-transplant (mean ± SEM)

	MPS		IGL-1	
	CS	MP	CS	MP
Creatinine (μmol/L)	238.0±46.9	152.0±12.0	164.2±9.4	165.0±22.1
Proteinuria (g/24h)	1.4±0.1	0.5±0.1*	0.6±0.1*	0.6±0.1*
Q-PCR (folds to control)				
TNFα	10.2±2.4	9.3±3.0	13.5±0.3	3.6±1.3*‡¶
C3	8.2±2.8	3.0±0.8*	4.5±1.2	1.8±0.6*‡
p47Phox	5.3±2.7	1.6±0.4*	1.5±0.4*	1.7±0.4*
IL-17	6.3±1.9	3.2±0.7*	3.4±0.7*	2.4±0.7*
Thrombospondin	4.2±1.0	6.1±2.7	5.7±2.3	2.1±0.6*‡¶

Statistical analysis: *p<0.05 versus MPS SC; ¶p<0.05 to MPS MP; ‡p<0.05 to IGL-1 SC.

Conclusion: We determined that machine perfusion using RM3 allowed for better chronic graft outcome on the functional and gene expression levels. Moreover, use of IGL-1 preservation solution is more efficient than MPS in maintaining graft integrity and guaranteeing long-term function.

P-701 ARE BMP7 AND HSP70 EARLY MARKERS OF CHRONIC KIDNEY GRAFT FUNCTION? PROTEOMIC AND GENOMIC ANALYSIS OF ISCHEMIA REPERFUSION INJURY

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Purpose: Renal ischemia reperfusion injury (IRI) influences early and long term graft outcome. Its severity correlates with chronic fibrosis and renal failure, but no accurate markers of IRI severity are available to guide diagnosis and therapy.
Methods: In a Large White autologous pig kidney transplantation model, we studied cold storage (CS, 4°C preservation for 24h using UW), warm ischemia (WI, renal arteries clamping for 60 min) and the association of the two (WI+CS). Analysis were conducted 3 hours, 3 days, 7 days and 3 month posttransplant.
Results: WI+CS displayed the worst function at 3 days (1822±186 μmol/L creatinine, p<0.01 to WI and CS groups), followed by CS (1031±58 μmol/L, p<0.05 to WI), and WI (435±6 μmol/L). This followed superoxide anion production (DHE fluorescence= 29.60 DU in WI+CS versus 0.01 in WI).
Proteomics revealed Hsp70 overexpression in WI group, 3hours (245.4±13.6% of control, p<0.01) and 3 days (133.8±7.6%, p<0.05) after reperfusion. In CS group, Hsp70 expression appeared increased at 3 days (198.3±47.3%). WI+CS group did not show Hsp70 variations.
In WI group, BMP7 expression decreased slightly at three hours (79.3±14.9%, p<0.01). CS group showed no changes, while WI+CS group displayed important BMP7 expression decrease at 3 days (22.6±8.3%, p<0.01).
Graft analysis at 3 months confirmed that severity of the lesions associated with the intensity of the ischemic injury, as evidenced by proteinuria, tubular atrophy and fibrosis. Inflammation was also increased, as was tubular staining for αSMA and Vimentin, linking Epithelial to Mesenchymal Transition with IRI.

Table 1. Renal functional and histological parameters at 3 months (mean ± SEM)

	WI	CS	WI + CS
Proteinuria (g/24 h)	0.5±0.2	2.8±0.5*	4.1±0.8*‡
Tubular Atrophy Score	14.4±0.1	26.2±4.0*	39.6±2.5*‡
Fibrosis (% Sirius Red)	16.8±2.7	29.0±4.6*	44.4±4.8*‡
Inflammation (CD3+ cell/field)	12.0±3.0	22.0±4.0*	31.0±6.0*‡
αSMA staining	16.2±0.8	28.8±1.5*	38.8±2.5*‡
Vimentin staining	11.6±0.5	20.6±0.8*	34.2±1.5*‡

Statistical analysis: *p<0.05 to WI; ‡p<0.05 CS.

Conclusion: Chronic graft outcome is associated with IRI severity. Early Hsp70 expression was linked with lesser IRI severity and better outcome; while intense BMP7 downregulation was evidenced in the group with the worst chronic graft phenotype. These markers could represent critical assets to diagnose and predict the outcome of transplanted kidneys.

P-702 IMPROVING DCAD GRAFTS: DIRECT THROMBIN INHIBITION PREVENTS DELAYED GRAFT FUNCTION AND ACUTE INJURY

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Purpose: Kidney transplantations from deceased after cardiac arrest donors (DCAD) display an increased occurrence of delayed graft function (DGF) and/or primary non-function, likely related to intense ischemic injury. Our hypothesis is that coagulation is central to IRI and thus Melagatran®, a direct thrombin inhibitor, can limit renal injury.
Methods: We used an autologous DCAD kidney transplantation model in Large White pigs. Kidneys undergo warm ischemia for 60 min before being preserved at 4°C for 24 hours using UW.
Results: Melagatran® increased animal survival (9/10 vs. 4/10 in UW Alone at 7days, p<0.05). Renal injury was reduced in treated groups: brush border injury and cell detachment score of 2 at 7days, versus 4 in UW Alone (p<0.05). Inflammation and tubulitis were also diminished (score 1 versus 3 in UW alone, p<0.05) as well as invading cells number (10±3 vs. 50±5 cells/field, p<0.05)
Melagatran® lowered the inflammatory status of circulating PBMCs: RT-PCR revealed downregulation of Rantes (4.7±0.9 folds over control versus 22.9±5.4 folds in UW alone, p<0.01); IL-1Rn (4.4±1.8 vs. 172.7±85.1 folds, p<0.05); IL-1β, (6.5±2.3 vs. 29.2±10.9 folds, p<0.05); CD40L (2.9±0.9 vs 9.8±3.6 folds, p<0.05); Fas (15.6±6.5 vs. 76.1±25.8 folds, p<0.05) and Trail (3.4±1.2 vs. 16.4±6.5 folds, p<0.05).
Melagatran® had a direct protective effect on endothelial cells in vitro, as

RT-PCR showed reduction of endothelial cells activation markers Thrombospondin (2.9±0.5 vs. 6.9±1.8 folds in UW Alone, $p<0.05$) and Pselectin (1.6±0.5 vs. 7.9±1.5 folds, $p<0.001$); pro-inflammatory cytokines IL-1β (3.6±1.3 vs. 11.2±3.9 folds, $p<0.05$) and MCP-1 (0.9±0.2 vs. 2.3±0.7 folds, $p<0.05$); oxidative stress markers LOX-1 (2.1±0.6 vs. 5.9±1.5 folds, $p<0.01$) and Nox2 (3.1±1.0 vs. 7.6±2.3 folds, $p<0.01$).
Conclusion: Direct thrombin inhibitor administration in the peri-conservation period reduced inflammation and oxidative stress, improving graft outcome in a model of DCAD.

P-703 HOW FREQUENTLY SHOULD ONE SEE A NEPHROLOGIST IN THE OUTPATIENT CLINIC AFTER A KIDNEY TRANSPLANT?

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Nephrologists are often involved in the care of post-transplant patients. We have previously described variations in nephrology visits post-transplant. We assessed the association of frequency of outpatient nephrology visits with renal allograft and patient outcomes in the United States. We studied frequency of outpatient visits during the first year post kidney transplant among 41,004 transplant recipients (Tx) transplanted between 1995-2003 using Medicare claims data. Follow-up was collected until December 31, 2003. 11%, 47%, 32% and 9% of Tx had a rate of 0, >0 and ≤1, >1 and ≤2, and >2 nephrology visits per month (mo) during their first year post-transplant, respectively. The adjusted and unadjusted relative risk of allograft failure or death for monthly nephrology visits during the first year post-transplant are shown in the figure.

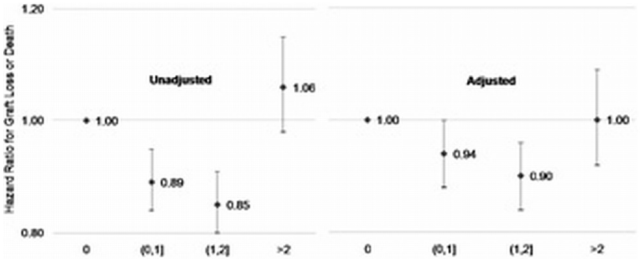

Figure 1. Rate of outpatient nephrology visits per month during the first year.

Adjustment was made for donor type, age, gender, race, Hispanic ethnicity, primary cause of kidney disease, OPTN region, distance from the center, BMI, transplant number, PRA, HLA mismatches, steroid use, initial IS regimen, rapamycin use, use of induction antibodies, inpatient days during the first year, and inpatient admissions during the first year. We conclude that both low and high rates of nephrology visits in the first year posttransplant are associated with worse renal allograft survival. The high rates are possibly associated with increased comorbid burden. Variation in nephrology visits is associated with differential renal allograft outcomes, and 1-2 nephrology visits per month on average during the first year was associated with the lowest risk of graft loss.

P-704 CARDIOVASCULAR MEDICATION USE FOLLOWING KIDNEY TRANSPLANT: DATA FROM THE PORT INTERNATIONAL DATA COLLABORATION

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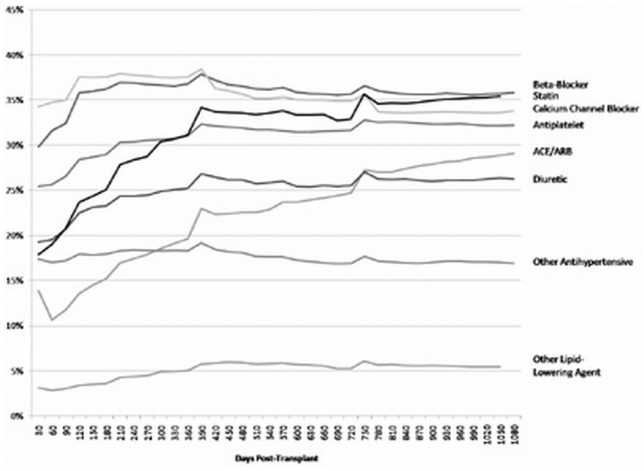
Cardiovascular disease remains the most common cause of mortality and morbidity following kidney transplantat. Despite the high rates of cardiovascular events, there are few studies examining the effects of cardiovascular medications, and these data have largely been limited to the use of statins. Analyses of registries have been limited by a lack of data on the use of cardiovascular medications, and little is known about the prescribing patterns for these drugs in transplant recipients. PORT is the largest multi-center, international collection of non-immunosuppressive medication data in existence in the renal transplant population. The goal of this study was to describe the use of cardiovascular medications during the first 3 years post-transplant. The study population included all adult kidney transplant recipients with graft function 30 days post-transplant from a subset of the 14 participating centers. 9 of 14 centers provided data on use of beta-blockers, ACEIs/ARBs, calcium channel blockers, antiplatelets, diuretics, and other antihypertensive drugs (N=12,150). One additional center provided data on use of statins and lipid-lowering agents. Medication use was defined as using the medication at any time during each 30-day period post-transplant.



Beta-blockers and calcium channel blockers were the most commonly used antihypertensive medications, with use in approximately 36% of the population during the first 3 years. Statin use increased from 18% during the first 30 days to 36% at 3 years. The use of ACEIs/ARBs also increased to 29% at 3 years post-transplant after an initial drop during the first 2 months. The use of other cardiovascular medications remained fairly stable. Despite the cardiovascular risk in the kidney transplant population, the use of medications that have been shown to be beneficial in the general population at high cardiovascular risk remains low.

P-705 POST KIDNEY TRANSPLANT ESTIMATED GLOMERULAR FILTRATION RATE BY CENTER: THE PORT INTERNATIONAL DATA COLLABORATION

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Lower estimated glomerular filtration rate (eGFR) at one year post-transplant has been shown to be associated with worse allograft survival. We examined the association of eGFR measured at one year with allograft survival up to 5 years post-transplant in the PORT database, an international collaboration of transplant data from 14 centers from North America, Europe, Japan, and New Zealand. We estimated one- year eGFR using the MDRD equation (non-IDMS traceable SCr version) in recipients at 9 of 14 centers that reported one-year serum creatinine measures in their patients (N=13,403). 12-month eGFR distributions were similar at the different centers (Figure 1).

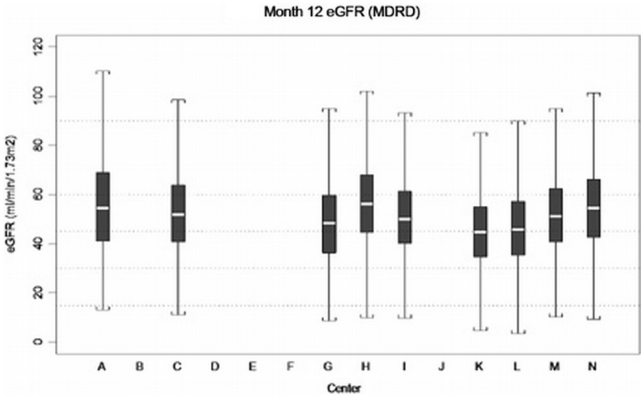

Figure 1

The majority of patients had one-year eGFR between 30 and 60. One-year eGFR was classified according to the KDOQI CKD classification system with an additional stage 3 split at 45 ml/min/1.73m^2. Graft survival varied significantly by one-year eGFR categorization ($p<0.0001$, Figure 2).
Five-year graft survival was 86%, 85%, 80%, 61%, and 17% for patients with eGFR ≥60, 45-59, 30-44, 15-29, and <15, respectively. After adjustment for age, sex, race, PRA, primary cause of renal failure, BMI, year of transplant,

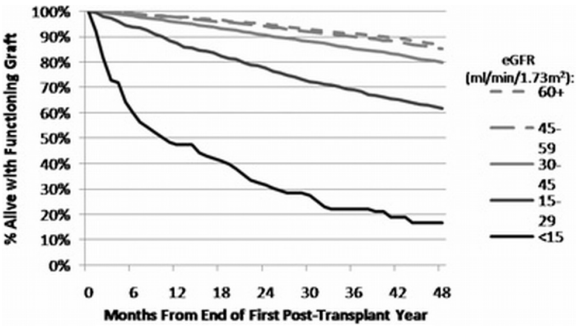

Figure 2

delayed graft function, and region, the adjusted hazard ratios for graft survival by eGFR group, compared with the 60+ group, were: eGFR 45-60: 1.15 (1.00-1.32, p=0.05); eGFR 30-45: 1.70 (1.48-1.95, p<0.01); 15-29: eGFR 3.77 (3.24-4.40, p<0.01); <15: eGFR 20.12 (15.72-25.75, p<0.01). In the PORT population with reported serum creatinine at one year post-transplant, eGFR was similar across participating centers, and eGFR below 45 was associated with increased risk of graft failure through 5 years post-transplant.

P-706 PREDICTION OF SLOW AND DELAYED ALLOGRAFT FUNCTION USING PERIOPERATIVE MEASUREMENTS OF ARACHIDONIC ACID'S METABOLITES

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Purpose: Arachidonic acid's (AA) metabolites, eicosanoids, are known to exert a tremendous influence on kidney function. Hence, in this study we have comprehensively examined the changes of eicosanoids' levels, generated via cyclooxygenase (thromboxane), lipoxygenase (hydroxyeicosatetraenoic-HETE acids) or cytochrome P450 oxygenases (20-HETE) pathway, which occur during early phase of renal allograft reperfusion, and have correlated our molecular observations with recipients' post-transplant outcome. Moreover, we have analyzed whether eicosanoids may serve as clinical predictors for slow/delayed graft function detection.
Material & methods: Renal transplant recipients (n=69) were retrospectively divided into early, slow and delayed graft function group (EGF, SGF, DGF respectively). Blood samples were collected intraoperatively directly before, and in the 1st and 5th minute of allograft reperfusion. Eicosanoids' concentrations were measured using spectrophotometry or ELISA. In order to conduct the multivariate assessment of the degree of dependence between the tested parameters, linear multiple regression model was used. Receiver operating characteristics (ROC) curves were constructed for all analyzed parameters' values, and the area under each ROC curve was calculated.
Results: The results demonstrated significant differences between examined parameters values and dynamics of changes, which were significantly correlating with recipients' post-transplant outcome. Moreover, in our study several parameters proved to be of much better diagnostic value for the prediction of early post-transplant graft activation problems, than already known parameters such as duration of cold or warm ischemia.
Conclusion: Our results demonstrate, that renal transplantations in humans are accompanied by significant changes in AA metabolism, that are strongly associated with recipients' early post-transplant outcome. Moreover, this study introduces several molecular parameters i.e. 5-, 12-HETE or thromboxane as a valuable perioperative markers of SGF and DGF that can be used in clinical practice for early post-transplant allograft activation problems prediction.

P-707 POST RENAL TRANSPLANTATION ERYTHROCYTOSIS

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Introduction: Post transplant erythrocytosis (PTE) is a common complication of renal transplant, that affects 10 to 20% of renal transplant recipients. It is a multifactorial condition. True PTE was defined as hematocrit (HT) a bove 52% and hemoglobin (Hb) above 17 g/Dl.
Aim: The aim of this study was to investigate the frequency of erythorcytosis among renal transplant recipients at our unit.
Materials and methods: We retrospectively examined the Hb levels and Ht of 90 patients who had undergone kidney transplantation.
Results: Of the 90 adult kidney recipients, 15 (16,6%) developed erythrocytosis. It was more frequent in male than female patients: 12 (80%) vs 3 (20%) respectively. The mean age was 29,93 years. No patient had polycystic kidney disease. The mean dialysis duration was 47,7 months. In all patients, the immunosuppressive medication regimen consisted of three drugs therapy (prednisolone cyclosporine – mycophenolate mofetil (MMf) or prednisolone – MMF – tacrolimus). Only 2 patients was treated by bitherapy prednisolone –MMF. PTE appeared at an average of 14,86 months of 16,2 months.
Most patients with PTE had well functionning grafts with a mean of creatinin serum 111,12 μmol/L. Five patients (30%) were treated with venesection. While 3 patients (20%) were given angiotensin –convecting enzyme (ACE) inhibitors. 3 Patients have a renal graft stenosis.
Isotopic measurements of red blood cell (RBC) mass and plasma volume was practiced for 5 patients and confirmed a true erythrocytosis. Remission of PTE Was seen in 13 cases. No thromoembolic complication was occured.
Conclusion: The PTE is a benign condition affecting 16,6% of renal transplant recipeints at our center.

P-708 MINIMALLY INVASIVE TREATMENT OF POSTTRANSPLANT RENAL TUMORS

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Purpose: Posttransplant malignancies have become a major source of posttransplant complications. Our aim was to assess the incidence of posttransplant renal tumors and the efficacy of conservative treatment, in our experience. Material & Method: We performed a retrospective study on 1000 renal transplants (826 living vs. 174 cadaver donors) performed in our institution between 1992 and 2008. Minimally invasive treatment included retroperitoneoscopic radical nephrectomy (RRN), partial nephrectomy (PN) or cryotherapy. The patients were assessed in terms of renal graft function preservation. Follow-up was 5 years
Results: All renal cell carcinomas were pT1a tumors. Twelve RCC were located in the native kidney (9 papillary and 3 multilocular clear cell) and 3 were located in the renal graft (clear cell). Other 12 PTLD affected the renal graft. Of them, 4 were nodular, strictly located in the graft. Standardized incidence ratio for RCC was 7.81. The mean time from transplantation to diagnosis was 11.33 months (range 4-18 months) in the case of PTLD and 33.67 months (range 17-60 months) in the case of RCC. All RCC developed in the native kidney underwent RRN, with the maintenance of renal graft function. Of the 6 cases with tumors developed in the renal graft, 4 were treated by laparoscopic cryoablation (1 RCC and 3 PTLD), one RCC was treated by partial nephrectomy, and one graft transplantectomy was performed because the tumor extended to the renal sinus. All nephron sparing treated patients had reduced immunosupression but with functional graft at follow-up. In adition, patients with PTLD underwent anti CD 20 treatment
Conclusion: Transplanted patients have an increased risk to develop renal tumors either in the native kidney or the renal graft. Early diagnosis is the key point for efficient minimally invasive treatment with renal graft function preservation.

P-709 ENZYMATIC ACTIVITY IN THE POSTTRANSPLANT LYMPHOCELE CONTENT AS AN INSTRUMENT FOR ESTIMATION OF ITS ORIGIN

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Introduction and objective: Lymphocele is a surgical complication of the kidney transplantation. There are two sources of its lymphatic content – transplanted kidney and iliac vessels. It is still unable to distinguish main source of the lymph contributing to the lymphocele content. We have tried to find it by the enzymatic activity in the lymph inside a lymphocele.
Methods: We have used gamma glutamyl transpeptidase (GGT) and creatine kinase (CK) for mapping of the lymphatic system. The lymph originating from a kidney shold have higher GGT activity (renal tubullar cells) and iliac lymph has higher CK activity due to high activity of the muscle mass in the lower extremity. We have analysed aspirated fluids from 40 renal cysts (Kidney). We have analysed 40 lymphatic samples from lymphatic nodes (Pelvis) and 40 lymphatic samples from the retroperitoneal lymphatic nodes localized closed renal hilum (Retroperitoneum) and 40 blood samples (Blood) as the referential values. All samples were drawn from non-transplanted patients. We have measured GGT and CK activity in all samples. We have calculated CK/GGT ratio in all samples. These data were computerized and the curve was constructed according to these data.
Results: see Table and figure.

CK and GGT activitis in the lymph

	CK (μkat/l)	GGT (μkat/l)	CK/GGT
Pelvis	4.764	0.301	24.477 ($p<0.01$)
Blood	0.755	0.451	2.653 ($p<0.01$)
Retroperitoneum	2.599	0.432	7.248 ($p<0.01$)
Kidney	0.061	0.470	0.451 ($p<0.01$)

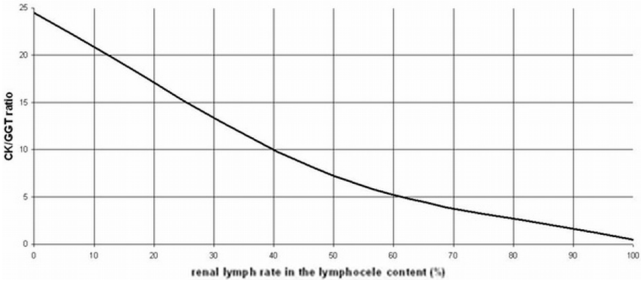

Figure 1. Renal lymph rate in dependency on CK/GGT.

Conclusion: There are significantly different levels CK and GGT in different lymphatic regions. The CK/GGT ratio evaluation in the aspirated lymphocele can be useful for the lymphocele content origin estimation. The presented nomogram is simple instrument for estimation of the lymphocele content and its origin. It needs percutaneous aspiration and CK and GGT evauation in the sample only. It can help us to better understand the lymphocele pathogenesis and it could improve our transplantation results.
Supported by research project MZO 00179906.

P-710 RECIPIENT GENETIC DETERMINANTS OF INFLAMMATORY PROCESS AND NON-STANDARD ATHEROSCLEROSIS RISK FACTORS AND THEIR PRODUCT CONCENTRATIONS AT EARLY POST TRANSPLANTATION PERIOD AFFECT KIDNEY GRAFT FUNCTION

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Background/Aims: The aim was an analysis of the connections between the recipient genetic features of selected factors and the twelve month graft function. The relationships between the occurrence of functional genetic polymorphisms of the genes for MPO, IL-1β, IL-6, CRP, fetuin A, and homocysteine, and gene product concentrations and twelve month transplanted kidney function were analyzed.
Material/Methods: The observation in 125 kidney recipients lasted min. 12; average: 30.9±13.0 months. *IL6* -174G/C, *IL1β* 3954C/T, *MTHFR* 677C/T, *MTHFR* 1298A/C, *AHSG* 1/2 SNPs were determined with SSP-PCR and *MPO* -463G/A and *CRP* -390C/T/A with RLFP analysis. ELISA was applied to mark MPO, fetuin A, IL-6, IL-1b and FPIA to mark L-homocysteine concentration.
Results: The highest CRP values were linked with presence of the TT genotype. The positive correlation of CRP concentrations and GFR was observed. Lower fetuin A concentration were linked with the 256Ser allele. A higher level of of fetuin A examined three months post transplantation was connected with better graft function. Worse graft function was connected with higher serum homocysteine concentrations three months after the transplantation.
Conclusions: Two polymorphisms (CRP, fetuin A) proved to have functional consequences in the recipient as in the general population.
None of examined genetic determinations had influence on long-term graft function.
Higher, though still within the norm, CRP concentration on the day of transplantation and after three months were related to higher values of eGFR in the twelfth month suggesting that the higher intensity of inflammatory reaction may be a manifestation of more effective healing of I-R injury.
Both homocysteine and fetuin A – products with known impact on the development of vascular complications showed long-term prognostic importance.

P-711 PITFALLS OF C2 MONITORING OF CYCLOSPORINE-MICROEMULSION ADMINISTRARION IN STABLE RENAL TRANSPLANT RECIPIENTS – CONDITIONS THAT ARE ABSOLUTELY NECESSARY IN C2 MONITORING

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Purpose: C2 monitoring of Ciclosprin-microemulsion (CsA-ME) has been reported as an effective method for renal transplantion. However, variability between meals and timing of CsA-ME administration may be associated with a serious problem. The aim of this study was to compare the effect of various timings of food intake on variations in C2 levels in stable renal transplant patients.
Methods: 10 patients (aged 45±11) were enrolled in this study. The time that had elapsed from after the transplant to the initiation of this study was 3.3±2.1 years. The dose of CsA-ME was adjusted according to levels of AUC0-4 sparse-sampling that was estimated using two sampling points (C1 and C2) once a month. The maintenance phase AUC0-4 was set at 2,000ng hr/ml. The time differences were the three patterns below that were selected.
– Pattern 1: drug administered 2 hours before meals.
– Pattern 2: drug administered immediately (within 10 minutes) before meals.
– Pattern 3: drug administered within 10 minutes after meals.
Based on the results, we next examined coefficient variation (CV) of the CsA-ME C2 levels where the pattern of CsA-ME administration had the most appropriate timing.
Results: The pattern of meal intake was changed individually and the CsA-ME C2 levels varied in the same individual depending on the pattern meal intake (%CV of intra-patients C2 were from 3.3% to 58.2%). Inter-%CV of pattern 3 was the most various in three groups (55.7%). Inter-%CV of pattern 2 was the lowest (pattern 2 vs pattern3, 18.1% vs 55.7%, p=0.014).

	Pattern 1 C2 (ng/ml)	Pttern 2 C2 (ng/ml)	Pattern 3 C2 (ng/ml)	Intra % CV
Pat. 1	391	433	380	7.0
Pat. 2	530	539	339	24.1
Pat. 3	656	645	355	30.9
Pat. 4	703	670	661	3.3
Pat. 5	668	508	845	25.0
Pat. 6	708	629	270	43.6
Pat. 7	733	512	822	23.2
Pat. 8	507	530	241	37.7
Pat. 9	417	752	420	36.4
Pat. 10	490	453	117	58.2
MEAN	580	567	445	–
SD	128	102	248	–
Inter %CV	22.0	18.1	55.7	–

Conclusions: The pattern of CsA-ME absorption varies for an individual according to the pattern of meal intake. Administration of CsA-ME immediately before meals is highly recommended when managing patients by C2 monitoring.

P-712 BLADDER CANCER AFTER KIDNEY TRANSPLANTATION. SINGLE CENTRE EXPERIENCE

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Aim: The aim of this study is to present our experience with bladder cancer in patients after succesful renal tranplantation.
Material and methods: We reviewed 10 cases of bladder cancer in our centre between 2002 and 2008. All patients used immunosupresive therapy based on calcineurin inhibitors. The average follow up was 43 months (9-72). 6 patients were men, 4 women. Average age at the time of diagnosis was 62 years (34-77). Average time after renal transplantation was 51 months (26-123). All the patients had first kidney transplantation, all grafts were cadaveric. We reviwed pathologic stage, histologic nuclear grade, progression and recurrence of superficial tumours. We also reviewed therapeutis approaches.
Results: In 8 cases (70%) we proved superficial bladder cancer (<pT1). In 2 cases (20%) we proved muscle-invazive bladder cancer (pT2). Histological nucelar grade of tumours was in 3 cases (30%) grade I, in 4 cases grade II and in 3 cases grade III. After transurethral resection of bladder tumous (TURB), we did not prove progression of the tumours, in 2 cases we proved down-stage of tumour (pT2 to pT1). We proved recurrence in 9 cases (90%). In all recurrent cases we proved recurrent diseas 3 month after primal resection. No patient of our study died of bladder cancer. We did not prove any metastatic diseas in our patients. The therapeutic approach was in all cases in first step TURB.

After positive follow up cystoscopic evaluation 3 month after primal TURB, we used sigle-shot intravesical chemotharapy. We did not make any changes in immunopupresive protocol.
Conclusion: Bladder camcer is uncommon compliaction after kidney transplantation. In therapy of superficial bladder cancer is not necesarry to change immunosuppresive protocol nor perform extensive surgical procedures.

P-713 IMPORTANCE OF ROUTINE CANCER SURVEILLANCE TO IMPROVE LONG-TERM RESULTS AFTER KIDNEY TRANSPLANTATION

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Purpose: Recent trends in kidney transplantation have led to a dramatic improvement. However, malignancy accounts for 28.6% followed by cardiovascular disease in our group of patients in the CNI era. Morbidity of malignancy was 4.0% and 1.5% in mortality at the end of 2004. Thus, we positively introduced a cancer examination that decreases the rate of post-renal transplant death due to malignant tumors.
Methods: An out-patient management system aimed at the early discovery of malignant tumors was created using 283 renal transplant recipients in the maintenance phase that visit this hospital. The aim was to bolster up tumor examinations by the screening tests below in a period of one year. Computerized tomography (CT), gastrointestinal endoscopy (GE), prostate specific antigen (PSA, men >50 years of age), mammography (Mam, women only) and cervical smear (CS, women only) were the tests performed once a year. Fecal blood testing (FBT) was performed once every three months.
Results: The ratio of patients that underwent CT was 257/260 (98.8%), GE 249/260 (95.8%), PSA 65/65 (100%), Mam 23/99 (23.2%), CS 28/99 (28.3%) and FBT 244/260 (93.8%). There was only one positive reaction of fecal blood findings, therefore 33 colonoscopies were performed. Neoplastic lesions were detected in 66.7% of the patients. In addition cancers were detected in two patients (carcinoma). Due to this bolstering of the tumor examination, 11 cancers were detected within first one year (2 stomach, 2 colon, 2 kidney, 2 prostate, 1 bladder, 1 uterus and 1 breast cancer). Incidence was 4.2%. Fortunately, all cancers were treated successfully.
Conclusions: Since kidney graft survival depends on patient survival, routine screening for cancer is essential. Making individual annual timetable for screening by specialized staff and patient education will be helpful for long-term follow up.

P-714 SUPERFICIAL FUNGAL INFECTIONS IN 222 CONSECUTIVE RENAL TRANSPLANT RECIPIENTS

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Background: During the last several decades, renal transplantations have been performed with increasing success, the number of recipients and graft survival are steadily growing.
However, renal transplant recipients are predisposed to greater number of skin complications especially to superficial fungal infections.
Objective: The aim of the study was to estimate the number and the type of superficial fungal infections among the kidney transplant recipients.
Methods: Between December 2005 and June 2008, 222 (95 women and 127 men) consecutive renal transplant recipients from two transplant centers underwent screening for the presence of superficial fungal infections. Skin scrapings and swabs were obtained from any suspicious lesions. Nail clippings were collected in case of any nail lesions. All samples were submitted to laboratory and cultured in Sabouraud dextrose agar.
Results: Superficial fungal infections have been detected among 134 (60%) of the 222 renal transplant recipients (55 women,79 men). 32% of patients were on cyclosporine, prednisone and mofetil mycophenolate. The most frequent localization of fungal infection was cutaneous – oral candidiasis (59%) followed by onychomycosis (57%) and fungal toe web infections (37%). The average age was 47,9 (18-77 years). In the group of kidney graft recipients the main agent for oral candidiasis was C.albicans (55%). Trichophyton mentagrophytes (26%) was the most common dermatophyte isolated. Pityriasis versicolor was not significantly more common among the renal transplant recipients.Superficial fungal infections were the most frequently isolated 1-5 years after transplantation.
Conclusions: The prevalence of opportunistic infections with cutaneous-oral candidiasis and onychomycosis caused by T.mentagrophytes is increased among renal transplant recipients. Renal transplant recipients are not at increased risk of Pityrosporum ovale infection and other dermatophytosis. Constant cooperation of transplant centers with dermatologist is needed to increase awareness of transplant patients on proper prophylactic behavior.

P-715 GENETIC PREDISPOSITION TO NEW ONSET DIABETES AFTER RENAL TRANSPLANTATION WITH CYCLOSPORINE AND TACROLIMUS IN SOUTHEAST ASIA AND ITS ASSOCIATION WITH LIPID LEVELS AND DRUG DOSAGE

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Purpose: Transplant recipients develop new onset diabetes after transplantation (NODAT) and Transplant Associated Hyperglycemia-TAH (NODAT or new onset IGT) with cyclosporine (C) and tacrolimus (T). 251 consecutive renal transplant recipients were analyzed for NODAT incidence and risk factors.
Materials and methods: Glucose Tolerance Test (GTT) pretransplant identified nondiabetics (n=102, IGT-24, NGT-78). Baseline immunosuppression was given with either C (n=70) or T (n=32). GTT 20 days (mean) posttransplant identified NODAT, normal (N) or impaired glucose tolerance (IGT).
Results: TAH was seen in 40.2% (40% in C and 40.6% in T) (p=0.5). NODAT developed in 13.7% (12.9% in C and 15.6% in T) (p=0.5). Overall, Hepatits C (p=0.007), HLA B52 (p=0.03) and lack of HLA A28 (A68/69) (p=0.03) was associated with TAH. In T group, higher day one dosage ($p<0.001$), HLA A1 (p=0.04), B13 (p=0.03) and lack of DR2 (p=0.004) increased TAH risk. In C group, HLA A10 (p=0.03), failure of triglyceride (TG) (p=0.001) or LDL (p=0.03) to lower or HDL to rise (p=0.001), and higher post transplant LDL ($p<0.001$) and cholesterol levels (p=0.02) were associated with NODAT or TAH. Post transplant Fasting Plasma Glucose (FPG) on day one had sensitivity - 54.5%, specificity - 50.1%, PPV - 18.1% and NPV - 84.8% for detecting NODAT
Conclusion: Incidence of NODAT was not different with T or C. There is a genetic predisposition to TAH in South Asia and a predisposition exists to the individual diabetogenic effects of the two drugs based on HLA type. TAH in patients on tacrolimus shares common pathogenesis with type 1 DM because both show the protective effect of HLA DR2, and there was no significant association with triglyceride levels (measure of insulin resistance). Lowering of TG,LDL and elevation of HDL after transplantation in patients on cyclosporine predicts a lower risk of TAH and metabolic syndrome due to lower levels of insulin resistance (lowering TG) and shows the importance of insulin resistance in cyclosporine group.

P-716 VITAMIN D METABOLITE-MEDIATED HYPERCALCEMIA WITH SUPPRESSED PARATHORMONE LEVELS IN PNEUMOCYSTIS JIROVECI PNEUMONIA AFTER KIDNEY TRANSPLANTATION

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Purpose: To describe high rate of vitamin D metabolite-mediated hypercalcemia (HCa) with low parathormone (PTH) levels during Pneumocystis jiroveci pneumonia (PJP) in kidney transplant recipients.
Patients and methods: In a 2 years period (2005-2007), 15 cases of PJP were observed in a cohort of more than 500 kidney transplant recipients. Attention was drawn on HCa in several of them. Sequential studies of calcium metabolism were undertaken.
Results: HCa, 2.71 to 3.17mmol/L, m=2.90±0.20mmol/L, was observed in 5 patients (33%) at the time of diagnosis, 10±10.7 months after grafting, in the absence of any therapeutic modification able to interfere with the phosphocalcic balance. HCa was associated with a decrease in levels of circulating PTH from 294±292ng/L 3 to 6 months earlier to 20±23.5ng/L (N=7-53ng/L). 1,25-$(OH)_2$ vitamin D levels were higher than expected: 54.66±23µg/L (N=25-56), whereas 25-(OH) vitamin D levels were low: 13.9±2.17µg/L (N=25-66). Serum phosphate remained in the normal range. Sulfamethoxazole-Trimethoprime therapy resulted in complete recovery in 4 cases with stable renal function, and one patient died. One month later, calcemia and PTH levels returned to normal values: 2.36±0.05mmol/L and 89±29.7ng/L respectively.

Conclusion: Clusters of PJP, as observed here, are known and could be due to nosocomial or environmental transmission sources. Fewer than 10 cases of PJP-associated HCa have been reported so far, less than 5 in transplanted patients, perhaps because the relationship between the two conditions has not been considered. As in other granulomatous diseases-induced HCa, extra-renal production of 1-α hydroxylase by activated macrophages anb by interferon-γ can result in increase conversion from 25-(OH) to 1,25-$(OH)_2$ vitamin D, and, consequently, in transient HCa and suppression of PTH secretion. Fortuitous discovery of HCa in transplant recipients with pulmonary symptoms must raise the suspicion of PJP or other fungal infections.

P-717 LONG TERM GRAFT SURVIVAL IN LIVING UNRELATED/ABO-INCOMPATIBLE RENAL TRANSPLANTS: A SINGLE CENTER RETROSPECTIVE ANALYSIS

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Background: The number of living, unrelated renal transplants and ABO-incompatible renal transplants are increasing because of the shortage of donor organs. The purpose of this study is to evaluate the long term graft survival in living unrelated and ABO-incompatible renal transplant patients. The long term graft survival of living donor renal transplants performed in our center was analyzed retrospectively.
Methods: At our center, 131 renal allograft patients who received the graft between May 2002 and December 2004 were analyzed retrospectively. A total of 19 patients were classified as living unrelated and ABO-incompatible (Group 1;LUR/ABO-i), 17 patients were classified as living related and ABO-incompatible (Group 2;LR/ABO-i),17 patients were classified as living unrelated and ABO-compatible (Group 3;LUR/ABO-c), and 77 patients were classified as living related and ABO-compatible (Group 4;LR/ABO-c). Among living related donors, parents were the most common donors, followed by siblings. In living unrelated donors, almost all were spouses. All recipients received our standardized immunosuppressive protocols at our center consisting of Basiriximab, cyclosporine (CyA), mycophenolate mofetil (MMF), and steroids. The 5-year graft survival rate was calculated by Kaplan-Meier estimation.
Results: The 5-year graft survival rate was 89.1% in Group 1, 94.1% in Group 2, 100% in Group 3, and 91.6% in Group 4.No significant difference existed among the 4 groups.

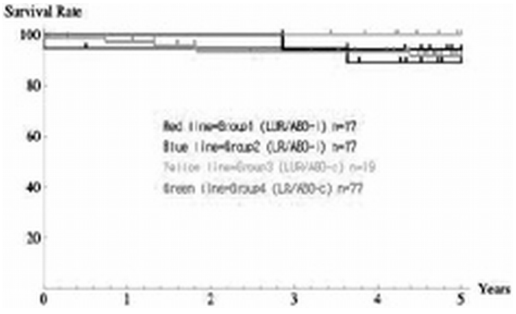

Figure 1. 5-year graft survival.

Kaplan-Meier estimation

	Group2	Group3	Group4
Group1	0.597	0.175	0.649
Group2	–	0.317	0.730
Group3	–	-	0.237

Conclusion: This research suggests that long term survival is equivalent in living, related and unrelated, renal transplants, even if the transplant was performed under the condition of being ABO-incompatible.

P-719 THE USE OF EXTENDED CRITERIA DONORS: A SINGLE CENTRE EXPERIENCE

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We assessed 1-yr and 5- yr outcome of transplantation of marginal kidneys (MK) versus standard kidneys (SK).
Methods: 223 cadaveric kidney recipients between 2001-2003. Grafts marginal if one or more of: Age $>$ 60, non-heart beating donors, cold ischaemia time $>$ 24 hrs, history of hypertension/diabetes. 1 yr follow up data on all, 5 yr in only 113. End points: Delayed graft functionDGF, 1 yr patient and graft survival (PS, GS), estimated glomerular filtration rate eGFR at 1 yr and rejection. Chi-squared, two-sample t-tests or Fisher's exact test; stepwise logistic and stepwise linear regression.
Results: 99 MKs,124 SKs. PS and GS similar at 1-yr. MKs had higher DGF than SKs (39.4% vs. 20.2%, p=0.002). MKs had lower eGFR (40.1 vs. 46.6, p=0.003) and higher sCr (172.3 mmol/l vs. 143.4 mmol/l, p$<$0.001) Those with DGF, had higher sCr at 12 months (184.3 DGF vs. 147.0 non-DGF, P$<$0.001) and lower eGFR (39.6 DGF versus 45.0 non-DGF, P=0.03). DGF not related to rejection. CIT was not related to any one of the outcome measures. Donor sCr $>$ 130 mmol/l significantly related to DGF (p=0.005) After 5 yrs, 113 patients under our care. 8 had lost their graft or died in the first year. Of the remaining 95, 7 died at 5 years, 5 of them with a functioning graft. Out of these 7, 2 had received MK. GS similar for both groups (MK 92.5% vs. SK 96.3% p=0.7)
Conclusions: MKs do not differ from SKs in GS and PS at 1 yr. MKs have more DGF and worse function after 1 year. 5 year follow up does not show an impact in those grafts which survived after 1 year.

P-720 ENDOTHELIAL AND THROMBOCYTE ACTIVATION ARE NO INITIATORS OF EARLY ISCHEMIA-REPERFUSION INJURY IN HUMAN KIDNEY TRANSPLANTATION

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Purpose: In addition to their evident role in hemostasis and thrombosis, thrombocytes are specialized cells of the innate immune defence and modulators of the inflammatory response. Upon reperfusion in human kidney transplantation, an inflammatory reaction is initiated that will account for later dysfunction of the graft. We reasoned that thrombocyte activation may initiate the cascade of inflammatory events upon reperfusion. In this study we assess whether endothelial cells and consecutively thrombocytes are activated after reperfusion in living and cadaveric donor kidney tranplantation.
Methods: We collected paired arterial and renal venous blood samples at successive time-points during the first 30 minutes of reperfusion. Eight living donor (LD), heart beating (HB) and non-heart beating (NHB) donor kidney transplantation recipients were included in each group. The paired samples were analyzed on markers of thrombocyte and endothelial activation, i.e. β-thromboglobulin, glycoprotein Ib, regulated on activation normal T-cell expressed and secreted (RANTES), platelet derived growth factor (PDGF), von Willebrand factor (vWF), and vWF propeptid. To assess whether release of these factors is specific for reperfusion, we included control arteriovenous samples collected during donor nephrectomy prior to inducing renal ischemia.
Results: No markers of edothelial activation were released from the reperfused kidney. Indicators of thrombocyte activation did not show a significant arteriovenous difference either in living or cadaveric donor kidney transplantation. Only RANTES was released from the kidney in small amounts in HB donor kidney transplantations.
Conclusion: The results of this study unequivocally show that there is no indication for the involvement of local endothelial or thrombocyte activation in early reperfusion injury in both living and cadaveric donor kidney transplantation. The release of RANTES in HB donor kidney transplantation rather indicates T-cell involvement than thrombocyte activation, as all other markers are negative.

P-721 AN INNOVATIVE APPROACH TO ASSOCIATE OUTCOMES RELATED TO ADHERENCE WITH PATIENT BEHAVIORS AND TREATMENT CHARACTERISTICS

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Purpose and methods: Immunosupressive (IS) regimens require life-long adherence to maintain the transplanted organ. Although calcineurin inhibitor (CNI)-based regimens are effective, dose optimization is critical to minimize both organ rejection and CNI-related toxicities. Effective dosing is challenged by conflicting approaches to dose monitoring and poor adherence to a twice-daily oral regimen over the long-term. The goal of this study was to describe the impact of patient behavior (adherence) and Cyclosporine (CsA) treatment characteristics (dose and exposure) on health outcomes (renal function).
We developed a model based on published adherence data coupled with a population pharmacokinetic model to describe the impact of drug adherence on CsA exposure variability and time outside therapeutic exposure range. In

addition, the model was used to simulate the impact of poor adherence on CsA exposure variability and renal function (health outcome).
Materials/Results/Conclusions: There is large variability in CsA exposure (area-under-curve) despite dose adjustments based on therapeutic drug monitoring of trough concentrations. Poor adherence translated to approximately two-thirds of patients experiencing a high coefficient of variation in CsA trough concentration (>30%) which was associated with worse renal and overall health outcomes, e.g., serum creatinine of 1.4±0.5 (low variance) vs. 1.7±1.2 (high variance), p=0.03 at 5 years post-transplant.
Quantitative modeling and simulation techniques employed in drug development can be an innovative way to characterize the relationship between drug exposure, patient behaviors in real-world settings and the consequences on health outcomes. This model indicates that in routine practice 2-hour AUC projections may underestimate the longer-term variance in CNI levels, potentially exposing the patient to erroneous dose adjustments and the resulting consequences. Characterizing the dose-adherence-exposure-outcome relationship supports the creation of patient-level initiatives that may maximize adherence to an IS regimen and optimize health outcomes.

P-722 THE EFFECTS OF DONOR FACTORS ON GRAFT OUTCOMES IN LIVING DONOR KIDNEY TRANSPLANTATION: SINGLE CENTER EXPERIENCE

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Background: The influence of donor factors on acute rejection rates and graft survival in living donor kidney transplantation has not been well characterized. Among living donor factors reported to correlate with posttransplant outcome are pretransplant glomerular filtration rate (GFR) and donor age.
Methods: Clinical data were retrospectively analyzed from 384 pairs who underwent living-donor kidney transplantation from January 1995 to November 2005. We compared donor sex, age, GFR and body mass index (BMI) to recipient GFR (at postop. 30day), acute rejection episodes and 5 years graft survival.
Results: The average donor age were 39.2 yr (17~63). The donor age & donor GFR were correlated with allograft GFR (P=0.001, 0.043). At the group of donor age < or= 45 yr, graft survival increased than other group (16%:22%, P=0.021), acute rejection episodes was no difference between groups (29%:33%, P=0.42). Allograft GFR, graft survival and acute rejection rate were no definite difference in each donor-recipient sex groups (P=0.751, 0.165, 0.405). Donor GFR was no significant difference in graft survival and acute rejection episodes (P=0.217,0.675). Donor BMI was not associate with allograft GFR (P=0.442). At donor BMI groups (~18.5, 18.5~24.9, 25~), graft survival and acute rejection rate were no difference (P=0.558, 0.778). The graft survival rate was correlated with allograft GFR (P=0.000).
Conclusions: Donor age and GFR seems to be a more important predictor of graft loss than other factors. This study suggest that routine analysis of donor factors may be useful as the consideration of recipient characteristics in predicting posttransplant graft outcomes.

P-723 OUTCOME OF KIDNEY TRANSPLANTATION CADAVERIC DONOR WITH ELEVATED SERUM CREATININE

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Introduction: The increasing need for kidney transplant has led to long waiting lists and forced authorities to step beyond their standard criteria for accepted kidneys from cadaveric donors. But the question remains about the benefit of these out bound kidneys.
Material & methods: We conducted a retrospective analysis of all kidney transplant preformed at Imam Reza Hospital of Mashhad, IRAN, during January 2002 to April 2008 from cadaveric donors. A total of 194 kidney transplants met the criteria of which 137 had donors with creatinine less than 1.5 mg/dl and 57 had creatinine greater than or equal to 1.5 mg/dl. Then required information was collected from transplant clinic to which all patients had regular visits.
Results: Average follow up was 33 (Maximum of 78). According to Kaplan – Meier survival analysis the graft survival rate for those with normal creatinine was 92% and 68% for I and 3 years after renal transplantation and for those with creatinine greater than or equal 1.5 ml/dl was 86% and 62% for I and 3 years after renal transplantation.
Conclusion: Although graft survival rate was 5% – 7% less in kidney recipients from cadaveric donor with creatinine above 1.5 but the different was not statistically significant. Even if significant, due to organ shortage crisis this would not be an appropriate exclusion criterion instead a good factor to justify the recipient.

P-724 SUCCESSFUL KIDNEY TRANSPLANTATION LOSE PERCENTAGE OF WATER, MUSCLE AND BONE BUT GAIN LIPID IN EARLY PERIOD; A BODY COMPOSITION ANALYSIS

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Successful kidney transplantation (KTx) can theoretically reconstitute body composition of a CKD patient normally. However, the actual change has not studied well. We herein evaluated the changes in body composition between before and after KTx. The study enrolled 37 male and 18 female (mean age at KTx: 43.5±13.6, mean period of dialysis before KTx: 53.4±68.4 months) kidney recipients eligible for the comparison of their BMI, body composition and lipid metabolism before and one year later after KTx. Fifteen had been induced quadruple immunosuppression consisted of CNI/MMF/steroids/basiliximab, while 40 were also same agents, however steroid were discontinued on POD3. The body composition was analyzed using bioelectrical impedance, Muscle-alpha. Their BMI, fat metabolism were analyzed as well. There was no significant change in BMI between two points (21.4±3.1 vs 21.7±3.5). Regarding body composition, the percentage of water decreased significantly (61.2±4.9 vs 58.3±5.3) ($p<0.05$), in contrast the fat percentage significantly increased (16.4±6.7 vs 20.3±7.1) ($p<0.05$). More interestingly, successful KTx significantly decreased the percentage of muscle and bone one year after KTx (37.3±5.1 vs 34.8±4.7, 16.3±2.1 vs 15.2±2.1) ($p<0.05$). Fat metabolisms were worsened after KTx supported by the significant increase of parameters such as TC, TG and LDL-C (161.2±40.0 vs 191.0±40.6, 95.2±38.8 vs 113.5±57.0, 87.7±29.3 vs 105.9±28.2) ($p<0.05$). In comparison of two different protocols, there was no difference in any item. In conclusion, KTx did not change BMI one year later. On the other hand, body composition significantly changes; the percentage of lipid increased and the percentage of water, muscle and bone decreased. Care must be taken even after successful KTx not to exhibit dyslipidemia, which is most risk factor of cardiovascular events and protocols to prevent from the progression of catabolism should be considered.

P-725 LATE ANTIBODY- MEDIATED REJECTION; SINGLE CENTRE EXPERIENCE

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Introduction: Late antibody-mediated rejection (late ABMR), clinically defined as progressive loss of renal function with hypertension and proteinuria more than 3 months after transplantation, is the leading cause of late allograft dysfunction. The hypothesis that a subset of chronic humoral rejection is mediated by antidonor antibody was tested by determining whether C4d is deposited in peritubular capillaries (PTC) and whether it correlates with circulating antidonor antibodies.
Methods: The objective of this retrospective single centre study was to analyze a renal function of patients with different phenotyphes of chronic humoral rejection. Documentation and biopsy material along with serology from 25 patients who underwent renal biopsy for decreased creatinine clearance between years 2002 and 2007 and revealed late ABMR were analyzed.
Results: We established that 11 out of 25 patients had elevated panel reactive antibodies before transplantation (PRA≥ 20%). Induction therapy with antithymocyte globulin or OKT3 was administered to 14 out of 25 of patients. Late ABMR was detected on average 2.78 years after renal transplantation. At the time of biopsy mean creatinine was 255.88±162.38 μmol/l, creatinine clearance 0.66±0.36 ml/s, mean proteinuria was 1.34± 2.518g/day. 9 out of 25 patients had positive flow cytometry cross-match (FXCM) and 7 out of 25 patients had positive cytotoxic cross-match (CDCXM), all patients had positive histological verification of C4d complement fragment in biopsies. Transplant glomerulopathy was present in all biopsy findings, with coincidence of acute cellular rejection in 13 out of 25 patients. 1-year graft survival from the diagnosis was only 64%. Patient survival was 100%.
Conclusions: The presence of C4d in biopsy findings and detection of alloantibodies indicates ongoing immunologic activity of the process. Earlier detection and treatment of chronic humoral rejection still remains a challenge.

P-726 RENAL TRANSPLANTATION FROM AgHBs POSITIVE DONORS TO AgHBs NEGATIVE RECIPIENTS

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Purpose: Using of kidney from Ag HBs+/anti-HBc+ donors in non-immunised or unprotected recipients is contraindication for renal transplantation. Kidneys from Ag HBs positive donors can be used in immunised patients by dissease or after vaccination
Methods: This is a retrospective study between January 2000 and December 2007 on 712 renal transplants. 22 of them (3. 08%) were AgHBs–/antiHBc– and recived kidney from Ag HBs+/anti-HBc+ donors. All of them had protective titre of anti-HBs at the moment of transplantation; 18 of them by effective vaccination before transplant (anti-HBs+/anti-HBc–) and they have recived kidney from living related donors; 4 were immunised by infection (anti-Hbs+/anti-HBc+), they reciving kidney from cadaver donors.
All the living donors had normal liver tests at the moment of donation; HBV-DNA was undetectable in 15 of living donors and 3 of them had mild viremia. 2 of cadaver donors had significant viremia and in 2 of them the viremia was undetectable. Also, the liver tests of donors were normal.
1 year after transplantation all recipients recived Lamivudine.
Follow-up interval was 2 years. After 2 years we studied: patient and graft survival, liver tests, serological markers for HBV (HBsAg, anti-HBs, anti-HBc) and HBV-DNA.
Results: All patients and grafts survived 2 years after transplantation. All of them had normal liver tests; AgHBs and HBV-DNA were negative in 21 of patients; just one of them (who recived the kidney from HBV-DNA positive cadaver donor) presented 2 years after transplantation AgHBs+ and mild viremia, with normal liver tests.
Conclusions: Kidney from AgHBs + donors can be used in immunised recipients. It is more safely if the donor HBV DNA is negative at the moment of transplantation.

P-727 CADAVERIC KIDNEY TRANSPLANTATION WITH THYMOGLOBULIN VERSUS MONOCLONAL ANTIBODY INDUCTION – A PAIRED KIDNEY ANALYSIS

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This study was performed to investigate the impact of induction therapy (Thymoglobulin *versus* a monoclonal Ab) in delayed graft function (DGF) and acute rejection (AR) rates and in the renal function 1year post-Tx.
Methods: A paired kidney analysis was used in order to minimize the donor variabilility and bias. All paired kidneys from deceased donors during 2006-2008 period, where one kidney was allocated to a patient receiving thymoglobulin *(group1)* and its mate allocated to a patient receiving a monoclonal Ab*(group 2),* were evaluated.
Results: 94 pts were included (mean age: 38.4±12.9 yrs; 60.6% males; time on dialysis: 4.1±3.2 yrs). No statistically significant difference was found between the groups according to recipient and donor age, gender, PRA, HLA mismatches and cold ischemia time (CIT) (*group 1:* 23.7±3.3 hs; *group 2:* 23.3±3.6 hs). The immunosuppressive protocol consisted of mycophenolate plus calcineurin inhibitors (tacrolimus in 89.4% of pts) in both groups and steroids in group 2. The *serum creatinine* at 12 months post-Tx (1.50±0.75 *vs* 1.37±0.66 mg/dl, p = 0.26) and the incidence of *DGF* (56.6% *vs* 63.0%; p = 0.52) was not statistically different between the two groups. The rate of any report of *AR* within 1 yr post-Tx was significantly decreased in group 1 (19.6 *vs* 45.7%; p = 0.008) and the incidence of *CMV disease* was similar in both groups (10.9 *vs* 15.2%; p = 0.53).
Conclusion: Thymoglobulin was associated with a significant reduction in 1 yr-AR rate in this cohort of paired kidneys, but not with a decreased rate of DGF, probably because of the prolonged CIT. There was no impact on renal function/CMV disease in the 1st year post-Tx with Thymo.

P-728 EARLY DETECTION OF BKVIRUS ASSOCIATED TO URETERAL NECROSISIN A RENAL ALLOGRAFT RECIPIENT

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An early BKVN case is reported post-renal transplant associated with ureteral necrosis.
A patient 61 years old, who was transplanted from a 59 years old woman There was immediate diuresis, but hemodialysis was required for 4 days.ATG induction was used in addition to steroids and mycophenolate.On day six tacrolimus was started. On day 20 he had fever and pain in the grafted area. Abdominal ecotomography showed a periureteral collection. Surgery was performed, showing extensive ureteral necrosis. Ureteral hystology showed infarcted areas with neutrophil infiltrate. Urine cytology studies performed 1 month post- transplant showed typical Decoy cells.Real time cuantitative polyoma virus urine PCR was positive with $1{,}847 \times 10^{11}$ viral copies/mL, and real time blood PCR was 1,139 ×10E3 viral copies. The poliomavirus was identified as BKV.
Graft kidney biopsy was performed showing positive isolated viral inclusions SV40, without evidence of interstitial nephritis. There was also evidence of anticalcineurinic toxicity, despite low tacrolimus levels (5-7 ng/mL). Retrospective search for BKV in the ureter from the donor kidney also showed the SV 40 viral inclusions in the urotelial cells only in the perforated area. Immunosuppressive therapy reduction, mycophenolate was discontinued, steroids were decreased while tacrolimus was reduced to 1.5 mg twice daily.(level 4 ng/ml). A viremia control was still high, leflunomide therapy started. Three months post-transplantation the patient is stable with serum creatinine (1.5 mg/mL)
This case shows that BKV detection can ocurr as early as 20 days post transplantation and also wtih of ureteral necrosis associated with BKV; thus, we suggest that there was a rol played by BKV in late ureteral necrosis. Longer follow-up period will provide the final answer. Finally, this case supports the need for early BKV screening in all transplanted patients.

P-729 ASSESSMENT OF KIDNEYS PROCURED FROM EXPANDED CRITERIA DONORS BEFORE TRANSPLANTATION

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Using expanded criteria donor (ECD) organs is one of the strategies for making more transplants available. In order to reduce the number of post-transplant complications and failures there is a need to create a comprehensive system of kidney evaluation prior to transplantation, especially for kidneys harvested from expanded donors.
Aim: The aim of this study was to assess which factors are most suitable for kidney evaluation before transplantation.
Patients and methods: One hundred and seventy two patients received cadaveric renal transplants between January 1, 2006 and August 31, 2008. Data on donors, recipients and preservation were collected. Patient and graft survival as well as immediate, delayed and slow graft function were analysed. Kidney function was assessed by serum creatinine concentration and creatinine clearance according to Cockroft-Gault formula at seven days, 1, 3, 6, 12 and 24 months post transplantation. The follow-up was completed on November 30, 2008. All patients were followed-up for three to thirty five months.
Results: Average 1-year graft survival was 86.9% for the whole group and mean creatinine concentration was 1.58 mg/dl. One case of primary non-function was observed (0.6%). More than 25% of transplanted kidneys were harvested from ECD.
A lower graft survival at six months after transplantation was observed in the group of organs harvested from ECD, those with histological lesions (HL) and those in which flow in the fourth hour of machine perfusion was lower than 0.4 ml/g.

Factors affecting kidney graft survival

	SCD	ECD	HL(–)	HL(+)	Flow (ml/g) ≥0.4	Flow (ml/g) <0,4
Graft survival 6 months after transplantation (%)	97.1	75.0	94.3	76.5	89.8	62.5

By using logistic regression model, chronic histological changes were proven to have influence on kidney survival at six months post transplantation. Additionally, ECD kidney recipients were more likely to have a creatinine concentration higher than 2 mg/dl at six months post transplantation.
Conclusions: Pre-transplant evaluation of expanded criteria donor kidney should include three variables: donor parameters, histological findings and machine perfusion parameters.

P-730 CORRELATION BETWEEN EXPANDED CRITERIA KIDNEY DONOR PARAMETERS AND CHRONIC HISTOLOGICAL LESIONS

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Using expanded criteria donor (ECD) organs is one of the strategies for making more transplants available. In order to evaluate kidneys from expanded criteria donors prior to transplantation donor parameters and histological findings were analysed in this study.
Aim: The aim of this study was to investigate the relationship between expanded criteria kidney donor parameters and histopathological lesions.
Patients and methods: One hundred and seventy two patients received cadaveric renal transplants between January 1, 2006 and August 31, 2008. Data on donors were collected. In one hundred forty seven cases, renal biopsy specimens obtained perioperatively were available. Cortical interstitial fibrosis, cortical tubular atrophy, arteriosclerosis, total inflammation, arteriolar hyalinization, glomerulosclerosis and thrombotic changes were evaluated.
Results: Average 1-year graft survival was 86.9% for the whole group and mean creatinine concentration was 1.58 mg/dl. One case of primary nonfunction was observed (0.6%). More than 25% of transplanted kidneys were harvested from ECD. ECD kidneys presented chronic histological lesions like cortical interstitial fibrosis, cortical tubular atrophy, arteriosclerosis, arteriolar hyalinization and glomerulosclerosis significantly more frequently than standard criteria donor (SCD) kidneys.

Histological changes in kidneys procured from SCD and ECD

	SCD (n=128)	ECD (n=43)	P
Interstitial fibrosis	0.9%	12.5%	0.002
Cortical tubular atrophy	3.7%	22.5%	< 0.001
Arteriosclerosis	22.7%	62.9%	< 0.001
Total inflammation	1.0%	5.4%	NS
Arteriolar hyalinization	17.8%	52.5%	< 0.001
Glomerulosclerosis $\geq$ 20%	2.2%	36.4%	< 0.001
Thrombotic changes	8.1%	13.5%	NS

Conclusions: Expanded criteria donor kidneys are more likely to contain chronic histological lesions on biopsy.

P-731 GENE EXPRESSION PROFILING UNDER DIFFERENT IMMUNOSUPPRESSIVE PROTOCOLS

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The aim of this study is to investigate the differences in gene expression profiling in protocol biopsies taken from patients using calcineurin inhibitors (CNI) and mammalian target of rapamycin inhibitors (mTOR-I).
Eight protocol biopsy samples obtained from patients using CNI (n: 4) or mTOR-I based treatment (n: 4) were analyzed. Control group consisted of five biopsy samples obtained at the time of implantation (zero hour). All biopsy specimens were evaluated according to the Banff Classification. Formalin-fixed, paraffin-embedded samples were used for microarray analysis. Microarray hybridization was performed using the Affymetrix GeneChipU133 plus2.0 Array. Data analyses were performed using Partek Genomics Suite6.4 and Ingenuity Pathway Analysis7.1. Differences in gene expressions were considered as significant at p value$<$0.05 and 1.5-times increase in fold change in expressions between groups.
In CNI and mTOR-I groups, patient age, donor age, biopsy duration after transplantation, creatinin level and proteinuria at the time of biopsy were similar. All patients had received first transplant from one haplotype match live donor. Acute and chronic Banff components were not different between CNI and mTOR-I groups. Mean donor age in control group was 45$\pm$6, and all were live donor.
In CNI and mTOR-I groups 1214 and 1515 up- or down-regulated genes have been found compared to control subjects, respectively. When the analysis performed to compare between CNI and mTOR-I groups, 29 genes in CNI group and 101 genes in mTOR-I group were up-regulated compared to each other. Mainly involved cellular and molecular functions were amino acid metabolism, small molecular biochemistry, antigen presentation, cellular movement and cellular growth and proliferation in CNI group. Whereas, antigen presentation, cellular movement, cell-to-cell signaling and interaction, cell morphology and cellular assembly and organization involved in mTOR-I group.
In spite of the presence of similar clinical course and histopathological appearances, different treatment strategies cause different gene expression profiles in kidney transplantation.

P-732 THE INFLUENCE OF CHRONIC HISTOLOGICAL LESIONS ASSESSED BY PERIOPERATIVE TRANSPLANT KIDNEY BIOPSY ON ITS FUNCTION AND SURVIVAL

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The number of patients with end-stage renal disease is growing, while the number of transplanted organs remains quite stable. Using expanded criteria donor (ECD) organs is one of the strategies for making more transplants available. Histological findings of biopsies obtained prior to transplantation may play a significant role in kidney evaluation.
Aim: The aim of this study was to investigate the influence of histopathological lesions on transplant kidney graft function and survival.
Patients and methods: One hundred and seventy two patients received cadaveric renal transplants between January 1, 2006 and August 31, 2008. Data on recipients were collected. In one hundred forty seven cases, renal biopsy specimens obtained perioperatively were available. Chronic histological changes were evaluated. Patient and graft survival, as well as immediate, delayed and slow graft function were analysed. Kidney function was assessed by serum creatinine concentration and creatinine clearance according to Cockroft-Gault formula at seven days, 1, 3, 6, 12 and 24 months post transplantation. All patients were followed-up for three to thirty five months.
Results: Average 1-year graft survival was 86.9% for the whole group and mean creatinine concentration was 1.58 mg/dl. One case of primary nonfunction was observed (0.6%). More than 25% of transplanted kidneys were harvested from ECD.
A correlation was observed between chronic histological changes "inherited" from the donor and graft survival/function. Cortical interstitial fibrosis, cortical tubular atrophy, arteriosclerosis, arteriolar hyalinization and glomerulosclerosis found in biopsies were associated with higher creatinine concentration and lower creatinine clearance. Additionally cortical interstitial fibrosis, arteriosclerosis and glomerulosclerosis were associated with higher incidence of graft loss.
Conclusions: There is a correlation between chronic histological lesions and kidney graft function and survival.

P-733 THE RISK FACTORS AND THE THERAPY FOR CHRONIC DIARRHEA RELATED TO IMMUNOSUPPRESSIVE AFTER RENAL TRANSPLANTATION

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Objective: To analyzed the risk factors and summarize the therapy for chronic diarrhea related to the immunosuppressive after renal transplantation.
Methodology: 404 cadaveric renal transplant receipts were observed for more than 18 months, they were combined with MMF and were separated CsA group, FK506 group, conversion group (from CsA to FK506). The chronic diarrhea were analyzed in three groups and were compared between pre and post conversion in conversion group. The rate of diarrhea was analyzed in different CYP 3A5 genetype group. The effect and safety were observed after the switching of immunosuppressive protocol for therapy of chronic diarrhea over 6 months.
Result: No one had chronic diarrhea in CsA group (n=145) and conversion group (n=93) before conversion. The rate of chronic diarrhea was 7.5% (7/93)in conversion group after conversion and 7.2% (12/166)in FK506 group. The dosage of MMF, renal allograft function have no difference among these groups. 214 receipts received CYP 3A5 genetype test. the rate of diarrhea in including *1 group (n=70) was lower than *3/*3 group (n=144)(1/70 vs 18/144 $P< 0.01$). 2 cases decreased the dosage of MMF without improvement and resulted in loss of allograft, 3 cases decreased the dosage of MMF with improvement of diarrhea, 14 cases switched immunosuppressive protocol with completely relief: 1 with CsA+MMF, 1 with sirlorimus+MMF and 12 with FK506+mizoribine. One receipt had acute rejection on the 7th month after switching;
Conclusion: The combination of FK506 with MMF can increase the risk of chronic diarrhea in renal transplant receipts contrast to CsA with MMF, the CYP3A5 *3/*3 type has a high risk for this side-effect. Conversion of immunosuppressive promptly was an effective and feasible therapy for these patients.

P-734 MANAGEMENT OF RENAL PERFUSION IN DONORS DECEASED FROM CARDIAC ARREST: COMPARISON OF IN SITU PERFUSION AND NORMOTHERMIC ECMO

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Purpose: In case of donation after cardiac death (DCD), organ perfusion can be performed either by immediate cold In Situ Perfusion (cISP) or by initial normothermic Extracorporeal Oxygenation Membrane Support (nECMO) followed by the regular organ harvesting procedure. The aim of this study was to compare the outcome of kidneys harvested by these 2 perfusion techniques in DCD donors.
Methods: Transplants were performed between May 2007 and January 2009 in a single institution. Six kidney transplants were perfused by nECMO and 11 were perfused by cISP. Donors were type I (70%) and II (30%) Maastricht categories. Grafts were all machine perfused (Lifeport®, ORS). Donor age and cold ischemia time were not statistically different between 2 groups. Analysis was performed with the Student T test.
Results: Recovery of renal function occurred earlier in the nECMO group as assessed by 1) date of diuresis recovery (PO day 0 in nECMO vs. 4.1±5.1 in cISP, $p<0.03$); 2) number of postoperative hemodialysis sessions (0.3±0.5 in nECMO vs. 3.8±3.1 in cISP, p=0.006), 3) time to serum creatinine $<$ 300 μmol/l (13.5±6.2 days in nECMO vs. 27.3±13.8 in cISP, p=0.016); 3) serum creatinine level at one month (143 μmol/l ± 55 in nECMO group vs. 245 μmol/l ± 102 in cISP, p=0.027). Consequently, patients in nECMO group were discharged earlier (19.8±6.8 days vs. 28.4±9.14 in cISP group, p=0.045).
Conclusion: According to our preliminary results, management of DCD donors with nECMO allows earlier renal function recovery and should be regarded as the method of choice to manage DCD donors.

P-735 POST-RENAL TRANSPLANT ANEMIA (PTA): PREVALENCE, ASSOCIATED FACTORS AND MANAGEMENT IN BRAZILIAN RECIPIENTS

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This study was designed to investigate the prevalence of PTA, its management and the associated factors.
Methods: We performed a retrospective cohort study enrolling kidney Tx recipients with a follow up $>$ 2 years. Anemia was defined as a Hb $\leq$ 12g/dl in women and $\leq$ 13g/dl in men (WHO criteria). Donor age, recipient gender, type of donor (living or cadaveric), creatinine, delayed graft function (DGF), acute rejection (AR) and therapy without steroids were investigated as risk factors. The variables reaching a significance of $p < 0.15$ in the univariate analysis were included in a multivariate logistical regression analysis.
Results: 258 recipients were evaluated (mean age: 38.8±11.4 ys; 60.5% males; cadaveric donor: 53.5%; 35.7% did not receive steroids). DGF and AR were detected in 38% and 14.7% of pts. Anemia was diagnosed in 83% (M1), 61% (M2), 55% (M3), 48% (M4), 44% (M5), 38% (M6), 33% (M9), 28% (M12), 32% (M24) and 45% of patients at the last follow up (5,4±1,9ys). A significant negative correlation was observed between SCr and Hb levels at M6, 12 and 24. *Donor age $<$ 50 ys* was associated with a lower risk of PTA at M6 (OR=0.183 [0.05-0.67]; p=0.011) and M24 (OR=0.074 [0.014-0.377]; p =0.002), as well as the *use of steroids* at M6 (OR=0.314 [0.17-0.56]; $p <$ 0.0001). *DGF* was independently associated with PTA at M6 (OR=3.657 [1.69-7.88]; p=0.001) and M12 (OR=2.847 [1.45-5.57]; p=0.002). The management of PTA included erytropoietin in 25.6%, iron in 36.4% and at least one blood transfusion in 18.6% of patients in the post-Tx.
Conclusions: The lowest prevalence of anemia was observed between M9 and M24 post-Tx and PTA was undertreated in the studied population. DGF was the most important factor associated to PTA.

P-737 CURRENT STATUS AND TREND OF LAPAROSCOPIC LIVE DONOR NEPHRECTOMY IN JAPAN

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Purpose: The increased acceptance of laparoscopic nephrectomy (LN) has been a driving force for live donor kidney transplantation. To investigate and clarify current status and trend of LN in live donors kidney transplantation, we surveyed all kidney transplantation centers for 6 years on LN.
Methods: A questionnaire on LN was sent by mail to all Japanese kidney transplantation centers every year from 2003 to 2009. The questions consisted of the experience, numbers of LN and open nephrectomy in live donors, as well as, detailed method and complications in donors and recipients in the previous one year.
Results: In 2009, we mailed to 148 centers, and 105 (70.9%) centers responded. These centers carried out 794 live donor nephrectomies. In these centers, 55 (52.4%) centers performed LN. In all donors underwent nephrectomies in all responded centers, 572 (72.0%) donors had LN and 222 (28.0%) had open nephrectomies. In 55 centers, 17 were performed hand-assisted (HA) LN, 26 non-HA, 3 both HA and non-HA, 2 both non-HA and laparoscope-assisted and 7 laparoscope-assisted. And 21 centers carried out peritoneal approach, 31 retro-peritoneal and 2 both. In 572 LN donors, no one had life-threatening complication. Blood transfusion was performed in 1 donor. Open conversions were 13 (2.3%). Minor complications not requiring long-hospital stay were reported in 19 (3.3%). The mortality was 0. On the other hand, in 572 recipients, primary non-function was reported in 1 case and 19 (3.3%) recipients needed hemo-dialysis after transplantation because of delayed graft functions. Urinary tract complications were noted in 17 (3.0%) recipients.
Conclusions: LN increases steadily in Japan. In donor complications, the incidence of blood transfusion decreased and that of open conversion increased. The results of this survey showed the validity of LN in live donor kidney transplantation.

P-738 SUCCESSFUL LIVING DONOR KIDNEY TRANSPLANTATION ACROSS POSITIVE CROSS-MATCH

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Although kidney transplantation is the treatment of choice for end stage renal disease, presensitized recipients are less likely to find compatible deceased donors. With desensitization prior to transplantation, these recipients could be offered a living donor and avoid the excessive waiting time. Herein, we report an initial experience on successful living donor kidney transplantation across positive crossmatch through desensitization.
Between September 2006 and October 2008, 8 consecutive sensitized candidates with crossmatch positive prospective donors underwent kidney transplantation after desensitization protocol. Antibody-reduction protocol consisted of plasmapheresis (PP) every other day starting 10 days before the scheduled transplant surgery, and intravenous immune globulin (IVIg), which was given after each PP session at a dose of 100 mg/kg. One dose of Rituximab (375 mg/m^2) was given intravenously 40 days before the scheduled transplant. Patients had additional course of alternate-day PP and IVIg for 1 week post-transplant. All patients received induction with one dose of 20mg Basiliximab and maintenance immunosuppression, which consisted of a combination of tacrolimus, mycophenolate mofetil and prednisone.
After aforementioned pretransplant immunomodulation, all 8 candidates underwent live donor kidney transplantation. Mean follow-up was 14 months. One-year patient and graft survivals were 100% and 87.5%, respectively. The overall incidence of biopsy-proven acute rejection within 1 year was 25.0%. The glomerular filtration rate, which was calculated with MDRD equation, at 2 weeks, 4 weeks, 3 months, 6 months, and 12 months was 65.7±8.3 mL/min (range 55.7-81.1 mL/min), 64.4±9.5 mL/min (range 52.7-78.4 mL/min), 59.4±10.2 mL/min (range 48.1-73.8 mL/min), 58.5±9.7 mL/min (range 47.8-71.8 mL/min), 60.9±18.8 mL/min (range 43.9-80.4 mL/min), respectively.
In spite of a very small study population, these results suggest that preoperative desensitization of positive crossmatch transplant candidates is feasible and could give a favorable short-term outcome to sensitized patients.

P-739 PREGNANCY AFTER KIDNEY TRANSPLANTATION - A SINGLE CENTRE EXPERIENCE

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Background: Successful pregnancy in hemodialysed women is rare. After kidney transplantation (KT) pregnancy is possible but the risk of maternal and fetal complications is increased.
Methods: We examined retrospectively the outcome of 15 pregnancies in 13 patients after KT in Gdansk centre in the period 1987-2008.
Results: Mean maternal age at pregnancy was 29.7±4,2 (range 24-37) years. Mean interval between transplantation and conception was 30.9± 18.6 (range 7-62) months. Mean creatinine concentration at conception was 1,35±0,39 (range 0,9-2,45) mg/dl, hypertension was present in 7/13 women (2 received more than 1 anti- hypertensive drug), none had urine spot proteinuria. There

were 2 conceptions within the first year of transplantation, and 6 within the second. Out of 13 women, 8 were primagravidas. At conception, 8 women received protocol with cyclosporine (CsA/MMF/P – 4, CsA/Aza/P – 4), 3 with tacrolimus (TAC/MMF/P-2, TAC/Rapa-1), and 2 azathioprine with prednisone. Mycofenolate mofetil was discontinued before pregnancy but rapamycine during the first few weeks of pregnancy. Fetal outcomes included: 13 alive births, 1 spontaneus abortion, 1 stillbirth. Main pregnancy age was 35,5±3,5 (range 26-39) weeks. There were 9 cesarean sections. Among the alive births, there was 1 neonatal death due to multiple lethal malformations, 1 child developed a severe neurological defect. There was 1 case of imminent asphyxia. Out of 15 pregnancies, maternal complications included ankle edema (4/13), worsening of blood pressure control (3/13), 1 imminent abortion, 1 cervical insufficiency, 1 anhydramion. One mother returned on dialysis 7 years after successful pregnancy, the other live with functioning grafts.
Conclusions: All mothers survived the pregnancy. None of the mother experienced rejection or graft lost as a result of pregnancy. Positive fetal outcome was noticed in 75% of pregnancies.

P-740 THE ECONOMIC IMPACT OF DIFFERENT REGIMENS TO PREVENT CYTOMEGALOVIRUS DISEASE IN RENAL TRANSPLANT RECIPIENTS

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Background: The aim was to determine the cost impact of four various strategies for prevention of cytomegalovirus (CMV) disease after renal transplantation (RTx).
Methods: Hospitalization data and medical resource utilization data were prospectively collected alongside two randomized trials. In the first trial (Transplantation 2005;79:317) the patiens were randomized to 3-month prophylaxis with either oral ganciclovir (1g t.i.d., n=36) or valacyclovir (2g q.i.d., n=35), and to the control group (n=12) managed by deferred therapy. In the second trial (Am J Transplant 2008;8:69) the patients were randomly assigned to 3-month valacyclovir prophylaxis (n=34) or preemptive therapy with valganciclovir (900mg b.i.d. for a minimum of 14 days, n=36) for significant CMV DNAemia. The cost analysis (expressed in 2009 euro) involved all real costs directly related to CMV during first year post-RTx.
Results: The average CMV-associated costs per patient were 4096, 2305, 7198, and 4442 EUR in patients in the ganciclovir, valacyclovir, preemptive, and deferred therapy groups, respectively ($P<0.001$). Valacyclovir prophylaxis was significantly less expensive than any other regimen. The cost of CMV disease was highest in deferred therapy group (($P<0.001$) while the cost of PCR CMV DNA monitoring was significantly higher in preemptive or deferred groups compared with both prophylactic regimens ($P<0.001$). Increased cost in ganciclovir group as compared with valacyclovir was due to higher cost of drugs given for prophylaxis (3029 vs. 1162, $P<0.001$).
Conclusions: Deferred therapy is the most expensive strategy for CMV management due to excessive cost of CMV disease. Valacyclovir prophylaxis is more cost-effective strategy compared not only with deferred therapy but, also with ganciclovir prophylaxis or valganciclovir preemptive therapy.

P-741 THE ROLE AND BENEFITS OF TRANSPLANT PHARMACISTS IN A KIDNEY TRANSPLANT DISEASE MANAGEMENT CLINIC

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Aim: The Kidney Transplant Disease Management Clinic (DMC) was set up in 2004 to care for kidney transplant recipients (KTX) with high immunological risk of rejection or complex post-transplant complications. DMC is run by a multidisciplinary team including transplant pharmacists. A prospective study was performed to analyze the recommendations made by transplant pharmacists and evaluate its clinical impact on KTX.
Methods: Between July 2008 and February 2009, 110 of 137 KTX on follow-up at DMC were seen by transplant pharmacists. At each visit, transplant pharmacists would conduct an interview on medication history, review laboratory results and drug therapy; recommendations made on drug therapy would be reviewed by the transplant physician when he/she sees the KTX. Data on the recommendations and their clinical outcomes was collected over 7 months.
Results: Transplant pharmacists made 525 recommendations and 78.8% were accepted by transplant physicians. Recommendations included therapeutic drug monitoring (TDM) of immunosuppressive agents (69.5%), optimization of drug therapy for complications [hyperlipidemia (9.0%), hypertension (6.7%), anemia (2.1%), proteinuria (3.2%)], anti-infective prophylaxis (4.0%) and avoidance of adverse drug reaction (0.8%). Drug classes mostly involved the immunosuppressive (67.4%) and cardiovascular agents (16.6%). Among the TDM recommendations, 92% achieved their intended target. KTX with adequate follow-up were analyzed, all achieved statistically significant ($p<0.05$) improvement in the measurable outcomes. 8 KTX with proteinuria had a median reduction in urine protein/creatinine ratio from 1.04 to 0.59 ($p<0.05$); 16 KTX with dyslipidemia achieved a median reduction in low-density lipoprotein cholesterol from 3.4mmol/L to 2.9mmol/L ($p<0.05$); 13 KTX had median systolic blood pressure lowered from 165mmHg to 141mmHg ($p<0.05$) and 5 KTX with anemia had median hemoglobin level raised from 8.8g/dL to 12.2g/dL ($p<0.05$) after recommendation. KTX maintained stable renal function with a median serum creatinine of 146umol/L.
Conclusion: The presence of transplant pharmacists at the DMC has made significant positive impact on outpatient care of KTX.

P-742 SHORT AND LONG TERM COST-EFFECTIVENESS OF HYPOTHERMIC MACHINE PERFUSION VERSUS STATIC COLD STORAGE IN KIDNEY TRANSPLANTATION

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Introduction: Static cold storage (CS) is the most widely used organ preservation method for deceased donor kidney grafts. Our recently conducted multicenter RCT (Machine Preservation Trial) showed that hypothermic machine perfusion (MP) leads to improved outcome after renal transplantation. We performed a cost-effectiveness analysis for the use of MP versus CS alongside this prospective study.
Methods: The clinical study included 336 consecutive kidney pairs from deceased donors, one of which was assigned to MP and one to CS. An economic evaluation was performed, combining short term results based on data from the study with a Markov model (20-year time horizon) to evaluate long term cost-effectiveness. Patient survival (life years) and quality adjusted life years (QALYs) were the clinical outcomes. Direct medical costs associated with hospital stay, dialysis treatment and complications were included. Data on long term survival, quality of life, and costs were derived from literature.
Results: MP significantly reduced the risk of delayed graft function (OR 0.57) and reduced the risk of graft failure (HR 0.52). Average total costs per patient in the first year posttransplant were €4,896 for MP and €5,309 for CS. The long term analysis showed an incremental cost-effectiveness ratio of minus €51,200 per life year gained in favor of MP. The corresponding incremental cost-utility ratio was minus €111,800 per QALY gained.
Conclusion: Our cost-effectiveness analysis suggests that MP is superior to CS in both the short and the long term. MP is associated with improved short term outcome, better long term survival and lower costs. When deceased donor kidneys are preserved by MP instead of CS, life years and QALYs can be gained while reducing costs at the same time.

P-743 THYROIDIZATION (THYROID-LIKE APPEARANCE) IN RENAL ALLOGRAFTS

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Thyroidization (thyroid-like appearance) in renal tissue, which is made up of a colloid-like hyaline cast formation of Tamm-Horsfall glycoprotein (THP), is a common finding in chronic pyelonephritis and obstructive nephropathy. This type of pathological change is sometimes observed in renal allograft specimens. We examined allograft specimens for thyroidization and other pathological findings related to thyroidization to characterize the conditions causing such changes. One-hundred and three patients, who underwent renal transplantation between January 2006 and April 2008 at Gifu University Hospital (251 renal allograft biopsy specimens) were enrolled in this study. Sixteen patients had thyroidization (11 mild, 4 moderate, 1 severe). In 4 patients, THP reflux on Bowman's capsule was found, and in 3 patients interstitial THP deposits were observed. In 4 patients, tubulointerstitial nephritis was diagnosed. Fifteen of 16 patients were examined for vesicoureteral reflux (VUR) with voiding cystourethrography (VCUG). Three of 15 patients had vesicoureteral reflux. In the past medical histories of the 16 patients with thyroidization, 3 had low capacity bladders, 2 had prostate diseases, and 6 had previous urinary tract infections. In cases of thyroidization with additional findings, including THP reflux into Bowman's space and interstitial THP deposits, we need to examine the patients for the presence of urinary tract diseases. In cases of thyroidization and tubulointerstitial nephritis, urinary tract infections were suspected. Such sub-

clinical urological diseases in the grafts might affect the prognosis of renal function. Therefore, appropriate management of urinary tract diseases is required

P-744 RESULTS OF KIDNEYS TRANSPLANTATION PROCURED FROM EXPANDED CRITERIA DONORS

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Kidney transplantation is the treatment of choice for patients with end-stage renal disease. Organ shortage is the main barrier to offering this treatment to all who need it. Using expanded criteria donor (ECD) organs is one of the strategies for making more transplants available.

Aim: The aim of this study was to assess the results of kidney transplantation procured from expanded criteria donor.

Patients and methods: One hundred and seventy two patients received cadaveric renal transplants between January 1, 2006 and August 31, 2008. Data on donors and recipients were collected. Patient and graft survival, as well as immediate, delayed and slow graft function were analysed. Kidney recipients function was assessed by serum creatinine concentration and creatinine clearance according to Cockroft-Gault formula at seven days, 1, 3, 6, 12 and 24 months post transplantation. The follow-up was completed on November 30, 2008. All patients were followed-up for three to thirty five months.

Results: Average 1-year graft survival was 86.9% for the whole group and mean creatinine concentration was 1.58mg/dl. One case of primary non-function was observed (0.6%). More than 25% of transplanted kidneys were harvested from ECD.

There were no significant differences in patient survival between recipients of standard criteria donor (SCD) and ECD organs. Graft survival was higher in the SCD group than in the ECD group (one-year survival–94.4% vs 62.5%, p=0.004). There were no differences in the incidence of primary non function and delayed graft function between the groups. Recipients of ECD kidneys were more likely to have slow graft function (69.2% vs 37.8%,p=0.033).

Conclusions: There is no significant difference in patient survival between recipients of kidney harvested from expanded and standard criteria donors. Expanded criteria donor kidneys have lower graft survival rates. There is no significant difference in incidence of delayed graft function between recipients of kidney harvested from expanded and standard criteria donors.

P-745 HISTOLOGICAL CORRELATIONS IN PROSPECTIVELY OBSERVED PATIENTS WITH CHRONIC ALLOGRAFT REJECTION/NEPHROPATHY

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Background: As we previously described C4d expression in patients with chronic allograft nephropathy predisposed to progression of histopathological chronic changes within one year period of observation and in these patients proteinuria was significantly Amore reduced after immunosuppression enhancement. No other correlations between histological factors were thus far published in prospective observation in patients with chronic allograft nephropathy/rejection.

Aim of the study: To independently assess correlation between clinical and histological data in patients with chronic allograft nephropathy who underwent baseline and control renal allograft biopsies.

Patients and methods: All clinical and histological factors were thoroughly analyzed in at baseline and control biopsies performed a year after inclusion in 26 patients with clinical features of chronic allograft rejection/nephropathy. Detailed statistical analysis using Spearman Correlations Coefficients was performed.

Results: The results are given in a table.

Conclusions: Observed correlations confirm that younger patients would start with lower creatinine levels and less advanced fibrosis and hyaline change findings and that chronic vascular and interstitial changes are reciprocally dependent. On the other hand surprisingly they point out that younger age predispose to higher baseline and control proteinuria as well as more advanced glomerulosclerosis itself has an impact on control higher proteinuria and control extension of glomerulosclerosis, interstitial inflammatory infiltrates and fibrosis within one year period of observation in patients with chronic allograft nephropathy. Other interesting information may also be deduced.

P-746 CLINICAL RESULTS OF PROLIFERATION SIGNAL INHIBITORS (PSI) BASED THERAPY FOLLOWING CONVERSION FROM ANTICALCINEURINIC (CNI BASED INMUNOSUPRESSION IN RENAL TRANSPLANT RECIPIENTS

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Long-term graft survival is still the great challenge for solid organ transplantation and Mammalian target of rapamycin inhibitors (mTORi, they are useful in chronic allograft nephropathy (CAN)

We analized 46 transplanted patients who were converted from CNI based therapy to PSI immunosuppression. The median conversion time was 6.3 years post-transplantation Tolerance to conversion was evaluated. Renal function was compared against pre-conversion values at 1, 6 and 12 months measuring serum creatinine, calculated creatinine clearance using Cockroft and MDRD formulas, hipertensión and incidente of acute rejection episodes following conversion.

Renal function at 1, 6 and 12 months improved significantly measured by Cockroft method (median value 51 – 61 ml/min at 12 months $p<0.05$ and MDRD (median 43 – 58 ml/min at 6 months $p<0.05$) and serum creatinine median 1.65 mg/dL at 1 month $p<0.05$. At 1 year post-conversion clearance creatinine averaged 59,6 mg/ dL, median 61, improving pre-conversion values p=0,034. Only one of 6 patients experienced a post-conversion rejection episode Four patients (9%) experienced early severe edema, proteinuria unrelated. Seventeen recipients (35%) had de-novo post-conversion proteiniuria. It ocurred one month (mean) post-conversion (58.8% $p<0.05$), and 6 (29.4% $p>0.05$) and 12 (11.8% $p>0.05$) months. No proteinuria ocurred in 46% of patients. Infections ocurred in 11% mainly bacterial. Renal function was predictive of renal function improvement post-conversion (OR 1,06, range 1.01-1.20) age adjusted. CNI withdrawal and PSI conversion leads to significant improvement in one year renal function, with low risk of rejection episodes, however, infectious com-

Abstract P-745 – Table 1. Clinical and histological correlations

	Age	Anuria at transplantation/min creat.	Acute rejection	Baseline creatinine/ aseline proteinuria	Glomerulosclerosis/ inflammatory infiltrate	Fibrosis/tubular atrophy	Arteriosclerosis/hyaline change
Age		/–		/+		–/	/–
Anuria at transplantation				+/	–/		
Min crea	–						
Acute rejection							
Baseline creatinine		+/	+ (p=0.08)				/+ (p=0.07)
Baseline proteinuria	+				–/		/–
Glomerulosclerosis				/+			/– (p=0.07)
Inflammatory infiltrate						/+	
fibrosis	–					/+	+/
Tubular atrophy					/+ (p=0.08)	+/	+/
Arteriosclerosis						+/+	
Hyaline change	–			+/– (p=0.08)	– (p=0.08)/		
Control creatinine			+			+/	/+
Control proteinuria	+			– (p=0.06)/+			
Control glomerulosclerosis					+/		
Control inflammatory infiltrate					+/	+/	
Control fibrosis					+/		
Control tubular atrophy	–					+/+	+/
Control arteriosclerosis							+/+
Control hyaline change							

plications forces us to consider immunosuppression decrease. mTORi adverse effects, mainly proteinuria, may force dose reduction or therapy withdrawal. Renal function prior to conversion was predictive of conversion therapy to PSI.

P-747 COMPLICATIONS OF TRANSPLANTATION OF KIDNEYS PROCURED FROM EXPANDED CRITERIA DONORS

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Organ shortage is the main barrier to kidney transplantation. In order to maximize organ utilization, expanded criteria donor organs have been used increasingly. Expanded criteria donor is defined as a donor older than 60 years or a donor older than 50 years with at least two of the following: hypertension, stroke as a cause of death or serum creatinine greater than 1.5 mg/dl.

Aim: The aim of this study was to assess the number of complicattions after transplantation of kidneys harvested from expanded criteria deceased donors in comparison to organs from standard criteria deceased donors.

Patients and methods: One hundred and seventy two patients received cadaveric renal transplants between January 1, 2006 and August 31, 2008. Data on donors and recipients were collected. Patient and graft survival as well as immediate, delayed and slow graft function were analysed. Kidney function was assessed by serum creatinine concentration and creatinine clearance according to Cockroft-Gault formula at seven days, 1, 3, 6, 12 and 24 months post transplantation. The follow-up was completed on November 30, 2008. All patients were followed-up for three to thirty five months.

Results: Average 1-year graft survival was 86.9% for the whole group and mean creatinine concentration was 1.58 mg/dl. One case of primary nonfunction was observed (0.6%). More than 25% of transplanted kidneys were harvested from ECD.

There were no significant differences in postoperative complications between recipients of standard criteria donor (SCD) and ECD organs.

Complications after transplantation

	SCD	ECD	P
Lymphocele	7.1%	0%	NS
Urinary leak	0.01%	0%	NS
Thrombosis	0%	0%	NS
Urinary tract infection	38.8%	28.6%	NS
CMV infection	14.3%	7.1%	NS

Conclusions: Recipients of expanded criteria donor kidneys experience a comparable rate of complications to recipients of standard criteria donor kidneys.

P-748 INFECTIOUS COMPLICATIONS IN KIDNEY TRANSPLANTATION: A RETROSPECTIVE ANALYSIS OF 114 PATIENTS

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Kidney transplantation (KT) has become a widely, utilized, and successful treatment for end-stage renal disease. Microbial infections, however, are a frequent life-threatening complication of transplantation.

Aim: Is to study the incidence of infections in 114 renal transplant (RT) patients operated between December 1998 and December 2006 in our transplant unit with a follow-up of 1 year.

Material and methods: All the patients received anti-infectious prophylaxis regimen after KT. Induction therapy was given to 94 patients (82.4%) and maintenance immunosuppression consisted mainly in Cyclosporin microemulsion (CyA-me) in 61 patients (53.5%) or Tacrolimus (Tacro) in 49 patients (42.9%) associated to Mycophenolate mofetil (MMF) and Prednisone (Pred). All demographic, epidemiological, medical, and surgical data in this retrospective study were compiled and analyzed by SPSS 13.0.

Results: 56 patients (49.1%) developed a total of 95 infections up to 1 year after KT. Among them, 46 infections occurred in 38 patients during their postoperative hospital stay. Bacterial infections were the most frequent (97.8%) mainly urinary followed by drain infections, central line catheter and pulmonary infections. The most frequently isolated bacteria were *E.coli followed by Klebsiella*, *Acinetobacter and Pseudomonas.* No viral infections were diagnosed. After the hospital discharge up to 1 year, 49 infections occurred in 26 patients. Among these, 79.5% were bacterial infections, mainly urinary tract infections mostly due to *E.coli* in addition to *7* cases of Cytomegalovirus (CMV) infection, 1 herpes infection and 2 cases of fungal infections.

Conclusions: To our knowledge, this is the first Lebanese study that deals with post RT infections up to 1 year in transplant patients. It shows the importance of monitoring these patients and following up on them. Comparison with international data shows similar patterns.

P-749 PELVIC VASCULAR CALCIFICATION IN RENAL PATIENTS AWAITING TRANSPLANTATION – CONTROLLABLE RISK FACTORS A WEST OF SCOTLAND PERSPECTIVE

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Vascular disease is common in patients receiving renal transplants, potentially leading to significant peri-operative complications, reduced transplant function and graft survival. Initially in the transplant assessment phase, pelvic calcification is assessed via a pelvic x-ray. If significant vascular disease is observed a CT Angiogram is requested. The purpose of this study was to ascertain if there any controllable risk factors in the incidence of significant vascular calcification, in our pre-transplant population.

Potential renal transplant patients with 1 or more risk factors for vascular disease were included in the study n=145. Risk factors included diabetes mellitus, hypertension, hyperparathyroidism, smoking history, other vascular disease, and previous transplant. Of those with risk factors 80/145 (55%) have no significant vascular calcification whilst 65/145 (45%) have moderate to severe vascular calcification of the external iliacs as judged by an independent radiologist.

The most significant potentially controllable independent predictor for moderate to severe calcification as found by logistic regression, is of duration of dialysis (OR: 1.1/month p=0.002). Other significant findings related to external iliac calcification are of the initial calcium phosphate product pre dialysis (p=0.01) and the difference between the calcium phosphate product pre dialysis and at the time of x-ray (p= 0.02). Risk factors associated with vascular calcification included vascular disease at other sites (p=0.007) and diabetes mellitus (p=0.05). There also appeared to be an association between the centre of dialysis and the number of patients with vascular calcification.

Our results suggest that the duration of dialysis and the calcium phosphate product pre-dialysis has a bearing on the extent of pelvic vascular calcification. Therefore these factors should be monitored and manipulated. With the hope that pelvic vascular calcification will be reduced, prolonging graft survival in our renal transplant population.

P-750 CHRONIC TRANSPLANT GLOMERULOPATHY – IMPACT ON GRAFT SURVIVAL

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Chronic transplant glomerulopathy is one of chronic lesions developing secondary to chronic, or repetitive injury to glomerular endothelium. It may occur in a response to humoral rejection, cellular rejection or thrombotic microangiopathy. There is limited data about histological and clinical characteristics of that lesion including its impact on graft survival.

The aim of the study was to clinically and histologically characterize TG and its impact on graft survival.

We retrospectively analyzed all 152 cases of chronic transplant glomerulopathy recognized in Transplantation Institute since 1996, and compared it with 86 non-TG cases matched for the stage of advancement of other chronic lesions, such as interstitial fibrosis, tubular atrophy, arteriosclerosis and arteriolar hyalinization. In both TG, and controls all the biopsies were performed due to deterioration of graft function and/or recent onset of proteinuria

Results: In comparison to control TG was associated with significantly lower survival rate (83% vs 49%, $p<0.0001$) higher incidence of proteinuria (34% vs 88%, $p<0.0001$), and higher incidence of HCV infection (45% vs. 33%, p=0.0033). There was no difference in max and last PRA values, nor number of HLA mismatches between two groups. Morphologicaly TG group characterized by higher incidence of C4d deposition in PTC (77% vs 1%, $p<0.0001$),

and glomeruli (66% vs 0%, p<0.0001), as well as an acute transplant glomeurlopathy (14% vs 0%, p<0.0001) and endarteritis ("v", 9% vs 0%, p=0.005). Banff scores for iinterstitial inflammation ("i" and "ti" score), and PTC-itis were significantly higher in TG group than in control (p<0.005 for each parameter)
Conclusions: In comparison to other chronic kidney graft lesions chronic transplant glomerulopathy is associated with poorer graft survival and higher proteinuria, as well as more common C4d deposition in both PTC and glomerular capillaries, and higher scores for interstitial and vascular inflammation.

P-751 KIDNEY TRANSPLANTATION WITH MULTIPLE RENAL ARTERY GRAFTS FROM DECEASED DONORS: PATIENT AND GRAFT OUTCOMES

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Purpose: Kidneys with multiple arteries are frequently transplanted. However, the long-term outcome of such kidneys harvested exclusively from deceased donors is not known. We therefore conducted a retrospective study to determine whether such grafts adversely affect long term graft survival and function.
Materials and methods: The outcomes of 259 consecutive kidney transplantations between 1996 and 2000 were reviewed. We divided the patients into two groups, multiple renal artery graft recipients (group I; n=70) and single renal artery graft recipients (group II; n=189). We compared the short-term complications and long-term outcomes (survival, post-transplantation, blood pressures (BP), creatinine clearance and proteinuria levels at 1, 3, 5 and 7 years post-transplantation) between the two groups.
Results: Early vascular complications were more common in group I than in group II (18.6% vs 7.9%; p=0.02), mainly because of occlusion of a polar artery in group I (7.1%). Urologic complications were not more frequent in group I than in group II (5.7% vs 5.3%; p=0.89). There was no significant difference between the two groups in terms of long-term graft survival (p=0.33) with a median follow-up of 9.05 years (extremes: 0.1 to 12.7 years). Creatinine clearance (59.4±22.6 ml/mn vs 55.9±20.3 ml/mn; p=0.47), proteinuria (0.77±2.1 g/24h vs 0.4±0.8 g/24h; p=0.19) and systolic blood pressures (133.6±14.5 mmHg vs 133.7±17.5 mmHg; p= 0.85) were not significantly different between the two groups 7 years after transplantation.
Conclusions: Our findings suggest that renal transplantation with multiple renal artery grafts does not significantly influence patient and graft outcomes.

P-752 URINARY COMPLICATIONS AFTER RENAL TRANSPLANTATION – SINGLE CENTER EXPERIENCE

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Kidney transplantation is the treatment of choice for patients with end-stage renal disease. Urinary complications used to be common after renal transplantation. Usually ureteral stricture, urine leak or both are observed.
Aim: The aim of this study was to assess the number of urinary complicattions following renal transplantation in our center.
Patients and methods: One hundred and seventy two patients received cadaveric renal transplants between January 1, 2006 and August 31, 2008. Data on donors, recipients and operative technique were collected. Urinary complications were analysed. The follow-up was completed on November 30, 2008. All patients were followed-up for three to thirty five months.
Results: Average 1-year graft survival was 86.9% for the whole group and mean creatinine concentration was 1.58 mg/dl. One case of primary nonfunction was observed (0.6%).
Most of the ureterovesical anastomoses were performed by using the single-stitch technique (81.9%). In 21 cases, anastomoses were completed with Lich-Gregoir technique (12.3%). In two cases, two ureters were found and one anastomosis was completed with single-stitch technique and second with continuous suture in both cases. Eight patients had atypical ureterovesical anastomosis.
Urinary complication was suspected in 7 cases (4.1%). In 5 cases (2.9%) surgical intervention was necessary. Ureteral necrosis was observed in 3 cases (1.7%) and urine leak in the anastomosis in 1 case (0.6%). The anastomosis at re-intervention in these four cases was completed by single-stitch technique. The difference in urinary complications in regard to ureterovesical anastomosis technique was not significant.
Conclusions: Urinary complications are infrequent in our center and independent of the surgical technique.

P-753 MALIGNANT DISEASES IN RENAL TRANSPLANT RECIPIENTS IN SLOVENIA

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Purpose: Renal transplant recipients are at increased risk of malignant diseases. The purpose of this retrospective review was to examine the incidence and mortality from malignant diseases in renal transplant recipients in Slovenia.
Methods: The historic cohort included 658 renal transplant recipients who received 700 renal transplants in the period between January 1984 and December 2007. Non-melanoma skin cancers were excluded from the analysis.
Results: In total, 40 (6.1%) renal transplant recipients developed 44 malignant diseases during the study period. Median time from transplantation to diagnosis of malignant disease was 58 months (range 4 to 179 months; interquartile range 40.5 to 106.5 months). Until the end of the study period 14 recipients (2.1%) died from a malignant disease. Median time from diagnosis to death was 12.5 months (range 0 to 141 months; interquartile range 1.75 to 30 months). Median follow-up of recipients with diagnosed malignant disease who survived to the end of the study period was 22 months (range 0 to 123 months; interquartile range 12 to 51 months). Cumulative incidences of the most frequent malignant diseases reported in our patients are presented in Table.

Table 1. Cumulative incidences and deaths from malignant diseases in renal transplant recipients in Slovenia

Type of malignant disease	Number of malignant diseases diagnosed	Number of deceased recipients
Renal and uroepithelial cancers	9	2
Lymphomas	5	
Cervical cancers	5	
Breast cancers	4	1
Lung cancers	4	3
Other malignant diseases	17	8

Conclusion: Excluding non-melanoma skin cancers, renal and uroepithelial cancers were most frequent reported malignant diseases in our patient cohort. In spite of a relatively low incidence of non-skin cancers, malignant diseases were a substantial cause of mortality. All efforts should be directed towards prevention and early diagnosis of malignant diseases in this specific high-risk group of patients.

P-754 QUALITY OF LIFE AFTER LIVING KIDNEY DONATION IN POLAND – EXPERIENCE OF ONE CENTRE

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Background: Kidney transplantation is the best treatment of end-stage renal disease. The benefits for recipients are obvious. The consequences for living kidney donors appear to be not so clear.
Objective: The objective of this study was to evaluate the quality of life after living kidney donation.
Patients and methods: A total of 66 living donor open nephrectomies were performed in the Department of General and Transplantation Surgery at the Warsaw Medical University between 1995 and 2005. The quality of life was assessed in 32 donors after nephrectomy. The study applied The Satisfaction With Life Scale (SWLS) developed by Ed Diener and colleages (Diener, Emmons, Larsen and Griffin, 1985) adapted in Poland by Juczynski and the questionnaire formulated by Jakubowska-Winiecka, Bieniasz and Domagala. Donor mean age was 46.3 years (range 31 – 69). Observation period ranged from 36 to 156 months after donation.
Results: The mean SWLS score in the investigated group was 22.8 (men – 21.5, women- 23.9). Mean life satisfaction in living kidney donors was comparable to general population in Poland. No donors regretted their decision about kidney donation. Mean pain score after donation was 3.2 in 5-item scale (1-severe pain, 5-mild pain). Medical care was 4.4 and 4.5 in 5-item scale (1-poor, 5-very good) before and after donation, respectively. Mean time of return to work was 3.5 months.
Conclusion: Living kidney donation in Poland has no significant impact on donors quality of life.

P-755 THE ASSESSMENT OF RESIDUAL KIDNEY FUNCTION AFTER LIVING DONOR NEPHRECTOMY

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Background: The number of patients on the waiting list for kidney transplantation is increasing as a result of cadaveric donor shortage. One of the ways to expand the donor pool is living donor transplantation. However, only 2-3% of kidney transplants in Poland are obtained from living related donors.
Aim: The aim of this study was to assess residual renal function and incidence of microalbuminuria in living kidney donors.
Patients and methods: Between 1995 and 2005, 66 living donor open nephrectomies were performed. Physical examination, blood and urine tests and ultrasonography were performed prior to nephrectomy and at every follow-up visit (every 12 months post-op) in the donors. Donor mean age was 40,9 years (range 29 – 60). The donors were predominantly female (52,5%). 27 donors did not report for follow-up visits. Observation period ranged from 36 to 156 months.
Results: Mean creatinine concentration increased from 0,89 mg/dl prior to donation to 1,12 mg/dl and 1,1 mg/dl at 36 and 84 months post nephrectomy, respectively. Mean creatinine clearance according to Cockroft-Gault formula decreased from 94,27 ml/min prior to donation to 80,2 ml/min and 72,2 ml/min at 36 and 84 months post donation, respectively. Microalbuminuria was observed in one patient (2,6%) at 84 months following nephrectomy.
Conclusion: Living kidney donation results in a reduced creatinine clearance in the donor. Follow-up of living kidney donors is essential in determining risk factors for deterioration of residual kidney function.

P-756 HYPERTENSION AND CARDIOVASCULAR DISEASE IN LIVING KIDNEY DONORS IN POLAND – ONE CENTRE EXPERIENCE

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Background: Living kidney donation is one of the few instances in medicine in which a healthy individual undergoes a surgical intervention for the principal benefit of someone else. The short-term complications of living donation are infrequent, making it a safe procedure. However, the long-term risk of hypertension and cardiovascular disease remains uncertain.
Aim: The aim of this study was to evaluate cardiovascular disease and hypertension in living kidney donors.
Patients and methods: A total of 66 living donor open nephrectomies were performed in the Department of General and Transplantation Surgery at the Warsaw Medical University between 1995 and 2005. Physical examination, blood and urine tests, ECG, ambulatory blood pressure measurement, cardiac echography and ophtalmoscopy were performed. Donor mean age was 40,9 years (range 29 – 60). The donors were predominantly female (52,5%). 27 donors did not report for follow-up visits. Observation period ranged from 36 to 156 months.
Results: Two patients (5,1%) were hypertensive before donation. One of them had well-controlled hypertension after nephrectomy. Hypertensive angiopathy on ophtalmoscopy was observed in a 57-year old woman six years after donation. Ten patients (25,6%) developed hypertension after nephrectomy. Hypertension was observed in 14,3% (3/21) women and 38% (7/18) men. Cardiovascular disease (silent myocardial infarction) was observed in a 58-year old man. There was no mortality.
Conclusions: The risk of cardiovascular disease does not increase after living kidney donation. The frequency of hypertension and cardiovascular disease after living kidney donation is lower than in the general population.

P-757 THE LIPID PROFILE OF LIVING KIDNEY DONORS

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Background: Living kidney donation is becoming more significant as the number of cadaveric transplants remains fairly constant and outcomes do not improve due to accumulation of aged patients with long times on dialysis. Only 2-3% of kidney transplants in Poland come from living donors. Lipid profiles of living donors need to be evaluated in order to stratify cardiovascular risk before donation.
Aim: The aim of this study was to assess the lipid profile of living kidney donors.
Patients and methods: Between 1995 and 2005, 66 living donor open nephrectomies were performed. Physical examination, blood and urine tests were performed prior to nephrectomy and at every follow-up visit (36 months and every 12 months post-op). Donor mean age was 40,9 years (range 29-60). There were 21 women and 18 men. 27 donors did not report for follow-up visits. Observation period ranged from 36 to 156 months. Hypercholesterolaemia was defined as total cholesterol concentration $>$ 200 mg/dl. Hypertrigyceridaemia was defined as triglycerides concentration $>$ 150 mg/dl.
Results: Hyperlipidaemia was present in 3 (7,7%) donors prior to surgery. 22 (56,4%) patients developed hyperlipidaemia after donation. Appropriate treatment was initiated for hyperlipidaemia in the diagnosed patients. 15 patients had mild hyperlipidaemia treated by diet modification and 7 patients needed statin administration. No cases of diabetes mellitus were observed.
Conclusion: Follow-up of living kidney donors lipid profile should be included in the work-up as prevention of cardiovascular disease.

P-758 EXCELLENT *VERSUS* INTERMEDIATE EARLY KIDNEY GRAFT FUNCTION AND CLINICAL OUTCOME

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It has been well established that delayed kidney graft function (DGF) is correlated with both worst short and long-term survival of the graft, increased occurrence of acute rejections and increased rate of graft function decline. But, the exact correlation of these outcomes with an excellent (EGF) or intermediate (IGF) early graft function has not been clear.
For that purpose, we designed a retrospective study of 483 patients that were transplanted in our center from 1989 to 2007. EGF was defined as a level of blood creatinine below 3 mg/dL at 5 days post-transplant and IGF the absence of hemodialysis need in the first 7 days.
Percentage of DGF, IGF and EGF were 6,3%, 22,8% and 71% respectively. No correlation was found between EGF/IGF and warm or cold ischemia time. On the other hand, EGF was correlated with lower donor age, less rejections and better GFR. The graft survival (censored to mortality) computed on a Kaplan-Meier graph showed that the patients with EGF had better graft survival that the ones with IGF (99% vs 95% at 12 months, 91 vs 74% at 5 years and 82% vs 67% at 10 years ($p < 0,05$)). This observation maintained statistical significance even when calculations were adjusted for the occurrence of acute rejections as a confounding factor. The kidney graft function was also superior in patients that had EGF (mean GFR: 59,1 vs 44.2 mL/min/1,73m^2 at 3 months, 60,8 vs 46,2 at 12 months and 61 vs 51,7 at 4 years ($p<0,05$)). The GFR was estimated based on the abbreviated ("four variables") MDRD equation.
In conclusion, we ascertained that patients with EGF had significant better outcomes that with IGF.

P-759 PARATHYROID HORMONE IN LIVING KIDNEY DONORS AFTER NEPHRECTOMY

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Background: Living kidney donors lose half of their renal mass in a single surgical event. After this loss, a series of compensations take place. Thus, living

kidney donors offer a unique opportunity to study the metabolic and functional consequences resulting from loss of renal mass.
Aim: The aim of this study was to assess parathyroid hormone (PTH) in living kidney donors after unilateral nephrectomy.
Patients and methods: Between 1995 and 2005, 66 living donor open nephrectomies were performed. Physical examination, blood and urine tests and ultrasonography were performed prior to nephrectomy and at every 12 months post operation. We assessed basal PTH level. Donor mean age was 40,9 years (range 29 – 60). The donors were predominantly female (52,5%). 27 donors did not report for follow-up visits. Observation period ranged from 36 to 156 months post nephrectomy.
Results: Mean creatinine concentration increased from 0,89 mg/dl pre-surgery to 1,12 mg/dl at 36 months and to 1,1 mg/dl at 84 months post donation. Mean creatinine clearance according to Cockroft-Gault formula decreased from 94,27 ml/min before donation to 80,2 ml/min at 36 months and to 72,2 ml/min at 84 months after donating the kidney. One patient (2,6%) had a PTH level elevated to 94 pg/ml at 78 months post operation. His creatinine clearance according to Cockroft-Gault formula was 102 ml/min. We also observed a lowered PTH level in one patient at 52 months after nephrectomy.
Conclusion: Living kidney donation does not result in serious changes in PTH levels in our investigated group. Further study with a longer observation period may be needed to evaluate parathyroid hormone imbalance in the long-term.

P-760 EXPANDED CRITERIA LIVING KIDNEY DONORS – SINGLE CENTER EXPERIENCE

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Using living kidney donor (LKD) organs is one of the strategies for making more transplants available. Results of kidney transplantation are superior when the kidney is obtained from a living donor. It is worthwhile to explain whether expanded criteria living donor kidney acceptance is safe and offers satisfactory recipient outcome.
Aim: The aim of this study was to analyse living kidney donors and to propose the definition of expanded criteria living kidney donor.
Patients and methods: Eighty four one live donor nephrectomies was performed between 2000 and 2007. Mean donor age was 41,3 years. The donors were predominantly female (59,2%). Open nephrectomy was performed in all cases, usually left-sided (71,4%). In 36 (42,8%) cases the harvested kidney was transplanted to a child. We analysed retrospectively the accessible data of seventy six donors. Donor age, body mass index (BMI), hypertension, lipid disorders, gout, nephrolithiasis, vascular abnormalities and past venous thromboembolic disease were evaluated among other things.
Results: We proposed risk factors that may affect both donor and recipient of the kidney. For each factor a specific number of points was assigned. Accordingly, a scale is suggested which defines expanded criteria living kidney donors.

Factor	Points
Age >60 years	2
BMI >25	2
Hypertension	2
Lipid disorders	2
Gout	1
Nephrolithiasis	1
Kidney disease	1
Family history of diabetes mellitus	1
Smoking history	1
Psychiatric disorders	1
HBV or HCV infection	1
Venous thromboembolic disease	1
Kidney cysts	1
Vascular abnormalities	1

Kidney donors were divided into two groups – optimal donors (0-5 points) and expanded criteria donors (more than 5 points). Seven cases (9,2%) of expanded criteria living kidney donors were observed according to the proposed definition.
Conclusion: A comprehensive system of living kidney donors evaluation as well as an assessment of influence of expanded living kidney donor factors on short- and long-term donor outcome and recipient and graft survival are necessary and shall be conducted in the future.

P-761 EARLY POSTOPERATIVE COMPLICATIONS OF EXPANDED CRITERIA LIVING KIDNEY DONORS NEPHRECTOMIES

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Organs from living donors with expanded criteria (ECLD) are one of the way to increase the number of transplantations. In recent years, these criteria have widened. Although the term “donor with expanded criteria” appeared a few years ago, there is no comprehensive definition of this status.
Aim: The aim of this study was to analyse early postoperative complications of living kidney donors with expanded criteria versus optimal donors' postoperative complications.
Patients and methods: The records of 76 living donors of 84 operated on between 2000 and 2007 were reviewed. Those included age, BMI, hypertension, and lipid disorders as major risk factors (assigned 2 points each), and gout, nephrolithiasis, nephrocysts, renal disorders in the family, diabetes, smoking history, HBC and HCV infections, venous thromboembolism, mental health disorders and vascular abnormalities as minor risk factors (assigned 1 point each). Patients were divided into two groups. The group of optimal patients (0-5 points), and group of extended criteria patients (6 points and more). According to this there were 69 patients in the fist group, and 7 patients in the second group.
Results: There were three patients with diagnosed complications in the expanded criteria group (42.8%), and twenty two patients with diagnosed complication in the optimal group (OLD) (31.9%).

Name of complication	OLD (69)		ECLD (7)		P
	No.	%	No.	%	
Wound infection	5	7.2	1	14.28	NS
Albuminuria	0	0	1	14.28	NS
Postoperative haemorrhage	0	0	1	14.28	NS
Respiratory insufficiency	0	0	1	14.28	NS
Fever	10	14.49	1	14.28	NS
Intraoperative haemorrhage	1	1.44	0	0	NS
Retroperitoneal haematoma	3	4.34	0	0	NS
Ileus	1	1.44	0	0	NS
Peritoneum opening	1	1.44	0	0	NS
Buttock burn	1	1.44	0	0	NS
Urinary infection	4	5.79	0	0	NS
Respiratory system infection	0	0	0	0	NS
Clostridium difficile infection	1	1.44	0	0	NS
Haematuria	0	0	0	0	NS
Hypertension de novo	1	1.44	0	0	NS
Hypertension aggravation	1	1.44	1	14.28	NS

There were no deaths and thromboembolism.
Conclusions: Nephrectomy in living kidney donors with expanded criteria is safe and there is no higher risk of early postoperative complications.

P-762 THERAPEUTIC DRUG MONITORING SAFELY SPARES DOSES OF MYCOPHENOLATE MOFETIL IN MIDDLE-TERM RENAL ALLOGRAFT RECIPIENTS

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Objectives: Short-term therapeutic monitoring of mycophenolic acid (MPA) has successfully enabled minimization of tacrolimus and steroid without increase in adverse events in our institutions. Middle-term outcomes of MPA monitoring were studied.
Methods: Two hundred renal allograft recipients in our institutions were included in this study. All recipients received tacrolimus, mycophenolate mofetil (MMF) and steroid (early withdrawal or chronic). The recipients who underwent MPA monitoring at 1, 2 and 3 years after transplantation (TDM group, n=100) and those who did not undergo MPA monitoring (noTDM group, n=100) were compared for 12 h area-under-the-concentration curve (AUC) of MPA (mcg.hr/mL), MMF dose (mg), MMF dose per body weight (MMF dose/BW, mg/kg), tacrolimus-AUC and serum creatinine. MMF doses in TDM group were adjusted to the target MPA-AUC of 35. MPA-AUC was retrospectively measured in noTDM group as well.
Results: Mean MMF doses at 1, 2 and 3 years posttransplant were 772, 817, 752 in TDM group and 1035, 1028, 812 in noTDM group. Mean MMF doses/BW were 15.8, 15.5, 15.4 in TDM group and 18.7, 19.2, 16.5 in noTDM

group, respectively. MPA-AUC levels were 33.2, 33.7, 34.0 in TDM group and 54.7, 54.1, 39.2 in noTDM group, respectively. MMF doses (/BW) and MPA-AUC were lower in TDM group at 1 and 2 years posttransplant than in noTDM group. There was no difference in tacrolimus-AUC or serum creatinine between the groups.
Conclusions: Middle-term monitoring of MPA resulted in MMF dose sparing and stable exposure to MPA without impairment in allograft function.

P-763 CO-MORBID FACTORS RELATED TO SURGICAL COMPLICATIONS IN 200 KIDNEY TRANSPLANTATION PATIENTS

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Objective: We have studied retrospectively the demographics and different post transplantation morbidities associated with surgical complications in 200 kidney transplant recipients between May 1997 and January 2008
Methods: Patients were divided into 2 groups: Group 1 included 177 patients without surgical complications and Group 2 included 23 patients who had surgical complications.
Baseline demographics and later co-morbidities were analyzed.
Results: The baseline characteristics between the 2 groups did not differ significantly, including types of surgical complications, donor/recipient age and sex, BMI, cause of original renal disease, transplantation date, dialysis duration, sensitization and pre-transplantation diabetes. However significant difference between the 2 groups included: pre and post-transplant hemoglobin level differences (2.6 mg/dl in group 1 versus 4.1 mg/dl in group 2), number of post-transplant transfusions (0.4 in group 1 versus 2.2 in group 2), duration of hospital stay (10.9 days in group 1, versus 17.5 days in group 2), creatinine upon discharge (1.47 mg/dl in group 1 versus 2.7 mg/dl in group 2), death and graft failure at 6 months post-transplant (2 in group 1 versus 2 in group 2 and 3 in group 1 versus 5 in group 2 respectively).
Conclusion: Surgical complications were associated with significant short and long term co-morbidities, including duration of hospital stay, creatinine upon discharge, and death and graft failures at 6 months post-transplantation.

P-764 RISK FACTORS AND EXPECTED CLINICAL OUTCOMES IN KIDNEY TRANSPLANTATION BASED ON 1 YEAR SERUM CREATININE LEVELS

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Objective: This retrospective study delineates the variable risk factors associated with differences in renal function at 1 year post kidney transplantation.
Methods: Records of 183 kidney transplantation patients were reviewed and patients were divided into 4 groups according to serum creatinine levels 1 year post kidney transplantation. Group 1 had creatinine levels <1.1 mg/dl, group 2 had 1.1mg/dl < creatinine <1.51 mg/dl, group3 had 1.51mg/dl < creatinine <2mg/dl, and group 4 had creatinine >2mg/dl.
Baseline demographics and variable risk factors were studied.
Results: Baseline demographics of all groups were similar, including transplantation dates, donor age, donor/recipient sex match, recipient sensitization and pre-transplantation hemoglobin levels.
There were significant differences between the groups according to hospital stay (10 days in group1, 11 days in group 2, 12 days in group 3, and 16 days in group 4), post-transplantation cholesterol (204 mg/dl in group 1, 211 mg/dl in group 2, 238 mg/dl in group 3, and 218 mg/dl in group 4), post-transplantation triglycerides (193 mg/dl in group 1, 195 mg/dl in group 2, 262 mg/dl in group 3, and 174 mg/dl in group 4), delayed graft function (2 in each group)and surgical complications (2 in group 1, 8 in group 2, 7 in group 3, and 1 in group 4).
Conclusion: Serum creatinine level post-transplantation is a powerful predictor of long term graft survival. Although some risk factors associated with graft survival are fixed, others can be optimized.

P-766 BASELINE OSTEOPROTEGERIN LEVELS AS AN INDEX OF PROGRESSION OF CORONARY CALCIFICATIONS FOLLOWING KIDNEY TRANSPLANTATION

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Background: Vascular calcifications are now recognized as a risk factor of death in patients with chronic renal failure (CRF). In CRF and diabetes, osteoprotegerin (OPG) is a potential calcification biomarker and a prognosis factor. We prospectively assessed the evolution of vascular calcifications and osteoprotegerin levels after one year of renal transplantation.
Methods: 83 patients transplanted between 2005-2006 were enrolled and followed-up prospectively during 1 year. Blood samples were collected before (baseline) and one year after renal transplantation for determination of mineral parameters (calcium, phosphate, alkaline phosphatase, parathormone and OPG). Coronary artery calcification (CAC) was measured during the first two weeks after transplantation (baseline) and one year later.
Results: In addition to age and dialysis duration, we identified baseline OPG as a risk factor for the presence of vascular calcifications before transplantation. A predictive threshold of 1008 pg/mL was defined by receiver-operating characteristic (ROC) analysis. Renal transplantation was accompanied by an improvement of mineral metabolism and bone regulating molecules such as OPG. CAC diminished in 11.8%, stabilized in 61.9% and significantly progressed in 26.3% of patients. Factors significantly associated with progression were age and baseline OPG levels.
Conclusion: OPG levels before renal transplantation are associated with coronary calcifications and are an indicator of progression after transplantation.

P-767 COMPARISON OF LONG-TERM POST-TRANSPLANT OUTCOMES IN PATIENTS WITH AND WITHOUT NATIVE ARTERIO-VENOUS FISTULAE FAILURES

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The aim of this study was to trace up the long-term post-transplant results in renal allograft recipients according to native arterio-venous fistulae (NAVF) surgery outcomes in pre-transplant period.
Patients and methods: The study included all patients who underwent NAVF surgery and then first kidney allotransplantation performed in a single transplantation centre from January 1, 1999 till December 31, 2002. Patients were divided into two groups according to NAVF surgery outcomes: group A (n=45, mean age 50±13 years, male/female 27/18) with primarely functioning NAVF; group B (n=39, mean age 51±11 years, male/female 17/22) with NAVF thrombosis episodes. Both groups were compared for renal allograft

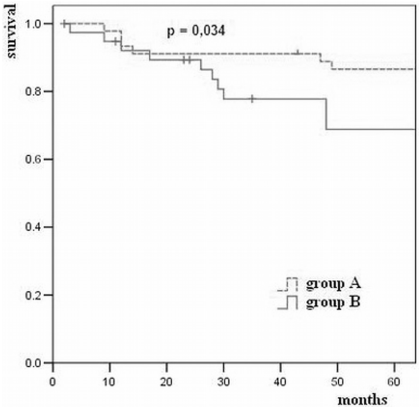

Figure 1. Renal allograft survival.

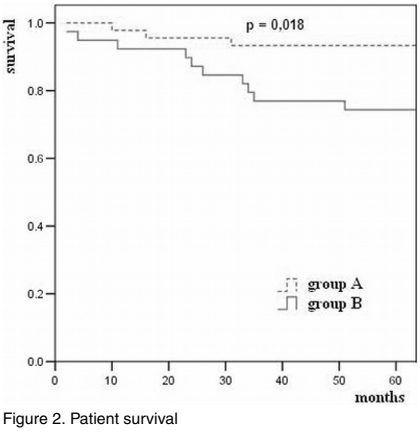

Figure 2. Patient survival

(death-censored) and patient five-year survival and its association with donor factors (age, gender, traumatic/non-traumatic cause of death), cold ischemia time, recipient factors (age, gender, duration of hemodialysis prior to transplantation), development af acute rejection and chronic allograft nephropathy in post-transplant period.
Results: Both graft and patient survival was much higher in patients with primarely well-functioning NAVF (p=0,034 and 0,018, respectively).
Graft loss was associated with development of chronic allograft nephropathy ($p<0,001$) and acute rejection episodes (p=0,057). Analysis of patient death episodes failed to show association with upper-mentioned factors. For functioning grafts there was no significant difference between groups A and B in the level of serum creatinine after 5-year of follow-up (0,16+0,06 and 0,15+0,04 mmol/l, respectively).
Conclusion: Factors that impact native arterio-venous fistula surgery results may impact also post-transplant outcomes. Patients with history of NAVF failure may need more detailed examination prior to renal transplantation and more attention in post-transplant period.

P-768 PREVALENCE AND RISK FACTORS OF UNCONTROLLED HYPERTENSION AFTER KIDNEY TRANSPLANTATION

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Objective: In renal allograft recipients, best practice guidelines recommend target arterial pressure $<$130/80 mmHg. Whether these values are achieved in routine clinical practice is not known. Our aim was to analyze the prevalence and factors associated with the presence of hypertension (HT, $\geq$ 130/80 mmHg) in a large cohort of patients followed annually in our center.
Methods: Blood pressure and renal function (glomerular filtration rate, GFR, urinary 99mTC-DTPA clearance) were evaluated in 456 subjects, 66% male, aged 51$\pm$12 yrs (mean $\pm$ SD) after a median follow-up period of 47 months (range 47-335) post first-kidney transplantation (Tx).
Results: From the 456 subjects, only 33 (7.2%) were normotensive without any antihypertensive treatment, 97 (21.3%) had well-controlled HT and 325 (71.5%) had uncontrolled HT. Among the 325 patients with uncontrolled HT, 69 (15.1% of the whole population) had resistant HT (at least 3 drugs including 1 diuretic) whereas 257 could not be considered as resistant HT since they received $\leq$ 2 antihypertensive drugs (1.3$\pm$0.8). As compared to controlled HT, uncontrolled HT were older (53$\pm$11 vs 50$\pm$12 yrs, p=0.026), received grafts from older donors (45$\pm$16 vs 38$\pm$16 yrs, p=0.001), had lower GFR (51$\pm$21 vs 56$\pm$19 mL/min/1.73m^2), and higher albuminuria (34 vs 19 μg/mL, $p<0.001$ after log-transformation) and fasting blood glucose (5.85$\pm$2.61 vs 5.31$\pm$1.35 mmol/L, p=0.053). No difference was found for gender, dialysis duration, delay after Tx, steroid doses or type of immunosuppression (cyclosporine vs tacrolimus). In multivariate logistic regression analysis, using controlled HT as the reference, the presence of resistant HT was independently associated with higher body mass index, albuminuria and higher donor age.
Conclusion: The major factor associated with persistent hypertension is the inadequation of antihypertensive therapy. However, obesity, albuminuria and older donor age are the main factors associated with true resistant HT.

P-769 POSTTRANSPLANT ENCAPSULATING PERITONEAL SCLEROSIS – ONE CENTRE EXPERIENCE

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Background: Encapsulating peritoneal sclerosis (EPS) is rare but serious complication in patients on peritoneal dialysis (PD). It is defined as intermittent or recurrent intestinal obstruction with or without signs of inflammation and the existence of peritoneal thickening, sclerosis, calcifications and encapsulation. EPS in many cases occurs after withdrawal from PD.
Aim: We describe 4 posttransplant EPS cases occurring in our centre.
Method: From December 1994 to December 2008, some 69 PD patients received kidney transplantation (KT) and 4 of them (3m, 1f) developed EPS. Mean age of all PD patients was 39.9$\pm$12.4 and those with EPS 48.3 (range 42-59) years. RRT duration time of all PD patients was 19.7 (range 1-93) months, while patients with EPS 103.8 (range 56-192) months. EPS patients were maintained on PD for 71.3 (range 56-89) months. All required high volume dialysis to achieve its adequacy (APD), two received icodextrin, all but one were high transporters, one had returning intra-peritoneal bleeding, all received beta-blockers, all had peritonitis incidents (1-2).
Results: Described patients developed severe symptoms of intestinal obstruction, and required surgical intervention within 1-3 months after KT. Diagnosis was based on: clinical symptoms, macroscopic inspection, radiological and histopatological findings. Treatment consisted of: adhesiolysis, parenteral nutrition (PN) (2/4) and tamoxifen. 49 months since EPS diagnosis and after 27 months of PN one patient died. The other live with well functioning grafts (19, 20 and 23 months after KT); one is still on PN, all receive tamoxifen, steroids, tacrolimus and mycophenolate mofetil.
Conclusions: EPS should be considered when bowel obstructive symptoms appear in long term PD patients undergoing KT. These patients may take advantage from such therapeutic measures as adhesiolysis, chronic PN and tamoxifen. Early enrolment to transplantation waiting list should be considered in all suitable PD patients.

P-770 EXPERIMENTAL KIDNEY TRANSPLANTATION IN A SWINE MODEL

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Introduction: For an organ preservation test we developed a model for kidney transplantation in swine pattern.
Method: On the first day kidney withdrawal was done with either UW preservation or Superswine preservation solution, cooled (4 grad Celsius) and implantation was performed 24 hours later. Transplantation was done in intubation anaesthesia with a median lapratomy. Kidney capsular was opened up front and the vessels exposed. Both Kidneys were removed and on one side (depending on the side of the kidney graft; same side implantation) implantation was performed having a 1 to 1.5 centimetre patch on both vessels in end to end technique. Running sutures were done with Prolene 6/0 (veine) and Prolene 5/0 (artery). A zero biopsy was performed after perfusion started. Afterwards implantation of the urety was done on the roof of the bladder with Monocryl 4/0. Closure of the bladder, Kidney capsular and abdomen was done. All animals received triple drug immunsppressive medication (TAC, MMF, Steroids) without induction therapy. Sacrification took place one week later.
Results: 13 swines underwent kidney transplantation whereof two died within the follow-up period (one intraoperative, bleeding, second after two days due to kidney failure). Median operation time was 125 minutes. Complications were: compensated renal failure (3), rupture of abdominal wall (1) In eight animals renal function was satisfying.

P-771 KIDNEYS FROM LIVING DONORS WITH ANEURYSM IN RENAL ARTERY CAN BE TRANSPLANTED, GETTING A GOOD RESULTS FOR DONOR AND RECIPIENT

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Purpose: To review aneurysm in the renal artery in living donors used for transplantation.
Methods: During the study protocol for kidney donation we perform in all donors bilateral renal angiography. From jan 1990 to Dec 2008 we performed 1808 kidney transplant, in a retrospective wiew we had four living donors with renal aneurism in one kidney and one deceased donor with aneurysm, we used those kidneys for transplant. All living donors had no sympotms, the anurysm was a finding during the angiography study. Mean of age was 50 (42-58) years, MAP was 80 (82-92) mmHg. they have no others patological condition for donation.
Results: We transplanted in the four cases the kidney with aneurysm, we did aneurysm resection ex vivo on cold ischemia. (figure 1 and figure 2) All recipients had primary kidney function, one recipient die after 6 years of pancreatitis, one return to dialysis after 2 years and three are alive with normal renal function after 13, 4 and 2 years. All donors are alive with normal renal function after 13, 13, 12, 4 and 2 years.
Conclusions: Incidence of aneurysm in renal artery is low from 0.3 to 1.5% ussually this is a finding during the angiography study, we can transplant these kidneys without risk for donor and recipients solving future pathology in the potential donor and getting a good renal allograft to the recipient after resection of aneurysm on the back table

P-772 QUALITY OF LIFE OF PATIENTS WITH KIDNEY TRANSPLANT IN COMPARRISON TO GENERAL POPULATION

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The aims of the research were to asses the overall quality of life of kidney transplant patients that participated in annual summer and winter World Transplant Games and to compare the results to that of the general population.
The health-related quality of life was assesed using the SF-36 Short Form Health Survey questionnaire on transplant patients (n=13) and on general population (n=16). This is a generic, 36-item instrument that measures health related quality of life, engagement in vigurous activities, family, social and oc-

cupational roles and performance of daily living activities. The questionnaire also explores whether limitations in these areas are because of physical or mental health issues. Scale scores range from 0 to 100; higher scores indicate better physical, mental and social functioning and freedom from pain.We also acquired laboratory results and Work Capacity Test (MET) for TP.
Patients with kidney transplant [TP] identified only slight limitations in the areas of physical functioning and the perception of their general health was lower when compared with general population [GP]. There were no major differeces found in mental health scores and social functioning perception.Their creatinine laboratory values were elevated (avarage of 145 μmol/l) and the values of haemoglobin were within normal limits (average of 132 g/l). The Work Capacity Test results showed that they are able to cope with a relatively high level of physical strain (average of 10 MET).

Results from Short Form Health Survey questionnaire in TP and GP

	Physical	General	Mental	Social
TP ± SD	91,92±11,28	65,31±19,12	79,08±11,21	88,46±14,84
GP ± SD	98,75±3,45	78,13±14,61	78,50±10,70	92,97±9,09
P-value	<0,05	<0,05	N.S.	N.S.

Despite their perception of lesser physical abilities kidney transplant sporstmen showed a high level of physical condition. They mostly feel limited in vigorous activities whereas they do not feel limited in moderate physical strain. A good rehabilitation is achieved after a kidney transplant and patients are able to fully function in everyday life and participate in sports activities.

P-773 POST-TRANSPLANT GLOMERULONEPHRITIS IN LIVE-DONOR RENAL TRANSPLANT RECIPIENTS: CLINICAL COURSE AND RISK FACTORS

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Glomerulonephritis (GN) post transplantation can be either De novo or recurrence of original disease. The major difficulty is lack of histological diagnosis of the native kidney pathology. The reported incidence of recurrent GN is thus judged by clinical suspicion and could be over- or under-estimates of the true incidence. Aim of the work was to study the incidence and impact of GN post-transplantation (De novo or recurrence) on the graft survival.
Material & methods: Out of 2000 transplant recipients (transplanted between 1976 to 2007), 250 patients (157 males, 93 females) suffered from end stage GN (35 mesangial, 22 membranous, 71 FSGS, mesangio-proliferative, 16 crescentic, 48 hereditary, 33 amyloidosis). Kidney donors were 77% related (37% parents, 36% siblings, 5% emotionally related) and 23% unrelated donors. Those groups of patients were compared with the other group as regard graft survival. Patients suffering from post transplant GN were classified into 3 groups according to their histopathological findings of graft biopsy. Graft survival were calculated using Kaplan Meier and compared using log rank test.
Results: 22 patients suffered from recurrent GN, 8 from De-Novo GN and 33 from transplant glomerulopathy. 88% of De-Novo GN suffered from hypertension post-transplant, 79% among transplant glomerulopathy and 59% among recurrent GN (P=<0.01). 50% of DeNovo suffered from diabetes, while only 5% among recurrent GN and 3% among transplant glomerulopathy suffered from diabetes (P=0.167). There was a significant difference in graft survival among the different post-transplant GN groups. Recurrent GN displayed a worse graft survival compared to De-Novo and transplant glomerulopathy GN (P= 0.044).

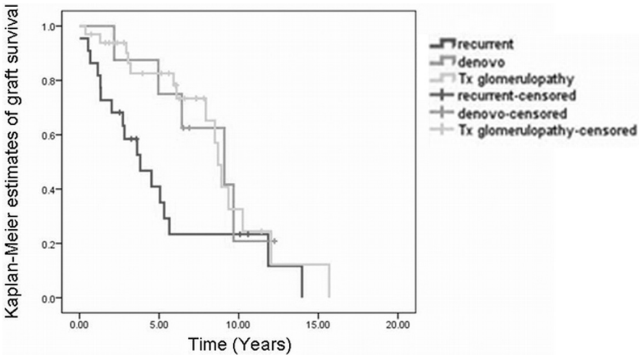

Figure 1

Conclusion: Unfortunate GN does not end by renal failure but it may continue after transplantation. Early identification of Denovo & recurrent GN post-transplantation and consequent management are critical issues for graft survival.

P-774 KIDNEYS RETRIEVED FROM NON-HEART-BEATING DONORS (NHBD) WITHIN THE OVERALL ACQUISITION PROGRAMME: MONOCENTRIC FRENCH STUDY OVER 18 MONTHS

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Purpose: The organ transplant programme has benefited from the steady increase of organs retrieved from brain-dead donors (HBD) [1]. However, there are not sufficient organs to meet a continually increasing demand. Induced by foreign experiments [2], a national protocol to retrieve organs from non-heart-beating donors (NHBD) was introduced in France in 2006. Our hospital volunteered and began NHBD organ retrieval in June 2007.
Methods: Prospective monocentric study measuring characteristics of organ retrieval from non-heart-beating donors for the first 18 months versus that of brain dead-donors during the same period.
Results:

Table 1. Non-heart-beating donors versus heart-beating donors kidneys retrievals

	HBD	NHBD	NHBD/HBD
Potentials donors	84	16	19%
Actual donors	46	6	13%
Kidneys retrieved	92	10	11%
Kidneys transplanted	90	6	6.6%
Age of donors	53 [7-80]	41 [20-54]	
Refusal rate	22%	12.5%	

Conclusions: Despite a lesser yield, this scheme has made it possible to increase the number of transplants in eighteen months in our centre by 6.6%. The results are promising. In addition, family refusal rates seem to be lower, and donors are younger, which allows transplants to younger recipients. The retrieval of kidneys from non-heart-beating donors seems to be a partial but effective solution to the shortage of kidney transplants that we are confronting today.
References: 1. *Rapport d'activite de l'Agence de la Biomedecine*. 2007.
2. Kokkinos, C., et al., *Outcome of kidney transplantation from nonheart-beating versus heart-beating cadaveric donors.* Transplantation, 2007. **83**(9): p. 1193-9.

P-775 DIFFERENT PARAOXONASE-1 (PON1) ACTIVITIES IN CHRONIC KIDNEY DISEASE AND RENAL TRANSPLANT PATIENTS

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Chronic (CKD) and end stage renal disease (ESRD) are coupled with oxidative stress (OS) and would reasonable to suppose normalization of OS parameters after kidney transplantation (Tx). Paraoxonase-1 (PON1) is a high-density lipoprotein-associated serum enzyme that protects lipoproteins from oxidative modifications. The aims of the present study were to evaluate the OS status, measured PON1 activity using a different two-substrate activity methods (paraoxon-POase/diazoxon-DZOase), to assess the relationship between different PON1 activities with renal function (estimated by GFR), markers of chronic inflammation [high sensitive C reactive protein (hs-CRP) and serum amyloid-A (SAA)] and lipids in CKD and Tx patients (pts). The study involved 97 pts: 48 CKD (25 males, aged 38.4±15.4 years, CKD duration 30.7±46.3 months, GFR 30.8±22.3 ml/min/1.73m^2) and 49 Tx pts (31 males, aged 41.9±10.6 years, Tx duration 8.1±3.4 years, GFR 39.6±15.0 ml/min/1.73m^2). Also, 50 controls were involved in the study. The OS/AOD status was estimated by measuring malondialdehyde (MDA) and superoxide-anion (O2*(-)) levels and superoxide-dismutase (SOD) activity. Rates of PON1 activity towards POase and DZOase were measured spectrophotometrically. Both CKD and Tx pts had significantly higher (O2*(-)) levels and lower SOD but higher DZOase activity compared to controls. In Tx pts POase activity was significantly lower (281.78±186.12 vs 429.13± 258.11 U/L) and CI markers were higher although the GFR was better compared to CKD pts. There is no differentiation among other OS parameters between groups. Significant correlation was found between POase activity and age (r=-256), hs-CRP (r=-385) and SAA (r=-236). In conclusion, both examined groups had higher OS compared to controls but POase activity was lower and CI was higher along with better renal function in Tx pts compared to CKD.

P-776 IMPACT OF BALANCED NUTRITIONAL INTERVENTION THERAPY IN LONG TERM GRAFT SURVIVAL OF KIDNEY TRANSPLANT RECIPIENTS RECEIVING MYCOPHENOLAT-MOFETIL (MMF) (THE DALMART-STUDY)

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Background: Data concerning the impact of nutritional support on gastrointestinal side effects in the posttransplant management of kidney transplant recipients receiving mycophenolat-mofetil (MMF) are rare.
Method: 193 kidney transplant recipients with a MMF mono- or combination therapy (MMF AUC target range of 30-60 mg/L.h) were enrolled into a single centre nutritional intervention trial prospectively (median age 52±12 yr). Patients were trained concerning their individual dietetic needs by dieticians and "Gastrointestinal Quality of Life Index (giQoL)" was evaluated at entrance to the study. Clinical parameters for gastrointestinal side effects of MMF were further noted during all the visits every 6 weeks. Laboratory screening of renal function tests (cystatin C, creatinine, urea, blood count) as well as serum albumin and prealbumin was performed on routine basis at every routine control.
Results: Compared to average data at entrance to the study cystatin C values decreased significantly in patients with MMF over a period of 12 months ($p<0.01$). 9 patients suffered from graft failure requiring consecutive haemodialysis. Only one acute transplant rejection were detected according to the BANFF criteria. GiQoL index could be extrapolated in 180 patients for further statistical analysis reaching an average value of 106,5 consistent with an excellent gastrointestinal well-being (with a maximum value of 144). Gastrointestinal side effects were rare, mainly diarrhoe combined with abdominal pain. Only one of 180 patients had to switched to a MMF free immunosuppressive therapy due to gastrointestinal side effects.
Summary: MMF in combination with a balanced nutritional intervention therapy can positively influence graft function as well as quality of life in kidney transplant recipients.

P-777 THE MDRD AND COCKCROFT-GAULT FORMULAS FAIL TO CORRECTLY DETECT A FAST GLOMERULAR FILTRATION RATE DECLINE IN RENAL TRANSPLANT RECIPIENTS

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Introduction: The ability of the MDRD and Cockcroft-Gault (C-G) formulas to predict the GFR evolution remains to be evaluated. The aim of our study was to assess the performances of these formulas to detect a fast decline of inulin-measured GFR.
Methods: All patients from our cohort of kidney recipients who underwent at least 3 inulin clearances, between 1994 and 2007 were restrospectively selected for the analysis. A serum creatinine measurement was performed at the beginning of each inulin clearance procedure (IDMS-traceable enzymatic assay). The GFR evolution, defined as the slope of the linear regression line, was determined for the inulin clearance, the MDRD and the C-G formulas. The sensitivity to detect a slope less than -1 mL/min/1.73m/year was determined, as these patients were considered to suffer from a fast GFR decline.
Results: Two hundred and seventy two patients were finally selected, corresponding to a total of 872 inulin clearance procedures with the following characteristics: they were mainly males (sex ratio 2.3), with a mean age of 49 years old and a mean body mass index of 24 kg/m. The mean GFR was 48 mL/min/1.73m, as MDRD and C-G formulas overestimated it (53 and 61 respectively). The overall GFR slope was -0.1 mL/min/1.73m/year as the mean MDRD and C-G slopes were -0.3 mL/min/1.73m/year and -0.2 mL/min/1.73m/year. The sensitivity to detect a GFR slope of -1 mL/min/1.73m/year was 65% [56-74] and 66% [57-75] with the MDRD and C-G formulas.
Conclusions: This study shows that about one third of the patients who exhibited a fast GFR decline were not detected with the two recommended creatinine-based GFR estimates.
The estimation of the GFR slope with the creatinine-based estimates should be use with caution in the renal transplant population.

P-778 USE OF HIGH DOSE HUMAN IMMUNOGLOBULIN IN HIGHLY SENSITIZED PATIENTS ON KIDNEY TRANSPLANT WAITING LIST – ONE CENTER EXPERIENCE

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Introduction: Waiting time for kidney in patients (pts) with high anti-HLA titers is much longer because of of the additional immunologic barrier. Intravenous infusion of pooled human immunoglobulin (IVIG) is immunomodulatory, neutralizes circulating Ab, reduces AR – all improve long-term outcome of Tx.
Methods: 10 adult ESRD pts listed for kidney Tx, aged 29-52, highly sensitized to HLA (historical PRA >80% and current 56-100%) were selected for high dose IVIG (1g/kg monthly for 4 Mo). Mean waiting time on list was 7.5y. Anti-HLA titers were monitored monthly by CDC before each and after last IVIG. Upon completion pts were put on urgent list and monitored as to Tx, incl. renal function and AR episodes.
Results: 9 pts completed the study. 1 pt was transplanted after 1st IVIG, and remaining pts (N=8) received all 4 doses. PRA did not change in 3 pts, in 5 pts was reduced by 8-28% (mean 14.4%). During 6 Mo follow-up 4 pts were considered for Tx (neg. crossmatch), 3 received Tx (1 disqualified – infection). Recipients received induction (ATG N=2; basiliximab N=2) and tacrolimus+mycophenolate+steroids as baseline immunosuppression. Protocolar biopsies (1, 3, 6 Mo) were performed in 3 pts (1 denied a consent). On biopsy: 1 pt – AR free, 1 pt – vascular AR II B acc. to Banff '05 (treat.: steroids, ATG, IVIG), 1 – humoral AR with thrombotic microangiopathy (treat.: steroids, IVIG). Mean creatinine was 1.5 mg/dL 1 year after Tx (range 1.0-1.9).
Conclusions: High dose human IVIG poorly reduces PRA in pts awaiting renal transplant. It is advisory to perform protocol biopsies in highly sensitized recipients because of frequent AR incl. antibody mediated. Short-term outcome of transplantation is promising.

P-779 RISK FACTORS FOR LOW BONE MINERAL DENSITY IN LONG-TERM RENAL TRANSPLANT RECIPIENTS: A CROSS-SECTIONAL AND LONGITUDINAL STUDY

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Purpose: To investigate potential risk factors for low BMD, we performed a cross-sectional and longitudinal study in long-term (>12months) renal transplant recipients (RTR).
Methods/Materials: BMD was measured at lumbar spine (LS) and hip (FN) by DEXA in 72 RTR (45 males, mean age 45±13years), 83 months post-transplant (median). iPTH, calcium, phosphorus, 25(OH)VitD and $1,25(OH)_2$VitD were also determined.
Results: 56% of women were post-menopausal. 95% of patients were on cyclosporine and all on corticosteroids. 25% of patients had taken corticosteroids before transplantation. iPTH>80pg/ml had 51% of patients. 60% had 25(OH)VitD<30ng/ml while 92% had $1,25(OH)_2$VitD>20pg/ml. Osteoporosis (BMD >2.5SD below peak adult BMD) at LS or FN was diagnosed in 45% of patients and osteopenia in 52%. Women had lower BMD than men at LS (-1.9±1.0 vs -1.7±0.8, p=NS) and FN (-2.5±1.1 vs -2.0±0.7, p=0.037). 64% of women were osteoporotic (87% of post-menopausal). Osteoporotic patients were older (50 vs 40years), had longer transplantation time (126 vs 78months), lower creatinine clearance (62 vs 78ml/min) and lower body weight (BW) (65 vs 75kg). Logistic regression analysis showed that advanced age, low BW and corticosteroid use before transplantation significantly increased osteoporosis risk (odds ratio 13.8, 9.4 and 9.0, respectively). DEXA was repeated in 45 patients after 2 years (median). In those receiving anti-osteoporotic treatment (alendronate or alfacalcidol, 25 in total), BMD was increased at LS (-2.0±1.2 vs -1.7±1.1, p=NS), while it worsened in those without treatment (-1.4±1.1 vs -1.8±0.8, p=0.026). No significant difference was observed at FN.
Conclusions: Osteoporosis is common in long-term RTR. Advanced age, low BW and corticosteroid treatment before transplantation are significant risks for post-transplant osteoporosis. Treatment with alendronate and vitD protects against further bone loss. Patients not receiving treatment should be closely monitored for the occurrence of bone loss.

P-780 SMILE, A NEW MOLECULE INVOLVED IN OPERATIONAL TOLERANCE IN TRANSPLANTATION?

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Background: Chronic injury is poorly influenced by immunosuppression treatments in kidney transplantation. Thus there is a concerted effort in the transplant community to find procedures to induce or to detect immune tolerance in patients under chronic immunosuppression in the hope to obviate the need for life-long exposure to these drugs.
Aim: Our team has studied several biomarkers in order to define set of genes differentially expressed in operationally tolerant patients compared with other

group of patients. In this study, we focus on SMILE, a biomarker of operationally tolerant patients, in order to confirm its potential diagnostic power and its role in the status of the patients.
Materials and Methods, Results: We have identified by microarrays a molecular signature associated with operational tolerance state in drug-free patients with stable graft function. Among the molecules composing this signature, SMILE is overexpressed in the blood of tolerant patients compared to patients with chronic rejection. Function of SMILE is unknown. SMILE contains tetratricopeptide repeats that generally initiate protein-protein interactions. We were able to confirm the microarray data by RT-PCR, showing that SMILE is increased in the blood of operationally tolerant patients and down-regulated in biopsies from patients with chronic rejection. The expression of SMILE was also analysed in different cDNA banks prepared from healthy human tissues and organs and found to be also increased in the human placenta. Moreover, we showed by a double hybrid approach that SMILE interacts directly with the retinoic acid receptor alpha *in vitro*, a key molecule of the signalling pathway of vitamin A that is involved in regulatory T cell differentiation.
Conclusion: We hypothesize that SMILE may increase our understanding of allograft tolerance and may reveal a new pathway of regulation of immune response against the allograft.

P-781 CECAL PERFORATION COMPLICATING DISSEMINATED HISTOPLASMOSIS AFTER KIDNEY TRANSPLANTATION

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Histoplasmosis caused by Histoplasma capsulatum is a progressive widespread fungal infection. It was often described in immunocompromised patients including HIV-infected patients and after solid organ transplantation.
We report herein a case of fatal disseminated histoplasmosis diagnosed in a transplant kidney recipient with a history of lymphatic filariosis.
A 55-year-old man from Ivory Coast received, in December 2005, a renal transplant from his wife with a good early outcome except the occurrence of lymphocele which revealed asymptomatic filariosis. He was admitted in our department three years later for fever, chills, diarrhea, mucosal ulcerations and subcutaneous nodules. At that time, his immunosuppressive therapy included prednisone, tacrolimus and mycophenolate mofetil.
These symptoms appeared 2 months ago with progressive aggravation in spite of the long-term use of broad-spectrum antibiotics. Microbiological culture and skin biopsies were positive for Histoplasmosis. Treatment by itraconazole, introduced after a short course of fluconazole, resulted in a good initial responses knowing that there were indirect features for vertebral, hepatic and deep lymph nodes localizations. Colonic histoplasmosis was also documented after the occurrence of cecal perforation necessitating the resection of the right colon.
The patient died few days later after a sudden respiratory distress.
This case illustrates the severity of disseminated forms of histoplasmosis especially those with late diagnosis and the importance of preventive measures in recipients from endemic areas.

P-782 RISK FACTORS FOR LATE OCCURING PNEUMOCYSTIS JIROVECI PNEUMONIA IN RENAL TRANSPLANT RECIPIENTS: A CASE CONTROL STUDY

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Background: The wide use of prophylactic regimens in the early post-transplant period has dramatically reduced the risk of Pneumocystis jiroveci pneumonia (PCP) in organ transplant recipients. However, there have been recent reports of PCP cases occurring after renal transplantation.
Methods: We conducted a retrospective descriptive and case-control study to determine risk factors for PCP in renal transplant recipients. Each case was matched with 2 controls defined as the patient transplanted immediately before and the patient transplanted immediately after.
Results: Eleven cases of PCP were diagnosed at our institution between January 2006 and March 2007. All cases occurred more than 12 months after transplantation with a median delay of 18 moths [IQR 15-96] between transplantation and PCP. There were 7 males (64%), with a median age of 53 years [IQR 28-73]. Eight patients (73%) had experienced rejection and 90% of the patients were receiving 2 or 3 immunosuppressive drugs as maintenance therapy. At PCP diagnosis, none of the patients was on TMT-SMX prophylaxis and median total lymphocyte counts was 440/μl [IQR 380-540].
Univariate analysis showed that patients with a prior history of rejection and a low total lymphocyte count were at high risk for PCP (OR 14.4 [2.1-inf] and OR 0.42 [0-0.8] per 100 cells/μl increase, respectively).
Conclusions: PCP still occurs late after transplantation in highly immunocompromised renal transplant recipients. In patients with past history of rejection, receiving more than 2 immunosuppressive drugs and with low total lymphocyte counts, maintaining prophylaxis should be proposed over the recommended 3 to 4 months post transplantation.

P-783 ETIOLOGY OF DELAYED GRAFT FUNCTION (DGF) IN RENAL TRANSPLANT RECIPIENTS UNDER DIFFERENT IMMUNOSUPPRESSIVE REGIMENS

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Purpose: DGF or need for dialysis within the first week post-transplant has adverse consequences on kidney allograft subsequent short- and long-term survival. The aim of our study was to determine causes of DGF in kidney transplant recipients receiving three different immunosuppressive protocols.
Material/Methods: The retrospective analysis of the influence of donor, recipient and transplantation variables on the first posttransplant week course was conducted in the recipients of cadaveric kidney, transplanted in our centre between 1998 and 2008 years. During this period, several protocols of immunosuppression (IS) were used: group 1, 102 patients (cyclosporine A+steroids + azathioprine); group 2, 33 patients (cyclosporine A + steroids + mycophenolate mofetyl); group 3, 84 patients (cyclosporine A + steroids + mycophenolate mofetyl + monoclonal antibodies to interleukin-2 receptor, as induction therapy).
Results: Frequency of DGF did not change significantly from group 1 to group 2 and group 3: 28,9% vs. 18,2% vs. 21,4% (χ^2-test). However, frequency of biopsy-proven acute rejection during first week dramatically changed: 56,6% vs. 36,4%* vs. 9,5%*† (*,†$p<0,05$ compared with group 1 and group 2, respectively). In parallel with IS changes, the use of kidneys from NHBD (100% vs. 42%* vs. 13,8%*†), and second warm ischemia time (42,6±33,8 vs. 24,2±14,9* vs. 23,4±9,6* min, M±SD, t-test) were reduced. Nevertheless, the donor age (34±12 vs. 39±20 vs. 42±20* years), frequency of stroke as a cause of donor death (11,5% vs. 11,1% vs. 37,2%*†), duration of pretransplant dialysis (16,1±13,1 vs. 27,9±22,1* vs. 30,8±24,7* months), cold ischemia time (14,4±4,3 vs. 19,7±19,0* vs. 15,7±3,9 hours) were increased.
Conclusion: In spite of reducing acute rejection frequency because of IS strengthening; minimization of NHBD use, improving of operative techniques, the frequency of DGF remains stable. This can be explained by increasing influence of such antigen-independent factors, as donor age, stroke as a cause of donor death and duration of dialysis treatment.

P-784 SPECIFICITY OF ELICITED ANTI-HLA ANTIBODIES IN STABLE RENAL TRANSPLANTED PATIENTS

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Introduction: The chronic allograft injury responsible for premature organ failure is multifactorial and elicited donor and/or non-donor specific anti-HLA antibodies could be involved in its onset.
The aim of this study is to shed light on the role of antibodies in the development of organ failure.
Methods: The humoral anti-HLA immune response was studied before and following transplantation in 35 PRA negative first renal transplant recipients. Antibody screening was performed at time of transplantation and subsequently at regular time points. Panel reactive antibodies (PRA) and single HLA antigen analysis are performed by Flow Cytometry using solid phase assays (kindly

provided by One Lambda, Inc.). Clinical parameters for renal function as well as histological and immunological evaluations are being analysed throughout the study.
Results: The range of enrolment time is 2-24 months with 24 patients at at least 6 months from transplantation. Ten out of 35 patients (28%) developed *de-novo* anti HLA antibodies at different time points. Out of the 9 patients tested, 4 presented both donor specific and non-donor specific class I or class II antibodies while the remaining 5 showed only non-donor specific specificities. Creatinine levels at the time of *de-novo* antibody detection ranged from 56 to 158 μmol/l (112.3±33.2). Interestingly, 2 of the 6 patients, where biopsy at the time of antibody detection was analysed, showed C4d deposition with no graft lesion or function deterioration.
Conclusion: These preliminary results indicate that a high percentage of transplanted patients with stable renal function develop *de novo* anti HLA antibodies precosciously. Interestingly, in all cases non-donor specific antibodies are present. Strategies aimed at modulating both donor and non-donor specific immune response are awaited to definitively determine the clinical role of antibodies in the onset of irreversible graft damage.

P-785 INITIAL EXPERIENCE WITH TRANSPLANT RENAL ARTERY STENOSIS ANGIOPLASTY AND STENTING DOES NOT CONFIRM ANTIHYPERTENSIVE OR RENAL FUNCTION BENEFIT

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Transplant renal artery stenosis (TRAS) affects 1-25% of transplant recipients and may lead to allograft loss. The most common presentation is hypertension or elevated serum creatinine concentration (sC); frequently asymptomatic TRAS is seen on routine Doppler US.
Objective: To evaluate early results of transplant artery angioplasty in our first referrals from a transplant center.
Method: 10 patients (7 male, 3 female, mean age 52.1 years) referred for hypertension (n=3) or elevated sC at various periods post-transplant (4-41 months) were diagnosed with TRAS by Duplex Doppler. All patients underwent balloon angioplasty and 9 had primary stenting. Follow-up ranged between 2 and 21 months with evaluation of arterial blood pressure (ABP), sC, creatinine clearance and number of antihypertensive medications.
Results: Four patients experienced restenosis of transplant renal artery, three required reintervention for refractive hypertension. No significant differences were observed pre- and post angioplasty in mean ABP (106.27 vs 105.36), sC (2.43mg% vs. 2.28m%), creatinine clearance (44.62 vs 46.9mL/min) or number of antihypertensive medications (3.1 vs 3.4). There were no graft losses or deaths, dilatation and stent placement were satisfactory at primary angiography in all patients.
Conclusions: Limited experience with a new group of patients does not confirm encouraging results from other centers in treating hypertension and deteriorating renal graft function secondary to graft arterial stenosis. A greater number of patients may help evaluate the impact of endovascular intervention on long-term graft function which may be influenced by other factors, such as chronic allograft nephropathy, immunosuppressant nephrotoxicity etc. Satisfactory angiographic result is not necessarily reflected by clinical course.

P-786 LIVING KIDNEY DONORS: LONG TERMS OUTCOME

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Due to organ shortage, the patients have to wait on dialysis for a long time prior to transplantation. Living kidney transplantation is a valid option to reduce waiting time. The overall evidence suggest that living kidney donors have survival similar to that non donors and they risk for end stage renal disease is not increased.
Objectives: To analyzed the renal function of living kidney donor, and the long term follow up of them.
Methods: Data of living kidney donors who was regularly followed up between May 1987 and December 2008. We evaluated 740 donors, all of the donor were apt for donation. We examined Creatinine clearance, proteinuria level and blood pressure before and after donation. In all of the cases we suggested a follow up after one month and six month and then annually after nefrectomy. We attempted to contact all donors o determine long-term outcome regarding their remaining kidney.
Results: 740 donors were evaluated according to requirement of the international guides before transplant. We obtained information on 240 (32, 43%), 130 were females. Mean age at evaluation was 41 years (sd) 6 (21-70). Mean level basal Creatinine was 0.89 mg/dl +0.019 (0.5 mg/dl-1, 1 mg/dl) Creatinine clearance) 107 (sd) 25 ml/min, mean proteinuria at basal control was negative. The mean Creatinine after donation was 1 mg/dl (sd) 0, 19 mg/dl, Creatinine Clearance was 90 ml/min (sd) 25 ml/min and proteinuria 0, 25 mg/24 hs. 5 donors became hypertensive (2,08%).
Conclusions: The correct evaluation of donors minimizing their risk of disease and renal failure and minimal risk of hypertension. There is a clear need to monitor the minimal risks with long term of follow up of donors to detect and treat any negatives side effects.

P-787 SKIN CANCER IN POLISH RENAL TRANSPLANT RECIPIENTS (RTR)

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Background: The immunosuppressive treatment necessary for prolonged survival of allografts significantly increases the risk of cutaneous malignancies in renal transplant recipients. Skin cancer following transplantation is an important cause of morbidity in long-term survivors, however the risk for Polish population is unknown.
Objectives: The objective of the research was to determine the skin cancer risk and its clinical features in Polish RTR.
Methods: We linked a population of 916 patients who had received renal transplant in Gdansk between 1980 and 2008 with the histopathological cancer registry, to identify all cancer cases which were registered. Additionally between December 2005 and June 2008 population of 235 patients was screened for skin cancer.
Results: After a mean follow up of 6,3 years 40 of 916 patients developed 58 nonmelanoma skin cancers. The were 14 women and 26 men, with the average age at transplantation 49.4years. The standardized incidence rates for non-melanoma skin cancer were significantly increased ($p<]0.001$). The risk for skin cancer was increased 216-fold compared with the nontransplanted population ($p<0.00001$). The ratio of BCC to SCC was 1.7:1.The highest risk was noted for face in men and the risk increased with time. No significant increase in malignant melanoma was noted. BCC was located mainly on the face, but on covered areas SCC was more common. Patients on cyclosporine had the same predisposition to BCC and SCC, however SCC was commonest in patients who received azathioprine.
Conclusions: The renal transplant recipients in Poland are at significantly increased risk for nonmelanoma skin cancer and must be closely followed throughout their lives by dermatologist. Cancer risk associated with transplantation is higher for sun-exposed than non-sun-exposed regions, even among populations living in moderate climate. The azathioprine in combination with UV and HPV may have direct effect on skin cell DNA.

P-788 PREVALENCE OF ANEMIA IN KIDNEY TRANSPLANT RECIPIENTS AND NON-TRANSPLANT PATIENTS WITH CHRONIC KIDNEY DISEASE

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Background: Anemia is one of the most common complications of chronic kidney disease (CKD). However, the incidence or prevalence of anemia in kidney transplant (KTx) recipients has not been well studied. The aim of this study was to assess the difference of prevalence of anemia in KTx recipients and non-KTx patients with native CKD
Methods: Cross-sectional study of all KTx recipients and non-KTx patients with native CKD (stage 3 to 5 CKD according to the KDOQI classification). Multivariate logistic regression analysis was performed to account for potential confounding variables.
Results: The mean hemoglobin (Hgb) levels were 12.4±2.3 g/dL (13.2±2.3 in men and 11.5±1.9 in women) in 312 KTx recipients; 26% of KTx recipients (12.3% men and 42.6% of women) had Hgb levels <11 g/dL. The mean Hgb levels were 10.7±2.1 g/dL (11.2±2.1 in men and 10.1±1.7 in women) in 1029 non-KTx CKD patients; 57.3% of them (48.5% men and 71.7% of women) had Hgb levels < 11 g/dL. However, KTx recipients with eGFR < 30 ml/min/1.73m^2 had higher prevalence of anemia than non-KTx patient. In both KTx and non-KTx patients, the percentage of patients with anemia increased with the severity of CKD. Compared to non-KTx patients, less KTx recipients with anemia received erythropoietin (52.7% vs 37%, $P<0.05$)

Conclusions: The prevalence of anemia in both KTx and non-KTx patients with CKD were remarkably high, and appeared associated with impaired renal function. The management of anemia in these patients seems inadequate.

P-789 KIDNEY TRANSPLANTATION IN ADULTS WITH AN ILEAL CONDUIT FORMATION – THE ONLY CENTER IN POLAND EXPERIENCE

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Dialyzed patients with serious pathology of the lower urinary tract (LUT) had not been qualified for kidney transplantation in Poland till 1999.
Aim: Prospective study in the only Polish centre, performing this procedure in adults, to compare the results to standard kidney transplantation.
Patients and method: Since 1999 we have performed 22 kidney transplants with an ileal conduit formation as urinary diversion. Out of 17 cadaveric and 5 living-related transplantations 2 ileal conduits had been performed prior to transplantation, 14 others at the time of procedure. Kidneys were positioned up-side down, with ureter anastomosed to ileal loop, fashioned by disecting 17cm of ileum near from caecum; bowel was immediately anastomosed, restoring the digestive tract. The deep end of the conduit was closed, while the other was brought out as a cutaneous stoma. The ureter was then anastomosed to the blind end of the conduit supported by a "pig tail" catheter brought out through the stoma for 10-14 days post transplantation.
Results: During follow-up ranging from 1 to 9 years, all but 3 kidneys survived with excellent function (one kidney was lost due to massive fibrosis of the urether in a patient with severe CMV infection, the second due to massive urinary infection with sepsis-both a year posttransplantation, the third was lost 5 year posttx due to chronic rejection). Several complications like ileus, ureter or loop necrosis, wound infection, hematuria and UTI all were treated succesfully. Mean creatinine level was 1.2mg% for living-related kidney grafts and 1.4mg% for cadaveric kidneys.
Conclusions: Kidney transplantation in patients with urinary diversion through an ileal conduit is a safe and effective procedure in patients with serious LUT pathology. Higher incidence of UTI does not influence graft function.

P-790 THE SKIN CANCER AWARENESS AND QUALITY OF LIFE IN RENAL TRANSPLANT RECIPIENTS

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Background: The renal transplant recipients (RTR) receive long term immunosuppressive treatment, which helps to sustain renal allograft but significantly increases risk of skin cancer. The condition of skin has important effect on patients' quality of life.
Objective: The aim of this study was to assess level of skin cancer awareness and its impact on quality of life in renal transplant recipients.
Methods: From December 2005 to June 2008 a group of 169 RTR (93 males and 76 females) from two Polish transplant centres was surveyed using standardized questionnaires including the Dermatology Life Quality Index (DLQI) questionnaire.
Results: 52,65% of patients considered RTR as high-risk group of skin cancer development – group A, 47,35% of RTR are not aware of the risk – group B. 28,4% of surveyed patients claims that skin cancer awareness has no effect on their life (32,58% in group A; 23,75% in group B); for 60,95% of patients it has small (53,93% in group A; 68,75% in group B)and for 7,69% moderate effect on their life (10,11% in group A; 5% in group B). For a group of 2,37% of surveyed patients skin diseases have very large effect (3,37% – group A, 1,25% group B) and for 0,6% extremely large effect on patient's life (none in group A; 1,25% in group B).
Conclusions: Awareness of the skin cancer and its prevention is still rather poor among kidney transplants recipients. The skin cancer awareness does not deteriorate the quality of life in renal transplant recipients as determined by DLQI.

P-791 TREATMENT OF URINARY COMPLICATIONS AFTER KIDNEY TRANSPLANTATION

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Introduction: Urinary complications after kidney transplantation can lead to graft loss.
We present the different methods of treatment in different clinical situations.
Material and methods: In the period of 1982-2008 we have transplanted 1500 kidneys in our Department, including 70 living related (5%). In this period 103 patients with urinary complications were treated (68 patients transplanted in our department and 35 referred from other transplant centers. In 63 patients complications occurred within 30 days after transplantation-in remaining 40 complications developed later on. Following urinary complications have been observed:
1. Early:
   – Urinary fistula 30
   – Necrosis of the ureter 21
   – Stricture of the urinary anastomosis 10
   – Urinary anastomosis to the peritoneum 2
   – Thrombus in kidney pelvis and the ureter 1
2. Late:
   – Stricture of the urinary anastomosis 39

Methods: The following treatment was performed
– Uretero-vesical reanastomosis
– Resection of the necrotic ureter and secondary anastomosis
– Resection of the ureter at the level of pelvis and anastomosis to the own ureter
– Reconstruction of the ureter with the Boari flop
– Ligation of the ureter and the permanent nephrostomy
– Transcutaneus pyelostomy

Results: In all but one cases good early and late results were obtained with preservation function of the transplanted kidney. In one fatal case the small arterial branch thrombosis resulted of kidney lower pool necrosis and massive urether and pelvis necrosis. Patient loosed the graft. In all other cases good technical and clinical result of performed surgery has been obtained.
Conclusions: Treatment of urinary complications after renal transplantation, need surgical and urological experience of the operating team. Definite treatment should be aimed during reconstructive surgery, since consecutive operations lead to a higher risk of a graft failure.

P-792 GIANT ANGIOMYXOID TUMOUR IN A RENAL ALLOGRAFT: A DIAGNOSTIC DILEMMA

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We report a case of a giant tumour in a failed transplant kidney presenting as an abdominal mass twelve years after transplantation.
A forty four year old gentleman with primary disease of Glomerulonephritis underwent a deceased donor renal transplant (mismatch 1:1:0) from a 32 year old male donor in 1996. He was immunosupressed with Neoral and Prednisolone. He had two episodes of steroid responsive rejection. The transplant failed in 2004 and he recommenced haemodialysis in 2005.
The patient was noted to have a protruding abdomen in January 2008. Examination revealed a large, firm mass arising from the pelvis and extending up to supra umbilical region. An abdominal CT scan showed a mass measuring $14\times18\times21$ cm. It appeared to be arising from the left transplant kidney, encasing the iliac vessels but with a well defined capsule. It was considered benign. Initially, the gentleman declined surgical intervention but consented 9 months later because of pressure symptoms. An initial embolisation of the renal artery was performed prior to surgery. The mass was excised completely in two stages from the iliac vessels with an uneventful postoperative course.
The Histopathologic appearance of the tumour has been discussed at three different UK centres and a final concensus of an angiomyxiod soft tissue tumour has been made. It is a tumour which is difficult to classify but has at least a potential to recur. The patient is well with no signs of recurrence at 6 months follow up.
The only benign tumour reported in a renal allograft is an angiomyolipoma.
This is our first experience of a giant benign tumour completely replacing the renal allograft and presenting as a large abdominal mass. We believe this is the first case of its kind to be reported.

P-793 THE IMPACT OF SKIN CANCER AWARENESS ON PROPHYLACTIC BEHAVIOR AMONG RENAL TRANSPLANT RECIPIENTS

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Background: Renal transplant recipients (RTR) are at significantly increased risk of developing skin cancer due to long – term immunosuppressive treatment. The most important risk factor for the disease, and the only one that depends on patient's behaviour, is exposure to ultraviolet radiation.
Objective: The aim of this study was to assess level of skin cancer awareness and its impact on methods of sun protection among RTR.
Methods: A group of 182 RTR (99 males and 83 females) was surveyed using standardized questionnaire. Before questioning all patients were informed about reasons and methods of sun protection.
Results: 51,65% of RTR considered themselves as a high-risk group for skin cancer development. Only 11,5% were able to fully explain the need of sun protection – skin cancer due to receiving long term immunosuppressive treatment – group A; 40,1% connected the need of sun protection with the skin cancer or with receiving long term immunosuppressive treatment – group B; 48,5% couldn't answer to that question – group C.
As much as 53,85% of patients never apply any sun protection (42,86% – group A; 46,57% – group B; 62,5% – group C). 13,18% of RTR claim to avoid sunlight irradiation (9,5% – group A; 6,85% – group B; 17,04% – group C). Still 54,4% of patients admit to have outdoor hobbies (66,7% – group A; 53,4% – group B; 52,27% – group C). 36,6% of RTR think that if they're tanned they'll look more attractive.
Conclusions: Awareness of the skin cancer and its prevention is still rather poor among kidney transplant recipients. Skin cancer awareness do not correlate with usage of sun protection. All RTR need repetitive educational messages regarding skin cancer performed by healthcare professionals in special transplant patient centres.

P-794 INNOVATIVE AND SUCCESSFUL USE OF KIDNEYS WITH RESECTED SMALL RENAL CELL CARCINOMA OR URETERIC INJURY FOR KIDNEY TRANSPLANTATION

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Aims: Kidneys with small renal cell carcinoma are a possible alternative source of grafts. 65 cases are reported with excellent graft and patient survival.
Methods: Our kidney recovery programme was initiated in 2007. 9 tumour-resected kidney transplants (TRK) have been performed. Mean tumour size in donor kidneys was 2.6cm. Of the 9 cases, 8 were Fuhrman grade I/II renal cell cancers, 1 was a benign angiomyolipoma. 1 other kidney was an ureteric-injured kidney. Transplant outcomes were compared with live-donor (LD; n=28) and deceased-donor (DD; n=32) transplant program in a single-centre during 2007-08. Survival was censored at 31st January 2009.
Results: Donors in the TRK program were older compared with LD and DD. 50% of TRK donors had vascular risk factors (treated hypertension and/or hyperlipidaemia and/or diabetes) compared $<$5% of LD and DD respectively. Mean donor creatinine were $<$80mmol/L in all groups. Recipients receiving TRK were older and had a greater number of HLA-mismatches compared to LD and DD recipients. Recipients of TRK had higher serum creatinine and proteinuria at 6 and 12 months compared with LD and DD recipients (12-month creatinine and protein/creatinine ratio were 184.9mmol/L / 93.1mg/mmol, 150.8mmol/L / 15.3mg/mmol and 129.5mmol/L / 16.5mg/mmol respectively). Despite a 40% incidence of delayed graft function or early urological complications, the death-censored graft survival was 100% in all groups. Urine leak occurred in the early phase of the program and is no longer a problem with improved preparation of the grafts. There was no tumour recurrence.
Conclusions: TRK are a suitable alternative source of kidneys but careful recipient selection and long-term follow-up are essential. Recipients of TRK have excellent outcomes and the higher creatinine and proteinuria at 12 months may reflect the older age of donors and recipients.

P-795 MONITORING OF ANTI HLA-ANTIBODIES IN LIVING RELATED RENAL ALLOGRAFT RECIPIENTS IN EARLY POST-TRANSPLANT PERIOD AND CORRELATION WITH PROTOCOL HISTOLOGY

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Introduction: – Role of antibodies in solid organ allografts rejection is increasingly recognized with development of improved techniques for the characterization of anti-HLA antibodies. A number of studies analyzing the incidence of anti HLA antibodies in patients with graft dysfunction have proved usefulness of their monitoring. However, none of the studies have correlated presence of anti-HLA antibodies with changes in protocol biopsies. Present study evaluated appearance of Class I & II anti-HLA antibodies in immediate post renal transplant period, and correlated it with simultaneous changes in histology in protocol biopsies done during first six months.
Methods: – Sera of 20 consecutive living related renal transplant recipients [mean age 31.0 $\pm$ 8.8 yrs, M:F 13:7, median follow up6 months] were screened for anti HLA class 1 and 2 antibodies by commercial ELISA [GTI Inc., Waukesha, WI, USA] at 1, 3 and 6 months after transplantation. The results were correlated with protocol biopsies and renal function. Forty-eight protocol biopsies were performed. Immunosuppression comprised of Tacrolimus, Mycophenolate and Prednisolone.
Results: – Class I antibodies were found in 25% of recipients, and class II antibodies in 10%. The incidence of acute rejection in these patients was similar to those who did not develop antibodies after transplant [33.3% vs. 28.5%, p=NS]. Two patients had Type III Banff rejection which was associated with presence of antibody. Early chronic allograft nephropathy was seen in 2 patients. One of these patients had Class I antibodies. Serum creatinine at 6 months in patients with anti-HLA antibody was 1.2$\pm$0.6mg% as compared to 1.4$\pm$0.4 mg% in those without antibody [p=NS].
Conclusions: Presence of anti-HLA antibody was associated with severe rejection episodes and may predict development of chronic allograft nephropathy.

P-796 INCIDENCE OF C4D DEPOSITION IN PROTOCOL BIOPSIES IN LIVING RENAL ALLOGRAFT TRANSPLANTATION

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Introduction: Deposition of the complement protein C4d in renal allograft is a sensitive marker of antibody-mediated acute rejection. It is not known whether the humoral pathways can produce subclinical pathology in the graft. The present study assessed the incidence of subclinical humoral rejection by C4d staining on protocol renal biopsies in living donor renal allograft recipients.
Material and methods: From April 2006 to December 2007, 50 renal allograft recipients underwent protocol biopsy within six months after transplant. Stable renal function was defined as serum creatinine $<$1.5mg%. The biopsies were assessed for c4d deposition [Cat B1-RC 4D, Biomedica] by immunofluorescence in addition to the standard histopathology. All patients were followed up for six months.
Results: Mean recipient age was 34.1$\pm$10.7 years, M:F 44:6, mean donor age was 39.8$\pm$11.2 yrs. Forty-one (82%) patients were on tacrolimus & mycophenolate, 8 (16%) on cyclosporine & everolimus and 1 (2%) patient received cyclosporine & azathioprine. All patients received Prednisolone. Two (4%) biopsies showed focal c4d positivity. None of the biopsies stained diffusely for c4d. Histopathologic evidence of humoral rejection i.e. PTC dilation and neutrophil margination was noted in 3 (6%) of the biopsies. Patchy dilation was noted in one (2%) of the biopsies. Five (10%) patients had evidence of subclinical cellular rejection. The mean serum creatinine at the end of six months was 1.16$\pm$0.3 mg%.
Conclusions: The incidence of C4d deposition in protocol biopsies in the early postransplant period is very low. This may be especially true in low risk situations like HLA and ABO compatible living donor transplantation and with the use of current powerful immunosuppressive therapy

P-797 ROLE OF ROUTINE IMPLANTATION BIOPSY IN RENAL TRANSPLANTATION

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Background: Implantation biopsy has been reported to predict graft function. The accuracy of this prediction and the risks of the routine use of this procedure in the clinical setting are unclear.
Aim: To evaluate the accuracy of implantation renal graft biopsy in predicting poor graft function at one year and to evaluate the complications of the procedure.
Methods: 53 adult patients who had cadaveric kidney transplantation successively between March 2006 and October 2007 underwent post-reperfusion implantation renal biopsy using a trucut needle. The biopsies were evaluated for chronic renal pathology using the Banff criteria. The pathology findings were converted into qualitative scores (ranging from 0-3) for each of four aspects i.e. glomerulosclerosis, tubulo-interstitial fibrosis, arteriolar hyalinosis and arteriosclerosis. Total biopsy score (TB) was calculated from the sum of individual scores (maximum score 12). Data regarding the graft-outcome at one year (graft loss or eGFR$<$30) was collected. The biopsy scores of functioning and failed grafts were compared. Data pertaining to the complications of biopsy was also collected.
Results: 53 grafts were included in the study. Chronic graft changes were seen in 33 biopsies. Most had mild changes with median TB scores of 1. At the end of one year, 3 grafts were lost. 4 functioning grafts had a eGFR $<$30. There was no difference in individual and total biopsy scores between functioning and failed grafts (Mann Whitney U, p=0.259). During this period four grafts had biopsy related complications. Two grafts developed AV fistulae, managed with angiography and coil embolisation (1 graft loss). Two grafts needed re-exploration for biopsy-site bleeding. There were no biopsy related deaths.
Conclusions: Routine implantation graft biopsy was not helpful in predicting one year renal graft survival. This could be because significant chronic pathology was infrequent in our study. The procedure was also associated with significant complication rate.

P-798 OPERATIVE INTERVENTION FOR AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY AND LIVER DISEASE: A UK SINGLE CENTRE EXPERIENCE

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Introduction: This study presents a single centre's 5 year experience of laparoscopic kidney and liver deroofings in patients with autosomal dominant polycystic kidney and liver disease (APKD). Recent NICE guidance regarding laparoscopic deroofing of simple symptomatic renal cysts does not address whether this intervention is efficacious in patients with APKD.
Methods: Eleven patients with APKD underwent a total of 17 laparoscopic interventions between September 2001 and November 2006 with a median follow up of 20 months (Minimum follow up of one year). Nine procedures involved laparoscopic deroofings of kidneys only. Four procedures solely de-roofed liver cysts (three on one patient). Four procedures involved simultaneous laparoscopic deroofings of kidney and liver cysts (in three patients). There were no conversions.
Results: Some degree of symptomatic recurrence occurred in 55% of all patients by 12 months and 33% underwent a second laparoscopic deroofing.
39% of all laparoscopic de-roofings suffered from complications. Acute on chronic renal failure occurred in two patients; one of whom required ITU admission (due to acute renal failure induced narcosis). Other complications were persistent port site wound discharge (n=1), chest infection (n=1), pneumothorax (n=1), Pulmonary Oedema (n=1) and PD peritonitis (n=1).
Conclusions:
Laparoscopic de-roofings offers patients short to medium term relief from the intractable pain of polycystic disease. However, complications related to impaired renal function and laparoscopic surgery need to be considered as does the and high rate of symptom recurrence.

P-799 LIVING DONOR KIDNEY TRANSPLANTATION (LDKT)- 10 YEARS SINGLE CENTRE EXPERIENCE

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Background: Kidney transplantation (KT) is considered the best treatment option for most patients with chronic renal failure. Available data show that living donor KT (LDKT) is a viable option in transplantation characterized by better short and long term results. In Poland number of LDKT accounts for only between 2 and 3% of all KT performed.
Aim: We present here 10 years LDKT experience of a single centre between 1999 and 2009. There were 23 LDKT performed, which accounts for 3.3% of all KT in this period.
Results: Most (83%) were living related donor KT. Mean recipient age was 33$\pm$11 years and mean donor age was 48$\pm$7 years. Most donors were women, 15 (65%). In most but 3 cases the LDKT was a first transplant. Mean number of HLA class I and II mismatches was 3.2$\pm$1.3. Mean cold ischemia time was 167$\pm$51 min. and warm ischemia time 37$\pm$36 min. 4 recipients (17.4%) received ATG induction and 3 (13%) daclizumab induction. 34% of recipients were placed on cyclosporin based immunosuppression and remaining 66% on tacrolimus. 59% received mycophenolate mofetil. All recipients received steroids. Delayed graft function was observed in 3 cases and in 4 cases acute rejection was diagnosed.
One year patient and graft survival were both 100%. Five year patient and graft survival were 100% and 93%, respectively. The mean serum creatinine levels at hospital discharge, 6 months, 1 and 5 years after KT were 1.91$\pm$0.4, 1.7$\pm$0.3, 1.55$\pm$0.4 and 1.64$\pm$1.09 mg/dl, respectively.
Conclusions: Our results confirm excellent outcomes reported previously in LDKT. This form of KT should be actively promoted in our country.

P-800 SUCCESSFUL ABO INCOMPATIBLE RENAL TRANSPLANTATION WITHOUT SPLENECTOMY AND/OR LOW-DOSE RITUXIMAB TREATMENT

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Introduction: In Japan, about 30% of living donor renal transplantation were in ABO incompatible setting (ABOi-RT). Previously, we have demonstrated the pathological evaluation of protocol biopsy in ABOi-RT with splenectomy (Spx). Recently, Rituximab (RXM) treatment was taken the place of ABOi-RT/Spx. In our center, Low-dose RXM treatment was adopted in the beginning of 2008. We compared the difference in management at peri-operation and post-discharge between two groups.
Methods: ABOi-RT was performed with Spx in 67 cases between 2002 and 2008, and with RXM in 14 cases. We compared the graft renal function, side effects, the subset of CD19 cells and the histology of the PBx within 1-year post-transplant period.
Results: Two cases of post-thrombotic glomerulopathy have been reported in the 6-month and/or 1-year PBx without episode Bx. All of three antibody-mediated rejection was reversible in 6 episode Bx, however, one of these led to graft loss 5 month after RT. No significant difference in the serum creatinine level and in occurrence of acute rejection was found between two groups. The number of CD19 strongly decreased by first administration of RXM, whereas no change in Spx group. Histological evaluation was needed because of the mixed type of ACR, arteriopathy and CAN, which will affect the therapeutic management. Strong C4d deposition was a non-specific but sensitive indicator for AMR. Especially, the finding of the post-thrombotic glomerulpathy seemed to be risk factor for graft survival in ABOi-RT. The post-operative haemorrhage for Spx and neutrocytopenia for RXM seemed to be a major complication.
Conclusion: ABOi-RT with Spx could be replaced with low-dose RXM, in which treatment lower incidence of CMV viremia and equivarent occurrence of acute rejection were achieved. PBx is useful in early detection of the borderline to mild ACR or CAN.

P-801 BIMODAL DISTRIBUTION OF MAJOR CARDIOVASCULAR EVENTS IN KIDNEY ALLOGRAFT RECIPIENTS

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Cardiovascular disease (CVD) is the major cause of death, both early and late after kidney transplantation.
The purpose of the present study was to determine the distribution of CVD events after kidney transplantation (event-time) and the changes of risk for CVD over the time (hazard-time) in kidney transplant recipients.
We have analysed CVD in 870 kidney transplant recipients from cadaveric donor, performed between January 1984 and December 2006. The mean follow-up time was of 2428 days (SD $\pm$ 1878, min 1 – max 6873 days after transplantation). The study of CVD risk over the time was performed through the fit of hazard function (H(t)). The results were considered statistically significant for a p-value $<$0,05. Statistical analyses were carried out with Stata 10 (Stata CorpLP, Texas, USA) and SPSS 15 (SPSS Inc., Illinois, USA).

A total of 143 patients (16,5%) experienced a fatal (74) or nonfatal (69) CVD after transplantation. We observed an higher frequency of cardiac events (59% of ischemic heart disease), with 15% of cerebrovascular disease, and 22% of peripheral vascular or aortic disease. In our group CVD were distributed in a bimodal manner, with higher incidence in the first post transplant year and a late cluster of CVD, eight years after transplantation. The risk of death (hazard function) for CVD increased dramatically getting over the eighth year of transplant.
This trend of CVD after kidney transplantation may be explained by inadequate evaluation and management of CVD risk factors during waiting list time and, after transplantation, by cumulative effect of traditional and non-traditional risk factors.

P-802 URETERAL STENT PLACEMENT AT ADULT KIDNEY TRANSPLANTATION: SINGLE CENTER EXPERIENCE

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Ureteral Double J stent (DJS) placement at kidney transplantation may reduce stenosis or leakage (S/L) complication rates. However, DJS placement may also increase risk for early urinary tract infection (early UTI; $<$ 3 months after transplant).
Material and methods: We analyzed retrospective data for outcomes in relation to DJS from adult recipients at Gazi University Transplantation Center, Ankara. At our center, DJS placement decision is given by transplantation surgery team during operation. Routinely DJS placements have been performed to all recipients in the operation. Removal of the DJS occurs by the 6th weeks after transplantation. All recipients receive trimethoprim/sulfamethoxazole for 3 months as prophylaxis. Immunosuppressive regiment consists of steroids, calsineurin inhibitors and mycophenoleic acide. In cadaver recipients, ATG 3mg/kg was used at the time of DGF onset.
Results: Among 71 recipients from 2006 to 2008, early UTI was seen in 6 (8,4%), no stenosis and 1 (1,4%) leakage. Mean DJS removal time is 6$\pm$1,5 weeks. Early UTI was seen in 3 out of 6 recipients who have Daibetes, small urine bladder due to long dialysis period (n=2) and augmentation+neurogenic bladder (n=1). In our study group, spontaneous stent migration (n=2) was the only the complications. We have seen crusting (n=1), but no breakage, hematuria, or stone formation.
Conclusion: We saw that DJS placement was not a significant risk factor for early UTI and but also has protective effect for stenosis. Although there is only 1 leakage, in our study group we have not seen any increasing risk factor forroutine DJS placement in adult renal transplantation. Regardless of DJS placement, when the recipient has additional systemic problems like diabetes, infection is becoming long term hurtle.

P-803 RISK OF MALIGNANT NEOPLASMS AFTER KIDNEY TRANSPLANTATION. SINGLE CENTER EXPERIENCE

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Purpose: Posttransplant malignancies have become a serious long-term complication especially for patients requiring intense immunosuppression. Our aim was to assess the role of immunosuppressive protocol type in malignancy incidence, in our experience. Material & Method: We performed a retrospective study on 1000 renal transplants (826 living vs. 174 cadaver donors) performed in our institution between 1992 and 2008. The patients were stratified in regard with the immunosuppressive protocol used and compared in terms of malignancy standardized incidence ratios (SIR), immunosuppression intensity, and the requirement for rejection treatment. Over time, three main immunosuppressive protocols were used: cyclosporine (CyA) + azathioprine (Aza) + prednisone (P) since 1992 (CAP group), CyA + mycophenolate mophetil (MMF) + P since 1998 (CMP group), and tacrolimus (Tac) + MMF + P since 2002 (TMP group)
Results: Seventy six posttransplant de novo cancers and 18 nonmelanoma skin cancers were found on a 5 years follow-up. The overall SIR was 2.47 (95% confidence interval 2.18-2.86). SIR was higher for the CAP group (3.07), lower for the CMP group (1.65), and intermediate for the TMP group (2.37), P$<$0.001. Acute rejection incidence in the first year after transplantation improved with time: 40.26% for the CAP group, 19.86% for the CMP group, and 10.94% for the TMP group (P=0.0241). Among recipients who developed malignancy, the induction with antilymphocyte polyclonal antibody was used in 80% (12/15) of the CAP group, in 86.67% (13/15) of the CMP group, and 61.36% (27/44) of the TMP group
Conclusion: The replacement of azathioprine by mycophenolate mophetil decreases both the standardized incidence ratio of malignancy and the acute rejection rate. Induction with polyclonal antibody is associated with an increased risk for malignancy. The intensity of immunosuppression is directly related to the risk of malignancy.

P-804 IS RENAL BIOPSY OF INTRA-PERITONEALLLY PLACED KIDENY TRANSPLANTS ASSOCIATED WITH AN EXCESSIVE RISK?

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Introduction: Renal transplant biopsy allows adequate diagnosis of graft dysfunction. However it has its complications. Renal transplants are occasionally placed intra-peritoneally particularly in simultaneous kidney pancreas transplantation (SPK). Biopsy from such kidneys is expected to be more challenging and fraught with complications compared to extra-peritoneally placed organs due to the absence of external tamponade.
Aim: Examine the safety and utility of kidney biopsies of intra-peritoneally placed renal (IPK) transplant in the setting of SPK.
Patients and results: All renal transplant biopsies of IPK were performed under ultrasound guidance using an 18 gauge automated biopsy needle. Biopsies were evaluated by light microscopy and further cores were taken if required for adequate pathological evaluation. Patients had bed rest six hours post biopsy with regular observation. If a patient was on warfarin or heparin it was stopped beforehand. However, aspirin was not stopped. All patients had their coagulation profile evaluated before biopsy.
From 1/2005 to 10/2008, 43 biopsies of IPK were performed in 20 patients out of 41 with SPK. All biopsies had adequate material for pathological diagnosis. 24 biopsies revealed rejection, while 19 biopsies revealed other pathological diagnoses (ATN, CNI toxicity). One patient suffered from bleeding that required exploration and 4 patients received blood transfusion (2 of them though because they had a low Hb prior to the IPK biopsy). There were minor episodes of post biopsy haematuria early following the procedure but none was associated with clots in the urine or required catheterisation for retention.
Conclusion: Renal transplant biopsy of intra-peritoneally placed adult kidneys in the context of SPK provides valuable information to aid diagnosis and management of patients, and it is safe, therefore it should not be avoided. However it should be dealt with more cautiously than biopsies from extra-peritoneally placed kidneys

P-805 HEMOLYTIC-UREMIC SYNDROME (HUS)/THROMBOTIC MICROANGIOPATHY (TMA) IN RENAL ALLOGRAFT RECIPIENTS-PROGNOSTIC FACTORS

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Methods: 74 cases of TMA were identified from the histopathology database of Department of Transplantation Medicine and Nephrology in Warsaw (Poland). Archived renal biopsy speciemen and accompanying medical records for each patient were obtained and reviewed. Patients were divided into 2 groups: A (n=32) who developed HUS till 1 month post-transplant and B (n=42) who developed TMA later. Data extracted from each clinical record included: HLA histocompatibility, CIT,treatment of HUS/TMA, infections, type of immunosuppresant drugs. Data extracted from biopsy speciemen included: presence of C4d deposits, PTC inflammatory infiltrates, necrosis of vascullar wall, thrombi presence, tubulitis, chronic vascular,glomerular and interstitial changes and interstitial inflammatory infiltrates. Cox Model was used and HR was estimated. End point was time to restarting hemodialisys
Results: Patients from group A became late dialysis dependent comparing to group B (observation time 108 months, HR =0,33;p$<$0,01). After 70 months of observation 73% of B group patients restarted dialysis and 33% of A group. Risk factors of restarting dialysis despite time of developing HUS/TMA were: thrombi presence (HR=3,076; p$<$0,01), necrosis of vascular wall (HR 3,921; p$<$0,0359), tubulitis (HR 2,373; p$<$0,0492), PTC inflammatory infiltrates (HR 5,467; p$<$0,0273). No correlation with C4d deposits were found
Conclusions: Negative prognostic factors might be connected with coexistance of acute interstitial and/or vascular rejection in renal biopsy speciemen.It can be speculated that histopathology findings usually considered connected with acute rejection should prompt additional clinical management. On the other hand C4d deposits seem not sufficient to unequivocaly diagnosed acute rejection and as a factor C4d did not differentiate our patients. Further investigation is mandatory.

P-806 HORSESHOE KIDNEY: SHOULD BE CONSIDERED FOR TRANSPLANTATION?

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Purpose: As organ shortage has become more severe, organs that not long ago would have been considered unsuitable for transplantation are currently being used. Horseshoe kidney, one of the most common anatomical renal variation, may be transplanted en bloc or they can be split and transplanted to two recipients. The aim of this abstract is to illustrate the split technique in horseshoe kidney transplantation and to report our results.
Material & method: From 1992 to 2008, three split horseshoe kidney grafts were transplanted: one from a related living donor and two from a cadaver donor. In the case of the cadaver donor, fusion anomaly was identified during the organ en bloc procurement process with subsequent back table dissection. In the case of the related living donor, complete investigations included arteriography and retrograde pyelography in order to assess the number as well as the position of the renal vessels and the urinary collecting system anatomy. One graft had 3 arteries reconstructed in a single arterial trunk. The other two grafts had two arteries which were reconstructed by latero-lateral anastomosis. The renal isthmus was sutured after a V-shape incision witch allowed the apposition of the renal capsule over a haemostatic sponge.
Results: All grafts showed immediate function with no intra or perioperative complication. At one-year, the mean serum creatinine level was 1.27 mg./ml
Conclusion: The results of horseshoe kidney transplantation are good, provided that attention is paid to certain technical details. The decision to divide a horseshoe kidney should be individualized, based on urinary collecting system and renal vessel anatomy. Even if horseshoe kidney transplantation requires greater skills and experience from the surgeons compared to conventional kidney transplantation, horseshoe kidneys can be considered a feasible option for transplantation in experienced hands.

P-807 URINARY NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN (Ngal): IS IT A GOOD MARKER FOR KIDNEY GRAFT FUNCTION?

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Introduction: Ngal is a protein present non only on neutrophils but also in epithelial cells of renal tubule. It is an emerging marker of acute renal injury and of subsequent reparative processes. We have studied the evolution of the urinary concentrations of this marker during the first hours after renal transplantation.
Materials and method: We studied Ngal protein in kidney cadaveric donor and recipients submitted to transplant. Urine samples has been taken from cadaveric donor at beginning and end of legal period for death ascertainment and during organ procurement. Urine samples from recipient has been taken 6, 12 and 24 hours after kidney transplantation. Untill now we have processed samples from 5 recipients and 4 donors. The Ngal was determined using a kit Trade Ngal AntibodyShop ELISA.
Results: Donors Ngal values was between 46 – 768 ug/g Creatinine, significantly lower than the observed in 5 recipients (range between 239 – 14,079 ug/g creatinine). In all 5 kidney recipients there was an immediate graft function and marked decrease in Ngal values at 12h and 24h as compared to the observed at 6 h post-transplantation. Our results was: Pz = RO 14079 (6h), 6895 (12h), 3389 (24h). Pz = 4061 AA (6h), 459 (12h), 1077 (24h). Pz.BB = 9869 (6h), 5743 (12h), 2547 (24h). Pz CL = 4596 (6h), 2190 (12h), 239 (24h). Pz SA = 8547 (6h), 1828 (12h), 1389 (24h). In all recipients studied there was normalization of serum creatinine within the first 3 days after transplantation.
Discussion: Preliminary result of our study showed a reduction of Ngal in post transplantation sample previous to creatinine lowering. If this data will be confirmed Ngal may became an early marker of good kidney graft function and ischaemia-reperfusion injury.

P-808 ABO INCOMPATIBLE TRANSPLANTATION WITH MINIMAL THERAPY; AVOIDING IVIG AND POSTOPERATIVE IMMUNOABSORPTION

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Purpose: Blood group incompatible transplantation (ABOi) is increasingly common and gives excellent short and long term results. The modern European regimen includes anti-CD20 therapy, pre- and post-operative immunoabsorption and IvIg (Tyden).In our institution we have moved to minimise this therapy.
Methods: 24 patients underwent ABOi, with a mean follow-up of 332 days. All were given rituximab 375mg/m^2 1 month before transplantation, and were given pre-operative imunnoabsorption or plasma exchange according to baseline titres. Immunosuppression consisted of tacrolimus. mmf and prednisolone. The first 11 patients were given 0.5g/kg IvIgG the day prior to transplantation and only the first 6 patients were given routine post-operative antibody removal.
Results: Graft survival was 100%, with a mean serum creatinine of 126umol/l at follow-up. 6 patients had an espidoe of acute cellular rejection, and 1 had acute vascular rejection; all responded to treatment. There were no episodes of humoral rejection. All titres remained within 2 dilutions of the post-operative value, and all were below 1 in 8 at follow-up.
Conclusion: Therapy for ABOi can be minimised, and both routine ivIgG and post-operative antibody removal can be omitted. Antibody rebound is rare and post-operative antibody monitoring might also be abandonded.

P-809 FRECUENCY AND INFLUENCE OF HEMOCHROMATOSIS GENE MUTATIONS IN KIDNEY TRANSPLANTED PATIENTS WITH OR WITHOUT HEPATITIS C VIRUS INFECTION

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Mutations in HFE gene cause an inappropriate high absorption of iron that induced iron overload and iron deposition in several tissues like liver, pancreas, heart, etc. Iron overload in the liver has been associated with a high risk of hepatocarcinoma and with a high touchiness to viral and bacterial infections.
The aim of this study was to describe the frequencies of HFE mutations in a kidney transplanted population with and without VHC infection, and its influence over liver status parameters.
We selected three populations: two of them of kidney transplanted patients, 60 patients with HCV infection and 56 without HCV infection, and third a control group composed of 50 healthy subjects.
We collected clinical data concerning the liver and kidney status such as Iron, Ferritin, Albumin, Creatinine, Gamma GT, GOT, Proteinuria, %Prothrombine and Bilirrubine.
HFE mutations were determined by PCR-RFLP using DNA from peripheral blood of the patients and controls. Frequencies for controls, transplanted patients with HCV infection and transplanted patients without HCV infection were:

Frequencies of three HFE mutations for controls and transplanted patients with and without HCV infection

	H63D	C282Y	S65C
Controls	0,16	0,02	0,002
Transplanted VHC+	0,17	0,008	0,008
Transplanted VHC–	0,22	0,02	0

We founded no statistical differences respect the frequencies of HFE mutations between controls and patients with or without HCV infection.
On the other hand, comparison of HFE mutation carriers versus no mutation in both groups indicates that any clinical parameter is associated with HFE mutations.

P-810 POST TRANSPLANT RENAL ARTERY STENOSIS – DOES THE SOURCE OF KIDNEY MATTER?

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Background: Transplant Renal Artery Stenosis (TRAS) is a recognised complication after renal transplantation. Known risk factors are long cold ischemia time, deceased donor grafts and kidneys with multiple arteries.
Aim: Identify incidence of TRAS and its risk factors.
Materials and methods: 488 renal transplants were performed from 1/1/2002 to 31/12/2007. Patients with clinical suspicion for TRAS were radiologically investigated to confirm the diagnosis. Recipient age and sex, donor age and sex, cold ischemic time, diabetic status of recipients, source of kidney and number of arteries in patients with TRAS and without TRAS were analysed.
Results: There were 308 male and 180 female recipients. 335 deceased donor (DD), 113 live donor (LD) and 40 donor after cardiac death (DCD) kidney grafts. The mean follow up was 42 months (range 10-83). The mean age of the recipient was 45 years (17 -81) and 46 (23-66) (P = 0.82), donor age 49 years (23-72) and 46 (2-79) (P=0.45), Cold ischemic time 16 hours (3-27) and 14 hours (1-33) (P=0.1), recipients with diabetes 3/16 and 60/472 (P=0.48) in the TRAS and without TRAS groups respectively. The overall incidence of TRAS was 3.2% (16/488). The incidence of TRAS in DCD grafts (12.5%, 5/40) was significantly higher compared to LD grafts (0.8%, 1/113, P=0.001) and DD grafts (2.9%, 10/335, P=0.004). There was no difference in the incidence of TRAS between DD and LD kidneys (P=0.82). The incidence of TRAS was also higher in kidneys with more than one artery compared to single artery

(7.7% vs 2.2%, P=0.008).All patients with TRAS were successfully managed by interventional radiology with no loss of grafts.
Conclusion: Transplanted kidneys from donors after cardiac death and the kidneys with multiple renal arteries have higher incidence of renal artery stenosis post transplantation.

P-811 CORRELATION BETWEEN FIBROSCAN, LIVER BIOPSY AND CLINICAL LIVER FUNCTION IN PATIENTS WTH HEPATITIS C VIRUS INFECTION AFTER RENAL TRANSPLANTATION

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Hepatitis C virus infection (HCV) is the most important liver disease (LD) after renal transplantation. Liver biopsy is the gold standard for the diagnosis and follow-up of LD. The aim of this retrospective study was to evaluate the correlation between Fibroscan, (a new non-invasive method for assessment of liver fibrosis), liver biopsy and clinical data in HCV renal transplants patients. Twenty four HCV/RNA positive patients with previous liver biopsy were selected to perform Fibroscan (transient elastography) and a clinical evaluation of liver function. Fibroscan values were expressed in Kilopascals. Two patients were eliminated by obesity and ascitis and 22 patients were analyzed.
Thirteen patients (60%) with fibrosis F0-F1 (METAVIR) by biopsy and normal liver function showed a mean Fibroscan score of 5kPa (range 2.3-6.8). Three patients (16.6%) exhibited F2 in the biopsy with normal liver function had a score of 8.2 kPa (range 7.3-8.9) in Fibroscan. Three patients (16.6%) with F3 by biopsy and abnormal liver function showed a high Fibroscan score 10.9 (range 10.5-11.6). The last three patients (16.6%) with F4 (cirrhosis) by biopsy and abnormal clinical data showed the highest Fibroscan values 14.2 kPa (range 8.9-18). In summary, in renal transplant patients with HCV the values of Fibroscan seems to be correlated with the degree of fibrosis by biopsy and with clinical liver function. Therefore, perhaps Fibroscan could be useful in the follow-up of these patients with LD. However these results should be anlyzed by caution by the small number and the retrospective nature.

P-812 LONG-TERM OUTCOMES IN RENAL TRANSPLANTATION AFTER MORE THAN 25 YEARS OF GRAFT SURVIVAL

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Background: The aim of this work was to study a cohort of 25 renal transplant recepients (RTC) with more than 25 years (range 25 and 32) of renal graft survival. The main point was to analyze if they have some characteristics or suffer less complications that could explain the better survival in comparison with other studies.
Material and methods: Descriptive study of 25 RTP transplanted between 1969-1983 with graft function more than 25 years later (N=105, 23,8% graft survival). Data of age, sex, cause of death were included as donor and recepients characteristics. Episodes of rejection, malignancy, cardiovascular diseases, graft function and cause of death were considered as long-term outcomes.
Results: The mean donors age was 28,79 years (SD 15,1), male sex in 79,1%, main cause of death was head trauma in 48% followed by brain stroke in 8%. In the recipients, 64% were male, mean age at transplant was 30,36 years (SD 8,41) and the main cause of cronic kidney disease was glomerulonephritis (68%). Two patients died between 25-26 years after transplantation. 23 patients have graft function with a mean follow-up of 27,2 (SD 1,9). The most important complications were cardiovascular diseases 28%. Tumors were present in 44% (skin, gastric, prostate and PTLD of B-origen). 21 RTP had episodes of acute rejection treated with steroid bolus (10 with more than 1). The actual mean creatinine level is 1,4 mg/dL (SD 0,63). Inmunosuppressive therapy was prednisone (n=25), azathioprine (n=14), MMF o MFS (n=10), sirolimus (n=1).
Conclusions: Percentage of outcomes were similar to data obteined from other publications with similar follow-up.
Prevalence of cardiovascular disease and tumors was very high.
The age of donor and recepient is the clue of having obteined these good long-term results in patients inmunosupressed initially with classic treatment.

P-813 POST-TRANSPLANT ANEMIA (PTA) REDUCES LONG-TERM GRAFT AND PATIENT SURVIVAL

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PTA is a common event in renal transplant (Tx) recipients. Etiology of PTA seems to be multifactorial. The effect of PTA on graft oucome is still discussed. The aims of our study were to evaluate, in a retrospective fashion, the incidence of PTA at 1 and 5 years post-Tx, to analyze the correlation between immunosoppressive therapy and PTA and to define the impact of PTA on graft and patient survival.
To this purpose, we evaluated 417 patients (135F, 282M) that received a kidney transplant between 1992 and 2002. Graft function was expressed as estimated creatinine clearance (eCrCl, MDRD formula). In all patients we evaluated heamoglobin (Hb) levels, immunosuppressive therapy and 5 years graft and patient survival.
At 1 and 5 years post-Tx, PTA affected the 29.2% and 28.2 of the patients, respectively. 6.8% and 6.7% of patients at 1 and 5 years post-Tx, respectively, received erythropoietin, while 13.6% and 12.4% of patients received iron supplementation. Hb level in our population was directly correlated with eCrCL ($r=0.25$, $p<0.0001$). Sirolimus (SRL, $\chi^2=9.6$, $p=0.002$) and mycophenolate mofetil (MMF, $\chi^2=3.6$, $p=0.05$) therapy was significantly associated with PTA. Multivariate analysis showed that only MMF was independently associated with PTA (HR2.18; p=0.003).
Anemic patients at 1 year presented a 5 years graft survival of 82.5% versus 92% of non-anemic patients (p=0.02). PTA remained significantly correlated with graft survival also when eCrCl was included in the Cox model (HR 1.62, p=0.01). Patient survival in anemic and non-anemic patients was 94.2% and 97.6% (p=0.01), respectively. PTA was independently associated with patient survival even when age and eCrCl were included in the multivariate analysis (HR 1.78, p=0.03).In conclusion, PTA has a negative impact on both graft and patient survival. Graft function and immunosuppressive drugs are the main variables affecting the onset of PTA.

P-814 DONOR-DERIVED INFLUENCE ON NON-INVASIVE FUNCTIONAL HEMODYNAMIC MEASUREMENTS IN RENAL TRANSPLANTS: A PAIRED KIDNEY ANALYSIS

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Purpose: Donor-related factors have a direct impact on renal hemodynamic and renal function in kidney transplants. We investigated if non-invasive color-coded duplex ultrasound techniques used at present to quantify renal allograft blood flow are appropiate to detect a donor-related influence on transplant hemodynamics.
Methods: 29 consecutive pairs of kidneys transplanted from the same donor to two different recipients were studied under standardized conditions. During the same examination, we measured mean renal resistance index of three different segmental arteries (RI) and dynamic tissue pulsatility index (TPI) and perfusion intensity (PI) of sub-segmental cortical perfusion calculated from sonographic videos over 2-3 heart cycles by an established software algorithm (see Scholbach et al. Transplantation 2005).
Results: Donor age was 53.9 years (mean; range 17-78), 48% were male. Recipient age at examination was 53.4 years (mean; range 30-77). 50% were male. Mean time after transplantation was 2.8yrs (range 0.7-5.5); mean CIT was 10 hours (range 3 to 20), 86% were first transplants, mean eGFR 61.1±23 ml/min. The results of a variance analysis between and within pairs of recipients for renal function and non-invasively measured hemodynamic parameters are displayed in Table 1. Renal function, expressed as eGFR calculated by Cockcroft-Gault formula (GC) of the recipient, was clearly dependent on donor-related factors. There was a trend towards a donor-derived influence on cortical TPI and PI, which was not seen for RI. Analysing only allograft pairs receiving a kidney from an older donor (>55 years) revealed a significant influence on renal function and cortical TPI- and PI-measures.

Variance analysis of donor-dependent influence on allograft function and non-invasive measures of renal hemodynamics in recipient pairs

	Mean squares within pairs		Mean squares between pairs		r - donor dependent		p total/donor >55yrs
	total	donor >55 yrs	total	donor >55 yrs	total	donor >55 yrs	
eGFR CG	339	178	773	762	0.39	0.62	0.02/0.01
TPI	0.36	0.39	0.56	0.87	0.22	0.37	0.12/<0.05
PI	0.20	0.16	0.31	0.44	0.23	0.46	0.11/< 0.05
RI	0.004	0.004	0.005	0.004	0.07	0.07	0.4/0.5

Total: n=29 pairs of recipients; donor age >55 yrs: n=14 pairs of recipients.

Conclusions: Intrinsic donor derived factors, especially in donors >55 years,

determine renal transplant function and renal hemodynamics are reflected by non-invasive measures of cortical blood flow such as TPI and PI but not by RI of segmental arteries.

P-815 CONNECTION BETWEEN COAGULATION PARAMETERS AND GRAFT FUNCTION IN EARLY PERIOD AFTER KIDNEY TRANSPLANTATION

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Introduction: Coagulation disturbances observed in patients with chronic renal failure (CRF) are complex. Successful kidney transplantation (KTx) gives a chance for withdrawal of some of these disturbances. Increase of plasma coagulation inhibitors activity after KTx is the most important effect.
The aim of the study was to analyze relation between plasma coagulation parameters in patients after KTx in early postoperative period and: graft function, duration time of CRF and dialysis.
Material and method: We studied 67 patients who received cadaveric kidney graft from 2005 to 2007. Patients were divided into 3 groups in respect to graft function: immediate (IGF)(N=23), slow (SGF)(N=21) and delayed graft function (DGF)(N=23). Activated partial thromboplastin time (APTT), prothrombin time (INR), fibrinogen and D-dimer concentration as well as activity of antythrombin III, protein C and S, VIII, IX and von Willebrand factor were measured. Blood was collected before surgery and on 1st, 7th and 14th postoperative day. Data was presented as mean±SD.
Results: Most of coagulation parameters values did not differ between IGF, SGF and DGF group. APTT in DGF group was significantly higher in 14th postoperative day than in SGF group (28,6±2,5 vs. 25,9±3,0 s) and in 7th postoperative day in comparison to IGF group (29,4±3,3 vs. 26,8±3,4 s). INR in 7th postoperative day was lower in patients with IGF than in patients with SGF and DGF (1,14±0,16 vs. 1,24±0,14 and 1,26±0,17 respectively). There was no relation between coagulation parameters after KTx and time of CRF or time of dialysis.
Conclusion: Function of transplanted kidney has a weak impact on coagulation in early period after KTx.

P-816 LIVE DONOR KIDNEY TRANSPLANTATION: UPDATING THE OCST SITUATION

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Evidences demonstrated the live-donor kidney transplantation (LDKT) as useful therapy in terminally uremia as well preemptive treatment to avoid dialysis. The aim of this work is to analyse recent changes in performing LDKT respect to preemptive-LDKT (preLDKT) and cadaver-donor kidney transplantation (CDKT) in Centre-South Transplantation Organization (OCST) area including nine Italian Regions.
Methods/Materials: From 2004 to 2008 in OCST were studied: CDKT, LDKT and preLDKT trends; CDKT waiting lists trend and cadaver donor (CD) retrieval activity. All kidney transplantation activity data were also stratified for donor and recipient age groups. Live donors information on performed surgical methods were reported.
Results: 2291 CDKT, 103 LDKTs and 25 preLDKTs were performed in OCST, see table1 also for OCST patients in waiting lists for CDKT at the end of year, transplanted kidneys and their ratio to utilised-CD (decreased from 1,79 to 1,53).

Annual CDKT waiting list, utilised-CD, CDKT and their ratio on u-CD compared with LDKT, pre-LDKT in OCST area

	2004	2005	2006	2007	2008
CDKT waiting lists registered at Dec.31	2619	2655	2521	2648	2427
Utilised-CD (u-CD)	300	249	282	278	286
CDKT	539	424	457	427	440
Ratio CDKT/u-CD	1.79	1.69	1.61	1.53	1.53
LDKT	28	21	20	22	12
pre-LDKT	4	1	6	4	10

Nevertheless, cadaver donor groups over-45 old progressively increased from 2004 to 2008 and mean time in waiting list decreased for over-45 patients (from 835 to 732 days). Laparoscopic nephrectomies from 2004 to 2008 were: 6 (18,7%), 13 (59,0%), 8 (30,7%), 6 (23,1%) and 8 (36,3%). Donor-recipient age groups consistency for CDKT and LDKT are compared in figures 1 and 2.
Conclusion: CD mean age raising up induced a decrease in utilised kidneys from CD and the allocation algorithms considering donor-recipient age compatibility exited in relative increasing CDKT for over-45 recipients, while the majority of LDKT were performed on under-45 recipients giving another treatment opportunity for this group. Considering the well known graft survival and functionality advantages in LDKT, pursuing the minimal surgical risk for live donors, also in OCST area the LDKT could be developed for under-45 and preemptive recipients becoming the alternative treatment to CDKT.

P-817 HLA CLASS-I (ABC) UP-REGULATION IN PERIPHERAL BLOOD CD8+ T LYMPHOCYTE IS A POTENTIAL PREDICTOR FOR ACUTE REJECTION IN RENAL TRANSPLANT

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Background: Kidney transplantation is the optimal renal replacement therapy for most patients with end-stage renal disease. But acute rejection (AR) is a major complication after renal transplantation and the biggest risk factor leads to chronic rejection. No clinical markers of renal rejection have been universally accepted.
Methods: Thirty-seven renal transplant recipients were collected during the period of September 2007 to April 2008. Peripheral blood samples were obtained immediately before the operation. After the transplantation, blood samples were obtained at days 3 and 7 when the patients were still hospitalized, and followed at weeks 2, 3 as well as months 1, 2, 3, and 6 after transplantation. For those patients with AR symptoms, blood samples were collected immediately before the administration of anti-inflammatory regents and at days 3 and 7 after the administration. The levels of HLA class-I (ABC) on the peripheral blood CD8+ T-lymphocytes were measured using flow cytometry.
Results: The levels of HLA class-I (ABC) on the peripheral blood CD8+ T-lymphocyte were consistently elevated during the first three weeks and declined gradually to the levels before the transplantation, afterward tapered and kept stable. There were no significant changes on HLA class-I (ABC) levels among the patients during the routine checkout either before the operation or during the 6-month period after the operation, except one month after the operation ($P<0.01$). However, the levels of HLA class-I (ABC) increased significantly for all 5 patients during the acute rejection episodes (ARE).
Conclusion: This study suggests that the up-regulation of HLA class-I (ABC) on the peripheral blood CD8+ T-lymphocyte can be used as an accurate and reliable indicator in predicting the AR after renal transplantation.

P-818 ASSESSMENT OF LIVER FIBROSIS IN KIDNEY TRANSPLANT RECIPIENTS WITH HCV INFECTION: USEFULNESS OF TRANSIENT ELASTOGRAPHY

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Approximately, 8-28% of renal transplant recipients die due to chronic liver disease and Hepatitis C is the leading cause. Post-transplantation HCV therapy is generally not recommended because of concerns regarding risk for precipitating acute rejection. Liver biopsy still remains the gold-standard to evaluate liver fibrosis. However is an invasive and uncomfortable method, non-free of complications. Transient Elastography (FibroScan) is a simple and noninvasive method to assess liver fibrosis by measuring liver Stiffness in kilopascals (kPa)
Aims: To analyze the applicability of Fibroscan in the assessment of liver fibrosis in Hepatitis C Kidney transplantation. To study if liver biopsy could be avoided using FibroScan
Material and methods: We prospectively assessed the performance of transient elastography in 11 kidney transplant patients diagnosed of hepatitis C. We prospectively study for the length of exploration, the success rate and the elasticity (stiffness).
Results: We studied 11 kidney transplant patients suffering from hepatitis C. The time average from the first transplant was 20,5 years (Range 14-28). 7 out 11 patients have received two or more kidney grafts. In 8 patients the liver function tests were normal. The overall rate of success of Fibroscan was 100%.

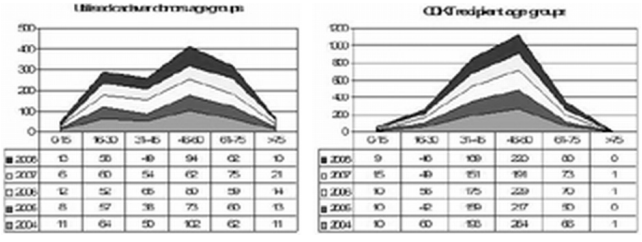

Figure 1

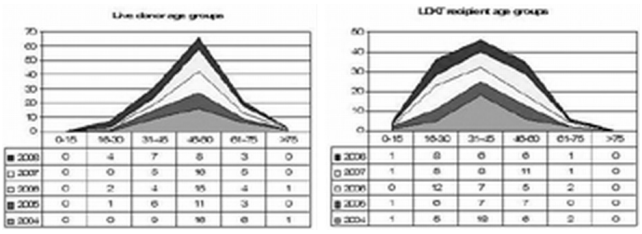

Figure 2

The average duration of the exploration was 260.09seconds, and the stiffness average was 8,1±5,2kPa. Just two patients had a significant liver fibrosis in FibroScan.
Conclusions: Hepatitis C is an independent prognostic factor of survival in kidney transplant. FibroScan is well tolerated and has a high success rate to evaluate liver fibrosis in hepatitis C patients. Liver biopsy could be avoided in cases with no significant fibrosis, using Fibroscan. Fibroscan can select patients with a significant fibrosis to perform liver biopsy and to evaluate the risk of treatment in kidney transplant patients.
This study has been supported by a Research Grant Gerencia SACYL 2008

P-819 LAPAROSCOPIC DONOR NEPHRECTOMY: EFFECTS OF LARGE VOLUME INTRA-OPERATIVE FLUID ADMINISTRATION

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Introduction: Administering large volumes of fluids to minimise the effects of pneumo-peritoneum during Laparoscopic donor nephrectomy (LDN) remains controversial. We intend to ascertain the adverse effects of this practice and ways to minimise the risks in otherwise healthy individuals.
Methods: Medical records were reviewed of 119 consecutive donors who underwent LDN between July 2002 and January 2008. Donors developing pulmonary oedema in the immediate postoperative period were identified using a set criterion. This group of donors were compared to donors with no adverse effects. We also assessed the impact of Oesophageal Doppler used in latter part of the series. Continuous data was analysed using non-parametric tests and categorical data were compared with Chi-squared and Fisher's exact tests.
Results: On average, a donor received 11.9mls/kg/hr of intra-operative fluids to maintain urine output above 100mls/hour as per our protocol. Five (4.3%) donors developed pulmonary oedema in the recovery room needing further treatment. In comparison to the donors with no adverse effects, donors with pulmonary oedema received significantly higher volumes (14.1mls/kg/hr Vs 11.0mls/kg/hr, $p<0.05$) of intra-operative fluids. They received far more colloids (7.9mls/kg/hr Vs 2.2mls/kg/hr, $p<0.001$) and lesser crystalloids (6.9mls/kg/hr Vs 9.6mls/kg/hr, NS). Donors with pulmonary oedema were also found to be older than the other group but showed no statistical significance (57 Vs 46 years). No difference was noted in ASA status, co-morbidities, length of stay, and discharge creatinine. Donors monitored with oesophageal doppler received slightly less fluids than the group with no monitoring (10.2mls/kg/hr Vs 12.8mls/kg/hr, NS) with no difference in recipient outcomes.
Conclusion: Pulmonary oedema as a complication of fluid overload was found to be associated with administration of large volume of colloids in comparison to crystalloids. Intra-operative oesophageal doppler monitoring may help in avoiding these complications by optimising fluid requirements.

P-820 THE IMPACT OF URETER ANASTOMOSIS TECHNIQUE ON UROLOGICAL COMPLICATIONS AFTER KIDNEY TRANSPLANTATION

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Introduction: Urological complications after kidney transplantation can lead to significant post-transplant morbidity, delayed graft function, graft loss and patient death. The choice of technique has been under debate, although it is assumed that both the Leadbetter–Politano and the Lich-Gregoire techniques are equal. In this day and era however, older, more marginal and even donors after cardiac death are accepted for transplantation, which may have an impact on the occurence of urological complications. Aim of this study was to evaluate our experience with these commonly used ureteroneocystostomy techniques including the use of a splint and to compare their influence on the development of urological complications after kidney transplantation after living donation (LD), donation after brain death (DBD) and donation after cardiac death (DCD).
Methods: In a retrospective comparison, patients who received a kidney transplant in our centre between September 2000 and December 2007 were analyzed. Group 1 (n=220) where the Lich-Gregoire technique was used was compared to Group 2 (n=231) with the classic Leadbetter-Politano technique applied. In both groups, incidence and type of complication were documented. Next, the type of anastomosis was tested to detect whether it was a predictor for urological complications.
Results: We found that the overall incidence of urological complications in patients in this cohort (n=451) was 5.5% (n=25). In Group 1 3.2% (n=7) developed urological complications versus 7.8% (n=18) in Group 2 (p=0.03). Complication rates were 2.1% in LD and 7.3% in deceased donors (p=0.03). No significant differences were seen concerning the types of urological complications.
Conclusion: This retrospective analysis demonstrates that in this era of older, more marginal donors and donation after cardiac death the Lich-Gregoire technique has in our hands a significant lower incidence rate of urological complications after renal transplantation compared to the classic Leadbetter-Politano technique.

P-821 RISK FACTOR FOR CHRONIC REJECTION IN RECIPIENTS WITH DE NOVO ANTIBODIES TO HLA ANTIGENS

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Evidence has accumulated that HLA antibodies may be responsible for the chronic failure and graft loss after kidney transplantation. With the recent availability of improved antibody detection methods, we wish to demonstrate conclusively, in a larger series of patients, that the presence of HLA antibodies does indeed predict chronic graft failure. Since only about 5% of functioning patients can be expected to fail in one year, it is difficult in short time to obtain a clear answer on this question.
Prettransplant sera of 273 recipients were obtained and between 1-32,2 years posttransplant. The presences of anti-HLA antibodies were determined with standard CDC and ELISA. Survival curves were estimated using the Kaplan-Meier method. Cox regression model was used to assess the significance of PRA, serum concentration of creatinine and graft survival. All P values are two-sided and considered statistically significant if less than 0.05 (STATA 7.0). 33.3.7% recipients had HLA reactive alloantibodies after transplantation and 73% among those who did not have pre-transplant antibodies. In subset of 180 patients, who did not have pre-transplant antibodies, 1.5% of patients had lost graft in this study period. 93 recipients with incidence of denovo anti–MHC alloantibodies (17.5%) failed. PRA, had statistically significant effect after transplantation for graft lost due to alloantibodies (P =0, 01) and 3.92 relative risk higher in this selected group. Four combination of immunosuppressive therapy (1.CsA+S+I; 2.CsA+S+CC; 3.CsA+S; 4. S+I) used in our transplant center, had statistically significant effect after adjustment. First and third combination of drugs, as compared with second, did increase the risk of graft failure (relative risk 1.79; $P<0.0158$).
Post transplant denovo alloantibodies are risk factor for chronic allograft rejection, suggesting that humoral mechanisms are rather the cause than consequences of chronic rejection.

P-822 SUCCESSFUL DESENSITIZATION STRATEGIES USING LUMINEX PRA IN ABO COMPATIBLE LIVING KIDNEY TRANSPLANTATION – ANALYSIS OF ACUTE REJECTION INCIDENT RATE WITHIN CASES OF NEGATIVE PRA RESULT

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Background: Panel reactive antibody (PRA) has been used for detecting high sensitized recipient with anti-HLA antibodies. Luminex PRA is considered more specific than flow PRA because it can detect donor specific anti-HLA antibody (DSA). The aim of this study is to provide superiority of Luminex PRA to flow PRA in term of predicting acute rejection by analyzing acute rejection incident rate retrospectively.
Method: Between 2000 and 2008, 232 cases of ABO compatible living kidney transplantation were performed in our institute. We had examined PRA test by flow PRA until 2005 (group 1: N=134), and after then examination had changed to Luminex PRA (group 2: N=98). PRA was determined positive when flow PRA was more than 10% or Luminex PRA detected DSA. Positive PRA cases were indicated preoperative desensitization such as double filtrate

plasmapheresis or administration of rituximab, whereas negative PRA cases were performed transplantation without preoperative desensitization. Acute rejection incident rate in negative PRA cases were analyzed and compared between each group.
Result: Totally, PRA was negative in 179 cases (group1: 104 cases, group2: 75 cases). Acute rejection occurred, despite negative PRA, 50 cases in group 1, and 11 cases in group 2. Acute rejection incident rate in negative PRA cases of each group was 48.1% and 14.7%, respectively ($P<0.0001$). Antibody mediated rejection (AMR) incident rate of each group was 11.5% and 0%, respectively ($P<0.0001$).
Conclusion: Avoiding preoperative desensitization on ground of negative PRA failed some cases, especially flow PRA group. This result suggests Luminex PRA could predict acute rejection more accurately than flow PRA. It seems Luminex PRA was superior to flow PRA not only specificity but also sensitivity in term of indication of preoperative desensitization

P-823 THE BURDEN OF MISDIAGNOSED RARE DISEASES IN RECIPIENT OF RENAL TRANSPLANTATION

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Introduction: A sizable number of patients in waiting list for renal transplantation (in our experience about 30%) have a disease of unknown origin, that will lay the transplant on the line. We describe the cases of a single patient and of a large family with unknown end stage renal disease (ESRD) that is correctly classified only after transplantation.
Patients and methods: A 67-year-old female suffered repeated renal colic for unknown causes, she underwent renal transplantation at our center. Following the transplant, there was no graft function recovery with urgency of biopsy.
A family of 100 people with 10 persons with ESRD (3 patients transplanted at our hospital) characterized by tubular-interstitial damage and corticomedullary cysts. We have suspected an uromodulin (UMOD)-associated renal diseases. UMOD hot spot regions were examined in blood samples by DHPLC.
Results: In the first patient renal biopsy and urine specimens showed crystals of unknown origin. Analysis by infrared microscopy showed that they were composed of 2,8-dihydroxyadenine (DHA). Studies on red cells with radiolabelled adenine showed Adenine phosphoribosyltransferase (APRT) deficiency. The patient was treated with allopurinol and a low purine diet with recovery of renal function.
In the large family were analyzed 35 subjects and we found a mutation c263G>A (pGly88Asp) in 17/35 persons, with a remarkable correspondence between genetic mutation and phenotypic renal disease. The renal biopsy showed only an unspecific pattern.
Conclusions: This two cases demonstrate the importance of diagnosis in patient underwent renal transplant. In the first patient the early recognition of APRT deficiency has been important because the correct therapy prevents renal failure caused by nephrotoxic 2,8-DHA crystals. The second case underscores the role of genetic analysis in people with positive history. Furthermore, one of the above reported mutation namely c263G>A has never been described in literature before.

P-824 HEPATITIS C VIRUS INFECTION AND THE OUTCOME OF THE KIDNEY TRANSPLANTATION

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The impact of hepatitis C virus (HCV) infection on the outcome of kidney transplantation is controversial, same as the role of HCV in pathogenesis of arteriosclerosis and cardiovascular events.
The study was conducted on 140 renal allograft recipients. The presence of HCV antibodies was determined by ELISA -III. Thickness of intima-media (IMT) layer as a parameter of the presence of atherosclerotic plaques of the common carotid artery was measured with Doppler ultrasound. All patients were evaluated with their demographic characteristics, post transplant period duration, cold ischemic time, and complete set of serum laboratories.
The mean age of the renal transplant recipients was 41.99 years with the mean post transplant period duration of 59.24 months. The mean age of the donors was 37.25 years. The presence of HCV antibodies was detected in 39.3% (55/140) of the renal transplant recipients.There was no significant difference in the common carotid IMT between HCV positive and HCV negative recipients (right: 0.69 ± 0.10 vs. 0.68 ± 0.13 mm, $p=0.818$, left: 0.71 ± 0.11 vs. 0.70 ± 0.11, $p=0.732$). HCV positive recipients were characterized with significantly longer post transplant period duration (68.67 ± 39.88 vs. 52.99 ± 29.77 months, $p=0.009$) and significantly higher serum levels of AST (27.92 ± 14.76 vs. 21.57 ± 12.14 U/L, $p=0.008$) compared to HCV negative ones. There were no significant differences between HCV positive and HCV negative patients regarding to their and donor's age, cold ischemic time, blood cell counts, serum levels of urea, creatinine, glucose, proteins, lipids, ALT, bilirubin, CRP, diuresis, and proteinuria.
There was no association between HCV infection and carotid intima-media thickness in the renal transplant recipients. Larger cohort studies are needed to elucidate the role of HCV infection on long term patient and graft survival.

P-825 ELDERLY LIVE KIDNEY DONORS: SAFETY ON LONG-TERM FOLLOW-UP

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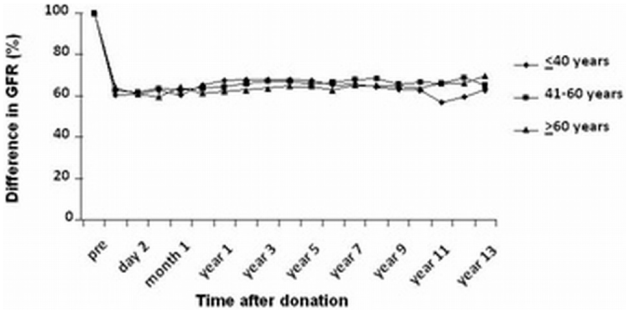
Purpose: Renal transplantation is the optimal treatment for patients with end-stage renal disease. Questions have risen about the outcome of elderly kidney donors and especially the decline in glomerular filtration rate (GFR) after donation. The aim of the study was to evaluate long-term renal outcome after live kidney donation in elderly kidney donors.
Methods: From 1994 to 2006 follow-up data of 539 consecutive live kidney donations were prospectively collected. Patients were categorized into three groups, based on age: $\leq$40 (n=162), 41-60 (n=260), $\geq$60 (n=117). Standard follow-up consisted of yearly serum creatinine, GFR (MDRD-formula), blood pressure measurements.
Results: Older patients had a lower GFR pre-donation compared to middle-aged and young patients (80, 91, 102 ml/min respectively, $p<0.001$). During a median follow-up of 5.5 years, mean maximum decline in GFR was $38\pm9\%$. There was no difference in percentage maximum decline in GFR between the groups (figure). At 5 years after donation, significantly more elderly patients had a GFR $<$60 ml/min compared to middle-aged and young patients (80% vs 47% vs 8% respectively, $p<0.001$). However, renal function stabilized during follow-up and no patient had a GFR of less than 30 ml/min during follow-up. After donation 10% of elderly patients developed hypertension versus 9% of middle-aged patients.



Conclusion: After kidney donation decline in GFR is similar in young, middle-aged, and elderly donors. As kidney function does not progressively decline, live kidney donation by elderly donors is considered as safe.

P-826 ORGANS FROM DONORS WITH RENAL CELL CARCINOMA – EXPERIENCES IN THE DSO-MIDDLE REGION

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Purpose: Transmission of cancer from organ donors to recipients is a tragic event. With the increasing age of donors this problem will become more evident in the future. Even in spite of careful diagnostics small tumors may not be recognizable before or during organ procurement.
Methods/Materials: We did a case-by-case follow-up study in 7 patients, who were transplanted with organs from 4 donors with RCC. 1 RCC was detected at time of organ procurement and 3 after implantation. All organs were procured in the DSO-middle region between January 1, 2006 and December 31, 2008.
Results: 7 organs (4 kidneys, 2 livers, 1 heart) came from 4 donors with RCC. Donor RCC were diagnosed during procurement (n=1) or after transplantation (n=3). RCC measured 0,9-2,5cm (pT1a), no metastases were detected. All tumors were well-differentiated (G1). Two kidneys with initially undetected RCC had been transplanted. Both kidneys were removed after diagnosis (day 6/14). Until now, there is no evidence of tumor recurrence. Two recipients who had been transplanted with contralateral kidneys do not show any sign of tumor transmission. One liver recipient, the only patient transplanted after confirmed

donor RCC, is also free of cancer. The heart recipient and one liver recipient died during follow-up of tumor-unrelated causes. Mean follow-up was 25,5 months (0,5-35 months).
Conclusion: Transplantation of organs from our donors with small, well-differentiated RCC did not result in any tumor recurrence or transmission in the recipients. Follow-up is to be continued. Immediate nephrectomy should be considered when RCC is diagnosed in the transplanted kidney after transplantation. This may not be necessary for other organs. Literature review corresponds with our results. Carefully selected recipients may benefit from these organs with a minimal risk for tumor transmission.

P-827 LONG-TERM RESULTS OF RENAL TRANSPLANTATION IN PATIENTS WITH ANTI HEPATITIS C ANTIBODIES

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The aim of the present study was to asses the long-term outcome of kidney trasplant patients with a positive serology for hepatitis C (HCV).
A retrospective evaluation of HCV (+) kidney transplants in two Spanish units during March 1990-March 2007 was performed. Recipients with pretransplant treatment with interferon, concomitant HBV infection and combined transplants were excluded. 468 patients fulfilled the inclusion criteria. Mean age was 46.6 (SD=14.3) years; 35% were transplanted from an HCV positive donor. Notably, the series exhibited a high immunological risk, 24% being hypersensitized patients and 42% having received previous kidney transplants.
Median follow-up was 65.2 months. Five and 10 year patient survival (Kaplan-Meier) was 86.4% and 75.3%. Corresponding estimates for death-censored graft survival were 71.7% and 55%. Risk factors for graft loss and patient death are depicted in the table.

Risk factors for graft loss and patient death in HCV positive kidney transplant patients*

	p	OR	CI95%
Graft loss			
Donor age	0.0001	1.022	1.012-1.032
%PRA > 50%	0.0001	1.912	1,367-2.674
Acute rejection	0.0001	1.778	1.304-2.425
DGF	0.032	1.417	1.031-1.949
Patient death			
Recipient age	0.0001	1.075	1.049-1.102
Pretransplant cardiovascular disease	0.051	1.850	0.997-3.432
Severe descompensate liver disease	0.003	2.883	1.447-5.746
PTDM	0.032	1.826	1.054-3.162

*Method: Cox regression

A decompensated severe liver disease was developed in 7.4%. Persistent elevation of ALT levels was related to this postransplant outcome (p=0.0001; OR 9.462; 95% CI 3.887-23.030). Only 3 patients were diagnosed of hepatocarcinoma.
In summary, HCV positive kidney transplant patients exhibit a high immunological risk, which does not preclude adequate long-term patient and graft survivals. Independent risk factors for death and graft loss seem to be similar to those described in the general population of kidney transplants. A persistent elevation of transaminase levels could be considered a surrogate marker for the development of an advanced liver disease.

P-828 REQUIEM FOR BK VIRUS NEPHROPATHY (BKN) – THREE-YEAR EXPERIENCE OF SYSTEMATIC SCREENING

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Out of 85 patients followed after renal transplantation (TP) at our centre during the period July 1999 to Oct 2003 eight patients (9,4%) were diagnosed with BKN. Three of these patients lost their grafts within less than a year after TP and another two patients within four years after TP. Of the remaining three patients two experienced a permanent deterioration of graft function.
Between Feb 2003 and March 2004 sera from 31 patients were collected monthly after TP and were retrospectively analysed for the presence of BK virus (BKV). Nine of the patients in this retrospective analysis were shown to have been positive for BKV at one occasion at least. Two grafts were lost in this series and two patients had a permanent deterioration of graft function.
From Feb 2006 all new renal TP patients are followed with qPCR for BKV monthly for the first six months and thereafter every three months for up to two years after TP. 69 patients have so far entered this screening programme with a FU from 1 to 24 months. Reactivation of BKV has been observed in 14 patients, in the majority by month 2-6. In patients with a viral load of $>10^4$ copies/ml (n=10) MMF has been tapered or withdrawn.
Diagnosis of BK virus reactivation should be done without undue delay. With the present screening programme we have seen no more graft losses or patients with permanent deterioration of graft function due to BKN. Given the high incidence of reactivation of BKV during the first six months post TP we recommend monthly screening during this period.
Summary: Early diagnosis of BKV reactivation is mandatory to prevent graft loss.

P-829 5-YEAR EXPERIENCE WITH THE EUROTRANSPLANT SENIOR PROGRAM

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Introduction: The aim of this retrospective analysis was to evaluate the results of patients in our transplant unit after kidney transplantation with donor/recipient pairs aged 65 years and older (Eurotransplant senior program; ESP), especially regarding outcome, long-term kidney function and complications.
Methods: Among over 600 kidneys transplanted in our centre, 39 (6.2%) patients exceeded an age of 65 years and were included in the ESP. The median age of the recipients was 68 years (range 65 to 79 years) and the median age of the donors was 68 years (range 65 to 84 years). The median follow-up-time was 32 months.(range 4 to 68 month).
Results: The median waiting time from first dialysis to transplantation was 11 months (range 1 week to 87.7 months). By topographic allocation and short shipping ways we reached a minimization of cold ischemia time to 11.2 hours. 7 patients (19.9%) suffered from postoperative complications (postoperative bleeding, anastomosis insufficiency, venous thrombosis). Currently, 33 of 37 (89.2%) patients are still alive with regular organ function in 28 (76%) patients. Median creatinine level is 190.3 μmol/l (range 75-314μmol/l).
Conclusion: The results reached in the ESP are comparable with those in younger patients. Therefore, ESP became routine in our centre. Our results suggest that short cold ischemia time and short waiting time are the main parameters predicting a good patient and transplant survival. However, the present analysis also shows a high complication rate mainly caused by vascular problems due to atherosclerosis in donor and recipient.

P-830 THE AVILABILITY OF ^{99} mTC-MAG3 RENOGRAPHY IN RENAL TRANSPLANTATION FROM NON HEART BEATING DONORS

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Purpose: Most patients who undergo renal transplantation from non heart beating donors (NHBD) develop ATN. For the evaluation of graft function during the ATN period, we performed ^{99}mTc-MAG3 renography regularly as soon after transplantation as possible. We estimated whether ^{99}mTc-MAG3 renography can predict the recovery of graft function during the anuria period.
Patients: Fifteen patients underwent renal transplantation from NHBD from 2 June 2005 to 24 May 2007. One patient was excluded from the study due to acute rejection which developed during the dialysis period. The medians of WIT and TIT were 6.5 and 847 minutes respectively. The median dialysis period after transplantation was 8 days (range 0–16).
Methods: The first ^{99}mTc-MAG3 renography after operation was performed as early as possible (within 4 days) and repeated weekly thereafter until the recipient was weaned from dialysis. We adopted RUNQ method to quantify MAG3, and calculated the corrected Tubular Extraction Rate (cTER) (ml/min/1.73m^2), that is MAG3 clearance corrected by body surface area.
Results: Corrected TER (cTER) was low (mean 53 ml/min/1.73m^2) immediately after transplantation, but increased gradually until 2-3 weeks after the operation, and then plateaued. Likewise, the change in the cTER based on the day of weaning showed an upward tendency during the dialysis dependent period, and plateaued 5-10 days after weaning.
By analyzing the relation between the early cTER and the dialysis dependent period, a significant correlation between these two parameters was found (R=-0,780, p=0.001). The following regression formula was obtained: y=0.269x+22.024 R^2=0.609 p=0.001.
There was no significant relationship between the early cTER and best cCCr, donors' age, WIT, and TIT.

Correlation with early cTER

	RR	p
HD period	0.609	0.001
Donor age	0.018	0.652
WIT	0.087	0.306
TIT	0.069	0.408
best C-Cr	0.345	0.027

Conclusion: Recovery of graft function can be monitored by routinely performing ^{99}mTc-MAG3 renography on transplanted grafts from NHBD.

P-831 APOPTOSIS OF TUBULAR EPITHELIAL CELLS IN PREIMPLANTATION BIOPSIES OF KIDNEY GRAFTS WITH IMMEDIATE, SLOW AND DELAYED FUNCTION

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Background: Apoptosis is a form of cell death observed in kidney grafts as a result of ischemia/reperfusion injury. Patients who develop slow (SGF) or delayed (DGF) graft function present worse kidney graft survival compared to those with immediate graft function (IGF). The aim of our prospective study was to analyse the occurrence of apoptotic cells in kidney tubules after cold storage in respect to post-transplant graft function.
Patients and methods: The degree of renal tubular damage was estimated as percentage (TUNEL method) of apoptotic cells in 72 pre-implantation kidney biopsies in proximal and distal tubules. Biopsies which not fulfilled Banff 97 classification (N=5) and of patients with early acute rejection (N=8) or early graft loss (N=3) were excluded from the analysis. IGF (N=17) was defined as serum creatinine level (SCr) $<264\mu$mol/l at 3rd postoperative day (POD); SGF (N=20) – as SCr $>264\mu$mol/l at 3rd POD and the need of maximum one dialysis; DGF (N=19) – when patient required more than one dialysis. Data are presented as means and 95% CI.
Results: The percentage of apoptotic cells was markedly higher in distal than in proximal tubules in all three groups. The highest percentage of apoptotic cells in distal tubules was found in IGF [3.02 (1.03-5.00)] than in SGF [1.66 (0.92-2.39)] and in DGF [1.76 (0.84-2.68)], however these differences did not reach statistical significance.
Conclusion: The enhancement of tubular epithelial cells apoptosis in kidney grafts after cold storage does not determine its early function.

P-832 RISK FACTORS FOR URINARY TRACT INFECTIONS IN RENAL TRANSPLANTATION

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Objectives: The aim of this study was to identify the risk factors for urinary tract infections (UTI) after renal transplantation;
Material and methods: This retrospective study included 136 kidney graft recipients (85 men and 51 women, mean age: 49.95 y) transplanted between January 2003 and December 2006. They were followed for one year. This population was divided in 2 groups: the group 1 including 58 patients with UTI and the group 2 with control renal graft recipients free of such disease. Within the group 1, patients were again divided in subgroups which have been compared: complicated UTI versus uncomplicated UTI and more than 2 UTI versus 2 or less UTI patients. The following parameters were studied: age, gender, etiology of chronic renal disease, presence of a residual diuresis, implantation and date of removal of JJ catheter, number of previous renal graft, type of immunosuppression, number of rejections, urological events and antibioprophylaxy. Statistical analysis was made through Chi-2 Test. A $p<0.05$ was significative.
Results: In the whole population, the UTI incidence was 42.7%. Complicated UTI was noted in 18%. For 81% of the patients, the first UTI developed during the first 3 months after graft. The women were mainly affected. The risk factors for UTI were urological events during the immediate post-graft period. The risk factors for complicated UTI were male sex and urological events. The risk factors for repetitive UTI were the female sex, urological events and past renal graft. The analysis of the other factors was not significatively conclusive.
Conclusions: UTI is frequent in renal transplant graft, especially in women or when urological events or operations are present. A second graft is also a risk factor for frequent UTI.

P-833 HAND-ASSISTED RETROPERITONEOSCOPIC VERSUS STANDARD LAPAROSCOPIC DONOR NEPHRECTOMY

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Purpose: To date live kidney donation is the most effective way to solve the shortage of donor kidneys. Laparoscopic donor nephrectomy (LDN) is less traumatic and painful than the open approach, with shorter convalescence time. The hand-assisted retroperitoneoscopic technique (HARP) could have benefits, such as shorter operation and warm-ischemia time and improved safety. We evaluated peri-operative and one year outcome of HARP alongside LDN.
Methods: From August 2006 to May 2008 the first 20 left-sided HARP were compared with the last 40 left-sided LDN. A prospective registration of operation- and warm ischemia time, intra- and post-operative complications and blood loss was performed. Creatinine clearance of the donors was recorded preoperatively, on day 1, 2, 3, 30 and yearly thereafter. Graft and recipient survival were recorded. Creatinine clearance of the recipient was registered preoperatively, during the first 14 days, day 21, 28 and every 3 months.
Results: Patients undergoing HARP tended to be older (57 vs 53 years, p=0.096) and more often female (75% vs 40%, p=0.017). Other baseline characteristics did not differ significantly. Median skin-to-skin operation time was shorter in HARP compared to LDN (180 min vs 225 min, p=0.002). Warm ischemia time was also shorter in HARP (median 3 vs 5 min, p=0.007). Intra- and postoperative complication rates for HARP and LDN (respectively 10% vs 25%, p=0.17 and 10% vs 18%, p=0.44) were not significantly different. Also, blood loss was similar (200 ml vs 150 ml for HARP and LDN respectively). During a median follow-up of 12 months creatinine clearance was similar in both donors and recipients. Graft- and recipient survival was not different.
Conclusion: HARP results in shorter skin-to-skin and warm ischemia times. Hand-assisted retroperitoneoscopic donor nephrectomy might be an alternative for laparoscopic donor nephrectomy.

P-834 PERITRANSPLANT NEPHRECTOMY IN AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE– INDICATIONS AND OUTCOME

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To define indications, timing and morbidity of peritransplant native nephrectomy in Adult Polycystic Kidney Disease.
Methods: Between 2003 and 2008, 29 peritransplant APKD patients underwent either unilateral (U/L) or bilateral (B/L) native nephrectomy. This group was analysed to define indications, timing of surgery and outcomes. Kidneys removed were divided into pre and post transplant groups with sub-groups of B/Land U/L nephrectomy.
Results: A total of 48 open nephrectomies were done. 28 nephrectomies, (14 (B/L) and 14 (U/L) in the pre Tx group and 20 nephrectomies 16 (B/L) and 4 U/L) in the post transplant group were performed.
The main indications for nephrectomy in pre Tx group were pain and discomfort (14), creation of space (7), haematuria (4) and sepsis (3). The major indication in the post transplant group was pain and discomfort (18). Two kidneys were removed in a patient because of Renal Artery Stenosis with uncontrolled hypertension.
9 patients required intensive care in the post op period. The major morbidity was intra-operative and post-operative bleeding (7 patients, 5 B/L and 2 U/L) and required ITU admission for short period. Chest infections (3) were more common in post transplant group.
Three pre-Tx patients died in the immediate post op period due to complications. Mean hospital stay in unilateral group is less than 10 days and bilateral group is 15days. Only one patient in post transplant group developed transient graft dysfunction.
Conclusion: The main challenge is the optimal timing of nephrectomy especially in the pre-Tx group which ideally should be delayed till the patient has been established on dialysis. The best outcomes are in the transplanted group with good graft function. Morbidity in the post transplant group does not tend to affect graft function.

P-835 HIGH INCIDENCE OF PARATHYROIDECTOMY AND NEPHROCALCINOSIS IN RENAL TRANSPLANT RECIPIENTS DISCONTINUING CINACALCET AT THE TIME OF TRANSPLANTATION

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Background: The calcimimetic cinacalcet is approved for treating secondary hyperparathyroidism in patients with chronic kidney disease on dialysis. Biochemical profiles and clinical outcomes in patients discontinuing cinacalcet at the time of transplantation have not been reported so far.

Methods: We performed a prospective observational study in 303 renal transplant recipients (2004-2008) with no prior history of parathyroidectomy (male 62.3%, age 53.8±13.5 yrs, dialysis vintage 30.5 months, median). Among these patients, 21 were on cinacalcet treatment at the time of transplantation (dose 30-90 mg, range; duration: 12.5 months, median). Median follow-up was 29.0 months. Parameters of mineral metabolism, determined at the time of transplantation and 3 months after engraftment, incidence/prevalence of parathyroidectomy and incidence of nephrocalcinosis (scored in the 3-month protocol biopsy) were compared between former cinacalcet patients (cases) and cinacalcet naïve patients (controls).
Results: Parameters of mineral metabolism at the time of transplantation were similar in both groups. Conversely, at month 3, serum ionized calcium (p=0.0007), calcitriol (p=0.02), biointact parathyroid hormone (p=0.06) levels and urinary fractional excretion of phosphorus (p=0.06)were higher, while serum phosphorus levels (p=0.06) were lower in cases. A high prevalence (28.6 vs 6.7%, p=0.0005 cases versus controls) and incidence rate (17.2 vs 2.6 per 100 pts years) of parathyroidectomy were observed in former cinacalcet patients. Nephrocalcinosis was diagnosed in 46.7% of the cases (versus 30.1% in controls, p=0.2). No difference in renal function was observed. In
Conclusion: The biochemical profiles and the high incidence of parathyroidectomy suggest clinically relevant rebound hyperparathyroidism in patients discontinuing cinacalcet at the time of transplantation. Risk/benefit studies are urgently required to define the role of continued calcimimetic treatment in renal transplant recipients.

P-836 LONG-TERM FOLLOW-UP OF A RANDOMIZED TRIAL COMPARING LAPAROSCOPIC AND MINI-INCISION OPEN DONOR NEPHRECTOMY

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Purpose: One year results after mini-incision open (MIDN) versus laparoscopic donor nephrectomy (LDN) show a benefit for LDN. At one year LDN was associated with better quality of life (QoL) and fatigue scores. However, long-term outcome i.e. physical and psychosocial effects of laparoscopic and open kidney donation are ill defined. Therefore, we evaluated long-term outcome of the randomized LiDo-trial, comparing LDN and MIDN.
Methods: Follow-up data of 100 live kidney donors, randomly assigned to either MIDN or LDN, were prospectively collected. Data included blood pressure, glomerular filtration rate, body image,QoL (SF-36), fatigue (MFI-20) and graft function. Subjective experience of donation was examined using a short questionnaire.
Results: After a median follow-up of 4 years complete data were available for 47 (94%) donors in both groups; QoL data for 35 (70%) in the MIDN group, and 37 (74%) in the LDN group. After 4 years follow-up, mean eGFR did not significantly differ between MIDN and LDN (75 vs 76 ml/min, p=0.39). Four donors (4%) (3 MIDN; 1 LDN, p=0.62) developed hypertension, but could be adequately controlled medically. In contrast to follow-up after 1 year, most dimensions of QoL and fatigue showed no difference between both groups at long-term follow-up, and most scores had returned to baseline. Body image scores did not differ between groups. Regardless of operation technique, all donors would donate again if possible. Graft failure and patient survival was similar for MIDN and LDN (10% vs 8% and 90% vs 94%).
Conclusion: Long-term outcome of live kidney donation is excellent from both the perspective of the donor and recipient. At long-term follow-up, surgical technique has only limited impact on quality of life.

P-837 LONG TERM KIDNEY FUNCTION AFTER PREEMPTIVE KIDNEY TRANSPLANTATION IN POLYCYSTIC LIVER ANS KIDNEY DISEASE

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Introduction: The aim of this retrospective analysis was to evaluate the changes in kidney function after preemptive kidney transplantation in patients with polycystic liver and kidney disease (PLKD) and to find out whether preemptive kidney transplantation in form of a combined liver-kidney transplantation is justified.
Methods: From 1998 to 2009 five patients with severe anatomic changes in both kidneys due to multiple cysts but only calm decrease of the clearance function received combined liver-kidney transplantation. While the evaluation of the patient for transplantation, a Technetium-99m mercaptoacetyltriglycine (Tc99m MAG3) scintigraphy was used to separate the function of each native kidney. The examination was repeated six month after transplantation, but now divided for all tree kidneys.
Results: Before transplantation creatinine levels ranged from 77 to 115 μmol/l and the Tc99m MAG3 clearance ranged from 141 to 163 ml/min/1.73sqm (74±8% of minimum-for-age values). Six months after transplantation the minimum-for-age clearance decreased by 12,5±11.5% in four patients, and increased by 26% in one patient. More than 3 years after transplantation the creatinine values were not significantly different from those before transplantation. The transplanted and the native kidneys assumed each about one third of total tracer clearance, only in one patient the transplanted kidney assumed 92% of the clearance function.
Conclusion: The results show that native kidneys are not functionally excluded after a kidney transplantation and they also show a division of the clearance between the native and the transplanted kidney. A preemptive kidney transplantation in PLKD patients does not improve the overall kidney function and should be well evaluated and only decided in exceptional cases.

P-838 KIDNEY TRANSPLANTATION MODIFIES THE CARDIOVASCULAR RISK PROFILE OF HEMODYALISIS (HD) PATIENTS

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Cardiovascular disease represents the main causes of mortality in HD. HD patients present a characteristic risk profile that includes both classic and novel risk factors for cardiovascular disease. Although cardiovascular risk is drastically reduced after transplantation, it remains significantly higher than in the general population.
The aim of our study was to evaluate whether kidney transplantation modifies the cardiovascular risk profile of uremic patients.
To this purpose, we evaluated 88 HD patients on the transplant waiting list (49M and 39F, mean age 51.6yrs, mean HD age 51.67 months, mean BMI 23.83kg/m^2) and 56 transplant recipients (35M and 21F, mean age 49.2yrs, mean transplant age 51.3 months, 89.66% in treatment with calcineurin-inhibitors and 10.34% with SRL, mean BMI 24.6 kg/m^2). Carotid intima-media thickness (IMT) was investigated by doppler ultrasound, as a marker of atherosclerosis. For each patient we evaluated the following cardiovascular risk factors: anemia, total serum cholesterol, systemic inflammation by serum C reactive protein (CRP) and insulin resistance assessed by HOMA index.
Total cholesterol levels were significantly (p=0.001) higher in transplant recipients (190.8±41.3mg/dl) than in HD patients (123.1±55.2mg/dl). The mean CRP serum level in the HD group (0.87±0.21mg/dl) was significantly ($p<0.001$) elevated compared to the transplant group (0.31±0.11mg/dl). The mean hemoglobin level was significantly (p=0.0002) higher in transplant recipients (12.1±1.4g/dl) than in HD patients (10.9±1.2g/dl). IMT was significantly ($p<0.0001$) higher in HD patients (0.97±0.12mm) than in transplant recipients (0.75±0.09mm). Interestingly, carotid IMT was independently correlated with CRP levels only in HD patients. On the other hand, a multiple regression analysis suggested that only HOMA index was associated with IMT after transplantation.
Our data show that most, although not all, cardiovascular risk factors are significantly improved after transplantation and that the cardiovascular risk profile is considerably different between HD patients and transplant recipients.

P-839 LAPAROSCOPIC VERSUS OPEN DONOR NEPHRECTOMY – THE EFFECT OF DONOR AGE AND BODY MASS INDEX ON OUTCOME

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Introduction: The use of living donors forms 36% of total renal transplant activity in the UK. Living donor grafts provide superior patient and graft survival compared to deceased donor transplantation. Donor age and obesity are important selection criteria for optimal quality grafts and donor health. This paper studies the outcomes of donor:recipient matched and mismatched renal transplantation in a live donor programme.
Methods: Short-term outcome following live donor renal transplantation in Leeds were studied in the period January 2005 to January 2009. Group A comprised donor:recipient pairs where donor age was greater than recipient age; Group B where donor age was less than recipient age. Group C comprised donor:recipient pairs where donor BMI was greater than recipient BMI: Group D where donor BMI was less than recipient BMI. Estimated GFRs were calculated using the 4 variable MDRD formula. Ordinal data were compared using a student t test.

Results: 145 live donor nephrectomies were performed using 86 female and 59 male donors. 94 nephrectomies were performed using an open technique and 51 using a laparoscopic retrieval. Mean donor and recipient ages in Group A were 49±11yrs and 33±13yrs respectively; in Group B these were 43±12yrs and 50±12yrs respectively. Mean donor and recipient BMIs in Group C were 28±3 and 23±3 kg/m^2 respectively; and in Group D these were 25±3 and 28±4 kg/m^2 respectively. Estimated 6 month GFRs differed significantly between Groups A and B (mean eGFR 55±17 *vs* 52±12 ml/min; p=0.011) but not in Groups C and D (mean eGFR 55±16 *vs* 51±13 ml/min; p=0.399).
Discussion: Discrepancies in BMI between live kidney donor and recipient have no impact on short-term graft function. Grafts from older donors, transplanted into younger recipients, show a significantly superior function in the short term.

P-840 CYTOKINE AND IMMUNE MODULATOR GENE EXPRESSION IN PERIPHERAL BLOOD MONONUCLEAR CELLS OF ACUTE RENAL ALLOGRAFT REJECTION

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Purpose: Despite advances in immunosuppression, renal allograft rejection remains the main crucial determinant of chronic and long term graft function. To solve this problem, there have been many efforts to explore the participation of cytokines and related gene expression in allograft rejection via advanced molecular biologic techniques like a RT-PCR using the genes from biopsy tissues. However, for rejection screening, allograft biopsy is too invasive to perform without a clinical clue. So, we studied time course expression of cytokine and other immune modulator genes extracted from peripheral blood mononuclear cells of renal transplant recipients in the immediate post-transplantation period and compared recipients who underwent rejection episode and no rejection episode.
Methods: Among renal transplant recipients who were followed up in Ajou university hospital volunteers included in this study, patients excluded because of other allograft dysfunction than rejection, eight recipients confirmed with acute cellular rejection. Peripheral mononuclear cells were extracted from venous samples at that times of immediate postoperative first or second day, clinically stable period before rejection diagnosis, and under steroid pulse therapy. The relative expression amount of cytokines and other immune-modulator genes including IL-2, IL-4, IL-10, IL-15, IL-17, INF-r, LGAL1, DEFA3, DNAJA1, HBA1, HBB, and SVEP1 were tested using RT PCR.
Results: Prior to clinical deterioration caused by acute allograft rejection, patients with allograft rejection showed lower mRNA expression of HBA1 and IL-10 than the patients without rejection.
Conclusions: The evaluation of immune-modulators and cytokine gene expression prove useful in the clinical identification of acutely rejecting transplant recipients and the monitoring of proper immunosuppression. And it could provide the justification of concomitant anti-rejection therapy before histological diagnosis confirmation.

P-841 THE ROLE OF INTERLEUKIN-6 HAPLOTYPES ON CARDIOVASCULAR OUTCOME IN A KIDNEY TRANSPLANT COHORT

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The role of inflammation as a key regulator in the development and maintenance of atherosclerosis is well established and impacts renal transplant outcome. In end-stage renal disease (ESRD) patients, Interleukin-6 and its underlying genetically determined levels, impacts cardiovascular morbidity and mortality. The role of genetically determined IL-6 differences in kidney transplantation is controversially discussed for cardiovascular and renal outcome. Here we try to clarify the influence of Interleukin-6-haplotypes on cardiovascular and renal outcome in a kidney transplant cohort.
352 patients, who received their first kidney transplant, were genotyped for the two “clade” Interleukin-6 polymorphisms (-174G/C and 1888G/T), and 2 missense polymorphisms (Pro32Ser, Asp162Val), which are known to influence patients’ IL-6 levels and outcome.
In our cohort 4 different Interleukin-6-haplotypes could be observed (CCAG: 57.0%, CCAT: 2.8%, GCAT: 39.2%, GCTT: 1.0%). After stratifying the different haplotypes into diplotypes in 3 different models we found no associations with early or late graft outcome, as well as all-cause or cardiovascular mortality/morbidity. However, there was a trend for earlier and more acute rejection in wild type group. Graft survival and function at 3 and 6 months, delayed graft function, and graft survival were also not affected by one of the haplotypes. These findings were also confirmed when each polymorphism was analyzed separately.
Despite evidence of associations in other transplant and ESRD cohorts, we could not confirm any association between Interleukin-6 haplotypes/diplotypes and cardiovascular or graft-related outcomes in our high risk population for inflammatory diseases. These results suggest an additional impact of ethnical backgrounds as well as treatment strategies/surveillance in these patient cohorts.

P-842 PREDICTION OF CARDIOVASCULAR AND RENAL OUTCOMES AFTER KIDNEY TRANSPLANTATION THROUGH INFLAMMATION MARKERS PRIOR TO TRANSPLANT

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Background: Markers of non-specific inflammation, such as C-reactive protein (CRP) or leukocyte count, may predict in end-stage renal disease patients adverse clinical outcomes. Recent studies have shown a link between pre-transplant inflammatory markers and kidney transplant outcome, but these analyses had been limited by sample size or enrolment bias. The aim of this study was to determine the association between pre-transplant CRP levels and clinical course after transplantation in our cohort of kidney transplant recipients.
Methods: 459 consecutive patients who underwent a first renal transplantation from July 1995 to December 2007 were included in our analysis. Both markers were obtained prior to transplantation and patients were grouped according to baseline CRP levels ($<$5 mg/l or $\geq$5 mg/l) or leukocyte counts ($<$10000/μl or $\geq$10000/μl).
Results: Acute rejection rates were higher (p=0.03), and the occurrence of an acute rejection was more rapid in patients in group B (p=0.02). However, delayed graft function or all-cause mortality showed no association. Besides elevated CRP-levels, no other inflammation markers could be established as predictor for transplant outcome.
In patients with elevated pretransplant CRP levels or leukocyte counts, we found higher rates of acute rejection after 4 weeks and 6 months. Furthermore, the occurrence of cardiovascular events was significantly associated with higher CRP-levels ($p<0.0001$), and a lower probability of patient survival after 6 months ($p<0.01$). However, leukocyte counts showed no association with cardiovascular outcome.
Conclusion: Elevated pretransplant serum CRP level is a risk predictor for cardiovascular events in renal transplant patients. It is also predictive, besides leukocyte counts, for early acute rejection episodes. Elevated CRP levels and initial high leukocyte counts may prove to be useful markers for posttransplant course and warrants the close follow-up of such patients.

P-843 LAPAROSCOPIC VERSUS OPEN DONOR NEPHRECTOMY – COMPARABLE OUTCOMES FROM A SINGLE CENTRE SERIES

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Introduction: The use of living donors forms 36% of total renal transplant activity in the UK and patient and graft survival are superior compared to deceased donor transplantation. Herein we study the outcomes of open and laparoscopic donor nephrectomy in a single UK centre.
Methods: Outcomes following live donor renal transplantation were studied from January 2005 to January 2009. Donor and recipient demographics, surgery and ischaemia times, and transplant outcomes (eGFR and graft survival) were compared. Ordinal data were compared using a student t test and nominal data using a χ^2 test.
Results: 153 live donor nephrectomies were performed (n=98 open *vs* n=55 laparoscopic). Donor and recipient ages (mean 43 *vs* 47 yrs donors; p=0.07 and mean 37 *vs* 41 yrs recipients; p=0.21) and BMIs were comparable (mean 27 *vs* 26 kg/m^2; p=0.11 and 24 *vs* 25 kg/m^2; p=0.16). Donor gender distribution was equal in the laparoscopic group (29F *vs* 26M laparoscopic; p=0.68) but there were more female donors in the open group (61F *vs* 37M open; p=0.015). Duration of donor surgery (mean 3h 1min laparoscopic *vs* 2h 43min open; p=0.13)and anastomosis time (mean 29 mins in each group; p=0.64) were comparable. Cold ischaemia time was prolonged in the laparoscopic group (mean 213 min *vs* 128 mins; $p<0.001$). For those with completed follow up

(n=130), estimated GFRs at 1 day (mean 26 *vs* 22 ml/min; p=0.22), 5 days (mean 69 *vs* 67 ml/min; p=0.87) and 6 months (mean 67 *vs* 59 ml/min; p=0.34) were equivalent. One year graft survival (99% *vs* 98%) was similar for both groups.
Conclusion: Open and laparoscopic donor nephrectomy can be performed with comparable durations of donor surgery. The rates of graft function and survival are comparable using either open or laparoscopic donor nephrectomy.

P-844 COMPARATIVE ANALYSES OF ELDERLY AND YOUNG DONORS FOR RETROPERITONEOSCOPIC LIVE DONOR NEPHRECTOMY

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Introduction: Laparoscopic surgery has become a mainstay for live donor nephrectomy, and recently the number of operations has gradually increasing in Japan, because it encourages kidney donation and enables faster restoration of quality of life than the ordinal open surgery. Our surgical staffs prefer the retroperitoneal approach for urological organs, usually performing the same approach for removing malignant tumors. The aim of this study is to clarify whether our method is feasible or not for both in elderly and young donors.
Methods: The surgery consisted of three operative stages as we mentioned in the previous literatures: a pure endoscopic procedure for mobilizing kidney, an open procedure through the hand port device for dissecting ureter, and a hand-assisted endoscopic procedure for dissecting renal vessels. Operative parameters and postoperative renal functions were evaluated, and further physicians at our nephrology department followed the mid-term renal functions.
Results: A total of 75 retroperitoneoscopic live donor nephrectomies were performed. The mean donor age was 56.1±11.5 years with a mean BMI of 23.5kg/m^2. Sixteen of the 75 (21.3%) were elderly donors (65 years or older), and half were obtained from female donors for male recipients. The mean operative time, warm ischemia time (WIT), blood loss, and estimated GFR according to MDRD (Modification of Diet in Renal Disease) study equation four weeks postoperatively were around 4 hours, 3 minutes, 200 ml, and 60mL/min, respectively. Comparison of these data and longitudinal observation of renal functions between elderly and young donors was not significantly different.
Conclusions: Our retroperitoneal approach to procure graft kidney is feasible for both in elderly and young donors, and may contribute to encouraging kidney donation. The future evaluation will provide more relevant renal prognosis based on a larger case series with long-term follow-up.

P-845 EARLY APPEARANCE OF *DE NOVO* ANTI-HLA ANTIBODIES FOLLOWING RENAL TRANSPLANTATION: PRELIMINARY RESULTS OF A MULTICENTER STUDY

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Introduction: Notwithstanding the development of novel immunosuppressive agents, the-long term survival of transplanted organs has only marginally improved, possibly as a consequence of the detrimental role of elicited anti-graft antibodies.
Methods: One hundred forty-seven *de novo* kidney recipients that were not sensitized to HLA on the last pre-transplant serum were included in a prospective, multicenter clinical study. The absence of HLA-sensitization was defined by CDC (72 cases) or by Luminex (75 cases). Monitoring for anti-HLA class I and class II antibodies, undertaken at the time of transplantation and post-operatively, was performed by flow cytometry or by Luminex (kindly donated by One Lambda, USA). Patients immunosuppression included a calcineurin inhibitor and mycophenolic acid in most cases.
Results: The current median enrolment time is 7 month (range 1-24 months). In those centers where the CDC was used to identify non-sensitized patients, high resolution tests revealed antibodies at transplantation in 13 cases (18% false negative results). To date, 20 patients have developed these antibodies, between 1 and 18 months posttransplantation. Interestingly, 14 out of 70 patients (20%) developed *de novo* anti-HLA antibodies within the first 6 months. Rejection episodes were detected in 11 patients and 5 of these elicited anti-HLA antibodies. The mean total mismatch number in patients with or without elicited antibodies was 4.1±1.25 and 3.6±1.0 (p=0.051), respectively.
Conclusion: Following renal transplantation, a considerable number of patients elicits an early *de novo* anti-HLA antibody response, with serum conversion at 6 months in 20% of the cases. As *de novo* anti-HLA class I and class II antibodies are associated with decreased long term allograft survival, routine antibody monitoring and specific intervention may become a necessary practice to improve long term results.

P-846 IDENTIFYING IMMUNOLOGICAL RISK FACTORS IN KIDNEY TRANSPLANTATION

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Purpose: To establish a safe way of reducing immunosuppression, a collective of low-risk patients has to be identified. Today there are hints that patients with high pretransplant levels of sCD30, HLA class I and II antibodies or low levels of IgA-anti-Fab autoantibodies are at a higher immunological risk than patients without those factors. In this study we investigated the influence of those antibodies allograft survival and rejection.
Patients and methods: In this prospective single-centre study we analyzed pretransplant levels of sCD30, HLA class I and II antibodies as well as IgA-anti-Fab antibodies in 224 patients that were on our waiting list in 2004. All already transplanted patients were included in this study (n=133). In total in 29,3% of patients at least one antibody was detectable. The mean age in group 1 (no antibody) was 54 years vs 50 in group 2 (≥1 antibody) (p=0,038). The groups didn't differ in HLA match, pretransplant PRA or cold and warm ischemia time.
Results: After a mean follow up of 2 years in both groups we didn't find any statistically significant difference in organ and patient survival, which was 94,7% and 95,5% in group1 and 97,8% and 97,8% in group2. We did observe a slightly higher rate of rejections in the group 1 20,5% vs 31,9%), whereas the rate in organ loss was lower in this group (2,1% vs 5,3%). Both effects were not statistically significant, this may be due to the low number of lost organs and patients.
Conclusion: In our patient collective we could not confirm the previously published data identifying a group with low immunological risk for organ rejection by detection of pretransplant HLAI/II, IgA-anti-Fab antibodies or sCD30. This may be due to a low number of patients and needs to be confirmed in further prospective studies.

P-847 CYCLOSPORIN A AND TACROLIMUS, COMBINED WITH MYCOPHENOLIC ACID, ARE EQUALLY EFFECTIVE IN PREVENTING THE ONSET OF *DE NOVO* ANTI-HLA ANTIBODIES

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Introduction: *De novo* appearance of anti-HLA antibodies has been associated with decreased long-term allograft survival. Here we have investigated whether patients treated with cyclosporin A (CsA) or tacrolimus (FK), in addition to mycophenolic acid (MPA), are equally protected from the appearance of such antibodies.
Methods: Over a 3 year period, we monitored 89 renal allograft recipients with stable graft function, with no anti-HLA antibodies at enrolment. Maintenance immunosuppression consisted in CsA (Group A; n=41) or FK (Group B; n=48), associated with MPA in all cases. Detection of anti-HLA class I and class II antibodies was performed by solid phase testing (One Lambda, USA). The elicited anti-HLA antibody response was compared between the two groups, as was creatinine.
Results: Three years following transplantation, *de novo* anti-HLA antibodies

were detected in 23% of the patients (n=20; 11 in Group A; 9 in Group B). In Group A, anti-HLA class I, class II, class I and II antibodies were observed in 10, 2 and 1 case(s), respectively; median class I and class II PRA was 5% (range: 0-26%) and 40% (range: 0-50%), respectively. In Group B, anti-HLA class I, class II antibodies were observed in 5 and 4 cases, respectively; median class I and class II PRA was 13% (range: 0-85%) and 7% (range: 0-50%), respectively. Median creatinine was 113 μmol/L (range: 66-333) and 137 μmol/L (range: 66-447) in Group A and B, respectively, without significant differences between patients with or without *de novo* antibodies.
Conclusion: Notwithstanding the use of MPA, *de novo* anti-HLA antibodies are frequently observed in kidney allograft recipients. Furthermore, when administered with MPA, CsA and FK are equally effective in preventing the onset of *de novo* anti-HLA antibodies.

P-848 IMPACT OF UTI ON THE LONG-TERM KIDNEY ALLOGRAFT FUNCTION IN ADULTS WITH URINE COLLECTING SYSTEM RECONSTRUCTION

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Bladder augmentation or urinary diversion may be necessary for kidney transplantation in lower urinary tract dysfunction (LUTD). Aim of study: to evaluate graft survival, incidence of UTI and it's impact on graft function in 25 adult kidney recipients transplanted1999-2008 with prior to or concomitant urinary tract reconstruction. Study group was compared (1:3 ratio) with controls matched for gender, age, procedure date.
In 14 patients ileal loop was created at engraftment, in 7 prior to procedure; 2 patients had continent urinary reservoir, 2 bladder augmentation, one cutaneous ureterostomy. Follow-up: 33.6±28 in LUTD and 33,1±27 month in control.
Kidney allograft survival was 97% in both groups.
Two LUTD patients lost graft– one was removed because of recurrent bacterial and fungal sepsis, other patient re-entered dialysis because of recurrent pyelonephritis, 3 were lost in control. There was no difference in acute rejection rate.
88%(n=21) of LUTD patients had at least one episode of urinary tract infection (UTI), in control group the incidence was 44%(n=30), $p<0.001$. Recurrent UTI's ($\geq$3 in post-transplant course) occured in 14 (58%) vs 6 (9%); $p<0.001$. The incidence of UTI requiring hospitalisation: LUTD 67% (n=16) vs controls 28% (n=19); $p<0.001$. Urosepsis occured in 4 study and 4 controls; p=NS. ESBL-caused UTI was 29% in study and 3% in controls, $p<0.001$. At the end of follow-up kidney allograft function was excellent, serum creatinine 1.29±0.5 in LUTD and 1.43±0.42 mg/dl in controls (p=0.17). There was no difference in UTI in patients withs prior vs concomitant with engraftment ileal loop operation.
Conclusions: Urinary tract infections do not negatively influence kidney allograft function in kidny recipients with alternative urine drainage. In our experience, although limited, the timing of bladder reconstruction did not influence the risk of infection.

P-849 LATE SURGICAL COMPLICATIONS MIMICKING CHRONIC ALLOGRAFT NEPHROPATHY

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Objective: Chronic allograft nephropathy (CAN) is the most common cause of late renal insufficiency after kidney transplantation (KT) and the loss of graft function is often inexorable. However, other causes of late, reversible graft dysfunction need to be differentiated from CAN.
Methods: In a continuative series of 2809 kidney transplants, performed between May 1969 and December 2008, 105 surgical complications are reported in 102 patients, occurring 2-24 years after transplantation and producing signs/symptoms similar to CAN, such as hypertension and graft dysfunction. 29 native kidney nephrectomies due to various pathologies (up to 17 post-transplant years), 28 urological complications (up to 17 post-transplant years), 18 renal artery stenosis primary or secondary to occlusive diseases of the iliac vessels proximal to the graft, 11 lymphoceles (up to 24 post-transplant years), 10 post-biopsy arteriovenous fistulas/aneurysms/clot retentions and 9 other complications causing graft dysfunction were recognized and treated after a differential diagnosis, either using open surgical approach or minor endoscopic radiological procedures. The success of corrective procedure was evaluated calculating the graft function in months until the return to dialysis, transplant nephrectomy, second transplant or patient death.
Results: No death was observed as caused from re-operation and the operative procedures were successful in 101 patients. Only one patient lost his graft after surgical correction of ureteral stenosis 2 years after KT; 2 patients were submitted to definitive cutaneous nephrostomy due to noncorrectable stenosis of the graft urinary tract. The operative corrections allowed the graft function to be lengthened for a mean of 5.3±4.2 years for a total of more than 550 transplant years.
Conclusions: A timely diagnosis and proper treatment can lengthen the transplant life even in late surgical complications.

P-850 IMPACT OF INDUCTION WITH BIOLOGICS IN KIDNEY TRANSPLANT PATIENTS WITH A POSITIVE SEROLOGY FOR HEPATITIS C: LONG-TERM ASSESSMENT IN A COLLABORATIVE STUDY

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The potential deleterious effect of lymphocyte depleting antibodies on the outcome of kidney transplantation in HCV positive recipients is a matter of concern. The aim of the present study was to evaluate the long-term impact of induction with biologics in this transplant population.
We retrospectively assessed the outcome of HCV positive kidney transplants performed in two Spanish units during March 1990March 2007. Recipients with pretransplant interferon treatment, concomitant HBV infection, combined transplants, induction with anti-CD25 antibodies and/or lack of information on induction were excluded.
Four hundred and eighteen HCV positive kidney transplant patients fulfilled the inclusion criteria: 117 received induction with OKT3 (11), Thymoglobuline (37) or ATGAM (69) (Group 1) and 301 did not receive induction (Group 2).
As expected, a higher percentage of patients were hypersensitized (64.3% *vs.*10%; $p<0.0001$) and/or had a previous history of kidney transplantation (60.7% *vs.*30.2%; $p<0.0001$) in group 1. Group 1 exhibited a longer time on dialysis [9.8 (SD=5.8) *vs.*5.8 (SD=4.8) years; $p<0.0001$) and a more frequent history of pretransplant cardiovascular disease (20.4% *vs.*12.3%; p=0.04).
Mean follow-up was 73.2 (SD=61.5) *vs.* 82.9 (SD=57.3) months in Groups 1 and 2, respectively (p=0.086). Notably, no significant differences in outcome were detected (table 1).
In conclusion, induction with biologics in selected high immunological risk HCV positive kidney transplant patients is related to a favorable long-term outcome, with no negative effect on postransplant clinical liver disease.

	Group 1 Induction (N=117)	Group 2 No induction (N=301)	p
5 year patient survival*	91.5%	85.3%	0.3270
10 year patient survival*	82.7%	73.5%	0.3270
5 year death-censored graft survival*	66.8%	73.8%	0.3378
10 year death-censored graft survival*	58.1%	54.3%	0.3378
Chronic liver disease**	7.5%	12.1%	0.203
Severe decompensated liver disease***	8%	7%	0.726

*Kaplan Meier; **ALT >2.5 times the upper limit >6 months; ***At least one episode of: ascites, hepatic encephalopathy and/or gastrointestinal bleeding due to ruptured varices.

P-851 FOURTH WHO GOAL IS "TO ADD LIFE TO YEARS": FOR RENAL TRANSPLANTED RECIPIENTS WE DID

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Introduction and aims: Kidney transplantation (KT) improves both survival and Quality of Life (QoL)in patients with ESRD. The aim of this study is to examine the changes of QoL in patients on waiting list for KT and to compare the results of the same patients, missing or doing KT. Then we focused the analysis of QoL on older patients.
Patients and methods: The prospective study was performed on 103 dialysis patients on waiting list for KT (time 0). SF-36 was administered at time 0 and after a minimum follow up of 12 months after transplantation (time 1). The transversal study involved 52 KT recipients (females 36.5%, men 63.5%) with a mean age at KT of 66.8 years with a minimum follow up of 12 months. The responses given by older patients were compared with national appropriate norms, and between sexes.
Results: All transplanted patients (n=63) showed significant improvement of QoL, whereas three of four significant QoL scales worsened in patients still on dialysis (n=40). Longer transplantation time was associated with greater improvement of QoL, while shorter time with lower BP freedom. Older women

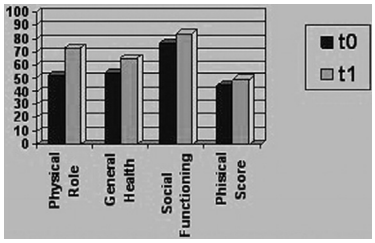

Figure 1. Kidney recipients (n=63).

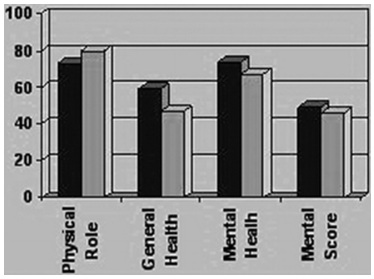

Figure 2. Patients still on dialysis (n=40).

reported significant limitations in SF, BP freedom and GH, while older men reported significant limitations in SF, BP freedom, RP and GH.
Conclusions: This is the first prospective study in patients on waiting list for renal transplantation.Our data confirm the improvement in physical domains after KT, with a great feeling of freedom immediately after, being pain still present, improving with time. Among older KT recipients, there was no difference between our population and national norm, but patients report significant limitations in social activities, lower vitality, greater perception of pain and worsening general health perception, without any difference between sexes.

P-852 MIMINALLY INVASIVE LIVING DONOR NEPHRECTOMY: IMPROVED RESULTS DURING RECENT YEARS – A SINGLE CENTER EXPERIENCE

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Introduction: In our single national Tx-center, we have since 1998 cautiously expanded the indications for laparoscopic living donor nephrectomy (LLDN). There has been an evolutionary kind of progress, both regarding technique and equipment, and we have during these years tried out various methods. During our randomised study (strictly laparoscopic vs open (2001-2004)) we experienced an unacceptably high rate of complications within the laparoscopic group, which urged us to explore alternative approaches.
Material/Methods: Since 2005, *160 hand-assisted LLDNs* have been registered in a prospective manner and compared to data from our randomised study. A Pfannenstiel incision (7-9 cm) has been used. The retroperitoneoscopic (RP) approach was abandoned after n=18 cases, for reasons explained below. After reintroduction of of the laparoscopic approach, 39 *right-sided* nephrectomies have been performed. In 2007 dissection/hemostasis with Ultracision was replaced by latest generation LigaSure.
Results: see Table 1 below.
Conclusions/Discussion: We consider the significant improvements in LLDN to be due to the following factors:

- Increased overall laparoscopic experience.
- The introduction of hand-assisted technique; affording increased security, both towards vascular incidents and gastrointestinal complications – and fast/efficient dissection.
- Major technical improvements, including 'High Definition imaging', improved handport (Gelport), blunt/non-cutting trochars, and above all, the latest generation LigaSure, taking care of all venous branches without clips.

Furthermore, we consider the 'laparoscopic approach' superior to the 'retroperitoneoscopic' for these reasons:

- The laparascopic approach exploits a large premade working space
- The retroperitoneoscopic space has to be created by extensive stripping of the peritoneum, potentially giving rise to 'traumatic peritonitis'. Besides, peritoneal perforations are hard to avoid – and the obtainable working space is smaller.
- The laparascopic approach is plain/more straight foreward and faster.

[Video-presentation]

P-854 CUSTODIOL VERSUS EUROCOLLINS: EFFECT ON EARLY GRAFT RECOVERY AND 24 MONTHS OUTCOME AFTER LIVING RENAL TRANSPLANTATION

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Introduction: Early graft recovery is beneficial factor for long term graft survival. The aim of our study is to asses the effect of Histidin-Triptofan-Ketoglutarat (HTC- Custodiol) as compared with Eurocollins (EC) on early graft recovery and long term clinical outcome after living donor transplantation.
Methods: A retrospective case control study was performed in 12 living renal transplant patients, 6 with EC and 6 with HTC. The sequential quadruple protocol with IL-2R antagonist and triple drug (MMF, CyA and steroids) maintenance immunosuppression was used in all patients. There were no significant difference between the groups in the donor's age (61±6 vs. 63±4), pretransplant GFR (78 vs. 75 ml/min), recipient's age (40± 9 vs. 40±12), warm ischemia time (4±1.4 vs. 3.5±1.4 min), cold ischemia time (225± 106 vs. 210±42 h) and HLA mismatch (2.4 vs. 2.6). The serum creatinine and GFR were evaluated during the first week, 30-th postoperative day and 24 months later.
Results: There was significant difference in the first postoperative week in serum creatinine between the EC and HTC groups (82.8±42 vs. 538±46), on day 30-th (97.6±20.4 vs. 140±5) as well as 24 months later (148±8 vs. 121.8 μmol/lit). The GFR in HTC group was also superior on day 7-th (76.9±13 vs. 41.3±2) on day 30-th (77.8±2. vs. 56.8±2)as well as 24 months later (58.9 vs 70.3 ml/min). There were no rejection episodes. In the EC group there were two pts with DGF.
Conclusions: Our results confirmed superior effect of HTC versus EC on early graft recovery and after 24 months of follow up even in living donor transplantation. The authors recommended use of HTC especially among the expanded criteria living donors.

P-855 EPIDEMIOLOGY OF INFECTIOUS COMPLICATIONS AND THEIR IMPACT ON THE OUTCOME OF RENAL TRANSPLANTATION RECIPIENTS (RTR)

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Infections represent a major cause of morbidity and mortality among renal transplant recipients.We aimed to analyse the epidemiology of infectious complications and their impact on the outcome of renal transplant recipients.
We analysed retrospectively 296 adults RT, performed at our department between 1986 and 2006. 56 (18.9%) were cadaveric, 240 (81.08%) were living transplants.Recipients were 194 males and 102 females, whose mean age (±SD) was 31.96±9.4 years (range 16-61 years).The median of the follow-up was 72.6 months
Prophylactic antibiotherapy was used at the time of transplantation and for up to 24 hours postoperatively. One single tablet of TMP-SMX was used during 4 to 6 months after transplantation in order to prevent infections with Pneumocystis cariini and Nocardia.
The patients were divided in 2 groups: G1 with infection and G2 without infection.244 (82.43%) patients presented at least one episode of infection during the follow-up, urinary tract infection is the most common infection (69.9%). 52 (17.56%) have never presented an infection.
The causes of death were infectious in 32 cases (58.18%): sepsis in 18 cases, pneumonia in 7 cases, tuberculosis in 2, viral in 4 cases
The actuarial patients survival rates at 1, 5 and 10 years in the G1 was re-

Abstract P-852 – Table 1

Mean (range)	2001-2004 Strict laparoscopic (n=63) All left-sided [Randomised study]	2005-2006 Hand-assisted (n=34) RP-scopic (n=18) + Laparoscopic (n=16) Left 27 + Right 7	2007-2009 Hand-assisted Laparoscopic (n=126) Left 94 + Right 32
Op. time (min.) [Experienced surgeon]	180 (110-295)	177 (130-240)	143 (100–185)
Periop. incidents	Vascular lesions: 2; Conversions: 2	Vascular lesions: 2; Conversions: 0	Conversions: 1 (GIA failure)
PCA-Analgesia Postop. days 0 + 1 (Morphine Equiv.)	28,1 (0-77)	40 (4-87)	32 (0-107)
Complications	Total: 6 (10%); Serious: 2 (intest. perf.)	No major	No major (1 reop. for s.c.-sinus)

Table 1

	G1	G2	p
Mean age (years)	31.7 ±9.4	33.1±9.3	0.33
Female gender	81%	18.6%	0.035
Acute rejection	38.1%	26.9%	0.003

spectively: 95.8%, 87% and 75.5%, whereas in the G2, was respectively 98%, 94.9% and 94.9%. The differences between the two groups were statistically significant (P = 0.01).
The prevalence of infections in our study remains high.Urinary tract infection iare the most common infection. In our study, acute rejection and female gender represent the main risk factors for bacterial infection.
Infectious complications in renal transplant recipients are still an important issue.

P-856 INFLUENCE OF ADVANCED AGE OF THE DONOR ON THE EVOLUTION OF RENAL TRANSPLANTATION

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Purpose: Regarding to increasing number of patients with renal failure, the recourse to marginal donors became more frequent. The goal of our study is to determine influence of advanced age of donors on the transplanted kidney.
Materials and methods: Retrospective, unicentric study of 153 kidney transplantations operated between February 1994 and December 2007. Grafts and Receivers were divided into two groups according to the age of donors. Group 1: age lower or equal to 50 years (G1: 117 cases) and Group 2: age higher than 50 years (G2: 36 cases). Pearson and Chi-square tests were used for statistical comparison. Patient and graft survival were compared between the 2 groups using Kaplan-Meier survivorship curves and results were compared using log rank test
Results: The mean age of donors was 39.4 years (21-50 years) for G1 and 56.7 years (51-72 years) for G2. All grafts of G2 were from living kidney donors. No factor of comorbidity was noted in the donors of G2. The rate of specific surgical complications was of 34.2% in G1 and 38.9% in G2 (p=0.6). A similarity was found between rates of vascular and urological complications (G1 vs G2), compared globally and individually. Graft Survivals were respectively 77 and 48% for G1, and 52 and 50% for G2 at 5 years and 10 years with no statistical significant difference (p=0.30). The mean survival half-time of the grafts of G2 was respectively 16.85 months and 18.66 months, for receivers aged between 20 and 40 years, and those of more than 40 years.
Conclusion: Although considered at high-risk, renal transplantation from older donors appears to have satisfactory results. Older donors can be selected according to well defined criteria to prevent organs penury without compromising graft function or receiver survivals.

P-857 EVOLUTION OF KIDNEY TRANSPLANTATION USING MULTIPLE ARTERIES RENAL GRAFTS

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Purpose: Kidney grafts with multiple arteries have been suspected to be associate with a higher incidence of vascular and urological complications, but effects of multiple arterial anastomosis has not been clearly defined. We intend to compare renal transplant short and long-term outcomes between grafts with single versus multiple arteries.
Materials and methods: Retrospective study, 153 kidneys transplanted between 1994 and 2007. Grafts were divided in tow groups: 122 with single renal artery (SRA) and 31 with multiple renal arteries (MRA). The 2 groups were compared regarding patients and grafts survivals, early and late vascular complications, urological complications, incidence of acute tubular necrosis (ATN), acute rejection and post-transplantation hypertension. Pearson and chi-square tests were used for statistical comparison. Patient and graft survival were compared between the 2 groups using Kaplan-Meier survivorship curves and the results were compared using log rank test.
Results: Patient and graft survivals were comparable in both groups: p value 0.18 and 0.17 respectively. Both groups were comparable regarding: acute rejection, post-transplantation hypertension, renal artery stenosis and urological complications. Only hemorrhagic complications and renal artery thrombosis were significantly higher in MRA: p value 0.027 and 0.03 respectively. Warm ischemia time was significantly longer in MRA without influence on incidence of ATN (p=0.2). Mean serum creatinine level at 1 year was 154.75±9,2 vs 171.37±18,8 (p=0.5) and at 5 year 165.8±8.9 vs 157.25±4.7 μmol/l (p=0,1) respectively in SRA and MRA. Return to hemodialysis was necessary for 18.8% of the SRA group and 16.1% of the MRA group. No death was noted in the MRA group.
Conclusion: The use of MRA allografts is a safe and successful surgical procedure, with no influence on patient or graft survival and without increasing of surgical complications rate.

P-858 ABO INCOMPATIBLE LIVING DONOR TRANSPLANTATION-THE FIRST CLINICAL EXPERIENCE IN SKOPJE

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Introduction: Due to the severe organ shortage in the Balkans we started accepting expanded criteria living donors including elderly, marginal and unrelated donors. In the last years ABO incompatible renal transplantation started, to. The first four cases are presented here.
Methods: A 40-yr mother (blood group A1B), 57-yr husband (B), 46 – yr wife (A1) and 39-yr mother (A1B) were considered as suitable donors for four recipients (blood groups B, 0, 0, and A1, respectively). The recipients serum anti-A1 and anti-B isoaglutinnin titer was in range from 1/64 to 1/128 before the procedure. A routine laparoscopic splenectomy was performed in 3 of 4 recipients 38, 42 and 180 days before the transplantation. In the 10 days pre-conditioning period we started with rituximab (375 mgr/m), 4-5 plasmaphereses to reduce the antibody titer below 1/4, and IvIg (0.5 gr/kgr/bw) one day before the surgery. Standard induction (Daclizumab) and triple drug therapy (CyA, MMF, steroids) was introduced. The routine 4-5 plasmapheresis was performed in the first two weeks after transplantation.
Results: Three of four kidney recipients are doing well 12 months after the surgery with un avarage serum creatinin of 199 μmol/lit and GFR 55 ml/min. Due to the reapeted rejection episodes the second recipeint with unrelated donor lost the graft after 3 months. The one month protocol biopsies showed sub-clinical acute rejections in two recipients and steroid pulse therapy was introduced. The regularly monitored anti-A1 and anti-B antibody titer in all recipeints was below 1/8.
Conclusions: The first short-term results despite the loosing of one graft encourage us to continue with this type of intervention. The authors consider ABO-incompatible renal transplantation as a safe and promising procedure that may ameliorate the actual organ shortage in the region.

P-859 ROLE OF CALCIUM PRELOADING IN PATIENTS UNDERGOING PARATHYROIDECTOMY FOR RENAL HYPERPARATHYROIDISM

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Introduction: Parathyroidectomy has an important role in the management of renal hyperparathyroidism refractory to medical treatment. Postoperative hypocalcaemia is the major complication occurring in up to 95% of patients. The aim of this study was to evaluate the role of pre-operative loading with calcium and its effect on the occurrence of postoperative hypocalcaemia.
Material & methods: Over a 12 month period (Jan'04 to Jan'05), 20 consecutive patients with renal hyperparathyroidism, who had failed medical treatment were included in the study.
All patients received 4ug of alfacalcidol for 4 consecutive days and 3 gm of calcium for 2 consecutive days prior to surgery. Preloading calcium and the immediate preop calcium values were noted. Total parathyroidectomy and a transcervical thymectomy were performed on all. A central line was inserted intraoperatively for intravenous calcium infusion, if required postoperatively. Postoperative calcium, alkaline phosphatase & parathormone (PTH) levels and presence or absence of hypocalcaemia were recorded.
Results: There were 8 males and 12 females in the study group with a median age of 52 yrs (24-82 years). 16 patients had secondary hyperparathyroidism while 4 had tertiary hyperparathyroidism. The mean preloading calcium was 2.66±0.22mmol/l while the mean post-loading calcium was 2.81±0.41mmol/l. Although a decline in serum calcium was noted, no patient had symptomatic hypocalcaemia or required intravenous calcium postoperatively. Mean lowest recorded calcium in the first week was 1.99 ± 0.21 mmol/l.
Conclusion: Preloading with calcium & vitamin D in patients of renal hyperparathyroidism undergoing parathyroidectomy appears to be safe and prevented symptomatic hypocalcaemia in all patients. It obviated the need for post operative intravenous calcium which is inherently dangerous. We commend preloading in all patients undergoing parathyroidectomy.

P-860 VASCULAR THROMBOSES AFTER RENAL TRANSPLANTATION

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Purpose: Vascular thromboses after renal transplantation becames rare but remains serious with generally the loss of the graft. Our objective is to study the ethiopathogenic, epidemiologic, diagnostic and therapeutic aspects of this pathology.

Material and methods: Retrospective study of 160 kidney transplantations carried out over 14 year's period (1994-2008). All cases of vascular thrombosis were reviewed.
Results: Vascular thromboses were noted among 6 patients, 3 men and 3 women. The mean age was 40 years (30-54). A patient was coronary with repeated thromboses of the arteriovenous fistulae. A patient had history of central retina vein thrombosis without homeostasis disorders at the pre-transplant assessment. Arterial thrombosis was noted in 3 cases, with multiple renal arteries graft in 2 cases. This complication was noted during transplantation in 1 case, requiring the refection of arterial anastomosis. In the 2 other cases, arterial thrombosis was revealed by anuria within post-operative 8th hour and 16th day respectively. The diagnosis was suspected on Doppler-sonography. A transplantectomy was necessary in a case of hemorrhage with heamodynamic disorders and in case of ischemic devascularized grat in the 2 other cases. Venous thrombosis was noted in 3 cases. It was suspected during surgery in 1 case, requiring the refection of the venous anastomosis. The patient was deceased after 2 days secondary to pulmonary embolism. In the 2 other cases, this complication appeared by a break of diuresis after 2 and 9 post-operative days respectively. A surgical exploration finds a cyanosite kidney in the 2 cases. The surgery consisted on a repair of the vascular anastomosis in 1 case, while a transplantectomy was necessary in the other case.
Conclusion: Vascular thromboses are the most frightening surgical complications of renal transplantation. Once the diagnosis is made, a surgical exploration must be tried rapidly to save the graft and its function.

P-861 EARLY mTOR INHIBITION BLOCKS GLOMERULAR HYPERTROPHY AFTER RENAL MASS REDUCTION

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Sirolimus (SRL) has been associated with a beneficial effect in terms of proteinuria and histological damage if initiated six weeks after renal mass reduction (RMR) in a rat model. The aim was to evaluate the influence of SRL treatment on proteinuria and renal histology if initiated before and very late after RMR in a rat model.
Methods: Rats either underwent cryoablation of 2/3 of the left kidney and subsequent right nephrectomy (group Nx; n=42) or sham operations (group S; n=29). Two weeks before (Early) or twelve weeks after (Late) RMR, treatment with SRL or vehicle (VEH) was initiated at 1.0 mg/kg three times a week. Creatinine clearance and proteinuria were evaluated in all 8 groups. 18 weeks after RMR, glomerular hypertrophy, glomerular sclerosis, tubular atrophy, interstitial fibrosis and chronic inflammatory infiltrate in the left kidney were evaluated.
Results: Immediately after RMR creatinine clearance was lower in rats with reduced renal mass (4.48 mL/min·kg vs. 1.81 mL/min·kg; $p<0.001$). At the end of treatment, creatinine clearance was not different between Nx+VEH and Nx+SRL (E and L). The development of glomerular hypertrophy was blocked by early SRL administration only.

Glomerular diameter (μm)

Early study		Late study	
S + VEH	142.8±8.3	s + VEH	154.0±6.6
Nx + VEH	227.9±20.3#	Nx + VEH	198.8±11.2#
S + SRL	128.9±7.5	S + SRL	134.2±9.8
Nx + SRL	170.8±14.3#*	Nx + SRL	196.5±23.7#

*$p<0.05$ versus VEH; #$p<0.05$ versus Sham

Four weeks after RMR, a significant increase of proteinuria was observed, SRL administration early and late after RMR led to a stabilization of proteinuria either after four weeks in the early administration or from the time of initiation of SRL in the late study, whereas the group Nx+VEH experienced a further increase of proteinuria. RMR rats treated with SRL have less structural damage in all evaluated parameters,.
Conclusion: SRL treatment has the potential to halt progression of proteinuria at any time during the course of progression in a model of reduced renal mass but only early SRL introduction blocked glomerular hypertrophy.

P-862 mTOR INHIBITION BLOCKS CARDIAC HYPERTROPHY AFTER RENAL MASS REDUCTION

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The objective was to evaluate the influence of sirolimus treatment on cardiac hypertrophy produced in a rat model of renal mass reduction.
Methods: Rats either underwent cryoablation of 2/3 of the left kidney and subsequent right nephrectomy (group Nx; n=16) or sham operations (group S; n=15). Six weeks after nephrectomy or sham operation treatment with SRL or vehicle (VEH) was initiated at 1.0 mg/kg three times a week. At the end of study, 18 weeks after nephrectomy, the heart was extracted to carry out the histological analysis. In the macroscopic analysis of the hearts, we defined two situations; normal or concentric hypertrophy. The interventricular septum and the left ventricular wall were also measured.
Results: 5/6 nephrectomy produced a significant increase of cardiac mass normalized by the tibia length (S+VEH =0.25±0.03 g/cm vs Nx+VEH = 0.32±0.06 g/cm, p=0.03). This effect was blocked in nephectomized animals treated with SRL (0.22±0.03 g/cm, p=0.004 vs Nx+VEH). Nx animals, VEH and SRL, presented concentric hypertrophy in 57% and 44% respectively. The group Nx+VEH presented a significant increment of the interventricular septum and the left ventricular wall, while SRL treatment impeded the coarsening of these parameters.
Conclusion: SRL treatment blocked cardiac hypertrophy in the reduced renal mass rat model.

P-863 BENEFIT OF RENAL TRANSPLANT BIOPSIES

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Histology of renal transplant biopsies is well established. But is there really advantage, when we do a biopsy?
Methods: About 1000 biopsies of renal transplants which were performed because of increase of creatinine or (new-onset) of proteinuria were evaluated. We have investigated two questions: First, if the histology can explain the cause why renal transplant biopsy was performed. Second question was, if the clinical conclusions can effect an improvement of the status.
Results: 1. Mostly renal transplant histology shows an explanation for transplant dysfunction. 2. Improvement of the status is dependent on cause for biopsy. It is achieved often in patients with acute increase of creatinine, less often in patients with creeping creatinine and patients with (new-onset of) proteinuria. Also the renal transplant histology suggests, if there will be an improvement after treatment.
Conclusions: Renal transplant biopsies can explain transplant dysfunction in most of the cases and can often predicte further outcome of the transplant. Therapy regimen mostly is not educible from the biopsy, but histology often contains fundamental references to treatment changes.

P-864 CLINICAL EVALUATION OF THE MECHANICAL SUTURE IN VASCULAR OPERATIONS IN END STAGE RENAL FAILURE AND POSTTRANSPLANT PATIENTS WITH COAGULOPATHY – AN OWN EXERIENCE

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Mechanical suture is not a standard mean of vascular anastomosis due to price of a set of 25 staplers – 50 times of standard prolene suture. There are situations, however when this cost may be fully compensated by an effect of the use of staplers in patients with coagulopathy when use of non penetrating staplers for anastomosis without making holes in prosthesis protects from serious bleeding which always hapens from needle punctures made in PTFE during standard suture. Therefore despite higher cost of staplers their application in patients with coagulopathy is fully justified for avoiding a serious complications like hematoma, infection and even PTFE graft loss.
We used vascular sutures in 47 dialysed or transplant patients while engrafting PTFE prosthesis in following operations:
– 31 straight arteriovenous (a-v) PTFE on arm ∗ 1
– 5 PTFE bridges femoro-femoral suprapubicus, ilio-iliac or ilio-femoral ∗ 2
– 6 PTFE loops on the arm or the femour ∗ 3
– 5 PTFE bridges of a-v or arterial posttransplant nanastomosis ∗ 4
Out of 47 vascular grafts 39 (83%) survived 12 months. Eight grafts have been removed (17%) 6 due to infection in diabetic patients 2 for thrombosis.
Five patients with thrombosis had operation with good result, some of them several times, including 1 patient with an aneurysm of the venous end of a-v fistula.
Not a single complication related to staplers themselves, including septic cases was observed. Very careful inspection of staplers prooved that even in cases requiring finally removal of PTFE, location and function of staplers was uncompromised.
Conclusion: Nonpenetrating vascular staplers, despite their high cost are strongly recomended in vascular operations with use of PTFE, especialy in patients with coagulopathy such as hemodialysis and posttransplant patients.

P-865 FUNCTIONAL AND METABOLIC EFFECTS OF EVEROLIMUS-BASED IMMUNOSUPPRESSION IN DUAL KIDNEY TRANSPLANTATION

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The old-to-old allocation strategy of extended criteria donors rises patients (Pt) cardiovascular and renal risk (CVR) related to immunosoppressive theraphy (IT) and traditional risk factors.
We evaluated the functional and metabolic impact of a sequential IT based on everolimus (Ev) and low dose cyclosporine (CsA) vs conventional triple IT with CsA in de novo dual renal transplant (DRT) recipients 6 months after transplantation (6MPTx).
Materials and methods: IT included basiliximab induction, differed CsA (serum creatinine <3 mg %) (SCr), mycophenolate mofetil (MMF) till Ev introduction after 3 weeks. CsA peak concentration (C2) was 350 ng/ml. IT Cumulative concentrations were targeted to 12 (Ev TLC + CsA C2/100).
6MPTx outcomes are: SCr, MDRD, Total CH, HDL, LDL, Triglycerides (TG), fasting blood glucose (FBG), post transplantation diabetes mellitus incidence (PTDMi), drugs (statins, ω3, insulin, antidiabetic oral agents (ADO)).
Results: *Ev IT Group* (11 Pt; 1f/10m; mean age 61.8±5.5y) 6MPTx results are (mean ± SD): SCr 1.35±0.5 mg/dl; MDRD 65.5±25 ml/min; Total CH 230.6±60.2 mg/dl; HDL 58.8±12.8 mg/dl; LDL 138.4±38.9; TG 200.5±82.4 mg/dl; FBG 102±9.2 mg/dl. PTDMi is 2 out of 11 Pt (18.2%), 2 Pt were on ADO (18.2%), 7 on statins (63.6%), 6 on ω3 (54.5%), 0 on insulin.
CsA Group (12 Pt; 3f/9m; mean age 61.8±5.6y) 6MPTx results are (mean ± SD): SCr 1.66±0.5 mg/dl; MDRD 45.5±13.5 ml/min; Total CH 201.9±46.1 mg/dl; HDL 50.7±18.8 mg/dl; LDL 120.4±35.9; TG 160.1±68.4 mg/dl; FBG 91±11.8 mg/dl. PTDMi is 1 out of 12 Pt (8.3%), 1 Pt were on ADO (8.3%), 3 on statins (25%), 2 on ω3 (16.7%), 0 on insulin.
Difference between Ev and Csa group mean MDRD and FBG ($p<0,05$) is significant.
Conclusions: DRT pt benefit from a renal function recovery with this IT; the negative effect on CVR by hyperlipidemia and rising glucose should be balanced by higher GFR.

P-866 ANAEMIA AND ERYTHROCYTOSIS AFTER KIDNEY TRANSPLANTATION AND 5-YEAR GRAFT SURVIVAL

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Introduction: Both anaemia and erythrocytosis frequently occur after kidney transplantation (KTx). However their influence on cardiovascular complications and the risk of kidney graft loss is not well documented. The aim of this study was to analyze the influence of both anemia and erythrocytosis on kidney graft function and patients outcome in long-term follow-up after kidney transplantation.
Patients and methods: Two hundred ninety nine consecutive patients with at least 12-month after successfully kidney transplantation were enrolled in this study. 90.1% of analysed patients had completed a 5-year follow-up period. Anaemia occurred in 29.5% of patients (in 16.1% Hb<11.0g/dl), while erythrocytosis in 19.1% of patients (including 9.0% with Ht>55%). We have analysed the graft function 12 months after KTx and the impact of anaemia or erythrocytosis on 5-year risk of death and graft loss.
Results: In 58% of anaemic patients low haemoglobin concentration did not reach normal range in the whole observation time after KTx. The mean eGFR-MDRD 12 months after KTx was significantly lower in patients with anaemia (44.9±18.8ml/min vs. 52.9±17.0ml/min; p=0.01). Better 12-month graft function was observed in patients with erythrocytosis (59.0±18.4ml/min). Anaemia but not erythrocytosis was associated with the increased risk of graft loss [RR=3.79 (1.97-7.29); p<0.001]. The risk of death was similar in all subgroups.
Conclusion: Anaemia after KTx is associated with a worse kidney graft function and is a strong predictor of graft loss. Erythrocytosis occurs in patients with excellent kidney graft function, nonetheless it did not increased the risk of graft loss or death when properly treated with phlebotomy.

P-867 USE OF STENTING IN LIVE KIDNEY DONATION: DOES IT REDUCE VESICOURETERAL COMPLICATIONS?

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Purpose: The risk of urological complications after kidney transplantation is between 2.5% and 30%. It has been suggested that routine use of an ureteral stent (splint) as prophylactic measure diminishes the risk of urological complications. However, the role of stents is not well defined and there is concern about potential stent related complications. Therefore the aim of this study was to assess the impact of prophylactic splint placement on the necessity of percutaneous nephrostomy (PCN)after live kidney transplantation.
Methods: From January 2003 to December 2007, 342 live kidney donations were performed. In 285 patients a splint was used and in 57 no splint was used. All patients with residual urinary production received a splint. Intra- and post-operative outcome was retrospectively collected. Multivariate regression analysis, adjusting for baseline characteristics, was applied to assess the impact of stent placement on the rate of PCN placement.
Results: Baseline characteristics were not significantly different, except for the number of transplantations: 31 (11%) with a splint versus 16 (28%) without had a history of >1 transplantation (p<0.001). Fourty-five (19%) of the stented group received a PCN <3 months after transplantation versus 12 (21%) in the non-stented group (p=0.71). Re-operation rate for urologic complications were similar for the stented and non-stented group (3% vs. 5%, p=0.43). In multivariate analysis, the risk for PCN was similar in stented and non-stented patients (HR 1.0, 95%CI 0.5-2.1). During a median follow-up of 37 months [IQR 23-52] recipient and graft-survival did not differ between both groups. Graft failure occurred in 26 patients (9%) in the stented group, and in 8 (14%) in the non-stented group (p=0.26).
Conclusion: Ureteral stent insertion is not associated with a reduced rate of PCN placement in live donor renal transplantation. Prospective studies according the use of a splint are warranted.

P-868 EARLY PREDICTIVE RISK FACTORS OF RENAL DETERIORATION IN TRANSPLANT RECIPIENT

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Chronic allograft dysfunction is one of the main causes of allograft failure.We are interested in detecting earlier predictors of late allograft dysfunction.
The aim of this study was to evaluate risk factors of worse renal function at 5 years after transplantation and its predictive values.
We performed a retrospective study of 196 patients (minimum follow-up: 60 months) transplanted in the last 10 years. We considered worse renal function (WRF) as patients whose serum creatinine values at 5 years were ≥1.55mg/dl, value that was determined by means of area under the ROC curve. WRF was found in 109 patients (55.6%). Univariate analyses showed that WRF was associated with older donors (47.7% vs 17.2%, P=0.000), cerebrovascular cause of death (62.4% vs 43.7%), p=0.010), delayed graft function (DGF) (35.8% vs 19.5%, p=0.017), proteinuria ≥0.5g/24h maintained a minimum of 3 months (38.1% vs 18.6%, P=0.002), worse serum creatinine and proteinuria levels during the follow-up ($p<0.05$). No differences were found in respect to immunosuppression, acute rejection episodes, blood pressure levels or antihypertensive treatment. Multivariate analyses confirmed donor age ≥55 years (HR 4.527, 95%CI 2.273-9.015, P=0.000) and proteinuria ≥0,5g/24h maintained (HR 3.031, 95%CI 1.508-6-090, P= 0.002) as stronger risk factors of WRF; after the exclusion of donor age, DGF appears as a risk factor of WRF (HR 2.020, 95%CI 1.024-3.985, P=0.042). Of these risk factors, positive predictive values (PPV) of donor age ≥55 years was of 77.6%, PPV of DGF of 69.6%, and maintained proteinuria ≥0,5g/24h, a PPV of 72.9%.
We conclude that increasing age of present donors, DGF, and maintained proteinuria (≥0,5g/24h), marker of tissue injury, were related to a worse renal function at 5 years with goods PPV. Preventive measures to reduce DGF, and early nephroprotection are needed to preserve renal allograft function in transplant recipients.

P-869 COMPARATIVE ANALYSIS OF ELDERLY VS YOUNG RENAL TRANSPLANT RECIPIENTS: SOUTH INDIAN EXPERIENCE

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Purpose: To compare graft survival between young (45- 60 years of age) and elderly (>60 years of age) renal transplant recipient.
Materials and methods: Retrospective study on cohort of 188 patients who underwent renal transplantation. We studied recipients aged 45 to 60 years (Group A) and recipients aged >60 years (Group B). Patient and graft survival were analyzed by Kaplan-Meier method.
Results: Group A (n=144) – mean age 51.51±4.02 years, 108 males (75%), 73 (50.7%) diabetics, 131 (91%) hypertensive, 27 (18.8%) Coronary artery disease (CAD), 26 (18.2%) smokers. 108 (75.5%), Hepatitis C 5.6% (8), Hepatitis B two (1.4%), CMV two (1.4%). Twenty-nine (20.3%) on Vit- D supplementation preoperatively. Mean creatinine (mg/dL) at 0, three and six months was 1.41±0.83, 1.27±0.74 and 1.26±0.26.Mean eGFR (mL/min/1.73 m^2) was 64.96±22.01, 72.92±35.01 and 65.81±17.60.

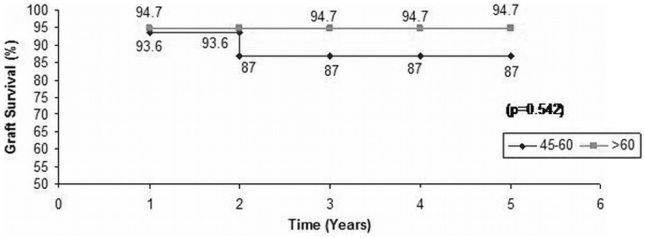

Figure 1. Death censored graft survival between group A & B.

In Group B (n=44) with mean age (63.06±2.81 years), there were 37 males (84.1%), 26 diabetics (59.1%), 42 (95.5%) hypertensive, 16 (36.4%)with CAD, 26 (18.2%) smokers, Hepatitis C 6.8% (3), Hepatitis B one (2.3%), pulmonary TB 4 (9.1%), CMV one (2.3%). Ten (22.7%) on Vit D supplementation preoperatively. Hepatitis C 6.8% (3) Hepatitis B one (2.3%), CMV one (2.3%). Mean creatinine (mg/dL)at 0, three and six months was 1.47±1.02, 1.29±0.23 and 1.2±0.29.Mean eGFR (mL/min/1.73 m^2)67.90±23.48, 67.02±12.76 and 75.23±15.19.

Patient survival – Group A at one, two and three years (92%, 89.8% and 88.9%), group B (88.1%) for three years (p=0.884). Figure 1 shows death-censored graft survival.

Conclusion: Although renal transplant recipients aged over 60 years have lower patient survival, they have higher graft survival compared to younger group. This may be attributed to decreased immunity with higher age. Co-morbidities such as CAD, rather than renal transplantation may contribute to higher mortality in elderly patients.

P-870 RESULT OF KIDNEY TRANSPLANTATION, EVOLUTION OF RENAL FUNCTION AND PROTEINURIA IN SPAIN IN THE ACTUAL IMMUNOSUPPRESSIVE ERA

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Aim: To prospectively evaluate the presence and risk factors of CVD after renal transplantation, we established a prospective database (no intervention)

Methods: We analyzed the results of all kidney transplanted patients during years 2000-2002 in 14 Spanish units (n=2600), most of them from cadaveric donors.

Results: Donors and recipient age were 46.9±17 and 49.7±13.7 years, 63% men, 16% were retransplanted and 12.5% hyperimmunized. The most frequent immunosuppressive protocol was Tac+MMF+St 45.9%. Steroids were wthidrawall in 30% of patients. Acute rejection rate at 1 year was 14.8%. Graft survival at 48 months was 85.6% (death censored), and 77.8% (death non censored). The first cause of graft loss was death with functioning graft during the first three years, and chronic allograft nephropathy at the 4th year. Mean serum creatinine and proteinuria were stable along these four years.

Renal Function

	Month 6	Year 1	Year 2	Year 3	Year 4
CrS (mg/dl)	1.63	1.63	1.57	1.7	1.5
Proteinuria (g/day)	0.4	0.4	0.4	0.5	0.59

Patient survival at forth years was 91.7%. Cox regression analysis showed that time on dialysis (HR=1.96, CI01.24-3.10, p=0.004) and renal function impairment (HR=1.52, CI=1.30-179, p<0.0001) were independent risk factors for graft loss at 4th year. Moreover, multivariate analysis showed that recipient age was the most important predictor of mortality (HR=2.5, CI=1.72-3.78, p<0.0001) whereas acute tubular necrosis (HR=1.5, CI=1,07-2,36, p=0.02) and renal function impairment (HR=1.3, CI=1,11-1,53, p=0.001) where other independent risk factors.

Conclusion: Results of renal transplantation in Spain are good. The patients achieve maintaining an stable renal function. Theses result are representing the clinical practice in our country.

P-871 THE INVOLVEMENT OF ACTIVATED T CELLS AND CYTOKINES PRODUCTIONS CORRELATES WITH CLINICAL OUTCOMES IN CHRONIC RENAL ALLOGRAFT REJECTION: HOW FAR/CLOSE WE ARE?

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We hypothesize that vascularized transplants have the potential to activate naive T cells in the absence of secondary lymphoid organs. The priming and effectors pathway could be operative for the lifetime of the allograft and thus contribute to the chronic rejection (CR).

To provide further insight the immunologic basis of CR, a cross-sectional analysis of cellular and humoral immunity in renal allograft recipients was performed. The study of possible risk factors for CR is based on 6, 7±3, 7 years. Whether peripheral T cells control inmmunosuppressed renal transplant patients, we analyzed the suppressive capacitie, level of cytokines (sCD30, TNF-α, IL-2 and IL-2R) and PRA, pre and post- transplant of 116 recipients. Cox regression model was used to assess the significance all tested parameters. All P values are two sided and considered statistically significant if less than 0.05 (STATA 7.0).

Allogeneic stimulation of patient's blood cells was associated with T-cell proliferation of individuals who responded to donor antigens and per group was statistically higher in CR patients (P<0.032). Significances was present between measurements r=1.163.66; P<0.05, CR/non CR. Mean level of TNF-α is significantly correlated with CR (P=0,025) and GFR. De novo alloantibodies in patients with functioning grafts presage subsequent failure (OR=3.92) with more failures in those who developed antibodies (P=0,01).

Alloreactivity against anti-donor T cells are readily detectable in allograft recipients during treatment with full dosage immunosuppression and long term function. Difference of TNF-α and renal function are interrelated. Immunological quiescence, like immune reactivity is thus not per se an inert situation, but an active state, in which checks and balances have resulted in responsiveness in recipients with chronic rejection.

P-872 DOES RENAL TRANSPLANTATION IMPROVE QUALITY OF LIFE?

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The common opinion is that successful renal transplantation improves quality of life. Studies are rare, data are not available.

49 patients after renal transplantation after living donation were investigated. Standardized questionnaires SF-12, PLC and FZL were used for characterizing quality of life.

Mean time between renal transplantation and psychological investigation was 4.75 years. The comparison of quality of life before and after renal transplantation shows significant improvement after renal transplantation (coefficient of correlation 0.370). Even interpersonal skills improved (coefficient of correlation 0.185). Allegiance was significant reduced after transplantation (coefficient of correlation -0.279). The results of SF-12 questionnaire showed wide influence of physical condition to the quality of life (p=0.018) than mental condition (p=0.087). Mental well being trends to correlate to fear of dialysis (p=0.054). Results of questionnaire SF-12 show an agreement between patients and physician in physical and psychological questions (Spearman rank correlation in all qualities of life p>0.05).

The investigation of quality of life of patients after renal transplantation shows better physical constitution with consecutive improvement of quality of life. Several mental domains were negative affected.

P-873 COMBINED LIVER AND KIDNEY TRANSPLANTATION (SIMULTANEOUS OR SEQUENTIAL) IN SPAIN

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Background: Patient survival in liver transplantation is 81% at first year, 73% at 3 years and 57% at 10 years. However, studies are needed to evaluate patient evolution in combined liver and kidney transplantation.

Objective and methods: Observational, retrospective and multicenter study assessing adult patients with combined liver and kidney transplantation (simultaneous or sequential) between 1991-2006 in Spain. Data were collected at time of transplant, at 6 months, 1, 3, 5, 7 and 10 years post-transplantation.

Results: 190 patients were included (150 simultaneous and 40 sequential transplant [4 kidney-liver KL- and 36 liver-kidney LK-]). Patients were mainly men and mean age was 51.3±9.5 years (simultaneous transplant), 47.3±6.1 years (KL) and 54.4±11.4 years (LK). Main reason for kidney failure was primary glomerulonephritis, whereas cirrhosis was the main cause of liver fail-

ure. The most common immunosuppressive regimen at discharge was anticalcineurins, mycophenolate acid and steroids. The mean creatinine clearance for combined transplant was 54.8 ml/min at 5 years and 61.3 ml/min at 15 years. At five years, 75% of patients with a combined transplantation were alive, and 55% at ten years Estimated mean patient survival was 9.1, 7.5 and 9.5 years for simultaneous, LK and KL, respectively. Main cause of death was infection. Hypertension and hyperlipemia were the most commonly reported complications. Graft loss in patients with simultaneous transplant was 15.3% for renal graft, and 14% for liver graft. Acute rejection (AR) rate of renal graft was 2.7% and 12.7%. for liver graft. All renal and 73.7% of liver AR episodes took place during first year postransplant.
Conclusions: Combined liver-kidney transplantation had good medium and long term outcomes, similar to those obtained in liver transplantation alone. This kind of transplants is a valid option for patients with end-stage liver disease who also suffer kidney failure.

P-874 INFLUENCE OF URETHER CATHETERYSATION ON FREQUENCY OF MAJOR UROLOGICAL COMPLICATIONS IN PATIENT UNDERWENT RENAL TRANSPLANTATION

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Major urological complications (MUC) after cadaveric renal transplantation occurs often and may lead to a lost of transplant in patients, among them the most common are: necrosis and stricture of the ureter's end, and urinary leakage.
The aim of the study was influence of the stenting of the uretero-vessical anastomosis with double J stents on incidence of major urological complication in patients after cadaveric renal transplantation.
Material and methods: Data from 223 patients who underwent renal transplantation, between 2006-2008 in Departament of Gnereal, Endocrine and Transplant Surgery of Medical University of Gdansk were analyzed. Patients were randomly divided into two groups due to double J catheterization. In the both groups the incidence and the type of MUC were noted and the rate and type of infection complications were analyzed.
Results: 20 MUCs (8,73%) were observed in both examined groups. Among them the most common were urinary leaks which were observed in 11 eleven patients with double-J stents and in one patient in non-stenting group.
In 4 cases of of the distal end of ureter necrosis only one of patient belonged to the group without stent, stricture of anastomosis was observe in 3 cases.
Double J stent was introduced in 87 patients, In that group only 2 MUCs were observed. Interestingly the incidence of the infectious complications were equal in both groups
Conclusions: The analysis of the data revealed that incidence of MUC in our material is decreased by the standard stenting of the uretero-vessical anastomosis, and do not influence on frequency of the infectious complications.

P-875 B CELL DEPLETION AT INDUCTION INCREASES ACUTE REJECTION

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B cell depletion is an effective treatment for a number of autoimmune diseases in which B cells were not previously considered important, for example multiple sclerosis. In renal transplantation, acute cellular rejection has been viewed as a T cell-dependent process, but B cells are required for alloantibody production and may also play other roles, including alloantigen presentation to T cells.
We performed an open label, randomized, controlled trial comparing rituximab, a B cell-depleting, chimeric, anti-CD20 monoclonal antibody, to an anti-CD25 monoclonal antibody (daclizumab) as induction therapy in renal transplantation. We planned to recruit 120 patients but the study was suspended following recruitment of the first 13 patients due to an excess incidence of acute cellular rejection in the rituximab group. Five of six patients (83%) who received rituximab experienced an episode of biopsy-proven acute rejection in the first three months post-transplant, as compared to one of seven patients (14%) in the daclizumab arm (p=0.01). All episodes of rejection responded to intravenous methylprednisolone, and allograft function was similar in both groups at 12 months.
Following rituximab, peripheral B cells were undetectable in all patients. Serum levels of TNF-α, IL-6, and IL-10 were increased following transplantation compared with baseline in some patients treated with rituximab.
Our findings are surprising; patients receiving rituximab not only had a higher rate of acute rejection than the control group (83% versus 14%), but also higher than that historically observed in patients who receive no induction therapy (35%). One possible explanation may be that pro-inflammatory cytokine release associated with B cell depletion might prime antigen-presenting cells. Alternatively, there may have been depletion of immunoregulatory B cells.

P-876 DE NOVO BRONCHIOGENIC MALIGNANCIES FOLLOWING KIDNEY-PANCREAS TRANSPLANTATION – A SINGLE CENTER REPORT

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Chronic immunosuppressive therapy (IS) implicates a higher risk for cancer development. In Europe, bronchial cancer (BC) is associated with the highest mortality rate compared to other malignancies. Aim of this study was to evaluate incidence and outcome of patients developing BC following kidney or simultaneous pancreas kidney (SPK) transplantation.
Retrospectively, we analyzed patients who underwent SK or SPK transplantation at our institution between 1997 and 2008 and later on developed BC. Among 1510 patients, 9 (0.6%) developed BC. 2 patients following SPK and 7 kidney transplantation; 2 patients were female. Median age at transplantation was 60 (range 39-72) years. 5 patients suffered from diabetic nephropathy, 2 from glomerulonephritis, 2 had nephrosclerosis. Prophylactic IS consisted of calcineurin-based therapy (5 cyclosporine, 4 tacrolimus). Pretransplant chest X-rays were without abnormal findings, even retrospectively reviewd. Only 1 patient had no smoking history. Median interval from transplantation to tumor diagnosis was 1075.5 (range 216-2456) days. In 8 patients (88.9%), carcinomas were diagnosed at UICC stage IV (1 Small Cell Lung Cancer, 7 Non Small Cell Lung Cancers). 5 patients were treated with palliative radiochemotherapy; 3 patients received symptomatic therapy. The only carcinoma diagnosed at UICC stage IB was curatively resected; the patient is still alive without recurrent disease after a follow-up of 390 days. All other patients suffered from progressive disease with a median survival of 137 (range 35-348) days.
The cumulative incidence (0.6%) of BC is higher when compared to a non immunosuppressed population. Nearly all tumors were already metastatic at diagnosis. Due to poor prognosis, screening strategies and intensive educational training of transplanted patients with a smoking history should be developed.

P-877 POLYOMAVIRUS BK-SPECIFIC CYTOTOXIC T CELLS AFTER KIDNEY TRANSPLANTATION: RATIONALE FOR A CELL THERAPY APPROACH TO VIRUS-RELATED DISEASE

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Recovery of T-cell immunity to polyomavirus BK (BKV) is positively associated to viral clearance in kidney transplant (KTx) recipients. We analyzed BKV-directed cytotoxic T-cells (CTLs) in the peripheral blood of 43 pediatric recipients of kidney allograft. Cytotoxicity was assessed by a standard ^{51}cr release assay after 9-day stimulation with overlapping peptides spanning the BKV proteins large T (LT) and VP1. After transplantation, BKV-seropositive patients who never reactivated the virus (group1, n=12) did not show a significant increase in cytotoxicity, while patients with urinary shedding alone (group 2, n=16) or with concomitant viremia (group 3, n=15), who had low/absent levels prior to BKV DNA positivity, showed a significant increase in BKV-specific lysis. In the latter cohorts, appearance of LT-specific lysis was significantly correlated with viral clearance, although, in group 3 patients, a significant increase in VP1-specific cytotoxicity was also observed. Evaluation of cytotoxic subpopulations, performed on viremic patients, indicated that LT-directed, CD8+ CTLs were detectable in 100% of analysed KTx recipients, with only a fraction of patients (37%) showing LT-directed CD4+ T-cells. Conversely, VP1-specific activity, observed in 75% of patients, was equally exerted by CD8+ and CD4+ T-cells. As CTLs seem to be a critical population able to mediate antiviral protection, we then proceeded to validate a protocol for GMP production of BKV-specific CTLs. Ten T-cell lines were generated, that were BKV-specific, since they showed a median proliferation to the BKV LT and VP1 peptide pools of 11730 and 5816 cpm/10^5 cells, respectively. BKV LT -specific lysis $>$10% at a 10:1 effector to target (E:T) ratio was observed for all T-cell lines. Our data show that it is feasible to reproducibly induce the generation of BKV-specific CTLs to be employed in cell therapy protocols.

P-878 ADIPOSITAS IN KIDNEY TRANSPLANTATION – AN ADDITIONAL RISK FACTOR IN RECIPIENTS OF THE EUROPEAN SENIOR PROGRAMME?

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Indroduction: Several factors contribute to a successfull Kidney Transplantation (KTX). Immunological aspects play an important role as well as cold and warm ischemic time (CIT/WIT)and donor age. The role of adipositas as a risk factor of kidney function after KTX is not evident, especially in the setting of the European Senior Programme (ESP). We evaluated if adipositas (BMI>= 25) is a risk factor for recipients in the ESP.
Methods: From 1999-2007 79 KTX in ESP were retrospectively analyzed. Mean donor age was 70,5y (65-86);mean recipient age was 67,0y (65-79). Mean CIT was 11,6h (4-24); mean WIT 29,2min (15-55). 58% of the these recipients presented at time of TX with BMI >25, 42% presented with BMI <25.
Results: 22,4% of recipients showed delayed graft function (DGF). Over all rejection rate was 16,5%. Although different, no significances (Chi-Qudr.) were seen between the two groups (BMI >25 vs <25) concerning DGF (31,4% vs 15,9%) and Primary Non-Function (8,6 vs 11,4%). 6 month creatinine did not significantly differ between the two groups (p=0,067). Over all post operative complications did not occur more frequently in adipose recipients (p=0,869).
Discussion: Adipositas may result in longer WIT due to difficult and time consuming operative procedure. However in our experience it does not necessarily end up with worse results. Therefore recipients with BMI >25 can be transplanted in ESP with good results and comparable risk.

P-879 HIGH INCIDENCE OF OVARIAN CYSTS AFTER RENAL TRANSPLANTATION UNDER IMMUNOSUPPRESSION WITH mTOR INHIBITORS

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Background: Successful kidney transplantation restores the hypothalamus–pituitary–ovarian axis. In most women of reproductive age, menstrual function and fertility are restored within 6 months after grafting. Menstrual disturbances have been observed in women with end- stage renal failure. Irregular, profuse or scanty menstrual bleedings that accompany mostly unovulatory cycles are frequent also secondary amenorrhea. In the normal ovarian cycle ovarian cysts appear and disappear at ovulation.
Materials and methods: We retrospectively analysed all female kidney transplant patients in our database from our centre up to October 2008. Diagnosis based upon ultrasound during routine examination. Size and appearance are used to characterize cysts as probably physiologic or probably pathologic. Simple cysts less than 2 cm in diameter are considered physiologic. Evaluation included a detailed menstrual and sexual history, including assessment of dysmenorrhea and contraceptive use and physical examination.
Results: We detected n=37 female kidney recipients out of 571 (6.4%), (mean age 37±11) who developed ovarian cysts with a mean time of (57 months) after transplantation. Three additional patients got a hysterectomia and ovarian cystectomy during transplantation. Sixteen patients with ovarian cysts received a mTOR inhibitor, 20 patients received an Calcineurin inhibitor (CNI) based therapy, and 1 patient azathioprine and steroids. In total 102/571 (17.9%) patients received mTor therapy at any time point after transplantation. Ovarian cysts were more frequently observed among patients receiving mTOR inhibitors (16/102 patients; 18.6%) than in those receiving no mTor inhibitor (21/469 patients; 4.7%; p<0.001).
Conclusion: Ovarian cysts were more frequently observed among patients receiving mTOR inhibitors than those receiving no mTor therapy. Before initiation of mTor therapy patients and doctors should be aware of the high incidence of ovarian cysts under mTor therapy.

P-880 ANTIBODY MEDIATED MICROCIRCULATION DAMAGE PLAYS A KEY ROLE IN LATE KIDNEY TRANSPLANT LOSS

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Failure of kidney transplants is common but in may cases the cause of graft loss remains elusive. We investigated the phenotype of failing kidney transplants in a prospective study of 234 consecutive (unselected) biopsies taken for clinical indications between 7 days to 32 years post transplant from 173 consenting patients. We analyzed histopathology, anti HLA antibodies, and death censored graft survival. Grafts biopsied late (>1 year post transplant) were more frequently associated with graft loss within three years (27/128) compared to grafts biopsied early (<1 year) (1/106). Late biopsies were more frequently associated with donor specific HLA antibody, particularly anti class II, and were more frequently diagnosed as C4d positive antibody mediated rejection and transplant glomerulopathy. Lesions of microcirculation injury were more frequent in late biopsies including microcirculation inflammation (glomerulitis, capillaritis) and deterioration (glomerulopathy, basement membrane multilayering), and staining for complement factor C4d. T cell mediated rejection and its associated lesions (tubulitis, interstitial inflammation, vasculitis) were not increased in late biopsies.
Multivariate analysis indicated that the features related to graft loss in late biopsies were donor specific anti class II, microcirculation inflammation and deterioration, and scarring, but not C4d or the current diagnostic criteria for rejection. The principal cause of graft failure in late biopsies (16/27) was anti-class II mediated graft microcirculation damage, but only half of these cases were C4d positive. Glomerulonephritis accounted for 4/27 late losses, whereas drug toxicity and unexplained scarring were uncommon.

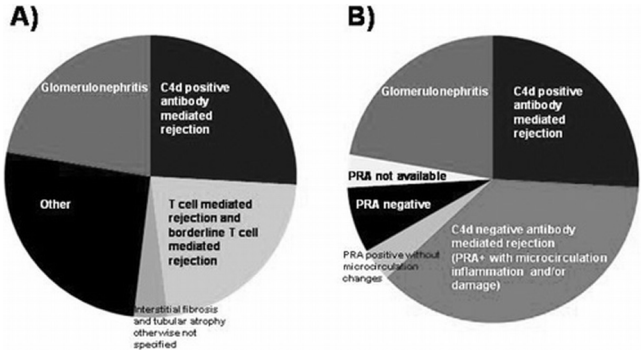

Figure 1. Phenotypes of failing renal allografts. The pie chart shows the distribution of phenotypes at the time of biopsy in grafts that were biopsied later than 1 year post transplant for clinical indications and failed during follow-up (n=27). Panel A shows the diagnostic categories according to standard histologic Banff criteria. Panel B shows the diagnostic groups according to the presence or absence of antibody mediated injury. Biopsies diagnosed as antibodiy mediated rejection by standerd Banff criteria formed one category. All other biopsies (with the exception of glomerulonephritis cases) were assigned into categories based on the presence or absence of HLA antibodies (PRA = panel reactive antibodies).

Thus HLA antibody-mediated injury is a major cause of allograft loss but that current diagnostic criteria requiring C4d staining fail to identify this disease.

Liver & intestine II

P-881 THE USEFULNESS OF A NEW REFRIGERATOR FOR PRESERVATION OF WHOLE BLOOD

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Background and aim: In developments of devices for organ preservation in clinical transplantation, it has been focused on cooling organs to ice temperature as soon as possible to reduce metabolism. We focused a new refrigerating chamber. This system can cool inside of material to the setting temperature with frequently sensing the temperature of both the inside and the surface of the materials, and is suggested to induce hibernation proteins of plants and fishes (apply for a patent; 2004- 166610). We previously reported that the use of this new refrigerating chamber can improve preservation injury of hepatic graft (the 13th ESOT). The purpose of this study was to evaluate the usefulness of this new refrigerating chamber in blood preservation.
Materials and methods: Whole blood samples from healthy individual were anticoagulated with CAPD. The samples were divided into two groups. Group 1 consisted of whole blood preserved in traditional refrigerating chamber at 4C for 15 weeks. Group 2 consisted of whole blood preserved in a new refrigerating chamber at 4C for the same terms. After the preservation period, ammonia, lactate, pH and ATP levels were analyzed.
Results: The ammonia concentrations in Group 2 were significantly lower than in Group 1 after preservation for 7 and 9 weeks (p<0.05). The lactate levels were significantly lower in Group 2 than in Group 2 after preservation for 8 weeks (p<005). The levels of pH in Group 2 after preservation for 5 to 13 weeks were higher than in Group 1 (p<0.05). The ATP levels were kept in Group 2 after preserved for 5 to 13 weeks.

Conclusions: These results suggest that the use of this new refrigerating chamber can keep good condition of whole blood during preserved, and may be able to preserve whole blood longer terms.

P-882 ENDOGENOUS PROTEASE INHIBITOR UPTAKE WITHIN THE GRAFT DURING REPERFUSION IN HUMAN LIVER TRANSPLANTATION

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Background: In experimental liver transplantation, endogenous protease inhibitors alleviate ischemia-reperfusion (I/R) injury both by inhibiting proteolysis and through direct anti-inflammatory actions. We explored their anti-inflammatory potential during reperfusion and effects on graft function in human liver transplantation.
Methods: Ten adult patients undergoing liver transplantation were studied. Circulating levels of protease inhibitors (secretory leukocyte proteinase inhibitor, SLPI; tissue inhibitor of metalloproteinases-1, TIMP-1) and proteolytic enzymes (elastase; matrix metalloproteinase-9, MMP-9) were measured with ELISA. As measures phagocyte activation, neutrophil and monocyte CD11b and L-selectin expression were determined with flow cytometry. To assess changes within the graft during reperfusion, blood samples from portal and hepatic veins were obtained simultaneously, and transhepatic gradient was calculated. Data are given as median (IQR).
Results: Circulating SLPI and TIMP-1 levels decreased gradually during surgery. During initial reperfusion, transhepatic SLPI gradient was -27 (-35 to -22) ng/mL, P=0.005; and TIMP-1 -510 (-636 to -362) ng/mL, P=0.005, indicating graft protease inhibitor uptake. Concomitantly, hepatic phagocyte activation, indicated by cell surface CD11b upregulation and L-selectin shedding, and sequestration occurred. Further, elastase and MMP-9 were released from the graft into circulation. Transhepatic SLPI gradient correlated with postoperative liver enzymes (ALT R=-0.648, P=0.043; ALP R=-0.661, P=0.038; bilirubin R=-0.821, P=0.004; and GGT R=-0.648, P=0.043).
Conclusions: An extensive and rapid endogenous protease inhibitor uptake takes place within the graft during reperfusion in human liver transplantation. Despite this, marked hepatic phagocyte activation and proteolytic enzyme release occur concomitantly. Hepatic SLPI uptake was most intense in grafts with the worst postoperative function. The results suggest a relative shortage of protease inhibitors within the liver during reperfusion, which may contribute to the development of graft injury.

P-883 PROLONGED HYPOMAGNESAEMIA AFTER ADULT LIVING DONOR LIVER TRANSPLANTATION (LDLT) FOR FULMINANT HEPATIC FAILURE (FHF)

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Purpose: Magnesium (Mg) is the second most abundant intracellular cation. It is essential for wide metabolic reactions. We aimed to evaluate hypomagnesaemia and its association with clinical outcome in (FHF) patients after (LDLT).
Methods/Materials: 59 adult patients with FHF were referred to our hospital for urgent LDLT between 1995 and 2008. Mean Age was 43.3±12.9 and 32 patients were males. Data was collected from medical records of patients. Serial measurements of Mg, other electrolytes, liver, renal function tests and Tracrolimus trough levels were obtained at preoperative, first 5 days, 1st and 3rd months, 1st, 2nd and 5th post-operative years.

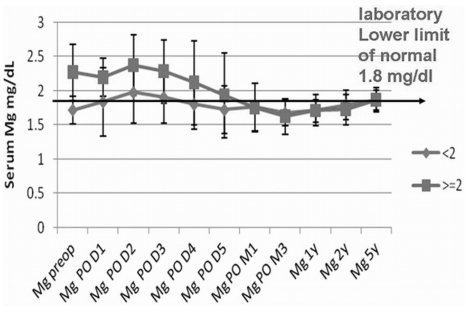

Figure 1. Mg follow up.

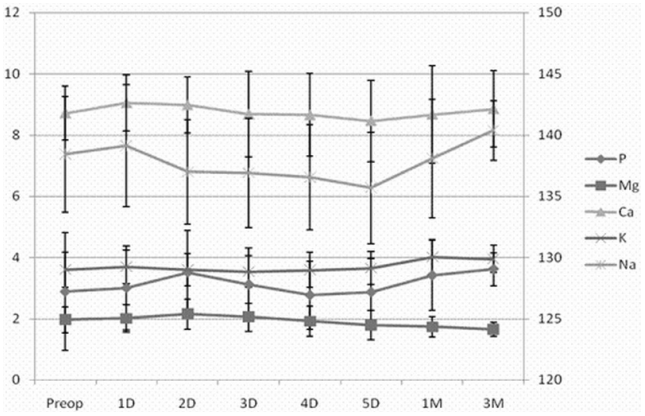

Figure 2. All electrolytes in FHF after transplant till 3 months duration.

Results: Pre-operative serum Mg of our patients was (1.9±0.4 mg/dl) and lastly reached (1.8±0.2 mg/dl) on the 5th PO year (P value < 0.01).This trend towards prolonged hypomagnesaemia was noticed in patients who had preoperative lower Mg levels and those had normal levels.
33.9% of patients had hypomagnesaemia before LDLT and normalization took a longer time (3.2±3.4 year), compared to other electrolytes as Na, K, Ca and inorganic phosphorus (Pi) which reached normalized value within 3 months after LDLT.
Only 44.4% of those patients had normal Mg levels at that time. Early postoperative, we noticed a significant correlation between postoperative Mg, Pi and k values.

Correlation between postoperative (PO) Mg and comparable Pi and K values

	Correlation	P value		Correlation	P value
Mg POD1-Pi POD1	R=0.286	0.063	Mg POD1-K POD1	R=0.294	0.056
Mg POD2-Pi POD2	R=0.505**	<0.01	Mg POD2-K POD2	R=0.541**	0.01
Mg POD3-Pi POD3	R=0.512**	<0.01	Mg POD3-K POD3	R=0.321*	0.024
Mg POD4-Pi POD4	R=0.446**	0.01	Mg POD4-K POD4	R=0.301*	0.035
Mg POD5-Pi POD5	R=0.479**	<0.01	Mg POD5-K POD5	R=0.131	0.339
Mg POM1-Pi POM1	R=0.009	0.947	Mg POM1-K POM1	R=0.388**	0.004
Mg POM3-Pi POM3	R= -0.390**	0.003	Mg POM3-K POM3	R=0.648**	<0.01

*Correlation is significant at the 0.05 level (2-tailed). **Correlation is significant at the 0.01 level (2-tailed)

However, there was no correlation with other parameters. One patient developed Torsades de Pointes during the anhepatic phase but there was no effect of hypomagnesaemia on the outcome.
Conclusion: We found prolonged Hypomagnesaemia in FHF patients up to 5 years after LDLT. Hypomagnesaemia may be associated with serious arrhythmia during operation. Failure of the body to restore normal serum levels for long time may represent cellular use of Mg during hepatic regeneration and the need for Mg supplementation for those patients.

P-885 LONG-TERM EFFECTS OF PROPHYLACTIC SPLENIC ARTERY LIGATION ON PORTAL OVERPERFUSION IN LIVING DONOR LIVER TRANSPLANTATION

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Objective: To investigate long-term impact of splenic artery ligation on portal overperfusion in living donor liver transplantation.
Methods: From June 2006 to December 2008, 33 patients who underwent ALDLT were included in this study. 33 recipients were divided into 2 groups: In group 1 (n = 19), we didn't regulate the portal vein flow; in group 2 (n = 14), we reduced the portal vein flow by splenic artery ligation. There were several criteria for splenic artery ligation during operation: GRWR<1%, or based PVP of recipient>20 mmHg (27 cmH2O). Hepatic hemodynamics, graft function, spleen regeneration, and outcome were evaluated. The spleen volume was measured by computed tomography preoperatively and 1, 3, and 12 months after LDLT. The PVF was measured by Doppler ultrasound on the same time schedule.
Results: The results showed that there was significant difference between two groups in decreasing of PVP after splenic artery ligation, but there was no significant difference between two groups in PVF in 1, 3, and 12 months after LDLT. In addition, the splenic artery ligation can significantly reduce spleen volume, which decreased by 30.2% after 3 months and 33.5% after 12 months, while the spleen volume almost unchanged in another group. We also found that the original hypersplenism of SAL group was alleviated in short period.

Conclusion: Our study suggested that the initial reduction of PVF using SAL could not only relieve portal overperfusion injury in the early postoperative period but also sustain continuously and improve long-term outcome of LDLT.

P-886 ORTHOTOPIC LIVER TRANSPLANT: MODIFIED TOTAL HEPATECTOMY WITHOUT ANHEPATIC PHASE

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Background: After the first liver transplant was performed by Starzl in 1963 several modifications have been described to the original "classical technique". Still, all variants of hepatectomy include the so called "anhepatic phase" defined as the period where the native liver is excluded from circulation leading to some disturbances, especially hemodynamic instability.
Methods: Since 1981 we have developed experimentally a modification to the Starzl's technique, which avoids the anhepatic phase and would eventually overcome the shortcomings presented by other techniques, including the classical one. The modification consists of a right lobectomy exposing the right aspect of vena cava. The graft is attached to the right hepatic vein with a small prolongation to the anterior wall. The new liver is then reperfused in standard fashion and the remaining liver is finally resected.
Results: This new technique was used in experimental settings using 30 male sheep receiving the usual per operatory management. All animals were monitored intra and postoperatively gathering information on hemodynamical variables and biochemical ones. All 30 animals showed stability of cardiac index and urinary output during the entire operation and a normal postoperative biochemical pattern in comparison with historic series of animals operated with classical technique. In 1992 the technique was used in two human patients diagnosed with alcoholic cirrhosis with satisfactory results
Conclusion: We conclude that this technique may be of some use in the armamentarium of liver transplant surgeons since it preserves the cardiac output by preventing total anhepatic phase. It has special advantage in those patients with no portal hypertension.

P-887 EFFECT OF DONOR HEPATECTOMY TIME DURING MULTI-ORGAN RETRIEVAL ON EARLY GRAFT FUNCTION FOLLOWING ADULT CADAVERIC LIVER TRANSPLANTATION

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Introduction: Time taken to recover the graft liver after aortic cross-clamp depends on both donor and surgeon factors. We aimed to investigate the effect of duration of donor hepatectomy (tHep) on the early outcomes after adult heart-beating donor whole liver transplantation (LT).
Methods: LT carried out in a single UK unit were analysed. To standardize retrieval protocol and cold ischaemia times, livers retrieved by our recovery team alone were included. tHep and pertinent donor and recipient data was collected from a prospectively maintained database. Post-transplant data in the form of primary non-function (PNF), hepatic artery thrombosis (HAT), initial poor function (IPF), graft loss within one month and deranged liver function tests (LFT) at 6 months (serum bilirubin $>$20 mol/l and serum alkaline phosphatase $>$500U) were collected. The effect of tHep on the incidence of above end-points was analysed.
Results: Data was available for 348 grafts transplanted between Feb 2000 and April 2006. The median hepatectomy time was 38 minutes. There were 7 patients with PNF, 21 with IPF, 6 HAT and 13 early re-transplants. Six month LFTs were available for 285 patients alive with the original graft liver. Fourteen patients had deranged LFT. There was no difference in tHep in patients with or without PNF, IPF, HAT or early re-transplant. tHep was longer in patients with deranged LFT as compared to patients with normal LFT (52 vs. 40 minutes, Mann Whitney U, p=0.042). Patients with prolonged tHep ($>$50 minutes) had a higher risk of deranged LFT at 6 months (7/70 vs. 7/215; p=0.023).
Conclusions: Prolonged tHep is associated with an increased risk of abnormal liver function tests at 6 months post-transplant. This may be a mark of re-warming injury sustained by the graft during a complicated recovery procedure.

P-888 ADVAGRAF IN LIVER TRANSPLANTATION: DOCE DE OCTUBRE UNIVERSITY HOSPITAL EXPERIENCE, MADRID, SPAIN

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Advagraf is the first calcineurin inhibitor designed for administration once a day.

Objectives: 1) Conversion to Advagraf in stable patients treated with Prograf. 2) Determining the efficacy and safety of the drug 3) level of patient satisfaction after the change.
Methods: A prospective, longitudinal and descriptive study (December 2007 to September 2008). The patients selected for treatment with Prograf conversion met twice daily and liver function were stable. The change was 1:1. We performed analytical and Advagraf levels after initiation of treatment (day 7). Identified side effects associated with Prograf and changes following the change of treatment. Finally a survey of satisfaction. Different variables were analyzed through the SPSS version 10 for Windows
Results: A total of 72 patients, mean age 54$\pm$13 years. Enolic cirrhosis was the most frequent cause indicated that the transplant. The average time of initiation of treatment from the transplant was 76$\pm$53 months, being the maximum and minimum value of 204 and 2 months respectively. The previous dose of Prograf was 3$\pm$1.86 mg/day, with an average of 6.3$\pm$2.6 ng/ml, while 22% of patients on dual therapy (n = 22). After changing the average dose was similar, with levels slightly lower (5.3$\pm$2.2 ng/ml). No patient had altered liver profile during the conversion. There were no changes in the levels of creatinine or MDRD with statiscally significance. Side effects were de novo headache in two patients (2.8%). Patients expressed their satisfaction to maximize adherence to treatment.
Conclusions: The change to Advagraf Prograf is an effective and safe in stable patients transplanted liver. The level of adherence and satisfaction exceeded expectations at the beginning of the proposed study.

P-889 BILIARY COMPLICATIONS IN LIVER TRANSPLANTATION: 12 DE OCTUBRE UNIVERSITY HOSPITAL EXPERIENCE, MADRID, SPAIN

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Objectives: To determine the biliary complications that patients who had received a liver graft and the treatment
Method: Descriptive, longitudinal and retrospective. Recipients of liver grafts 1998-2008. Biliary complications early or late ($<$ or $>$3 months, respectively) in the postoperative period. Statistical analysis SPSS version 10 for Windows.
Results: During the study period were a total of 707 liver transplants, 7% (n=55) had biliary complications (early and late n=25 n=30). The biliary reconstruction was used as a T-tube tutor biliary in 13 patients (20%). Within the biliary complications, fistula and stenosis n=15 n=40, respectively. Stenosis of the anastomosis was the most frequent complication of the group that received full graft (p=ns) whereas fistulas were more frequent in the group receiving a partial graft (p=0.002). The diagnosis was made by ultrasonography and/or MRI. The biopsy showed changes postreperfusion harvest by 45% (15% steatosis). When comparing the findings of the biopsy with the type of biliary complication was not reached statistical significance. In the post 9 cases (17%) CMV infection preceded the biliary complication. 76% of patients had at least one episode of acute rejection (chronic rejection n=4). No significant differences were found when comparing the type of immunosuppression used. ERCP was performed in 7 cases, CTPH 22 patients were operated and 27 underwent a biliary bypass in 19 cases. Actuarial survival at 60 months was 60% and 75% for graft and recipient, respectively
Conclusions: The incidence of biliary complications was low in our series. The multimodal treatment was in most cases, including percutaneous or endoscopic dilatation and surgical exploration, identifying in each case the necessary treatment.

P-890 HIGH MELD SCORE AND ELDERLY PATIENTS: GOOD RESULTS FROM BAD COMBINATIONS

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Purpose: High MELD score and the elderly recipients are considered as risk factors for liver transplantation outcome. The goal of this study was to analyse the outcomes of two groups of patients, transplanted with high MELD scores ($\geq$30), the elderly patients ($\geq$60 yrs) and the younger patients ($<$60yrs).
Methods/Materials: The data of 240 liver transplant realized between July 2005 to March 2009 were reviewed, with 84 transplanted with MELD score $\geq$ 30. The patients were separeted in two groups according to their age, and those transplanted for acute liver failure or retransplants were excluded. Hospital and Intensive care length stay, intraoperative transfusion, and postoperative complications were compared between the groups.
Results: Group $\geq$ 60 (n=11): mean age was 65,55 (range, 60 to 74), mean BMI was 27,29, and the mean MELD score was 38,27. For the Group $<$60 (n=27): mean age was 46,52 (range, 22 to 59), mean BMI was 28,11, and the mean MELD score was 35. The mean ICU length stay were 36 days for

Group I (range, 1-97) and 16 days for Group II (range, 1-103). Both Groups had the mean of 3 packed red blood cells and 1 platelet, Group I received 5 fresh frozen plasma and Group II, 4 fresh frozen plasma. Some post-operative complications were similar at both groups, as vascular and biliary problems, allograft dysfunction or rejection, but Group I presented 80% of infection and renal failure, while Group II had 55,55% of infection and 62,96% of renal failure. The overall survival was 90% at Group I and 70,37% at Group II (p=ns).
Conclusions: Our results suggest that advanced age should not be a contraindication for liver transplantation, even when considering recipients with higher MELD scores.

P-891 THE INFLUENCE OF RETROGRADE REPERFUSION ON THE ISCHAEMIA-/REPERFUSION INJURY AFTER LIVER TRANSPLANTATION IN THE RAT

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Purpose: Dysfunction of the graft after liver transplantation caused by ischaemia-/reperfusion (I/R) injury is a serious clinical problem. The aim of this study was to evaluate the influence of different kinds of reperfusion on I/R injury in a rat model.
Materials: Arterialized orthoptic rat liver treatment was performed on male LEWIS-(RT(1))-rats. Three groups (n = 7) were formed.
Methods: Group I: antegrade reperfusion with a 6-min delayed reperfusion via the hepatic artery. Group II: Antegrade reperfusion, simultaneously, via the portal vein and the hepatic artery. Group III: Retrograde reperfusion via the vena cava. Serum parameters were determined one, 24 and 48 h after operation. Furthermore, after 48 h, the liver was taken for histological assessment.
Results: After 48 h, rats of group III showed significantly lower aspartate amino transferase and alanine amino transferase serum levels compared with group I and group II rats. Forty-eight hours after transplantation, glutamate dehydrogenase serum level was significantly lower in group III than in group II. In histology, group III livers showed significantly less necrotic spots than group I and group II livers. Maximum size of the necrotic spots was significantly lower in group III than in group I. Also, significantly more necrotic spots were seen in the 'Rappaport's zone' 1 and 2 of group I than in group III.
Conclusion: Our data suggested that the expression of I/R-injury correlates with the type of reperfusion. Furthermore, under standard conditions, this study was able to demonstrate that in a rat model, the retrograde reperfusion leads to a lower expression of I/R-injury than the antegrade reperfusion.

P-892 PREOPERATIVE DIAGNOSIS OF POORLY DIFFERENTIATED GRADE IN PATIENTS WITH LARGE HEPATOCELLULAR CARCINOMA: A PROSPECTIVE CONTROLLED STUDY

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Background/Aims: In patients with a large hepatocellular carcinoma (LHCC: tumor diameter larger than 3 cm), surgical treatment is the only potentially radical surgery. Tumor grade is the main predictor of post-surgical HCC recurrence, but preoperative biopsy has shown a poor diagnostic sensibility, especially in patients with LHCC.
The aim of this study is to increase the diagnostic sensibility of preoperative biopsy in detecting pathologic poorly differentiated grade (PDG) by an association of needle and core sample procedures.
Methods: Thirty-three patients with LHCC undergoing both needle and core biopsies before surgery were prospectively enrolled and represented the study group. An historical cohort of 44 patients with LHCC undergoing a single diagnostic procedure (needle or core biopsy) before surgery represented the control group. In both groups, the diagnostic agreement of preoperative biopsy PDG detection was compared with the final surgical pathologic PDG diagnosis as reference.
Results: Baseline clinical characteristics were comparable in the 2 groups. Pre and post surgical histological evaluations in both groups were done in the same pathologic Institute. There were no false positive cases in both groups (specificity = 100%). In the study group, 8/12 (sensibility = 67%) PDG cases were correctly predicted before surgery, whereas there were only 4/11 (sensibility = 36%) in the control group ($p<0.05$).
Conclusions: The association of needle and core biopsy in patients with LHCC has the potential to significantly increase the sensibility of preoperative PDG HCC diagnosis. Moreover, preoperative biopsy, single or double, showed a very high specificity (100%) in detecting PDG HCC cases.

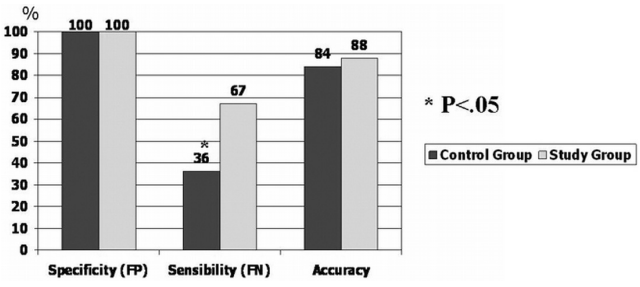

Figure 1. Specificity, sensibility and accuracy of preoperative biopsy in detecting PDG. Control group (retrospective): 44 pts with needle OR core biopsy before surgery. Study group (prospective): 33 pts with needle AND core biopsy before surgery.

P-893 COST-UTILITY OF THE MOLECULAR ADSORBENT RECYCLING SYSTEM (MARS) TREATMENT

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Purpose: To determine the short-term (3.5-year) cost-utility of molecular adsorbent recirculating system (MARS) treatment and its impact on the patient's health-related quality of life (HRQoL) in acute liver failure (ALF) and acute-on-chronic liver failure (AOCLF) patients.
Methods: The study was conducted retrospectively in a liver disease specialized intensive care unit (ICU) in Finland. Ninety ALF and 49 AOCLF patients who were treated with MARS during 2001-2005 were compared with a historical control group of 17 ALF patients treated in the same ICU during 2000-2001. Three-year outcome and the number of liver transplantations were recorded. All direct liver disease-related medical expenses which incurred from six months prior to treatment to three years after treatment were determined. The HRQoL prior to MARS treatment was estimated by a panel of ICU doctors, and the HRQoL after treatment was determined by using a 15-dimensional HRQoL questionnaire via mail. The HRQoL, cost, and survival data were combined, and the average cost/quality-adjusted life year was calculated. Costs and outcomes of MARS treatment were compared with those of conservative treatment in ALF patients from the perspective of the health care provider. In AOCLF patients, the costs and outcomes were reported without any comparative analysis due to the lack of a suitable control group.
Results: In ALF patients, MARS treatment was less costly and more effective than the best conservative medical care. The average cost/quality-adjusted life year was lower for MARS-treated ALF patients compared to the control group (53.845€ vs. 106.958€). In MARS-treated AOCLF patients, the mean cost/quality-adjusted life year was 118.053€.
Conclusion: Although MARS treatment of ALF and AOCLF patients in an ICU setting is expensive, it is more cost-effective than the best conservative medical care without MARS in ALF patients.

P-894 SHORT AND LONG-TERM OVERALL RESULTS WITH LIVER RETRANSPLANTATION: "12 DE OCTUBRE" HOSPITAL EXPERIENCE DURING THE LAST 10 YEARS

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Introduction: Liver retransplantation is the only option for patient survival when the first graft fails. The rate of retransplant in Spain is about 6%. Main causes are primary non-function, vascular complications, chronic rejection and recurrence of liver disease. The results are worse than the first transplant.
Patients and methods: Retrospective study of our experience with 54 retransplants performed between January 1992 and December 2006 (5.6% of 960 OLT during this period).

Results: 34.7% of the retransplants were performed 4-30 days after the first transplant and other 34.7% one year after. 48.9% of the retransplants were performed in urgent situation. The main cause of retransplant during de first month was primary hepatic failure (14 cases) and vascular complications (4). After the first month the main causes are chronic rejection (9) and recurrence of the hepatic disease (3) and biliary complications (4). Postoperative mortality was 23.9% and morbidity of 76.3%. 21.2% of the patients needed a third transplant. The overall patient survival was 60.4% (32 patients) and graft survival of 56.6% (30). The 5-years actuarial graft survival was of 65.4% with an mean survival time of 89.84±8.72 months and the 5-years patient survival was 64% with a mean survival time of 114.7±12.53 months. Worst survival was observed in chronic rejection and in retransplants performed between 31 to 360 days.
Conclusions: Liver retransplant has more surgical complexity than first transplant but is a good option for patients with failure of the first graft with a 5-year survival around 65% for patient and graft.

P-895 IS IT THE PREOPERATIVE ALPHAPHETOPROTEIN VALUE A PROGNOSTIC FACTOR FOR THE LONG-TERM RESULTS OF PATIENTS TRANSPLANTED WITH HEPATOCELLULAR CARCINOMA

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Introduction: LT is the choice treatment for patients with cirrhosis and hepatocellular carcinoma.
Background: To analyze our experience looking to the relation of the AFP level with the long-term results.
Patients and method: From April'86-December'06 we performed 151 OLT in HCC, 30.5% of them unknowm.
Results: AFP was larger in known patients at the transplant: 795.25 ng/ml vs 9.59 ng/ml (p=0.3) and there are no patient with an AFP level >200 ng/ml between the incidental tumors and 16% between the known tumors and 56% with 10-200 ng/ml versus 9% between incidentals (p=0.0001). AFP >200 ng/ml had more tumoral necrosis (40% vs 27%), more vascular invasion (40% vs 17.6%), shorter well differentiated tumors (66.7% vs 91.9%) and more patients out of Mazafferro's (60% vs 14.9%) and California's criteria (53.3% vs 12.2%). With a pretransplant AFP <10 ng/ml have shorter recurrence (5.9%) than 10-200 ng/ml (20.8%) and >200 ng/ml (58.3%) with statistical differences (p=0.0001). It was earlier with a greater AFP level (>50% before one year with >10 ng/ml versus nobody with <10 ng/ml). DFS survival was shorter between the patients with a level >200 ng/ml (16.7%) than with 10-200 ng/ml (58.5%) and than <10 ng/ml (63.2) with a p=0.01. The 5-year actuarial DFS was 68.6% between patients with level <10 ng/ml, 62.5% with level 10-200 ng/ml and 30% between >200ng/ml (p=0.012).The same with the long-term mortality cause: mainly due to recurrence between patients with a level >200 ng/ml (62.5%) versus 12% between patients with a level <10 ng/ml (p=0.1).
Conclusions: All the patients with a incidental tumor had an AFP level shorter than 200 ng/ml. Level larger than 200 ng/ml is related with worse histological prognostic factor, larger recurrence rate and shorter disease-free survival.

P-896 THE RISK OF CHRONIC RENAL DYSFUNCTION IN LIVER TRANSPLANT RECIPIENTS

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Objective: The aim of this study was to identify the risk of chronic renal dysfunction (CRD) in liver transplant recipients.
Material and methods: We evaluated 110 liver transplant recipients. None of the 110 patients presented kidney affection before transplantation. Standard immunosuppression protocols were used. We evaluated the risk of developing chronic renal dysfunction in the absence of pre-existing renal conditions. Kidney affection was considered in case of: proteinuria >3 gr/24 hours or hematuria > 2000/min (Addis-Hamburger probe), the presence of cilinders in urine spot or a creatinine clearance of < 90 mL/min calculated using the MDRD formula (Modification of Diet in Renal Disease).
Results: Proteinuria > 3 gr/24 hours and hematuria (>2000/min) were present in 3.27% of transplanted patients. II-nd degree chronic kidney failure developed in 44.26% of cases and III-rd degree chronic kidney failure in 29.5% of all transplants. Chronic renal dysfunction was found in 28% early (after 3–12 months),and in 45,76% late-onset (>12 months). Renal substitution therapy was not necessary in any of the patients.
Conclusions: Kidney affection occurs frequently after liver transplantation (73.76%). Tacrolimus, as well as Cyclosporin, may be considered as risk factors for kidney affection. Although kidney function was found to be significantly restricted in these cases, renal substitution was not necessary in any patients.

P-897 EXPERIENCES IN THE EARLY MOLECULAR ABSORBENT RECIRCULATING SYSTEM (MARS) TREATMENT OF *AMANITA* MUSHROOM POISONING

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Purpose: To evaluate the outcome of ten MARS treated *Amanita sp.* mushroom poisoning patients.
Methods: The study was a retrospectively analyzed case series. Ten adult patients with varying severity of accidental *Amanita* poisoning were treated in a liver disease specialized intensive care unit (ICU) during 2001-2007 in Finland. All patients received MARS therapy together with the standard medical therapy for mushroom poisoning (including fluid resuscitation, silibilin, N-acetylcystein and per oral charcoal). The demographic, laboratory and clinical data from each patient were recorded at ICU admission. The poorest laboratory values during the whole hospital treatment period were used for further analysis. The primary end point, 1 year survival and the need for liver transplantation, were recorded.
Results: The median age of patients was 46 years (range 36-81). The median time from the mushroom ingestion to hospital admission was 18h (range 14-36h). MARS treatment was started within 4 days of mushroom ingestion on all patients (median 48h, range 26-78h). All ten patients survived the follow-up of one year. The non-transplanted patients showed no signs of chronic liver damage in follow-up controls. One patient underwent a successful liver transplantation. No serious adverse side-effects were observed with MARS treatment. The median length of ICU treatment and the total hospital stay in non-transplanted patients were 2 days (range 1-6) and 6 days (range 3-14), respectively.
Conclusions: MARS treatment seems to offer a safe and effective additional treatment option in *Amanita* mushroom poisonings.

P-898 LIVER TRANSPLANTATION FOR HEPATOCELLULAR CARICNOMA: CAN WE INCREASE THE MILAN CRITERIA TO INDICATE IT?

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Introduction: In the last years there is an increasing in the indication of LT for HCC out of the Milan criteria, like San Francisco criteria, with good results.
Background: In our experience, analyze if there a change in the long-term results attending to the selection criteria (Milan vs San Francisco).
Patients and method: Of the 151 LT performed in HCC we excluded 46 incidental tumors during a period from 1986 to 2006.
Results: 22/105 pac (21%) did not fulfilled Milan criteria at listing and 28.6% at the transplant. 15.2% of the patients did not fulfill California criteria at listing and 23.8% at transplant. In the liver explanted 32.4% of the patients did not fulfilled Milan criteria and 25.7% California criteria. Patients that fulfilled Milan criteria had a recurrence of 15.2% being 36.7% between the patients that did not ($p<0.05$). 16.4% of the patients that fulfilled California criteria had recurrence and 39.1% between the patients that did not ($p<0.05$). Patients that fulfilled California but that did not fulfilled Milan had a recurrence of 28.6% vs 15.3% between the patients that fulfilled Milan (p=0.3). Patients that fulfilled Milan at listing and not at transplant had more recurrence: 57.1% vs 13%(p=0.003), without clear differences between the California criteria: sin 37.5% vs 16.2% (p=0.139). Of the 27 patients that did not fulfilled the Milan criteria at transplant, 5 fulfilled California with a 60% of recurrence vs 13% between the patients that fullfilled Milan criteria (p=0.006) or 41% between the patients that did not fullfilled both criteria.
Conclussion: In our experience Milan criteria are right criteria to decrease recurrence after LT for HCC. To increase the selection criteria is related with an increasing in tumor recurrence.

P-899 PROPHYLACTIC INTRAVENOUS ANTIBIOTICS DO NOT INFLUENCE THE OUTCOME OF ACUTE LIVER FAILURE

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Purpose: Acute liver failure (ALF) is a rare event associated with a high rate of mortality. The prophylactic administration of antibiotics has been suggested to reduce the incidence of infectious complications. The objective of the present study was to evaluate the impact of prophylactic antibiotics on the incidence of infections and on the outcome of patients with ALF.
Methods: Patients admitted for ALF to the CHUM liver unit between 1991 and 2002 were included in this retrospective study. Patients were divided into two groups according to whether they received prophylactic intravenous antibiotics or not.
Results: 115 patients with ALF were identified. 3 patients were excluded from the study because they were infected and treated with antibiotics before their transfer to our unit. Group 1 (no prophylactic antibiotics) included 88 patients and group 2 (prophylactic antibiotics) included 24 patients. The proportions of patients with hyperacute, acute and subacute liver failure were not statistically different in the two groups, nor were the etiology of ALF, patient age, gender, INR, creatinine and grade of hepatic encephalopathy on admission. 69% of group 1 patients and 71% of group 2 fulfilled King's College Hospital criteria for liver transplantation ($p = 0.89$). 51% of group 1 patients developed an infection compared to 33% in group 2 ($p = 0.12$). The cumulative incidence of infection, determined using the Kaplan-Meier method, was similar in both groups (72% at 1 month in group 1 and 71% in group 2, $p = 0.67$). A similar proportion of patients of the two groups died, was transplanted or survived without transplantation.
Conclusion: Among patients with ALF who received prophylactic intravenous antibiotics, the proportion developing an infection tended to be lower than in patients who did not receive antibiotics but the patients' outcomes were similar.

P-900 THE SUSTAINED VIROLOGICAL RESPONSE AS MARKER OF IMMUNOLOGICAL COMPLICATIONS ASSOCIATED WITH TREATMENT COMBINED WITH PEGYLATED INTERFERON AND RIBAVIRIN FOR RECURRENT HEPATITIS C AFTER LIVER TRANSPLANTATION

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Background: One of the main drawbacks of combined antiviral therapy with pegylated interferon and ribavirin for recurrent hepatitis C after liver transplantation are the adverse effects, including immunological alterations induced by interferon, such as chronic rejection and de novo autoimmune hepatitis.
Material, methods and results: We compared two groups of patients who had immunological complications related to antiviral treatment (out of 79): 4 patients developed de novo autoimmune hepatitis (AIH) (International Autoimmune Group scoring system) and 7 patients developed chronic rejection. In both groups, the average time of duration of treatment was 12 months. In the first group, 3 patients archived a sustained virological response (SVR) and one had a complete response with virological relapse after discontinuation of treatment.In the second group, 7 patients archived RVS. The average time of onset of HAI was 11 months after completion of treatment, while chronic rejection appeared during the therapy, with a mean time from the start of treatment of 5.8 months. In the first group, 4 patients received immunosuppressive regimen with tacrolimus and in second group, 6 of 7 with cyclosporine. Ribavirin was discontinued in 3 patients of the second group because of toxicity.
Conclusions: The development of immunological complications associated with combined antiviral therapy for recurrent hepatitis C after liver transplantation is uncommon but very serious, including de novo autoimmune hepatitis and chronic rejection. The presence of sustained virological response seems to be associated with the appearance of them.

P-901 THE ROLE OF THE TRANSFORMING GROWTH FACTOR B-1 POLYMORPHISM (CODON 10 AND 25) IN THE DEVELOPMENT OF GRAFT FIBROSIS AND FIBROSIS PROGRESSION AFTER LIVER TRANSPLANTATION FOR HCV-INDUCED LIVER DISEASE

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Background: Hepatitis-C-reinfection after liver transplantation occurring in nearly 100% forwards individually different development of graft fibrosis. Aim of our study was to analyze fibrosis progression after liver transplantation due to HCV-reinfection based on protocol liver biopsies and to evaluate the role of genetic variants of TGF-b1 in the hepatic fibrogenesis.
Methods: 200 patients who underwent a liver transplantation for HCV-induced liver disease were genotyped for TGF-b1 codon 10 (C->T) and 25 (A->G) by polymerase chain reaction on genomic DNA from leucocytes using sequence specific primers. Histological evaluation based on protocol liver biopsies of overall 922 biopsies performed after 1, 3, 5, 7 and 10 years after transplantation identified 92 patients with fibrosis progression and 108 individuals with a stable disease according to the Scheuer score. We compared the prevalence of alleles that were reported to be associated with high secretor phenotypes of TGF-b1 among the two groups.
Results: No difference was observed between the group with fibrosis progression and stable disease regarding allelic frequencies, genotype/haplotype distribution of TGF-b1-polymorphisms at codon 10 and 25, incidence of hepatocellular carcinoma before transplantation, recipient's age and inteferon-therapy response. Both frequency and rate of homozygosity of the TGF-b1 alleles were not statistically different between the two groups and its prevalence was not associated with progression of HCV-associated transplant fibrosis.
Conclusions: In this trial with the largest sample size of TX-patients to date we demonstrated that the two most fuctionaly relevant TGF-b1 polymorphisms do not play any role in the development of graft fibrosis due to HCV-reinfection after liver transplantation. We could confirm the importance of donor age in the development of graft fibrosis.

P-902 EVEROLIMUS AS A RESCUE THERAPY IN LIVER TRANSPLANTATION: EXPERIENCE OF THE DOCE DE OCTUBRE UNIVERSITY HOSPITAL, MADRID

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Aim: To describe the indications for salvage therapy with everolimus in liver transplantation. To determine the safety and security of treatment.
Methods: Descriptive, prospective and longitudinal study (January to September 2008). The inclusion criteria were: 1) novo tumor, 2) recurrence of HCC and IRC, 3) intolerance to Sirolimus or antimetabolites. Statistical analysis was performed using the program SPSS version 10 for Windows.
Results: We included a total of 20 patients. 65% of the cases involved patients with cancer. The most frequent indication (n=7, 35%) was renal failure in patients with a history of HCC in the native liver at high risk of relapse. The average age was 60 ± 9 years. The mean interval from transplantation to conversion to everolimus was 42 ± 5 months. Follow-up was 6 ± 3 meses. The scheduled starting dose was 1.5 ± 0.5 mg/day, with an average levels were 5.30 ± 1.8 ng/ml. Three patients (15%) had altered liver profile after conversion. The findings were acute cellular rejection grade 1 (n=1), grade 2 (n=1) in a patient who had discontinued treatment voluntarily and a third patient toxicity of excess immunosuppression (n=1). The increase in total serum cholesterol was the most common side effect (n=6, 30%) followed the lymphedema of the lower limbs (n=3, 15%).
Conclusions: The incidence of acute rejection was acceptable, although the experience will improve the results. Among the side effects dyslipidemia and lymphedema were the most common side effects, although drug treatment in both conditions decreased the severity of symptoms. Longer term monitoring will be necessary to demonstrate the hypothetical protective effect on tumor recurrence or de novo in patients at risk.

P-903 RESULTS OF LIVER TRANSPLANTATION FOR TYROSINEMIA IN IRAN: A SINGLE CENTER EXPERIENCE

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Tyrosinemia could arise from an inborn error of tyrosine metabolism and mainly

lead to death in case of no treatment. The best choice of treatment especially in those with critical conditions is liver transplantation. In this study we report the outcome of liver transplantation in patients with tyrosinemia in our institution. Between January 2007 and September 2008, 14 patients [4.54±3.40 years (1-14 years), 15.30±5.48 kg (8-28 kg), 8 male, 6 female] with tyrosinemia and liver cirrhosis, which were confirmed by detecting plasma succinylacetone, have been receiving liver transplantation. Only 1 of the patients had been treated by NTBC preoperatively for 6 months. Twelve of 14 patients had received livers from living donors and the rest received split grafts from deceased donors. Four patients had preoperative renal tubular acidosis. We used methylprednisolone pulse therapy as induction and only oral tacrolimus (blood level 12-18 ng/ml for first 6 months) and low dose prednisolone for maintenance immunosuppression. Two patients had pathologically confirmed hepatocellular carcinoma without metastasis. Complications included: re-exploration for internal bleeding (n=2), wound infection (n=1) and biliary leakage (n=1). The mean duration of hospital stay in these patients was 17±6.02 days. Diagnosis of acute rejection was made for 6 patients and has been treated with pulse of methyl prednisolone. One patient developed post transplant lymphoproliferative disorder and died after 11 months. Follow-up was 16.54±6.32 (4-24) months.
In conclusion, Despite of some complications, liver transplantation in our patients as the same as the other reports could be presented as an effective treatment for tyrosinemia resulting in clinical and biochemical improvement with good quality of life

P-904 ONE THOUSAND LIVER TRANSPLANTS FROM A SINGLE EUROPEAN CENTER

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Purpose: To analize changes over time in donors, recipients and results of a series of 1000 liver transplants (LT) performed in our center.
Patients and methods: Between 1985-2007,1000 LT were performed (789 adults, 211 children). We have compared the first 100 LT with the last 200 among adults, and the first 100 with the last 100 among children.
Results: *Adults:* Donors in the last period were older (30 years (r: 7-64) vs 54.5 years (r: 7-83), $p<0.001$)). The main cause of death during the 1st period was traffic accident (47%) and cerebrovascular disease in the 2nd period (54.9%). Recipients were older (53.5 years (r: 16-66) vs 57.4 years (r: 20-69), $p<0.001$) and had more comorbidity in the 2nd period (DM 14% vs 29.5%, HTA 6% vs 14.3%; $p<0.05$). In the last period, there were more patients with HCC (14% vs 27.5%, $p<0.005$) and patients HIV+ started to be transplanted. In the 1st period, the surgical technique used was: Piggy-Back technique (45%), bypass (33%) and classical (22%), ($p<0.001$). In the 2nd period, the Piggy-Back technique was used in all patients. Initially, the T-tube was used in 46% and in the 2nd period scarcely (6.6%), ($p<0.05$).
One-, 3- and 4-year actuarial patient survival in the first and last period was 64%, 50%, 48% vs 86%, 78%, 75%, respectively, ($p<0.05$).
Children: During the last period, transplanted children were younger: 1.3 years (r: 0.08-16.5) vs 4 years (r: 0.6-15), ($p<0.05$). There were no differences in weight: 15kg (r: 4.4-68) vs 10kg (r: 2.5-78). The main reason for transplantation was biliary duct atresia in both groups. In the last group, more partial grafts were used (17% vs 44.1%, $p<0.05$): less reduced grafts (15% vs 20.4%), but more "split" (2% vs 19.4%) and the beginning of the living donor ($p<0.05$).
Conclusions: Despite the use of older donors,partial grafts, more comorbidity and extreme ages, survival has improved throughout the years.

P-905 LIVER TRANSPLANTATION IN IRAN: A 15 YEARS EXPERIENCE

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Background: Liver transplantation (LTx) is the ultimate treatment for end-stage liver disease (ESLD). LTx was initiated in Iran in 1993 and we report here our experience of 611 cases of LTx during a 15 years period.
Patients and methods: From January 1993 to February 2009, 611 patients received an LTx at the Shiraz transplant center, Namazi Hospital, Shiraz, Iran, only 8 cases in the first 5 years. 23 cases underwent the classic technique and 588 underwent piggy-back technique. The main immunosuppression included methylprednisolone pulse therapy for induction, and cyclosporine or tacrolimus plus mycophenolate mofetil as maintenance with some modifications in specific groups.
Results: 611 patients (375 male, 236 female, mean age of 35.5± 13.3 y/o, range: 7 months- 73 years) were transplanted during this period. 503 received whole organ from deceased donor, and 76 cases received a partial liver graft from a living donor. 32 cases were received a split liver graft included 6 in situ and 10 ex situ splitting. The causes of ESLD were cryptogenic cirrhosis (n=119), hepatitis B (n=116), autoimmune hepatitis (n=101), primary sclerosing cholangitis (n=83), Wilson's disease (n=59), and hepatitis C (n=24) and other causes (n=109). Complications included: biliary complications (n=65), re-exploration for bleeding (n=45), wound dehiscence (n=29), hepatic artery thrombosis (n=28), portal vein thrombosis (n=8), and hepatic vein thrombosis (n=3). 1 year mortality was decreased from 37.5% in first 5 years to 10.5% in 2008. The overall 1 year survival rate was 91.5% in 2007-2008 period.
Discussion: After acquiring training and improving patient selection, now our 1-year survival rate is acceptable and it is converted to a routine procedure in Shiraz transplant center. Due to cultural and social barriers prevail, contributing to the shortage of donor organs, we should improve our living donor and split liver transplantation program.

P-906 INTESTINAL AND MULTIVISCERAL TRANSPLANTATION IN ADULTS RECIPIENTS: A THERAPEUTIC OPCION IN SPAIN

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Background: Actually intestinal transplantation is indicated for patients with chronic and irreversible intestinal failure who depend on total parenteral nutrition (TPN) and who meet serious complications due to TNP.
OBJETIVE: To know the results from the first Spanish series of intestinal transplant in adults recipients.
Material and methods: Between June 2004 and December 2008 we performed a total of 12 intestinal transplants in 11 recipients amongst a group of 36 potential candidates assessed. Mean age of patients transplanted was 38.42± 8.72 years, seven were males and four females. Crossmatch was positive in five recipients and matching CMV Do/Re was +/+ in 10 patients and +/– in 2.
Results: Of the 12 transplants, 10 were isolated intestinal and 2 were multivisceral. Indications for transplantation were desmoids tumours due Gardner syndrome (n=4), retransplants (n=2), short bowel syndrome secondary to abdominal trauma (n=2), secondary to mesenteric ischemia (n=1), secondary to Crohn's disease (n=1), secondary to GIST tumour (n=1) and Budd Chiari Syndrom (n=1). All patients received induction with alemtuzumab except one who received thymoglobulin. At this moment with a mean follow-up of 17 months, 7 patients are alive (63%) with grafts functioning and complete digestive autonomy (58,33%). Five patients had rejections episodes,four were grade II (effectively treated with OKT3 10 ml/iv/24 h for 10 days) and three were grade III (refractory to OKT3). The causes of graft loss were: rejections grade III (n=3), lymphoproliferative syndrome grade IV (n=1) and sepsis (n=1). Three patients developed postransplant lymphoproliferative syndrome,two were grade 1 (effectively treated with rituximab) and one were grade IV. Actuarial survival rate of grafts was 57.3% and actuarial survival of patients was 77.9%.
Conclusions: Intestinal and multivisceral transplantation represents a therapeutic option in our country. Acute rejection represents the most important complication and the first cause of graft loss in our experience.

P-908 THE EVALUATION OF LEARNING EFFECT AND FUNCTIONAL CAPACITY IN LIVER TRANSPLANTATION CANDIDATES WITH THE SIX MINUTE WALK TEST

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Introduction and objective: The six-minute walk test is simple, safe, easy to be administered, has low operational cost using a normal day-to-day activity and has been commonly used in research to evaluate the physical performance. The aim of this study was to evaluate the functional capacity and the possible learning effect in the six-minute walk test.
Methods: A prospective study with 10 patients was conducted, with average age of 59±10.5 years, on the liver transplantation waiting list at the Hospital das Clinicas of UNICAMP. The patients performed two walking tests with a rest interval of 30 minutes. They were evaluated regarding physiological effects (pulse oximetry and blood pressure) and the subjective sensation of dyspnea at rest in the 6th and 9th minutes after each walking. The statistical analysis was performed by paired Student's t-test with the Pearson test for correlation of independent variables, and the Wilcoxon test for correlation of walking distance with age and body mass.

Results: In both tests it was observed that the distance traveled was lower than predicted by the Enright and Sherril formula (585,7±45,5), with no significant difference between the first 6MWT (467.2±76.6) and the second 6MWT (467±83.9) period. No significant differences were observed for the physiological variables between both 6MWT. But, the physiological variables showed significant differences ($p<0.05$) between the evaluated periods (rest and 6 minutes).
Conclusion: The functional capacity of the candidates for liver transplantation was lower than expected, the 6 MWT was an effective tool to evaluate the functional capacity of patients with terminal liver disease and no learning effect was found.

P-909 INFLUENCE THE OF USE OF INCENTIVE SPIROMETRY IN RESPIRATORY MUSCLE STRENGTH ON CANDIDATE FOR LIVER TRANSPLANTATION – CASE REPORT

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Background and objective: The terminal liver disease is responsible for important alterations of metabolism that lead to malnutrition, loss of lean body mass and decrease of muscle strength. These changes interfere with physical capacity, daily activities, and quality of life. This study aimed at implementing a training series with the incentive spirometer (*Respiron®*), and assess its influence on the strength of respiratory muscles.
Case report: A male patient, 53 years old, diagnosed with liver cirrhosis, followed at the Liver Transplantation Unit (Gastrocentro UNICAMP), presented a maximal inspiratory pressure (MIP) of -72 cmH_2O and a maximal expiratory pressure (MEP) of 59 cmH_2O. He was invited to participate of the study that had a phase at the outpatient and another phase at home. The training with the incentive spirometer was carried out for four weeks and after the training the patient progressed to a MIP of -149 cmH_2O and MEP of 123 cmH_2O. The Child-Pugh classification was C (10) and the MELD score was 20. Both remained unaltered in the waiting list during this study.
Conclusion: The training with the incentive spirometer in a candidate for liver transplantation, who had weakness of respiratory muscles, contributed to the increase of both inspiratory and expiratory muscle strength.

P-910 LIVER TRANSPLANTATION FOR HOMOZYGOS FAMILIAL HYPERCHOLESTROLEMIA

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Homozygous familial hypercholesterolemia (HFHC) is a rare inherited condition with an incidence of 1 in a million. It is associated with severe premature atherosclerosis and early death from cardiovascular complication. Mutation in the gene that encodes the synthesis of the cellular receptor for low density lipoprotein (LDL) is responsible for this metabolic disorder. Currently, the only effective treatment for this disease is liver transplantation, which alone or in association with medications, normalizes plasma cholesterol level. The authors report the results of liver transplantation for 2 cases of HFHC in Shiraz transplant unit, Shiraz, Iran. First case, a 15 y/o boy, received whole liver from a deceased donor and the second an 11 y/o boy who received left lobe from a living donor (his mother). The older boy had severe atherosclerotic heart disease and undergone coronary artery bypass grafting 5 months before transplantation. Both had preoperative plasma cholesterol level higher than 750 mg/dl which didn't respond to medical therapy. Thyroid and liver function tests were normal. After the operation the patients received methylprednisolone as a pulse therapy followed by oral prednisolone, mycophenolate mofetil and tacrolimus for immunosuppression. Their hospital stay was 24 and 13 days respectively. The lipid concentration returned rapidly to normal range in the 1st week after operation and remained in this range in the first 6 moths of follow-up. In conclusion, liver transplantation offers highly effective treatment for HFHC. It's better to operate the patients before severe atherosclerotic changes in the coronary arteries. All patients must be undergone complete cardiac evaluation before the surgery.

P-911 DONOR SERUM CYTOKINES AFFECT EARLY BUT NOT LATE LIVER TRANSPLANT FUNCTION

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Inflammatory response with increased serum cytokines has been studied in brain-dead donors. However the significance of this phenomenon and its effect on post transplant organ function is very poorly understood. The aim of this study was to correlate levels of cytokine panel in the donor with early and long-term liver graft function.
Methods: Blood samples were drawn from 20 brain dead liver donors immediately prior to organ retrieval. Samples were centrifuged and sera were deep-frozen (-80°C) and stored until further analysis. Concentrations of IL1β, IL2, IL4, IL6, IL8, IL10, IL12p70, TNFα, IFNγ and GMCSF were later determined with Bedlyte human multicytokine detection system 3 on Luminex 100 hardware. Demographic and clinical donor and recipient data were obtained and analyzed. Post-transplant liver function was assessed daily for the first two weeks and periodically thereafter. Mean follow up was 22,5 months.
Results: All measured cytokines but IFN and GMCSF showed strong, positive correlation with early post transplant recipient AST and INR.

Correlation of donor serum cytokines and maximum recipient AST and INR

	IL1β	IL2	IL4	IL6	IL8	IL10	TNFα
AST: Pearsons R	0,66	0,74	0,88	0,51	0,55	0,47	0,55
(p)	(0,001)	(0,001)	(0,001)	(0,013)	(0,007)	(0,02)	(0,007)
INR: R	0,66	0,62	0,54	0,60	ns	0,48	0,49
(p)	(0,001)	(0,002)	(0,008)	(0,002)		(0,02)	(0,017)

With time, this correlation was gradually lost and was not seen after day 10. Only IL-4 affected liver function until one month after transplantation. When recipients were grouped according to maximum post transplant AST (IF ≤1000 U/L, PIF >1000 U/L), significantly higher IL1b, IL4 and IL6 levels were noted in PIF group (respectively IL1: 17,6 vs 2,4; IL4: 4,8 vs 0,47; IL6: 951 vs 85,5 pg/ml versus IF).
Conclusion: Inflammatory response observed in brain dead donor affects early, but not long term liver graft function.

P-912 RISK FACTORS FOR NON-ANASTOMOTIC BILIARY STRICTURES FOLLOWING LIVER TRANSPLANTATION

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Background: Non-anastomotic biliary stricture is a frequent complication of liver transplantation and may lead to retransplantation.
Aim: To identify the risk factors for non-anastomotic biliary strictures.
Method: Non-anastomotic biliary stricture was defined as the appearance of at least one stricture (intrahepatic and/or extrahepatic) not involving the biliary anastomosis on at least two imaging investigations. Non-anastomotic biliary strictures were identified in 96 out of 397 (24%) adult liver transplants performed between January 1990 and May 2008 in the Liver Transplant Unit Victoria. Donor, recipient and operative variables were entered into univariate analysis with calculation of odds ratios and factors with a P value less than 0.1 were then entered into logistic regression.
Results: The following variables were associated with an increased risk of non-anastomotic biliary stricture: diagnosis of PSC, recipient CMV negative status, donor positive/recipient negative CMV status, donor HLA A28, donor HLA B18, donor HLA DR103, recipient HLA DR8, HLA total match 1, graft macroscopic appearance poor perfusion, graft macroscopic appearance other (not good or poor perfusion), perfusion solution HTK, Roux-en-Y biliary anastomosis, tacrolimus or azathioprine as immunosuppression. The following variables were associated with a decreased risk of non-anastomotic biliary stricture: diagnosis of HCV, donor cause of death other (not stroke or trauma), recipient blood group AB, donor HLA B62, donor HLA DR4, recipient HLA B50, recipient DR 15, graft macroscopic appearance good, end-to-end duct-to-duct biliary anastomosis, hepatic artery thrombosis. The following variables were significant on multivariate analysis: perfusion solution HTK, graft macroscopic appearance other, Roux-en-Y biliary anastomosis, end-to-end duct-to-duct biliary anastomosis.
Conclusion: Use of perfusion solutions other than HTK, careful selection of grafts based on macroscopic appearance and avoidance of Roux-en-Y biliary anastomoses, if possible, may help reduce the risk of non-anastomotic biliary strictures in liver transplantation.

P-913 NON-ANASTOMOTIC BILIARY STRICTURES AFTER LIVER TRANSPLANTATION. A SINGLE CENTRE EXPERIENCE

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Introduction: Non-anastomotic biliary strictures (NABS) are important complications after liver transplantation.
Methods: Data was collected by case note review. 22 patients (1.7%) were diagnosed to have NABS.

Results: Seven (32%) patients had received non-heart-beating grafts. 4 patients had early hepatic artery thrombosis (HAT) and underwent emergency revascularization. Ten (45%) patients presented within 3 months of transplant. Four patients had involvement of the extra-hepatic bile ducts alone, 6 of intrahepatic bile ducts alone and 12 had involvement of both. Intra-hepatic duct involvement varied from single sectoral duct (2), multiple duct strictures (11) and diffuse involvement (5). CT angiography identified 3 with late HAT and 7 with hepatic artery stenosis (5 angioplastied). All patients received oral ursodeoxycholic acid and antibiotics. This was the definitive treatment in four patients. ERCP was carried out in 11 patients with suggestion of a dominant extrahepatic stricture. Of these, 5 patients had trial stent placement and 2 had stricture dilation (1 success). Percutaneous stricture dilation was attempted in two patients (1 success). Biliary reconstruction was carried out in 4 (2 successes). 2 further patients await biliary reconstruction. Re-transplant was not possible in 3 patients (2 were unfit, one refused). 10 (45%) were re-transplanted due to late HAT or failure of other therapies. At median follow up of 56 months graft survival was 9/22 (41%) and patient survival was 16/22 (73%).
Conclusion: NABS have an ischaemic aetiology. Management should be multi-disciplinary and tailored to each patient. Optimum use of all therapeutic modalities including re-grafting improves patient survival.

P-914 NEW THERAPEUTIC OPPORTUNITY IN MANAGMENT OF INFECTION BY MULTIRESTENT GERMS IN PATIENTS UNDERGOING SOLID ORGAN TRANSPLANTATION. ROLE OF A NEW TETRACICLIN TIGECICLINE

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In recent years infections by multi-resistant bacteria have become one of the most dangerouse complications can occur in patients who undergo solid organ transplant.
Enterococci spp glicopetides resistant and ESBL-producing Klebsiella spp, increasingly isolated. Our experience with the tigecicline new tetracycline injecting with broad spectrum of action and peculiar pharmacokinetic characteristics involved 10 patients undergoing organ transplant patients admitted in the post-transplant Intensive Care Unit. The patients were aged from 34 to 72 years 4 patients undergoing liver transplantation, 6 kidney transplant.
The infections treated were predominantly abdominal (colangitis, urinary tract infection, endoabdominal abscesses)in one case pneumonia.
The etiological agents were Enterococci faecalis, Enterococci faecium, Klebsiella oxitoca and Klebsiella pneumonia.
The average duration was 12 days, the dosage used provided for an initial dose of double later, the administration was carried out twice a day.
Results: Eight patients was achieved with rapid clinical recovery and the colture of blood body fluids became negative in a few days,in two cases in spite of the coltures were negative there was a severe insufficency of organ
During treatment there were no remarkable side effects. There has been no pharmacology interference with other drugs taken by patients
Conclusion: Management of infections by multi-resistant bacteria in transplanted patients is a challenging and ever more frequently we are defeated. Our experience, even if small numbers but made with a group of high-risk patients such as organ transplant recipients there is reason for hope on the role that can play the Tigeciclina in the management of infections by multi-resistant bacteria. But we must not be easy to make but enthusiasm continue to use this new molecule always supported by microbiological and laboratory data.

P-915 CYTOMEGALOVIRUS, HUMAN HERPESVIRUS-6 AND RECURRENCE OF HEPATITIS C VIRUS AFTER LIVER TRANSPLANTATION

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Background: Human herpesvirus-6 (HHV-6) belongs to the beta herpesvirus together with its close relatives cytomegalovirus (CMV) and human herpesvirus-7 (HHV-7). Among liver transplant recipients, HHV-6 and CMV have been related to clinical consequences, including fever, encephalitis, interstitial pneumonitis, and bone marrow suppression. Cirrhosis caused by hepatitis C virus (HCV) infection is the leading indication for liver transplantation, and HCV viremia persists in up to 95% of posttransplantation patients. The interaction between herpesvirus and HCV has been proposed to be clinically important in HCV-infected liver transplant recipients.
Objective: To analyze the HHV-6 and CMV presence in liver biopsy from recipient liver transplantation and the association with HCV recurrence after transplantation.
Methods: Twenty-eight patients submitted to orthotopic liver transplant due to HCV, were investigated for the presence of CMV and HHV-6 genomes in liver biopsies, using the Nested- PCR technique. The biopsies were obtained after operation, when indicated by the Liver Transplant Unit team when HCV recurrence was suspected. All the patients were followed prospectively in a double-blind study.
Results: Of the 28 patients, 12 (42.8%) had hepatitis C virus recurrence disease. Of these 12 patients, 10 (35.7%) of them showed DNA-HHV-6 positivity and 8 (28.5%) of them showed positivity for DNA-CMV. The relationship between the presence of DNA HHV-6 and recurrence HCV was significant ($p = 0.0049$).
Conclusion: HCV and HHV-6 coinfection was associated with more severe forms of HCV recurrence maybe due to immunomodulatory effects.

P-916 CMV, HHV-6 AND HHV-7 IN ADULT LIVER TRANSPLANTATION RECIPIENTS: DIAGNOSIS BASED ON ANTIGENEMIA

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Introduction: Beta herpesvirus remains latent after primary infection and can be reactivated during immunosupression following organ transplantation. CMV active infection is known as a major infectious complication after transplantation and has been considered an important cause of morbidity and mortality in transplant recipients. HHV-6 and HHV-7 have been acknowledged only recently. CMV has been currently monitored by PCR and/or antigenemia but HHV-6 and HHV-7 active infections are frequently diagnosed by PCR.
Objectives: The purpose of this study was to monitor herpesvirus CMV, HHV-6 and HHV-7 in patients after liver transplantation by the technique of antigenemia and to correlate these results to PCR, to better understand the issues surrounding the infection and active co-infection of herpesvirus.
Methods: Twenty-eight adult liver transplant recipients were enrolled in this study. HHV-6 and HHV-7 antigenemia were performed in peripheral blood mononuclear cells (PBMCs) using monoclonal antibodies and immunoperoxidase staining. CMV active infection was diagnosed by pp65 antigenemia in polymorphonuclear leukocytes (PMNLs).
Results: CMV antigenemia was found in 8 (28.5%) patients (median 28.5 days, range 0-302), HHV-6 antigenemia was positive in 12 (42.8%) patients (median 9 days, range 0-37) and HHV-7 antigenemia was positive in 4 (14.2%) patients (median 16 days, range 0-33). Co-infections were not frequently found. Compared to PCR positivity pattern in our research center antigenemia was similar although positive PCR were frequently more persistent after first detection.
Conclusion: The results found indicate that few patients remain free of beta herpesviruses but most patients who had active infection were infected sequentially and not concurrently. Antigenemia presented results similar compared to PCR techniques.

P-917 RIGHT SUBCOSTAL INCISION IN LIVER TRANSPLANTATION

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The midline of abdomen and the junction of upper midline and transverse incision has been reported as more frequent site of incisional hernia (IH) occurrence. We previously published the feasibility of liver transplantation through only right subcostal incision (SI), with better perioperative outcome and reduction of abdominal wall complications incidence, compared to more extensive incisions attending the midline.
In 77 out of 106 liver transplantations (OLT) we used right subcostal incision and in 29 OLT the incision attended midline of abdomen wall (12 Mercedes, 11 J shaped, 6 bilateral subcostal).
Right subcostal incision had better results compared with others incisions in term of operating time (330 min. vs 415 min.) and perioperative blood products consumption (4 Packed Cell Unit (PCU) vs 7 PCU). In 99 patients with at least 3 months follow-up, incisional hernia occurred in 5 out of 72 subcostal incision (6.9%) and in 6 out of 29 others incisions (22.2%).
In conclusion right subcostal incision, when possible, should be the incision of choice in liver transplantation, with better perioperative outcome and significantly reduced incisional hernia rate.

P-918 OPTIMIZATION ON THE WAITING-LIST USING DONORS OLDER THAN 75 YEARS FOR HEPATOCARCINOMA

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Introduction: Whether the indication of Hepatocellular carcinoma should be a criteria for prioritizing the waiting list and whether the donors of the elderly should be devoted to a selected group of recipients is controversial. We analyze the results of liver graft function and survival in 19 patients transplanted during a period of two years with donors older than 75 years.
Patients and methods: Over a period of two years (2007-2008) were performed a 105 liver transplantation in our hospital, having used 19 donors older than 75 years (18%), giving priority to the following recipients of the waiting list: 11 hepatocarcinomas (6 virus C, 3 B virus, 1alcoholic, 1CBP) 1 Klatskin, 1 urgent retransplant and 6 benign chronic liver diseases prioritized by severity.
In all cases a Piggy-back technique were performed, minimizing the maximum cold ischemia time (on average less than 5 hours). No cases of Hepatocellular carcinoma was treated pretransplant.
We assessed the following variables: early graft function (Quick), early mortality (first month after surgery), and actual survival.
Results: 1 patient presented a severe early graft dysfunction and normalization of the Quick over 70% from the third postoperative day was recorded in all remaining cases. 2 (10.5%) died during the postoperative period (28th postop day for sepsis and FMO, and another at 29th postop day by sepsis and colostasis). One patient died due to an aggressive early recurrence of the virus C (2nd month). 16 patients are alive (84%), with an average follow up of 16.6±7.9 months. All recipients with hepatocellular carcinoma are alive and disease free, except one who suffered for the early recurrence of virus C infection.
Conclusion: The use of organs from donors over 75 years allow prioritize liver malignancy with excellent short-term results.

P-919 AMANITINE INTOXICATION IN A PORCINE MODEL: WHEN TRANSPLANT, WHEN WAIT FOR REGENERATION?

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The toxin of Amanita phalloides causes liver failure mostly in not pre-injured livers with a high regeneration potential. The clinical decision models for transplantation were evaluated and new parameters were identified in a porcine model.
Intoxication was induced in 8 German Landrace pigs (32±2 kg) by an intravenous application of 5mg or 10mg amanitine in deep anesthesia. The animals were keep analogous to the human setting of a maximum intensive care (respirator, invasive blood pressure monitoring, hourly blood gas analysis, HES, NaCl, noradrenaline, electrolytes on demand).
The mean survival of the animals was 137 h (38,5-163,5 h). Liver synthesis stopped and by the end of day 2, the PT of all animals was below 40%. Four out of 8 animals spontaneously recovered as measured by an increase of the PT above 80% on day 5. The serum activities of transaminases was at no time predictive for liver regeneration. Values increased up to 2500 U/l for AST in animals that spontaneously recovered. The increase of serum creatinine above 106 μmol/l was observed in a transient way. In animals that recovered, creatinine levels decrease whereas in animals with a fatal outcome kidney failure became manifest.
In all animals with a regeneration of the liver, platelet count never dropped below a limit of 300×10^6 per ml. The difference clearly became predictive on day 3, more than 24 hours before the onset of regeneration seen by synthesis parameters.
The animal model confirmed most of the clinical observations. The platelet count is an easy accessible parameter to help on the decision when to transplant. The role of platelets as stimulator for liver regeneration is currently discussed, thus this observation may be directly related to the mechanism.

P-920 SALVAGE OF THE TRANSPLANTED LIVER IN A CASE OF KINKING OF CAVOPORTAL ANASTOMOSIS

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Although portal vein thrombosis is not currently an absolute contraindication for liver transplantation, it is considered high risk because of the complex surgical procedure of transplantation with subsequent morbidity and mortality.
We present the case of a 50-year-old woman with hepatitis C virus liver cirrhosis (MELD 15.3) with complete portal vein thrombosis extended to superior mesenteric vein which required cavoportal hemitransposition in order to ensure adequate portal flow.
The patient presented multiple episodes of encephalopathy, refractory ascites, upper gastrointestinal bleeding and recurrent right hydrothorax.
The preoperative assessment showed an incomplete portal vein thrombosis. The patient underwent full size graft liver transplantation in October 2007 and intraoperatively a complete portal thrombosis was discovered. An attempt to thrombectomy and an end-to-end porto-portal anastomosis failed (the intraoperative Doppler ultrasound showed no portal flow) and an end-to-end cavoportal anastomosis with IVC division was performed.
In the first postoperative day the patient developed a kinking of the cavoportal anastomosis and a reoperation was required to convert the cavoportal anastomosis to end-to-side fashion. The patient presented also a transient renal dysfunction.
The initial immunosuppressive regimen consisted of tacrolimus, mycophenolate and steroids, but it was changed to cyclosporine and mycophenolate because of neurological disorders. At 3 months the patient developed hepatitis C virus reactivation and the introduction of antiviral therapy failed because of secondary pancytopenia.
At 1.5 years postoperatively the patient has a good clinical condition with mild ascites, normal renal function and mild hepatocytolysis due to hepatitis C virus reactivation.
Cavoportal transposition is an option for extensive portal vein thrombosis in order to ensure an adequate portal flow. Kinking of the cavoportal anastomosis should be avoided, otherwise reoperation and correction of the kinking is necessary.

P-921 ANTI-TUBERCULOUS THERAPY STRATEGY IN PATIENTS WITH ACUTE LIVER FAILURE (ALF) BEFORE AND AFTER LIVER TRANSPLANTATION (LT)

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Management of patients with ALF and tuberculosis, by unusual anti-tuberculous therapy, is not very well known. In addition, the anti-TB treatment after LT is not commonly established.
Patients: From 1986 to 2008, 566 patients with ALF were referred to our liver intensive care unit. Among them, 16 patients (11F, 5M, mean age: 40±13 years) presented an ALF (2.82%) related to an anti-TB therapy (14 patients), miliary tuberculosis with liver injury (1 patient) and DRESS syndrome (Drug Rash with Eosinophilia and Systemic Symtoms) due to carbamazepin associated with tuberculosis (1 patient). Drugs responsable of ALF were pyrazinamide (9 patients) and isoniazide (5 patients).
Results: At admission, all anti-TB therapy were stopped. 5 patients had a hepatic encephalopathy. Mean values for factor V, ALT, total bilirubin, were 38+28%, 1040+648 IU/L, 237+188 μM/L respectively. After admission, 2 patients were traited by ciprofloxacine/ethambutol/streptomycine, 2 by rifampicyne/levofloxacine/ethambutol/amiklin, 1 by isoniaside/ethambutol/moxiflacine, 1 by ethambutol/rifampicyne, 1 by rifampicyne/isoniaside/pyrazinamide/ethambutol, and 2 by rifampicyne/ethambutol/moxiflacine. 8 patients spontaneously improved, 7 underwent LT and 1 died. After LT, anti-tuberculous therapy included rifampicyne/ethambutol/levofloxacine in 2 patients, rifampicyne/isoniaside/ethambutol/moxiflacine in 1, isoniaside/ethambutol/moxiflacine/amiklin in 1, and rifampicyne/streptomycine in 1. Tolerance of anti-tuberculous therapy was good. In 5 transplanted patients receiving rifampycine, 4 presented an acute rejection of which 3 were treated by bolus of prednisolone. 11 were alive and free of tuberculosis and 5 died of witch one of disseminated tuberculosis.
Conclusion: Unusual anti-tuberculous treatment is safe and effective in patients with ALF and it can be continued after LT. Risk of acute rejection may be increased by rifampycine and its use must be discussed. Moxifloxacine seems to be effective treatment with little sides effects.

P-922 HEPATOCELLULAR CARCINOMA IN UNRELATED VIRAL CIRRHOSIS: DOWNSTAGING AND LONG TERM RESULTS AFTER LIVER TRANSPLANTATION

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Introduction: Chronic viral hepatitis is considered the most significant risk factor for developing Hepatocellular carcinoma (HCC). Nevertheless, about 5%-15% of HCC occurred in patients virus free. HCC natural history in term of incidence and tumoral progression is different according to the underlying cancerogenic factors. Therefore, we can expect different long term results in patients affected by viral hepatitis or virus free, both transplanted as a consequence of HCC.
Methods: From January 2000 to December 2007, 179 patients underwent liver transpalntation (LTx) due to HCC. One-hundred-fifty-seven (87.8%) of them was affected by virus relate cirrhosis (88 HCV, 50 HBV, 19 HCV-HBV) (Group-A); while 22 (12.2%) had virus unrelated cirrhosis (13 alcoholic, 1 Hemochromatosis, 2 Primary Biliary Cirrhosis, 6 Cryptogenetic Cirrhosis). HCC downstaging was performed in 128 cases. One-hundred-seven patients in group A and 15 patients in group B were Milan IN at time of transplantation.
Results: As far as patients oncological features at time of HCC diagnosis and the histological analisys on the explanted livers are concerned, none significant differences were detected. The 3- and 5- year disease free survival between the grouop A and group B is 90.8% and 89.6%, 85.6% and 85.6% respectively (P-value = NS). The 3- and 5-year overall long term survival between the grouop A and group B is respectively 81% and 75%, 85% and 78.4% (P-value = NS).
Conclusion: In our experience, despite the different baseline cancerogenesis in the two group of patients (viral vs. non viral) transpalnted as a consequence of HCC, the overall results in term of recurrence free survival and long term survival rate resulted not significantly different.

P-923 INACCURACY OF PREOPERATIVE IMAGING AND THE INFLUENCE ON PATIENTS WITH LIVER TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA

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Purpose: CT and ultrasound are most common imaging techniques used for the staging of HCC. Discussing Milan criteria suggests, that preoperative staging is correct. But proposed tumor sizes in the CT/US often significantly differ from pathohistological findings in the explanted liver. We conducted a study to evaluate the frequency and significance of these differences referring to Milan criteria.
Methods: This is a retrospective analysis from our database of all patients transplanted for HCC between 1999 and 2006 at our center. Preoperative tumor size had been evaluated using CT and ultrasound and was compared to postoperative pathohistological findings. Patients were grouped according to their pathohistological meeting or not-meeting Milan criteria. End-points were overall and disease-free survival, statistics included the Kaplan-Meier-method, log-rank- and t-test.
Results: Excluding transplantation after liver resection for cancer, HCC was found in the specimens of 99 patients who underwent liver transplantation between 1999 and 2006. Ninety-seven patients had been transplanted for HCC and had received CT-scan and ultrasound preoperatively, two patients were transplanted for other reasons – incidental HCC – they had received only liver ultrasound. One patient had to be excluded from the study exceeding Milan criteria preoperatively.
The remaining 98 patients were grouped according to their meeting (77/98 patients; 78,5%; group A) or exceeding (21/98 patients; 21,5%; group B) Milan criteria in pathohistological specimens. The two groups' basic data were similar. But five-year overall survival (70,30% versus 46% respectively, p=0,048.) and five-year disease-free-survival (91,6% vs. 55,9%, $p<0,001$) differed.
Conclusion: At our center the rate of inaccurate staging HCC in preoperative imaging when applying Milan criteria is comparable to other centers' published data. There might be a relevant difference in 5-year disease-free and overall survival for miss-staged patients. Before expanding Milan criteria, staging inaccuracy should be considered.

P-924 INITIAL EXPERIENCE OF MICRODIALYSIS AS A METHOD OF MONITORING INFLAMMATORY, ISCHAEMIC AND IMMUNOLOGICAL EVENTS FOLLOWING LIVER TRANSPLANTATION

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Introduction: Microdialysis offers a new approach to monitoring acute events within a solid organ transplant in the immediate post-operative period and may allow earlier identification of acute rejection and ischaemic insults. In this study we have investigated the feasibility of utilising this technique in liver transplantation.
Methods: During 2008, 11 patients undergoing liver transplantation were monitored for the first post-operative week with intra-hepatic and subcutaneous 100kDa microdialysis catheters. The liver function markers lactate, pyruvate, glucose and glycerol were measured between 1 and 3 hourly and correlated with clinical events. Cytokine production was monitored daily and the expression pattern of intra-hepatic cytokines identified.
Results: The technique was successful in all but 1 patient in whom the catheter failed after 2 days. There were no complications attributable to the microdialysis catheters and they were removed without problems on day 7. In all patients there was initially high lactate/pyruvate ratios and glycerol, both values, rapidly falling to baseline levels. Raised L/P ratios subsequently occured in patients with evidence of ischaemic damage.High levels of IP-10, IL-8, TNF-b were detected in the majority of patients whereas only low levels of TNFa, IL-2, IL-10 and IL-12 were found in most patients. Rises in both L/P ratios, glycerol levels and IP-10 production were associated with subsequent development of rejection. In one patient high levels of TNFa and TNFb were associated with systemic infection and a raised CRP.
Conclusion: Our initial experience with microdialysis would suggest that this maybe a useful tool for more accurate monitoring of the liver post-transplant and may in time be able to be used to monitor graft perfusion especially in the context of inotrope usage and possibly allow the earlier diagnosis of events such as acute rejection.

P-925 FACTORS INFLUENCING THE INDOCYANINE GREEN (ICG) TEST: ADDITIONAL IMPACT OF ACUTE CHOLESTASIS – A PILOT STUDY

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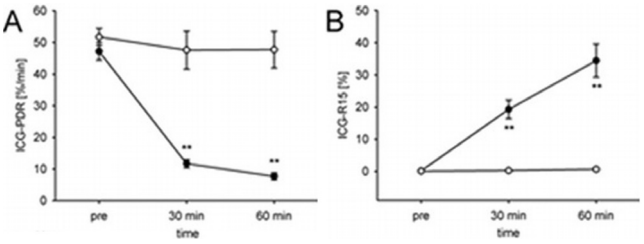
Introduction: Liver function is being assessed by the indocyanine green (ICG) test since decades. However there are known factors influencing its results like: liver blood flow, ICG dose and hyperbilirubinemia. Patients with cholestasis have reduced ICG disappearance rate (ICG-PDR). In this study we investigate if acute biliary obstruction without considerable hepatocyte damage can lead to false impaired ICG-test result.
Methods: ICG-PDR and ICG retention at 15 min (R15) were determined using pulse dye densitometry in a rat model. Rats were either shame operated, or underwent a bile duct ligation (BDL). ICG test was performed before, 30, and 60 min after operation. Standard liver damage serum parameters (ALT, bilirubin), as well as liver histology (H-E) were compared between the groups. To confirm those experimental findings we analyzed the ICG-test results of two liver donors with an early postoperative cholestasis cured with ERCP.
Results: Only slight increase of ALT and bilirubin, and no difference in the histological staining was noticed between the groups. R15 was significantly increased and ICG-PDR reduced in the BDL rats ($p<0.005$, figure). Patients with acute cholestasis caused by anastomotic stenosis were diagnosed by ERCP and stenosis was resolved by stent placement. ICG-PDR improved directly after intervention.



Conclusion: ICG-PDR decreases and R15 increases in acute BDL situation before hepatocyte damage occurs. Acute BDL seems as well experimentally as clinically independently influence ICG-test results. This could be of major relevance in the postoperative phase after liver transplantation and has to be investigated in future studies.

P-926 LIVER TRANSPLANTATION FOR FULMINANT HEPATIC GVHD AFTER BONE MARROW TRANSPLANT FROM THE SAME LIVING DONOR: CASE REPORT

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Purpose: We report a rare case of living donor liver transplantation for a patient with fulminant hepatic failure due to graft-versus-host disease (GVHD) after bone marrow transplant (BMT) from the same living donor.
Case: A thirty-year-old woman suffered from acute lymphocytic leukemia, and received BMT from her HLA-identical brother. Four weeks later, acute GVHD (grade III, stage 2 in skin, stage 3 in intestine, stgae 0 in liver) occurred, which seemed to be successfully treated with steroid and cyclosporine. However, after cessation of steroid and weaning of cyclosporine, liver dysfunction occurred one year after BMT and led to fulminant hepatic failure. Liver biopsy showed severe degeneration of hepatocytes, bile-duct and small vessels with marked lymphocytic infiltration, which suspected hepatic GVHD. In spite of steroid pulse therapy and apheresis, jaundice and coagulopathy were not recovered, and CT examination showed marked atrophy of the liver. Then, she underwent living donor liver transplantation from the same donor without any special precaution against GVHD recurrence. Before the operation, we confirmed no recurrence of leukemia and GVHD in other organs. Liver specimen showed massive and submassive necrosis of liver with lymphocytic and plasmacytic infiltration. After the liver transplant, she received standard immunosuppression with tacrolimus and steroid for prevention of recurrent GVHD. She is doing very well one year after liver transplant under low dose of tacrolimus without recurrent GVHD or leukemia.
Discussion: Liver transplant from the same BMT donor is efficacious and safe for hepatic GVHD. Theoretically, immunosupression is not essential for a transplant between HLA-identical siblings, but advisable in terms of GVHD prevention. In addition, anti-CD3 monoclonal antibody, anti-thymocyte globulin, or irradiation to liver graft may be possible countermeasure to diminish or inactivate "passenger leukocytes" that are responsible for GVHD.

P-927 EFFECT OF ANGIOTESIN II AND BRADYKININ INHIBITION IN RAT REDUCED-SIZE LIVER TRANSPLANTATION

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Previous studies reported that inhibition of Ang II actions through ACE inhibitors or AT1R antagonists protect against warm hepatic ischemia-reperfusion (I/R) injury. Also, ACE inhibitors not only inhibit the Ang II generation but also increase Bradykinin (BK) levels. This study examined whether Ang II blockers (AT1R antagonist and ACE inhibitor) could reduce hepatic injury and improve regeneration in reduced-size orthotopic liver transplantation (ROLT) and whether the beneficial effects of PC in ROLT could be explained by changes in Ang II.
We employed a rat ROLT model in the presence or absence of PC (10 min of ischemia followed by 10 min of reperfusion) and with or without pharmacological modulation with ACE inhibitors, AT1R antagonists or BK. We show that small liver grafts generate Ang II after ROLT and that this is associated with increased angiotensinogen and ACE mRNA expression. Furthermore, inhibition of Ang II does not contribute to PC-induced protection in ROLT. All Ang II blockers reduced hepatic injury but none of them promoted liver regeneration. BK receptor antagonist improved liver regeneration but did not reduce hepatic injury in ROLT. Finally, the combination of Ang II blockers and BK receptor antagonist in ROLT reduced hepatic injury and improved liver regeneration. In conclusion, the treatments with either Ang II blockers or BK receptor antagonists cannot, on their own, improve the outcome of ROLT. Although Ang II blockers can reduce hepatic I/R injury and BK receptor antagonist can promote liver regeneration, neither confers both benefits at the same time. Consequently, it may be of clinical interest to apply both treatments simultaneously.

P-928 SEQUENTIAL TREATMENT OF HCC IN A PATIENT WITH HBV CIRRHOSIS AND LUNG TUBERCOLOSIS CAVITATION: LOCAL ABLATION, LEFT LUNG PNEUMONECTOMY, LIVER TRANSPLANTATION

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Introduction: Tubercular active disease with lung cavitation is a contraindication to liver transplantation. We report the preoperative, surgical and postoperative management of liver transplantation (LT) in a patient suffering from HCC and HBV cirrhosis with left lung tubercular infected cavitation.
Case report: In Dec. 2006 a black 30 year old man with active tuberculosis, HCC and HBV cirrhosis, underwent local ablation of HCC. In Jan 2007, because of progression of liver cirrhosis and worsening of pulmonary function due to infection of the left lung cavitation, the patient began evaluation for LT. At first a tubercular disease eradication was obtained with surgical left lung pneumonectomy followed by 8 months of anti-tubercular drug therapy. When no signs of relapse of tubercular disease was detected, he underwent oncologic evaluation and cardiopulmonary testing wich reported a severe reduction of lung volume with restrictive pattern (Spirometry FEV1 1,53 lit) and an estimated pulmonary artery pressure of 37 mmHg. In June 2008 the patient underwent LT with anesthesiologic management tailored to mantain the preload status at the lower limit avoiding hypoperfusion and lung protective mechanical ventilation. LT was performed without venous bypass and with latero-lateral caval anastomosis.The operation was uneventful, no packed RBCs was administered, and the patient was extubated after 6 hours of mechanical ventilation. The postoperative period was characterized by persistent ascites, moderate renal failure with no permanent reliquates. After 9 months the patient is being well and no tubercular relapse is still observed.
Conclusion: In this case an adeguate anesthesiologic management and a correct surgical technique allowed to overcame a liver transplantation contraindication. To our knowledge there is no evidence of another successful case of liver transplantation in a patient previously treated with pneumonectomy.

P-929 PREDICTION OF TACROLIMUS BLOOD LEVELS DURING THE FIRST WEEK AFTER LIVER TRANSPLANTATION BY THE NEW LiMAx TEST

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Background: The narrow therapeutic range of tacrolimus requires a careful dosing regime with therapeutic drug monitoring. Toxic levels cause severe adverse effects. Metabolic rate of tacrolimus is dependent from graft function. The primary study hypothesis was, that patients with initial poor graft function had a higher risk of developing toxic levels.
Methods: Ninety-three patients receiving liver transplantation were examined in a prospective observational study. Graft function capacity was measured by the LiMAx-test: ^{13}C-labeled methacetin was injected intravenously and was metabolized in the liver. A continuous breath analysis determined emerging $^{13}CO_2$ for 60 minutes. The test was performed six hours after graft reperfusion and at days 1, 3, and 5. Tacrolimus trough levels were determined each day by a commercially ELISA kit.
Results: Toxic levels ($>$20ng/mL) were recorded in 41 patients (44%), but only in ten subjects (11%) for longer than one day. Insufficient levels ($<$5ng/mL) were recorded in 38 subjects (41%), and in 19 patients (20.5%) for longer than one day. At the second day patients with poor graft function showed tacrolimus trough levels of 20.1$\pm$11.6ng/mL in comparison with patients with fair function (13.7$\pm$7.8ng/mL) and good function (9.5$\pm$4.4ng/mL; $p<0.0001$) Receiver operating characteristic yielded an area under curve (AUROC) of 0.757 (95%CI 0.63-0.88; p=0.001) for prediction of toxic levels by the LiMAx test. Comparison of mean LiMAx and mean levels revealed a correlation coefficient of r=-0.513 ($p<0.0001$) during the first postoperative week.
Conclusion: Initial graft function is a major factor influencing tacrolimus kinetics. LiMAx test can accurately classify graft function directly after surgery. Patients with initial poor function should receive reduced tacrolimus dose, whereas patients with good function should receive higher doses. In conclusion, adequate tacrolimus levels could be provided earlier and might reduce the incidence of adverse effects.

P-930 A MULTI-FACTORIAL BIOLOGICAL MODULATION PROTOCOL THAT AMELIORATES ISCHEMIA-REPERFUSION INJURY SIMULTANEOUSLY REDUCES BILESALT TOXICITY IN PORCINE LIVER TRANSPLANTATION FROM NON-HEART BEATING DONORS

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Introduction: Biliary Strictures (BS) represent a serious complication after Liver Transplantation (LTx) from Non-Heart-Beating-Donors (NHBD). Ischemia and biliary bilesalt toxicity have been identified as important factors in the pathogenesis of BS. We reported that prolonged Warm Ischemia (WI) in NHBD leads to the formation of toxic bile (increased biliary bilesalt-to-phospholipid ratio) in porcine LTx *(Tx 2008).* We developed a multi-factorial Biological Modulation (BM) protocol targeting previously identified mechanisms of WI & ischemia/reperfusion injury (IRI), and that reduces primary-non-function.
Aim: To investigate whether this BM protocol not only reduces IRI but also ameliorates biliary bilesalt toxicity after NHBD-LTx.

Methods: BM protocol: *in donors,* (prior to 4°C HTK preservation), flush with warm ringers (avoiding cold-induced vasoconstriction), streptokinase (eliminating thrombi) and epoprostenol (vasodilator & platelet aggregation inhibitor); *in recipients*, IV administration of glycine (Kupffer cell stabilizer), 1-acid glycoprotein (anti-inflammatory protein), a MAPKinase inhibitor (pro-inflammatory cytokines inhibitor), tocopherol & glutathion (anti-oxidants), and apotransferrin (redox-iron chelator). After LTx, bile was collected during 72 hours. Total biliary bilesalt concentration was measured spectrophotometrically using 3α-hydroxysteroid dehydrogenase. Biliary phospholipid concentration was analyzed using a commercially available enzymatic method. The biliary bilesalt-to-phospholipid ratio in BM livers was compared to ratios obtained in a historical control group of 5 surviving pigs following LTx of grafts exposed to prolonged (≥30' WI) (*LTx 2005, 2008*). Total course of the biliary bilesalt-to-phospholipid ratio post-LTx was compared by using the area under the curve.
Results and conclusions: Biliary bilesalt-to-phospholipid ratio post-LTx was lower in BM versus controls pigs (1128±447 versus 4836±4619; p=0.05).
A cocktail containing several biological reagents targeting IRI reduces biliary bilesalt toxicity. Translating this strategy into the clinics may reduce BS after NHBD-LTx, leading to wider and safer use of these grafts.

P-931 WORSE PATIENT SURVIVAL IN LIVER TRANSPLANT RECIPIENTS WITH HISTORY OF TOBACCO USE

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Background: Tobacco use is associated with multiple medical problems including vascular and pulmonary disease and increased risk of cancer. This study is a retrospective chart review of a large number of liver transplant recipients to determine if a history of tobacco use is associated with decreased post-transplant graft and patient survival.
Methods: The records of 1013 consecutive liver transplant patients from 2001 to 2008 were reviewed. Tobacco use was determined from the initial psychological evaluation for transplant candidates which includes a history of substance use, and from other medical records if this evaluation was incomplete. "Current smoker" included anyone actively smoking at the time of listing or who had quit for less than 1 month at the time of listing. "Previous smoker" included anyone who had previously smoked routinely but had quit for at least 1-month prior to listing. "Never smoker" included persons without any history of regular tobacco use.
Results:

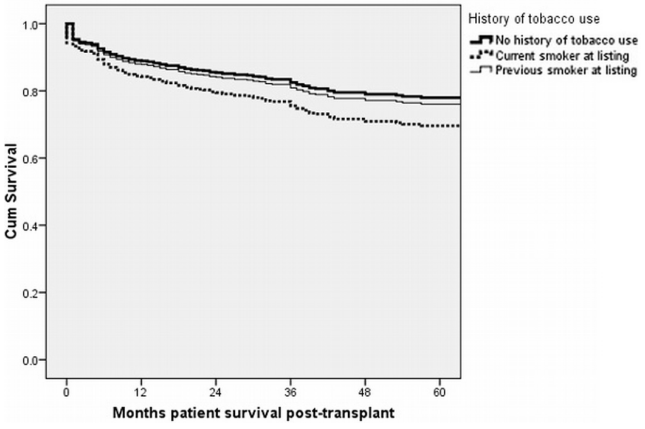

Figure 1. Cox regression post-liver transplant 5-year patient survival in 1000 patients stratified by smoking status at time of transplant.

Conclusions: Patient survival is lower from smokers throughout the follow-up period. Previous smokers have a survival similar to never smokers up to 36 months, but then survival worsens slightly thereafter. These results indicate a clear increase in risk of early post-transplant death for current and previous smokers when compared to never smokers.

P-932 RESULTS OF LIVER TRANSPLANTATION IN THE TREATMENT OF HEPATIC ALVEOLAR ECHINOCOCCOSIS

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Background: Alveolar echinococcosis (AE) is a rare disease caused by the *Echinococcus multilocularis* larvae growing in the liver. This observation suggests that liver transplantation (LTx) may be indicated when other therapies become ineffective and no extrahepatic lesions are founded.
Objective: The purpose of this study was to assess the value and timing of LTx in the treatment of AE of the liver.
Material & methods: A retrospective study was carried out, including all cases of LTx for AE performed in years 2000-2009: 11 cases of AE (M/F-9/2 in middle age of 39±9,4). 8pts (72%) had previous surgical therapy in about 3 months before LTx. Lesions in 81%(9pts) were located in 4th segment of the liver. Mean diameter was about 10cm. In 4 (36%) cases cysts infiltrated hilus of the liver. Indications for LTx were liver failure with associated jaundice and portal hypertension in 3 cases, lesions resected nonradically because of close location to the portal vein in 6 cases and oversized tumor in 2 cases. 7 classical and 4 piggy-back LTx from cadaveric donor were performed. All of the patients received additionally albendazol, prior to and after LTx – mean period 2 years. In immunosuppressive therapy predominated regimen were tacrolimus and steroids.
Results: In the study group 1 death due to complications of bile ducts necrosis 18 months after LTx was observed. In group of 3 patients appeared immunological exponents of infection recurrence in ELISA test, without changes in imaging examinations, after 24±12 months. Actuarial survival rate after LTx was 100%/91%/91% at 1/3/5 year.
Conclusion: Echinococcosis multilocularis of the liver in late stage can be considered as one of the indications of LTx, especially when other therapies are scarce and ineffective. In those cases LTx may be an appropriate option of radical treatment with excellent long term survival.

P-933 THE RISK FACTORS OF EARLY DYSFUNCTION OF THE LIVER GRAFT

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Aim: To discover the risk factors of initial poor function of the liver graft.
Material: 269 consecutive orthotopic liver transplantation were performed in the Department between 2004 and 2006. Donor, recipient, graft and transplantation process data were collected into the study. Tested parameters are listed below. Endpoint of the study was dysfunction of liver graft (AST or ALT >2500 IU/L or prothrombin index < 50% during first 7 days after LTx).
Results: The significant increase/decrease of hepatic early dysfunction by 25% requires the change of the levels of the following risk factors by: 13 minutes (WIT), 1.7 kg/m^2 (donor BMI), 7 years (donor age), 22.4 IU/L (donor GGT), 9.4% (donor prothrombin index), 5% (macrovescicular steatosis) and 7% (microvescicular steatosis). For non significant factors the following changes are required: 223 minutes (CIT), 75 minutes (TIT), 37 years (recipient age), 37 (MELD), 9 days (ICU stay), 32 mmol/l (sodium concentration), 223 IU/L (AST), 74 IU/L (ALT), 0.5 mg/dl (bilirubin level), 14 s (APTT) and 0.15 (INR).
Conclusion: The main conclusion is that the every increase WIT by 13 minutes during implantation of the graft increase the early liver poor function by 25%. 7% of microvescicular and 5% of macrovescicular and 13 minutes of WIT are equivalent to a predictors of early hepatic dysfunction.

P-934 THE USE OF EXPANDED CRITERIA DONORS IN LIVER TRANSPLANTATION IN SWEDEN DOES NOT COMPROMISE GRAFT OR PATIENT SURVIVAL

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Introduction: Sweden has a history of using a high percentage donors with conditions which classify them as expanded criteria donors (ECD). This retrospective study analyzed the outcome of ECD in liver transplantation (Ltx) and compared them with standard criteria donors (SCD).
Methods: Between 2000 and 2005, all first-time Ltx performed at Karolinska University Hospital were reviewed. ECD were defined as donors with age ≥ 65 years, macroscopic steatosis ≥ 30% or cold ischemic time (CIT) ≥12 hours. Graft function was analyzed by laboratory liver function tests and hepatic excretion fraction (HEF) using scintigrams at day 4-14 (HEF-1) and 3 months postoperatively (HEF-2).
Results: 103 donors (53%) were classified as SCD and 93 (47%) as ECD. The cause for ECD classification was CIT in 47.3%, age in 26.9%, and steatosis in 10.8%.
79 ECD (84.9%) had one ECD criterion, 11 had two (11.8%), and 3 had three (3.22%). The recipient demographics were comparable between the two groups. The peak S-Bilirubin post transplantation was 88.3±93.4 mmol/L in the SCD group and 100.1±78.2 mmol/L in the ECD group (p=NS). SCD-HEF-1 was 46±26% and ECD-HEF-1 was 43±26% (p=NS). At 3 months post transplantation SCD-HEF-2 was 80±25% and ECD-HEF-2 was 75±27%(p=NS).

The use of ECD livers was not associated with increased risk for primary non-function, delayed non-function, or increased post operative complications. Patient- and graft survival was similar in both groups.
Conclusions: Almost 50% of liver donors transplanted in Stockholm are ECD. The improvement of hepatic function within the first 3 months was comparable in the two groups. The use of ECD livers is safe and should be practised in Ltx.

P-935 LATE BILIARY COMPLICATION AFTER SPLIT-LIVER TRANSPLANTATION. A REPORT OF A PERCUTANEOUS TRANSHEPATIC BILE DUCT ABLATION WITH N-BUTYL CYANOACRILATE

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Biliary complications continue to be a major cause of morbidity after split-liver transplantation (SLT) with a reported negative incidence between 10% and 32%. In this report we describe an uncommon late biliary complication. One year after SLT the patient developed severe cholangitis episodes. A doppler ultrasound and a magnetic resonance cholangiography (MRC) showed an intrahepatic bile duct dilatation. The patient underwent a percutaneous transhepatic cholangiography (PTC) associated with the placement of percutaneous biliary drains inside the distended biliary tract. The segmentary bile duct of hepatic segments VI-VII draining in the left bile duct was unidentified and tied at the time of the in-situ split-liver procedure. We decided to perform a permanent obliteration of the dilatated intrahepatic ducts by a percutaneous embolization using a non-resorbable agent. With a fluoroscopic guidance through a transhepatic access we injected the tissue adhesive agent n-butyl cyanoacrilate (NABC) mixed with ionized oil (Lipiodol). This solution completely filled the biliary duct and the occlusion was almost totally accomplished in a few seconds. Acomputed tomography scan performed 6 months later showed no sign of hepatic abscesses and the bile duct dilatation was almost completely occupied by the NBCA lipiodol. One year after the procedure the patient showed normal liver function tests. The management of biliary complications after SLT requires a multidisciplinary approach. Chemical bile duct embolization treatment could represent an altrenative solution to solve an uncommon biliary complication. The use of NBCA in obliteration of a dilatated bile duct seems to be a safe procedure with good results providing a less invasive option than hepatic resection and decreasing the morbidity associated with chronic external biliary drainage.

P-936 PSYCHOLOGICAL SUPPORT, QUALITY OF LIFE AND ADAPTATION AFTER LIVER TRANSPLANTATION: THE VERONA EXPERIENCE

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Liver transplantation can cause emotional and psychological distress which affect Quality of Life compliance and adaptation.
In order to reduce these effects, a specific program of psychological assistance was set up. It includes: a psychological evaluation of the patients before their inclusion in the waiting list; an evaluation of theirs coping abilities and family support; an early taking in charge of the patients and theirs relatives.
This study describes the variations of the QoL and adaption (anxiety, depression) of the patients during the waiting time list, at six and at twelve months after transplantation.
157 patients ('xage= 53years) candidates to liver transplantation were evaluated; 121 of them were included in the waiting list and 109 had a liver transplantation. All these participated at the program of psychological assistance and filled self-report questionnaires aimed to check theirs perception of QoL (SF–36), Anxiety (STAI) and Depression (B.D.I) before and after transplantation.
Patients just six months after transplantation improve significantly theirs perceptions about QoL compared to the waiting list period ($p< 0.05$); in particular there are significant differences in Physical Pain, p=0.006 Physical Role p=0.02; General Health $p<0.0001$; Vitality $p<0.001$; Social Activity, p=0.0001; Emotional Role p=0.009 and Mental Health p=0.001. All these perceptions became more stable after twelve months (p=ns.). As regards depression, 50% of the patients who start the work-up show at least "light" level of depression which decreased after six months (20,51%), but tends to increase after twelve months (27,66%); the anxiety was: 20% at work-up, 9.76% after six months and12,5% at twelve months.
Liver transplantation improves QoL after just six months and this, associated with low levels of depression and anxiety, indicates a good level of adaptation. The program of psychological assistance improves Quality of Life, compliance and adaptation.

P-937 RATIONALIZATION OF LIVING DONOR LIVER TRANSPLANTATION USING NON MICROSCOPIC ARTERIAL RECONSTRUCTION

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Smaller diameter of the hepatic artery is the one of the complexity of living donor liver transplantation (LDLT). We investigated saving effect of the direct arterial anastmosis x3.5 surgical lope on rationalization of operative process instead of the ordinary fixed operative microscope. Two hundred and nine LDLT were carried out from 1996 to 2008, and the procedure of arterial reconstruction was changed from the fixed operative microscope to the direct method after 2004. There was not the significant difference in an age components of a Micro group (n =92, pediatric 20, adult 72) and the non-Micro group (n =117, pediatric 12, adult 97). Both ends of artery are longitudinally cut and are spatulated, and a running suture is started by the extra-luminar manner using 7-0 or 8-0 proline. In adults, arterial anastomosis was carried out between the lober artery of the graft and the native lobar or proper hepatic artery. But the lobar artery of the graft was anastomosed to the common hepatic artery in chirdren. The hepatic volume/body ratio in pediatrics is larger than that in adults, and hepatic artery of the child of biliary atresia got thick by accelleration of artery by cirrhosis. Therefore, non-microscope anastomosis is generally possible even in pediatrics. Hepatic artery thrombosis was happened 3 cases in Micro group, and 2 cases in non-Micro group. Significant difference was observed in operation time between two groups, 745 vs. 581 munities, respectively ($p<0.0001$). Intra-operative blood loss had also significant difference, 192 vs. 132 ml/kg ($p<0.05$), but there was no significant difference in survival rates. The non microscopic anastomosis is of use for rationalization of LDLT.

P-938 FOREIGN BODY GRANULOMA: A RARE CAUSE OF BILIARY OBSTRUCTION AFTER LIVER TRANSPLANTATION

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Background: Patients who undergo living related left lateral or left lobe liver transplant (LDLT) have been reported to have a high incidence of biliary complications. Some studies suggest that most patients will ultimately need operative revision. LDLT is essential in light of the scarcity of organs available for transplantation. Biliary complications are reported to occur between 14-38% and include leakage and stricture. Biliary intervention via endoscopic techniques is rarely possible in pediatrics because of Roux-en-Y reconstruction and in small patient size. Percutaneous management, however, is successful in the majority of cases.
Case summary: A 5 year old boy, a case of biliary atresia, who was a candidate for a living related liver transplant, receiving the left lateral segment of the donor's liver, underwent liver transplantation. The surgery and immediate postoperative course were uneventful. A few weeks postoperatively he developed fever and abdominal pain, and due to bile leakage he underwent a revision of the Roux-en-Y ductojejunostomy. He was discharged after a full recovery. Six years after the corrective surgery he developed jaundice and pruritus, an magnetic resonance cholangiopancreatography (MRCP) showed biliary dilatation and liver function tests were not in favor of rejection, so a percutaneous transhepatic cholangiography intervention (PTC) was performed. After each percutaneous intervention his symptoms would be alleviated but would again recur shortly thereafter. The final PTC showed a narrowing in the distal of the biliary tree. An exploration was performed via a laparotomy. At the site of the orifice of the ductojejunostomy a small knot was seen which had changed into a granulomatous tissue acting as a one way valve, causing obstruction to the passage of bile. In it there was a remnant of the silk suture which had been used in his previous surgeries.

P-939 PERCUTANEOUS RADIOFREQUENCY (PRFA) AS A BRIDGE TO LIVER TRANSPLANTATION (LT) FOR HEPATOCELLULAR CARCINOMA (HCC)

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Aim of the study: To evaluate the risk and the efficacy of RFA through the comparaison of criteria of necrosis on pre-transplant imaging and on histopathology of the explanted liver.

Patients and methods: From 1998 to 2007, 27 patients with HCC on cirrhosis were treated by pRFA in the waiting time for LT. All but 3 patients had a single nodule. Mean size of the tumor was 24.5 mm (10-41) with 4 patients with a size between 30-40 mm. Grading of cirrhosis was Child Pugh A in 16 patients, B in 5 and C in 6 patients. A complete work up excluded any extrahepatic deposit. Follow up was conducted for every 3 months up to LT.
Results: There was no mortality related to the procedure and 3 patients (11%) presented a minor complication. Total devascularization of the tumor on CT was obtained in 96%, 89%, 85% and 85% at 1,3,6 and 12 months respectively after pRFA. pRFA was considered successful in 23 patients (85%). The mean waiting time for LT was 12.9 months (1-35) from the onset of RFA. On the liver specimen after LT, among the 23 patients with complete response, a total tumor necrosis was demonstrated in 13 patients (55%) and a necrosis $>$ 50% in 10 patients (45%). Additional HCC were found in the explanted liver in 12 patients (44%). After a mean follow up of 32.5 months after LT, 20 patients were alive without recurrence, 1 alive with recurrence and 6 died, 2 of whom from tumor recurrence.
Conclusion: pRFA is safe and locally efficient but, despite apparent efficacy on imaging, only 55% of the patients demonstrate complete pathological necrosis at LT and 44% had additional undiagnosed nodules.

P-940 DIFFERENT IMMUNSUPRESSIVE DRUG SELECTION AFFECTS THE QUALITY OF LIFE FOLLOWING LIVER TRANSPLANTATION

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Purpose: Liver transplantation (LTx) is a well established procedure for end stage liver diseases. Since long term survival rates are satisfactory, nowadays quality of life (QOL) gains increasing interest. Once postoperative surgical course was successful QOL during maintenance therapy depends on individualized immunosuppressive drug selection (IDS). We investigated QOL employing the EYPASCH questionnaire in de novo patients as well as under maintenance therapy with different combinations of immunosuppressive agents.
Method: We analyzed postoperative courses of n=420 liver transplant recipients (de novo n= 80 and maintenance therapy n=340). Besides gastrointestinal symptoms potentionally related to mycophenolat mofetil (MMF) treatment or IDS, general QOL was accessed using EYPASCH's QOL query form (group 1: day 1 to 180; 2: day 180 to 540; 3: $>$ 540 days post LTx).
Results: *Gastrointestinal symptoms:* 1. Cyclosporin (CSA) shows significantly better results (p=0,001) compared to Prograf in all groups. 2. MMF in combination with calcineurin inhibitors (CNI) significantly (p=0,032) decreases LQ in group 3.
General QOL: 1. CSA shows significantly (p=0,002) better QOL compared to Prograf. 2. MMF significantly (p=0,090) decreases QOL in group 1.
Conclusion: 1. CSA based IDS (CSA plus Steroids) offered significantly improved QOL in de novo patients as well as under maintenance therapy. 2. Noteworthy, gastrointestinal symptoms obviously related to MMF decreases QOL in maintenance therapy. 3. Decrease of general QOL in group 1 is probably still due to operative trauma. 4. Relation of QOL with incidental rejection is currently under investigation.

P-943 THE IMPACT OF DIABETES MELLITUS IN LONG-TERM OUTCOME OF LIVER TRANSPLANT PATIENTS FOR HEPATITIS C

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Aim: Diabetes Mellitus (DM) has been implicated as a risk factor for bad evolution of HCV recurrence after liver transplantation.The aim of this study was to asses in our center the relationship between Diabetes mellitus and evolution of HCV after liver transplant.
Material and methods: From 2000 to 2005, 115 HCV positive patients has been submitted to liver transplantation.DM has been defined as patients with glucose levels over 120mg/dL confirmed on at least 2 occasions. Thirty four patients were diabetic before transplant and 81 were not.After transplant 50 patients were diabetic and 65 were not. To see the comparability of both groups pre and post-transplant, the demographic characteristics of recipients donor and surgery were compared.Type of immunosuppression,incidence of rejection,CMV infection, glucose values, BMI, hepatic function,type and severity of recurrence, viral load and outcome were compared between both groups pre and post-transplant.
Results: Patients with DM pre-LT had a tendency to be older,with higher incidence of cardiopathy, longer preservation time, higher incidence of rejection, than the non-diabetic (p=ns), but rejection has been treated wih lower amount of steroids (p=0.04) and liver dysfunction was more severe at 6 months post-LT (p=0.013). BMI and levels of immunosuppression were similar.Glucose values were stastically higher during all the follow-up in the diabetic group.Incidence of early recurrence of HCV was similar, but late recurrence of HCV beyond the second year appeared specially in diabetic patients.Viral load and evolution of recurrence did not show statistically significance.
When we compare the patients according to DM post-LT,liver dysfunction was more severe as early as 3 months post-LT in the diabetic group ($p<0.05$),but the rest of results were similar.
Conclusion: In our experience,DM pre-LT or post-LT,defined as levels of glucose above 120 mg/dl,did not afect the outcome of HCV recurrence after liver transplantation.

P-944 DONORS AND RECIPIENTS CHARACTERISTICS ASSOCIATED WITH LIVER GRAFT FAILURE IN CHIRROTIC RECIPIENTS: A EUROPEAN SINGLE CENTRE EXPERIENCE

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Introduction: The survival benefits of liver transplantation depends on candidate disease severity and on liver donor quality. Several recent studies focus on donor-recipient matching, but the issue is still open.
Methods: Between April 2003 and March 2008, 231 adults received a primary isolated liver transplant (LTx) at our centre. We reviewed 143 (47 female, 96 male) cirrhotic recipients, mean age 51.2$\pm$9.8, without hepatocellular carcinoma: donor and recipient parameters were investigated.
Results: Mean MELD was 20.46$\pm$8.4. Mean follow up was 986$\pm$609 days. Mean donor age was 54.5$\pm$17.9 years old, with mean intensive care unit stay 4.01$\pm$4.2 days. Mean cold ischemia time (CIT) was 401.9$\pm$117.5 minutes. 128 patients received a whole graft, 15 a split graft and mean GRWR was 2.1$\pm$0.6. Cox regression model identified only donor age between 65 and 80 years old (yrs) as independently predictor of graft failure (p=0.02), while split liver graft was not associated with graft failure. Split and whole graft population were comparable except for shorter CIT (p=0.02) and younger donor age (p=0.00). For donor age between 65 and 80 yrs (n=42): HCV (p=0.01)and MELD between 20 and 25 (p=0.03) were risk factor for graft failure. If donor age was between 40 and 65 (n= 63) anoxia as cause of donor death and MELD higher than 25 were associated with graft failure (p=0.00 and p=0.01).
Conclusion: Donor age higher than 65 yrs is an indipendently predictor of graft failure. In HCV positive recipients donor age between 65 and 80 yrs and MELD between 20 and 25 are risk factor for graft failure

P-945 WEIGHT GAIN AND METABOLIC SYNDROME AFTER LIVER TRANSPLANTATION: INCIDENCE AND PREDISPOSING FACTORS

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Introduction: Metabolic syndrome (MS) is a common complication after orthotopic liver transplantation (OLT). This cluster of metabolic disorders increases the risk of cardiovascular disease. Incidence is reported beyond 44,5%.
Patients and methods: Prevalence of MS (National Cholesterol Education Program-Adult Treatment Panel III criteria, NCEP-ATPIII) was assessed in 97 stable liver transplant recipients during routine follow-up. Patients were divided into Group A (without MS) and Group B (with MS). Pre-and post-OLT data were collected, including MELD score, BMI, lipid status, immunosuppression, cardiovascular events and educational level.
Results: Incidence of metabolic syndrome was 55,7%. There was no difference concerning presence of diabetes pre-and post-OLT, hypertension, and lipid status between Group A and B. There was also no difference in level of education, incidence of cardiovascular events and rejection episodes, presence of acute or chronic renal failure, need for hemodialysis, and renal transplantation. Type of immunosuppressive regimen had no influence on weight gain and the development of MS after OLT. Mean BMI was 24,521$\pm$4,072 in Group A, 28,353$\pm$4,869 in Group B, which was significantly higher ($p<0,0001$). Mean BMI increase after OLT was 2,388$\pm$3,837, which was significantly different between the groups ($p<0,006$).
Conclusions: As MS is very frequent after OLT, and as it is strongly correlated with BMI and weight gain after OLT, a special focus on metabolic disorders, especially weight control during follow-up after OLT is very important.

P-946 THE RELEVANCE OF PCT AFTER ORTHOTOPIC LIVER TRANSPLANTATION

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Introduction: Procalcitonin (PCT) was shown to be a reliable marker for SIRS and sepsis. Aim of study was to evaluate PCT as an early prognostic marker for occurrence of postoperative complications.
Methods: 32 patients (pts) who underwent 33 OLTs and PCT-levels were analysed. The highest PCT was defined as peak-PCT. Patients were stratified in non-complication and complication group. A secondary stratification was performed using a peak-PCT of 5ng/ml in each group. Further, we analysed the risk of occurrence of a complication according to a peak-PCT of 5ng/ml and the course of PCT after OLT in each group.
Results: The peak-PCT occurred between the 1st and 3rd postoperative day in 30 pts, followed by halvening every second day. A constantly rising PCT or a secondary rise was seen in 2 pts and associated with fatal outcome. 18 pts were stratified in the non-complication group (10pts: >peak-PCT<5ng/ml). 14 pts with 15 transplantations were stratified in the complication group. The odds ratio of running a complication was 11.2 (10.81-11.59;$p<0.025$) when the peak-PCT was higher than 5ng/ml.
Discussion: A decline was seen in 31 cases, a constantly rising level was observed in 2 pts, who died. This observation was described before for non transplant patients. In transplant patients, an elevation of PCT was seen in bacterial infections, but not in rejection or wound infection. There was a rise of PCT in respiratory failure and sepsis, but not in renal replacement therapy, ascites, pleural effusion, rejection or bleeding. An initial high PCT is described not to indicate a poor prognosis. Patients of complication group had a higher mean PCT, which turned significant after the 7th day, most probably because of high variation of levels. A peak-PCT above 5ng/ml has an odds ratio of 11.2 for pts experienced a complication.

P-947 THE IMPACT OF ANTIVIRAL THERAPY ON FIBROSIS PROGRESSION DUE TO HCV RECURRENCE AFTER LIVER TRANSPLANTATION (LT)

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Background: After LT few patients are elegible for combined antiviral therapy (AT) with PEG-IFN plus Ribavirin due to several, severe side effects.Whether AT is worthwhile in ameliorating liver fibrosis in the long term is still controversial.
Aim: To asses the impact of AT on fibrosis progression due to HCV recurrence after LT.
Methods: All consecutive LT-HCV+ patients undergoing AT for HCV histological recurrence (Scheuer's stage of fibrosis (S) >=1) on per protocol liver biopsies (LB) performed before and after AT, were included. The fibrosis progression rate (FPR) was expressed as fibrosis unit per month (FU/mo). Patients were stratified in 3 categories based on when LB was performed: 0-24; 25-48; 49-72 months after LT, respectively, at 6-12 months after AT.
Results: 27 patients underwent AT,16 M, 11 F, mean $\pm$ SD age 54$\pm$8 years, mean follow-up 38.7 months (range12-95). 25 patients were genotype 1b, 1 2b and 1 2a/2c. 19 (70%) were on tacrolimus, while 8 (30%) were on cyclosporin. The mean time of starting AT since the transplant was 25 months (3-98). 10/27 (37%) patients withdrawn from AT due to side effects before the end of treatment (12 months). Overall SVR was 33.4% (9/27). Mean S was 2.05 pre-AT and 2.51 after-AT (p=ns). In SVR+, pre-AT S was 2.05 and post-AT S was 2.22 (p=ns), in SVR-, pre-AT S was 2.05 and post-AT was 2.66 (p=ns). According to the time interval from LT 15 patients started AT at 0-24 months, 8 24-36 and 4, 36-72 interval, FPR, in SVR+ versus SVR- was 0.031, 0.013, -0.041 and 0.054, 0.027, 0.036 respectively (p=ns).
Conclusion: Liver fibrosis due to HCV recurrence after LT progresses despite the antiviral therapy, but slower in patients with virological response.

P-948 BLOOD SALVAGE DURING LIVER TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA: INFLUENCE ON RECURRENCE AND SURVIVAL

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Background: Blood salvage during orthotopic liver transplantation (OLT) has become standard technique in order to reduce homologous transfusion. The aim of this study was to evaluate the influence of intraoperative blood salvage during OLT for hepatocellular carcinoma (HCC) on recurrence rate and survival.
Materials and methods: Twenty-seven patients who had undergone OLT in piggyback technique for HCC were retrospectively evaluated. Influence of intraoperative blood salvage, HCC stage, viral hepatitis, MELD-score, immunosuppressive regimen, and preoperative downstaging techniques on recurrence rate and survival were retrospectively evaluated.
Results: Univariate analysis revealed patients with HCC beyond the Milan Criteria to have significant higher recurrence rates than patients within ($p<0,025$). Patients with multiple tumor nodules also had significantly higher HCC recurrence after OLT. Multivariate analysis revealed exceeding of Milan criteria and multiple tumor nodules to be significant and independent risk factors for HCC recurrence after OLT. Intraoperative blood salvage had no influence on survival and recurrence rate ($p<1,0$). Patients who received rapamycin significantly showed lower HCC recurrence rates ($p<0,047$), though immunosuppression had no significant independent influence on HCC recurrence, as well as technique of downstaging (chemoembolisation vs. radiofrequency ablation (RFA) vs. tumor resection prior to OLT). Patients with hepatitis C showed a trend towards lower recurrence rate than those without ($p<0,124$).
Conclusions: The results of this study suggest that intaoperative blood salvage during OLT for HCC has no influence on survival and recurrence rates. Multivariate analysis revealed HCC beyond Milan criteria as well as multiple tumor nodules to be significant and independent risk factors for HCC recurrence after OLT. Immunosuppression with rapamycin positively influences recurrence-free survival.

P-949 ALLOIMMUNIZATION TO RED BLOOD CELL ANTIGENS IN LIVER TRANSPLANT PATIENTS IN STATE UNIVERSITY OF CAMPINAS

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Transfusion support is an important part of liver transplantation. Liver transplant recipients have a greater incidence of RBC alloantibody, over 14% in current literature.
We present the frequency of alloimmunization and the specificity to RBC antigens in 302 patients undergoing liver transplantation at the School Hospital of the University of Campinas from 1997 to 2008.
We performed a screen for unexpected antibodies, and a direct antiglobulin test (DAT). A positive antibody screen was investigated with an antibody identification panel using commercial RBC reagent cells. Positive DAT was followed up with elution and antibody identification.
A total of 74 RBC alloantibodies were identified in 70 patients (23%), and 10 patients (3.3%) had an unspecific antibodie identified. We identified autoantibodies in 51 patients; 47% auto anti-I and 45.2% IgM without specificity. DAT was perfomed in 227 patients with positivity of 34%, only 3 eluitions were positive, all with specificity against the Rh system.
The most common RBC alloantibodies were directed against Rh system antigens with 31 (41.9%) directed against the E antigen; 8 (10.8%) anti-c; 5 (6.7%) against anti-D, anti-C and anti-C^w respectively; 4 (5.4%) anti-Jk^a and anti-M each and only 3 (4%) against K antigen, 9 (12%) of patients developed other alloantibodies such as anti-e anti-Fy^a, anti-Lu^a, anti-Di^a, anti P_1 and anti-Le^a.

Specificity and Frequency of RBC Alloantibodies

Antibody	No. alloantibodies	Patients with alloantibody (%)
Anti-E	31	41.9
Anti-c	8	10.8
Anti-D	5	6.7
Anti-C	5	6.7
Anti-Cw	2	6.7
Anti-e	3	2.7
Anti-K	4	4
Anti-Jka	4	5.4
Anti-M	2	5.4
Anti-Lea	1	2.7
Anti-Fya	1	1.4
Anti-Fyb	1	1.4
Anti-Dia	1	1.4
Anti-P1	1	1.4
Anti-Lua	1	1.4

We identified a high number of patients with clinically significant alloantibodies (23%). 75% of the antibodies were directed against Rh system antigens with 31 (41.9%) directed against E antigen. Despite the heterogeneity of our population we have a low incidence of anti-K (4%), usually found in African-American patients. This finding represents a special challenge in providing safe blood during transplantation showing that screening for the presence of RBC alloantibodies is an important part of pre-transplant evaluation.

P-950 MODIFIED PIGGYBACK TECHNIQUE OF LIVER TRANSPLANTATION IN CHILDREN

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Purpose: In the modified piggyback technique (MPBLTx) introduced by Belghiti a side-to-side cavocaval anastomosis not only preserves partial caval flow but also decreases the risk of outflow disturbance. Our aim is to report the experience of this technique in children at our department.
Method: From 2003 till now a total number of 9 children underwent MPBLTx. The evaluated parameters were: demographic data, indications of LTx, cold ischemia time, type of preservation solution, duration of operation, and blood loss. Furthermore, postoperative complications, graft and patient survival were analyzed.
Results: There were 2 girls and 7 boys with median age of 10yr (range 3-15). LTx indications were: cirrhosis due to chemotherapy (n=1) and extrahepatic biliary atresia (n=1), biliary cirrhosis (n=1), Wilson (n=1) and Byler disease (n=1), chronic liver failure following LTx (n=1), acute liver failure (n=1), mucovisidosis (n=1), and citrullinemia (n=1). The Child score was: Child-A (n=2), Child-B (n=4) and Child-C (n=3). Seven liver grafts were preserved in histidine-tryptophan-ketoglutarate and two in UW solution. The median blood loss, duration of operation and cold ischemia time were 600cc (range 200-5000), 5hrs (range 4-10) and 9hrs (range 6-14), respectively. There was one case of reLTx after complicated piggyback LTx. Two stenoses of bile duct anastomosis occurred which were managed conservatively in one case and with a bilio-digestive anastomosis in the other one. Except one child with no follow-up after one year, the rest showed 100% graft and patient survival.
Conclusion: We could show MPBLTx is feasible and beneficial in children with a promising rate of complication and graft survival. However the risk of caval stenosis after several years as a result of visceral growth is an important factor. Although we have not encountered this complication so far, longer follow-ups are warranted. Finally, this procedure should be performed in high case load centers and by experienced transplant surgeons.

P-951 BILIARY RECONSTRUCTION USING A SIDE TO SIDE CHOLEDOCHO-CHOLEDOCHOSTOMY WITH OR WITHOUT T-TUBE IN DECEASED DONOR LIVER TRANSPLANTATION – A RANDOMIZED TRIAL

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Objective: The biliary anastomosis is still one of the major causes for morbidity after liver transplantation. The optimal method of reconstruction remains controversial. The aim of the study was to assess biliary complications after liver transplantation with or without a temporary t-tube.
Background: Several reports have suggested that biliary reconstruction without t-tube is a safer method with a lower rate of biliary complication.
Methods: 194 recipients of deceased donor liver grafts were randomized. In group 1 the biliary reconstruction was performed by side to side choledocho-choledochostomy with (n=99) and in group 2 (n=95) without a t-tube. The t-tube was removed after 6 weeks. Statistical analysis included Fisher's exact and Chi-square test.
Results: The overall biliary complication rate was increased in group 2. Biliary leaks occurred in 5 patients in group 1 and in 9 patients in group 2 (5.05% vs. 9.47%; P=0.2756 ns). Anastomotic strictures of the bile duct were seen in 7 patients of group 1 and in 8 patients of group 2 (7.07% vs. 8.42%; P=0.7923 ns). Papillary stenosis occurred in 3 patients with t-tube insertion and 3 patients without t-tube insertion (3.03% vs. 3.16%; P=0.9591 ns). 2 of the patients in group 1 and 2 patients in group 2 developed an ischemic type biliary lesion (3.03% vs. 2.11%; P=0.9668 ns). No complications after removal of the t-tube were observed.
Conclusion: An increased rate of biliary complications in the group without t-tube insertion was observed, however not reaching statistical significance. In summary our results indicate that the usage of t-tubes is safe and an excellent tool for the quality control of biliary anastomoses.

P-952 CAUSES OF DISCOUNTINUATION OF RAPAMYCIN-BASED IMMUNOSUPPRESSION IN LIVER TRANSPLANTATION: A RETROSPECTIVE SINGLE CENTER ANALYSIS

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Background: Rapamycin is a potent new immunosuppressant with a mechanism of action that is distinct from that of calcineurin inhibitors, but few clinical data on rapamycin in liver transplantation are available. Hence it is necessary to evaluate the efficacy and side-effects of rapamycin-based immunosuppression in liver transplant patients.
Patients and methods: We retrospectively analysed 60 liver transplantation patients who took rapamycin as an immunosuppressant. This series consisted of 21 patients with alcohol related cirrhosis, 16 patients with hepatocellular carcinoma (HCC), 13 patients with HCV related cirrhosis, 3 patients with fulminate hepatic failure, 3 patients with HBV related cirrhosis and 4 patients with others pathologies. All patients received rapamycin-based immunosuppression.
Results: In the 16 patients with HCC, the one-year survival rate was 87% without any tumor recurrence. The acute rejection in 7 patients was relieved in 1-2 weeks after the administration of rapamycin. All the 11 patients who received rapamycin monotherapy survived for at least 12 months and liver function tests and biopsy showed nothing abnormal. Jaundice in 10 patients with chronic rejection was reduced sharply after use of rapamycin.
Conclusions: Rapamycin given alone or in conjunction with calcineurin inhibitors appears to be an effective primary immunosuppressant regimen for liver transplantation patients. Further studies are warranted to evaluate the efficacy and side-effect profile of rapamycin in liver transplant patients.

P-953 TWO RARE CASES OF GASTROINTESTINAL COMPLICATIONS ASSOCIATED WITH PERFORATION AFTER ADULT LIVING DONOR LIVER TRANSPLANTATION

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We report two cases with rare gastrointestinal complications associated with perforation after adult living donor liver transplantation, with a review of the literature. Both cases were women in their 50s who underwent living donor transplantation due to primary biliary cirrhosis. During the postoperative period, Case 1 developed chronic cellular rejection, which we treated with four immunosuppressants: tacrolimus, prednisolone, mycophenolate mofetil, and sirolimus. About 1 year postoperatively, she suddenly developed nausea and vomiting. An abdominal x-ray showed free air and emphysematous change in the bowel wall and mesentery. Abdominal CT showed the same changes, but no portal venous gas. Gastrointestinal perforation was suspected, but there were no physical findings suggesting acute peritonitis. The blood examination was essentially normal, except for a slightly increased C-reactive protein. We diagnosed her with pneumatosis cystoides intestinalis (PCI) and initiated conservative therapy consisting of fasting and hyperbaric oxygenation. Her problems resolved without aggravation of her symptoms. Case 2 suddenly developed a high fever and septic shock twenty-five days postoperatively. We diagnosed an intestinal perforation based on the drainage and amylase titer, and performed emergency surgery. The small intestine was perforated about 90 cm from the ligament of Treitz. No other abnormal obvious findings were seen. We performed a loop jejunostomy using the perforation site. However, the gastrointestinal tract perforated again on postoperative day 43 and she died on postoperative day 52. At autopsy, multiple jejunal diverticula were seen in the intestine in the region between 10 and 90 cm from the ligament of Treitz, and one of them had perforated. In summary, with the diagnosis of gastrointestinal perforation, it is necessary to consider the possibility of PCI and small bowel diverticulosis, and during treatment, to consider the possibility of multifocal, heterochronous perforation.

P-954 HEPATOCELLULAR CARCINOMA RECURRENCE AFTER LIVER TRANSPLANTATION IN PATIENTS ACROSS MILAN/UCSF CRITERIA

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Background and aims: Liver transplantation (LT) represents a cornerstone in the management of early-stage hepatocellular carcinoma (HCC).Expansion beyond the Milan criteria (UCSF criteria:1 lesion <or= 6.5 cm,2-3 lesions each <or= 4.5 cm with total tumor diameter<or= 8 cm) for liver transplantation remains controversial. The aim of this study was to investigate whether expanded criteria could be used to select patients with HCC for LT.
Methods: Between 1997-2007,196 patients with HCC fulfilling expanded criteria were included as candidates for LT. Survival and recurrence rates were compared (Milan vs UCSF) according to tumor staging.
Results: Pre-operatively,68 out of 196 (34.6%) patients exceeded Milan criteria. The two groups were comparable for:age,gender,aetiology, Child-Pugh and MELD score, type of graft,era of transplantation, immunosuppression regimen and co-morbidities.One-3-and 5-year survival rates of the transplanted

HCC patients within Milan criteria vs exceeding them but within UCSF criteria were 90 vs 88%, 85 vs 81%, and 77 vs 74%, respectively. Pathological staging showed:106 patients within Milan criteria, 28 patients exceeding them but within UCSF criteria, 34 patients exceeding UCSF criteria and 28 false positive patients.Tumor recurrence rates at 5-year were 5/106 (5%), 6/28 (21%), and 17/36 (47%) in each of these groups.The tumor recurrence difference rate between Milan vs UCSF criteria reached a statistical difference (p=0.003).The recurrence was treated with a multimodal approach in all patients.
Conclusion: In conclusion, following UCSF criteria could increase the number of HCC patients who could benefit from LT, without worsening the survival rates at 5-year of follow-up. However, in our series the disease-free survival rate statistically differ between the two groups (Milan vs UCSF). Because of the limits of this retrospective series, these data need a final validation.

P-955 LIVER TRANSPLANTATION ACROSS THE UCSF CRITERIA: A RETROSPECTIVE ANALYSIS BASED ON MACRO- AND MICRO-VASCULAR INVASION

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Introduction: Many papers discussed the outcome in patients across the Milan criteria-(MC).Others, have been proposed to expand those (ex.UCSF-criteria).Therefore, many patients are transplanted within the MC or UCSF preoperatively criteria but at the definitive histhology were excceeding both criteria.Here, we report our retrospective experience of liver transplantation (LT) in recipients exceeding the UCSF-criteria.In particular, we reported the macro/micro-vascular invasion of this cohoort of patients.
Methods: From 1997 to 2007 we performed 221 LT on 196 recipients for hepatocellular carcinoma (HCC).Of these, preoperatively 128 were into the MC, 58 into the UCSF-criteria and 10 exceeding.At the definitive histology of the native liver we had:106 patients into the MC, 28 into the UCSF-criteria, 34 across UCFS-criteria and 28 false positive.In 34 exceeding patients we analyzed outcome, recurrence rate, specificity/sensibility of the preoperative assessment and vascular invasion.
Results: The survival rate after LT at 1,3,5 yrs within histological MC was 90%, 85% and 77%, within UCSF-criteria was 88%, 81% and 74% and in patients across UCFS was 66%, 59% and 39%,respectively.Recurrence rates at 5-year were 5/106 (5%), 6/28 (21%), and 17/34 (50%) in each of these groups.The sensibility of the preoperative assessment was 85%.Overall angioinvasion was 20.4% (40 patients).The patients transplanted across the UCSF-criteria 22/34 had vascular invasion (64.7%) in particulary,17 (77.2%) had macrovascular-invasion and 5 (22.8%) had microvascular-invasion.11/17 (64.7%) died for recurrence, 4/17 (23.5%) are alive without recurrence, 2/17 (11.7%) died for others causes.Of the 4 patients with microvascular invasion 1 (25%) died for cancer recurrence,2 are alive and 1 died for GVHD.
Discussion: The survival and the HCC recurrence rate are inversly proportional with the tumor extension.However a difference in survival and the recurrence rate between patients with macro or microvascular invasion suggests that angioinvasion may be a preoperative prognostic factor in patients with larger HCC.

P-956 ADULT SPLIT LIVER TRANSPLANTATION WITH eRLG FROM EXTENDED CRITERIA DONORS UNDER MELD PATIENT ALLOCATION

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Split liver transplantation (SLT) is an efficient tool to increase the number of available grafts. Children are benefiting most from SLT while among some adult liver transplanters remain concerns that by splitting a liver, a good quality graft is turned into a marginal one. We performed a single center retrospective review to adress this issue.
Methods: Between July 2001 and August 2008, 22 liver transplants using eRLG were performed in 21 adult patients. From 2007 on, we adopted a rapid technique minimizing warming of the graft during the ex-situ splitting.
Results: Eleven ECD were used (50%), 4 (20%) presented 2 or more criteria. In addition 4 standard criteria donors (20%) presented hemodynamic instability during harvesting. Eighteen (82%) splitting procedures were carried ex-situ. Mean cold ischemia time was of 9h 40'$\pm$2h. Four transplants (20%) were performed in high urgency patients. Median waiting list time was 130 days, range (1-628). Median MELD was 15, range (7-40). Median ICU time was 4 days, range (1-60), while the median in-hospital stay was 28 days, range (8-269). Median follow-up was 16 months, range (4-92). One PNF (4.5%) was observed, 4 patients (18%) presented vascular complications and 2 (9%) presented biliary strictures. No graft was lost due to vascular or biliary complications neither related to high urgency transplantation. No early mortality ($\leq$3 months) was observed. Three-year patient and graft survival rates were 84% and 79% respectively. SLT after 2007 (50% of patients), yielded a 100% patient and graft survival. No significant differences were found between the studied parameters from donors or recipients prior or after 2007.
Conclusions: After a certain learnig curve and provided careful selection, exceptions to classical donor criteria for splitting can be accepted with success.

P-957 PORTAL VEIN CLAMPING TIME, BACTERIAL TRANSLOCATION AND MELD SCORE IN LIVER TRANSPLANTATION: A PROSPECTIVE STUDY

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Introduction: The cirrhosis and the portal hypertension are associated with a high incidence of bacterial translocation (BT). BT could cause severe episodes of sepsis especially in patients underwent to LT. A prolonged portal clamping during LT may increase the BT. We report our prospective study comparing the portal vein clamping duration with the BT rate.
Methods: In 48 consecutive randomized patients submitted to50 LT,performed in a period of one year,we performed a portal vein blood sampling for culture at the end of the vascular clamping.We conseder two groups apiece the develop of post-operative complication and we evaluated the correlation behind the complication rate and the patient's perioperatives variables (Child score, MELD score, age, portal clamping time, cold ischemy time and the portal vein sampling).
Results: All the LT were made on piggy back procedure.No shunts portocaval were perfomed.The overall mortality was 4% and overall morbility was 27%.MELD and Child score, age, intervenctional and clamping time were not statistically different behind the two groups considerated.We not found any correlation between the duration of the portal clamping time and the blood colture positivity.Considering the two group of patients, in the group B (complicated pts) the rate of positive portal vein sampling was 70% instead of group A (uncomplicated pts) in witch the portal vein sampling resulted positive for gram + and gram – bacteria just in 11% of cases.
Conclusion: We observe a higer incidence of complications in the group of patients with a portal vein samplig positive even if the colture in the late post-operative time was negative.Our short series suggest that the portal vein sampling should be considerated at least a predictive factors of advese post-operative course considering the loose of correlation behind the post-operative hemoculture and the complication rate.

P-958 TWO RARE RECURRENCES OF HEPATOCELLULAR CARCINOMA WITHIN THE MILAN CRITERIA AFTER LIVING DONOR LIVER TRANSPLANTATION

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The reported recurrence rate of hepatocellular carcinoma (HCC) within the Milan criteria after liver transplantation is very low. We experienced two rare recurrences of HCC within the Milan criteria. We report these cases with a consideration of the literature. Case 1 was a 47-year-old man who had three HCCs each about 2.5 cm in diameter. The postoperative pathological diagnosis was one moderately differentiated HCC and a multicentric outbreak of suspected multiple well-differentiated HCC 3-4 mm in diameter. It recurred as a stalked polyp in the hypopharynx 22 months postoperatively. A polypectomy was performed, but two years after that procedure, it metastasized to the cervical lymph nodes. A cervical lymph node resection was performed, and he was alive without further recurrence 5 months postoperatively. Case 2 was a 61-year-old woman with one 4.0-cm-diameter HCC. All tumor markers were negative, including CEA, CA19-9, PIVKA-2, and AFP. The HCC was hypovascular on dynamic computed tomography (CT) and positive on fluorodeoxyglucose-positron emission tomography/CT (FDG-PET/CT; SUV 5.66). The postoperative pathological diagnosis was undifferentiated HCC accompanied by sarcomatoid alteration. It recurred in the retroperitoneum, mesenteric lymph nodes, and lumbar spine in the early postoperative period. When following patients, we have to consider metastases not only in the graft, lung, bone, and adrenal glands but also in the head and cervical region via the portal-vertebral venous system. Some transplantation centers have reported that, in addition to tumor size and number, tumor differentiation and pathological vascular invasion may

contribute to recurrence. But these predictive factors are not clear preoperatively. If atypical HCC is recognized, based on hypovascularity, strongly positive FDG uptake, and negative for tumor markers, it may be necessary to exclude transplantation, despite meeting the Milan criteria.

P-959 PREDICTIVE FACTORS FOR MORTALITY OF HIV/HCV INFECTED PATIENTS ON THE WAITING LIST OF LIVER TRANSPLANTATION

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Liver transplantation (LT) is the only therapeutic approach in HIV/HCV infected patients with end stage liver disease. However specific prognostic criteria defining the optimal time for LT are lacking for this subgroup of patients. The aim of this study was to identify predictive factors of death in a cohort of HIV/HCV co-infected patients on the waiting list in a single centre.

Patients and methods: 78 HIV/HCV co-infected patients (64 males, 14 females, mean age 42.8±5 yrs) with an indication of LT were retrospectively studied from March 1999 to December 2007. Child-Pugh, MELD, MELD-NA and ASA scores were analyzed. The different prognostic variables were studied by univariate and multivariate analysis according to a logistic regression model.

Results: 16 patients (20.5%) died, 52 patients (66.7%) have been transplanted and 10 patients (12.8%) were alive during the studying time. At the time of inscription, by univariate analysis, a significative difference concerning MELD and MELD-Na scores between the deceased patients group and the transplanted patients group was observed with mean values of 22.3, 25.7 and 18.8, 21.6, p=0.04, respectively. By multivariate analysis, presence of antiretroviral therapy at the time of the first referral (p=0.04), ASA (p=0.04) and Child-Pugh (p=0.02) scores at the time of inscription were significantly associated with mortality.

Conclusions: Child-Pugh rather than MELD score should be used to predict mortality in HIV/HCV co-infected patients. Global scores as ASA score could be applied in this subgroup of patients.

P-960 DUCTOPLASTY USE IN LDLT: A COMPARISON BETWEEN TWO DIFFERENT INSTITUTIONAL EXPERIENCES

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Background: Biliary complications (BC) in adult-to-adult living donor liver transplantation (LDLT) are a major cause of morbidity affecting early and long-term outcomes. We reviewed retrospectively the incidence, risk factors and overall morbidity of 115 consecutive LDLT comparing two different surgical approaches.

Materials and methods: Data from 115 consecutive LDLT from Ghent (77) and Milan (38), performed from September 1999 to November 2007, were evaluated. Recipient's M/F ratio was 71/44, median age was of 52 y (range 19-67). Pre and perioperative differences were: Cholangio-CT for donor evaluation, intraoperative cholangiography (IOC), bile-duct cutting after parenchyma transection and HTK perfusion (Ghent); Cholangio-MRCP for donor evaluation, no IOC, bile-duct cutting before parenchyma transection and Celsior perfusion (Milan). Ductoplasty for joining 2 single apart ducts in one anastomosis were identically performed. Duct-to-duct anastomosis was done when possible and external biliary drainage routinely applied.

Results: Median FU was of 46 m (range 12-106 m). Ductoplasty was performed in 21% of patients. A total of 38/115 (33%) patients experienced early (leaks) and 26/115 (22%) late (stenosis) BC (p=ns between centers). Ductoplasty was significantly associated with early and late BC ($p<0.05$ for both centers). Ductoplasty was a significant risk factor for early BC at multivariate analysis. Ductoplasty and small ducts (<4mm) were significantly associated to late BC at the univariate analysis and the multivariate analysis confirmed ductoplasty as independent risk factor. According to this experience 5/115 (4,3%) grafts were lost due to BC. Overall graft survival was of 70% and 64% at 5-y respectively in patients with and w/o BC (p=ns).

Conclusions: BC represents a significant source of morbidity potentially leading to graft loss in LDLT. BC originating from ductoplasty were not related to the perioperative surgical approach and its avoidance may significantly lower the morbidity.

P-961 RISK FACTORS OF LIVER TRANSPLANTATION AND DONOR TO RECIPIENT MATCHING: IMPACT ON OUTCOMES IN THE EUROPEAN LIVER TRANSPLANT REGISTRY (ELTR)

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Liver transplantation (LT) is increasingly used as result from improved patient survival (71% at 5 years). Introduction of strict selection criteria and identification of prognostic factors have been key issues.

Aim: The aim of our study was to identify and evaluate the survival impact of combined donor and recipient factors.

Material & methods: Data from ELTR of 46,529 first transplants in adult recipient (year 1995-2007) were studied. All the variables of the recipient, donor, surgery and era of transplantation were assessed. Date of graft failure was the date of either re-transplantation or death. Survival was computed using Kaplan-Meier method and all variables were evaluated by univariate and multivariate analysis (Cox model). Finally, we assessed the donor-recipient matching that gives the best results.

Results: The analysis revealed 15 statistically independent risk factors of graft failure: incompatible group matching; reduced LT; heterotopic LT; HCV; Cancer; donor age $\geq$ 65 years; acute hepatitis; split liver; urgency; recipient age $\geq$ 65 years; LT before 2000; ischemia time $>$ 12 hours; compatible group matching vs isogroup; use of other than UW preservation liquid and female donor to male recipient (all factors $p<0.001$).

Combination of donor-recipient risk factors revealed: (1) best results when both donor and recipient are less than 65 years old; (2) worse results in female donor to male recipient; (3) highest impact of donor age in recipients with HCV; (4) worse results when reduced or split liver are used in urgent situation; (5) no higher impact of ischemia time on elderly livers ($\geq$ 65 years) compared to younger ones.

Conclusion: Advances in LT have improved graft survival. Combination of donor to recipient characteristics is critical to minimize the risk of LT and optimize recipient outcome.

P-962 DE NOVO DIABETES MELLITUS FOLLOWING LIVER TRANSPLANTATION. THE HUNGARIAN EXPERIENCE

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The incidence of de novo diabetes mellitus following liver transplantation (also called posttransplantational diabetes mellitus-PTDM) is approximately 15%. It's known risk factors are: the amount of postoperative steroid, and tacrolimus; age of the recipient, hepatitis C virus (HCV) infection, preoperative impaired fast glucose (IFG), and obesity. In case of the impact of PTDM the cumulative patient survival is significantly worse. The aim of this study was to evaluate the incidence and main risk factors of PTDM in the Hungarian practice. In our retrospective study we examined 277 liver transplanted patients' datas, from 1995 to 2008 in the Transplantational and Surgical Clinic, Semmelweis University. We also made two subgroups in the PTDM group: transient (T-DM) and persistent (P-DM) group. The incidence of transient de novo diabates was 10%, the persistent was 16%. The 1, 3, and 5 year cumulative patient survival was significantly worse of the transient de novo diabetes group compared the control group (71%, 71%, 65% vs. 90%, 86%, 83%, p=0,024). The main risk factors for T-DM are: operation time (p=0,037), and warm ischemic time (p=0,05). In the T-DM group the co- morbidities following liver transplantation were significantly higher (vascular complication, infection, biliary complications, p=0,003;0,005;0,007, respectively). The cumulative patient survival of

the P-DM group was not different significantly from the control group. Main risk factors for P-DM are: donor age (p=0,088), BMI (p=0,013), genus (p=0,042); recipient age and BMI (p<0,001); HCV as indication (p<0,001). We did not found statistical difference between the time and type of recurrency and de novo diabetes.
Conclusion: De novo diabetes is a common complication following liver transplantation. HCV is the most common risk factor for developing PTDM. There is no difference between the examined groups in the time and type of HCV recurrency.

P-963 QUALITY CONTROL OF THE EUROPEAN LIVER TRANSPLANT REGISTRY (ELTR) REPORT OF THE LIVING DONOR LIVER TRANSPLANTATION AUDIT

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Low data reliability in registries can bias the statistical analysis in unpredictable ways, causing both underestimation and overestimation of effects.
Aim: To determine if clinical data derived from the ELTR are reliable when compared to hospital charts, and to compare Living Donor Liver Transplantation (LDLT) data to Cadaveric Liver Transplantation (CLT).
Material and methods: The ELTR coordinating committee appointed an independent team of five auditors to check the reliability of data contained in ELTR. Centers to be visited and 10% of each center's files were selected at random. The rates of completeness and consistencies of LDLT files were compared to the cadaveric donors (CLT) files, for 25 variables common to the two procedures. We evaluated also the quality of variables specific to LDLT (Relationship donor to recipient, early complications, min PT or max INR, max serum bilirubin, cause of reoperation, outcome and outcome date, and cause of death).
Results: 905 LDLT files from 44 centers were audited between May 2002 and December 2007. The rate of LDLT completeness was 95.4%, and the rate of consistency between the files and ELTR was 96.7%. These rates were not different from those of CLT overall (95% and 97.8%, respectively). When considering LDLT specific variables, the rate of missing data was 33% for the outcome of donors and 31% for post donation min PT or max INR. Moreover, the rate of inconsistencies was 22% for max serum bilirubin and 21% for min PT or max INR.
Conclusion: The results of audit visits indicate that ELTR data are reliable for both LDLT and CLT. However, some LDLT specific items should be targeted for improvement. Mostly, the outcome of unrelated living donors and the peak of laboratory values.

P-964 IMMUNOHISTOCHEMICAL STAINING OF LIVER GRAFTS WITH A MONOCLONAL ANTIBODY AGAINST HCV-ENVELOPE 2 FOR RECURRENT HEPATITIS C AFTER LIVING DONOR LIVER TRANSPLANTATION

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Aim: We evaluated the expression of hepatitis C virus (HCV) antigen on liver grafts by immunohistochemical staining (IHS) using IG222 monoclonal antibody (mAb) against HCV-envelope 2 (E2).
Methods: The study material was 84 liver biopsy specimens obtained from 28 patients who underwent living donor liver transplantation (LDLT) for HCV infection. The biopsy samples were examined histopathologically, and by IHS using IG222 mAb against HCV-E2. Serum HCV-RNA level was measured in all patients. The IHS grades were compared among the three groups classified according to the time elapsed from LDLT (at 1-30, 31-179 and ≥180 days post-LDLT) and among four post-transplant conditions, including acute cellular rejection (ACR).
Results: Immunoreactivity to IG222 was detected in 78.6% of the specimens obtained during the first month after LDLT, and there were no significant differences on the IHS grades between the three groups classified according to the time elapsed from LDLT. The IHS grades were significantly stronger in definite recurrent HCV (n=12) and probable recurrent HCV (n=7) than in definite ACR (n=7) and other complications (n=8). There were no significant differences in serum HCV-RNA levels among the four post-transplant conditions. There was no significant correlation between the IHS grades using IG222 mAb and serum HCV-RNA levels when data of 84 liver biopsy specimens were analyzed.
Conclusions: The strong HCV-E2 expression on liver grafts were associated with recurrent hepatitis C after LDLT, but the serum HCV-RNA levels were not.

Pancreas

P-965 PERITONEAL DIALYSIS VS. HEMODIALYSIS IN THE INCIDENCE OF INTRA-ABDOMINAL INFECTIOUS COMPLICATIONS IN PATIENTS WITH SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANT

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The concept, that the peritoneal dialysis is a risk factor for the intra-abdominal infections after a simultaneous pancreas-kidney transplant, is controversy.
Patients and method: We studied the incidence of intra-abdominal infections and the graft survival in 98 patients undergone to SPK transplant among 1996 and 2008. All the patients received dialysis before the transplant, the means of duration of peritoneal dialysis (PD, n=23) and hemodialysis (HD, n= 75) were 25±35 months and 17±10 months respectively.
Results: 98 patients were studied. The age, time of ischemic, time of dialysis, time of diabetes and the type of exocrine drainage were similar between two groups. The intra-abdominal infectious complications developed were 23 (30%) in HD group and 6 (26%) in PD group (p= 0'41). In the HD group the 62% of complications were grades 3 and 4, which needed surgery, and only a 32% in the patients with PD were grades 3 and 4. The one year pancreatic graft survival was 88% in HD and 94% in PD group (p= 0'67) with a mean of follow up of 55±38 months. Also, there are not differences in acute rejection episodes, renal graft survival, and the length of hospital stay.
Conclusions: In our experience the PD before the SPK transplant don't increase the intra-abdominal infectious complications.

P-966 KIDNEY AND/OR PANCREAS RETRANSPLANT IN DIABETIC-UREMIC PATIENTS WHO PREVIOUSLY UNDERWENT SIMULTANEOUS KIDNEY AND PANCREAS TRANSPLANTATION

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Purpose: We present complications and long-term results in a group of patients (pts) with pancreas-kidney-transplant (PKT) who lost their grafts and were retransplanted.
Methods/Materials: Sixteen pts (9 male/7 female; mean age 35.8 years) with PKT lost one or both grafts. Causes of graft loss were chronic rejection in 8 (5 kidneys and 3 pancreas) and surgical complications in 8 (2 PKT and 6 pancreas). They were part of 80 PKT performed until 12-2008 (53 male/27 female; mean age 48,8 years; mean diabetes duration 24,2 years; mean dyalisis time 1,7 years).
Two pts received a pancreas-kidney-retransplant (re-PKT), 9 pts a pancreas-retransplant (re-PT) and 5 pts a kidney-retransplant (re-KT). The waiting time for re-KT was 19-270 days and for re-PKT 270-360 days. In the re-PT group, 3 were early (within 11 days) and 6 were late (180-330 days). The early re-PT group didn't have re-induction therapy.
Results: In the re-PKT group, 1 pt suddenly died for recurrent venous thrombosis and pulmonary embolism and 1 has functioning grafts (follow-up 72 months). All 5 pts who received a re-KT have a functioning kidney (mean follow-up 70 months). Of 9 pts who underwent re-PT, 6 have a functioning pancreatic-graft (mean follow-up 89,3 months) while 3 with early re-PT lost their graft for chronic rejection.
Conclusions: Pts who receive PKT can experience failure of one or both grafts for surgical and/or immunological complications. Since these pts need once again insulin and/or dyalisis and are exposed to progression of secondary complications, retransplant should be proposed. In our experience results are comparable to those at first PKT. However, good patient stabilization and re-induction therapy seem to play a major role in long term patient and graft survival.

P-967 MODIFIED RELEASE TACROLIMUS IN DE NOVO IMMUNOSUPPRESSION AFTER SIMULTANEOUS PANCREAS KIDNEY TRANSPLANTATION – A FIRST SINGLE-CENTER EXPERIENCE

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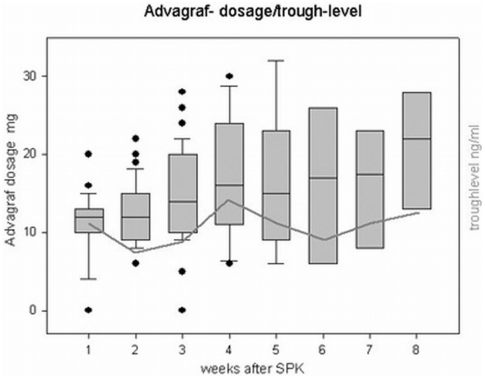
Purpose: Modified release tacrolimus is a new once-daily oral formulation of

the established immunosuppressive agent tacrolimus. Little is known about de novo immunosuppression after simultaneous pancreas transplantation using modified release tacrolimus.
Methods: To test the feasibility of modified release tacrolimus in simultaneous pancreas-kidney transplantation (SPK), we conducted a prospective study of 20 consecutive transplants using modified release tacrolimus (Advagraf©, MMF and low-dose corticosteroids as the initial immunosuppressive regimen. Patient and graft survival, the rates of acute rejection, graft function as well as ADV dosages and trough-levels (Cmin) were investigated after a mean follow-up time of 13.0±3.1 months.
Results: Overall patient, kidney- and pancreas graft survival were 100%, 100% and 90%. Two pancreas grafts were lost due to vascular graft thrombosis. The incidence of rejection episodes at 12 months was 38%. ADV was well tolerated in the majority of patients. Only in one case tacrolimus (ADV) was stopped because of psychotic symptoms. In week 2 and 3 post-transplant a significant adjustment in the ADV-dosage was necessary to achieve sufficient tacrolimus trough levels.



Conclusions: The results of this case series report demonstrate that patients after SPK can be safely treated with modified release tacrolimus. Further studies are needed to investigate pharmacokinetic profiles of modified release tacrolimus after SPK.

P-968 EVALUATION OF CORONARY MICROVASCULAR FUNCTION BY CORONARY FLOW RESERVE (CFR) MEASUREMENT IN SIMULTANEOUS PANCREAS AND KIDNEY TRANSPLANTATION (SPK) ALLOGRAFT RECIPIENTS

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Purpose: In SPK recipients, 50% of deaths are due to cardiovascular diseases. We sought to evaluate coronary flow reserve (CFR) by transthoracic Doppler echocardiography, as an index of coronary microvascular function, in SPK recipients.
Methods: 23 SPK recipients (11 male, aged 42±8 years) without clinical evidence of ischemic heart disease, and 26 controls matched for age and sex were studied. Coronary flow velocity in the left anterior descending coronary artery was detected by transthoracic Doppler echocardiography at rest and during adenosine infusion. CFR was obtained as the ratio of hyperaemic diastolic flow velocity (DFV) to resting DFV. A CFR ≤2.5 was considered abnormal. Time from transplantation was 42±32 months.
Results: Compared with controls, no differences were found regarding prevalence of coronary risk factors other than hypertension (80% vs 4%, $p<0.0001$). In SPK recipients CFR was lower than in controls (2.58±0.7 vs 3.55±0.8, $p<0.0001$). CFR was abnormal in 12 (52%) recipients compared with controls (1%) ($p<0.0001$). In these patients compared with the remaining population CFR was lower (1.98±0.2 vs 3.23±0.6, $p<0.0001$), total cholesterol and LDL levels were higher (206±65 vs 147±28 mg/dl, p=0.02 and 132±57 vs 70±16 mg/dl, p=0.01 respectively).
Conclusions: CFR is impaired in SPK recipients demonstrating the presence of coronary microvascular dysfunction. Determination of CFR in the follow up of SPK recipients could be a useful tool in the evaluation of the effects of normoglycemia in the progression of microvascular complications.

P-970 LONG TERM OUTCOMES AFTER PANCREAS-KIDNEY (SPK) TRANSPLANT AND INFLUENCE OF GRAFT FAILURE

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Purpose: To analyse the long-term results after SPK and the consequences of graft loss.
Methods/Materials: Retrospective analysis of 164 consecutive SPK transplants (1996-2008) in a single institution.
Results: Patient, pancreas and kidney survival at 1 and 5 years are shown in table 1.

Table 1: One- and five-year patient, pancreas, and kidney survival after SPK

	1 year	5 years
Patient	97%	93%
Pancreas	91%	84%
Kidney	93%	88%

Patients with a failed kidney graft had a 5-year patient survival (censored for death with functioning graft) of (n=8/16) 50% (relative to 97% for patients with a functioning kidney graft, log rank 42, $p<0.001$). Patients with a failed pancreas graft had a 5-year patient survival of (n=14/20) 70% (relative to 96% for patients with a functioning pancreas graft, log rank 14, $p<0.001$). Failure of both organs was a strong predictor of poor outcome (odds ratio 21.0 (95% C.I: 5.9-74.6), $p<0.001$), relative to patients with both grafts functioning.

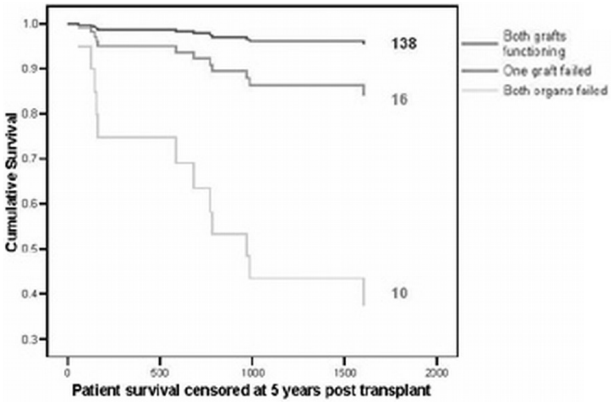

Figure 1. Five-year patient survival: (1) both organs functioning (n=138); (2) one organ failed (n=16); (3) both organs failed (n=10). (Cox proportional hazards model, graft loss censored for patient death.)

When the results of the whole program were analysed, counting patient death as a cause of graft failure:

Table 2: Causes of pancreas and kidney failure

	Pancreas Failure	Kidney Failure
Surgical/technical	39% (11/28)	15% (4/27)
Immunological	32% (9/28)	22% (6/27)
Death of patient with functioning graft	29% (8/28)	33% (9/27)
Chronic allograft nephropathy	–	26% (7/27)
Thrombotic Micro-angiopathy	–	4% (1/27)

28/164 (17%) pancreatic grafts failed and 27/164 (16%) renal grafts failed.
13/28 pancreas grafts failed within the first year (range 1-355, median 55 days) and 15/22 after the first year (range 370-3896, median 796 days).
Of the 12 patients alive with pancreas graft failure, 7 have continuing kidney function for 275-3538 days (median 888).
21/164 (13%) patients lost both organs at a median time of 681 days (range: 1-4453) after SPK (11/21 due to patient death).
Conclusion: Long-term outcomes in SPK transplantation give reason for optimism. Failure of one graft does not preclude function of the other graft for a significant time. Loss of both grafts has a significant influence on further patient survival.

P-971 EXPERIENCE WITH PERCUTANEOUS BIOPSY OF THE PANCREAS GRAFT

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Introduction: Since number of pancreas transplantation (PTx) has increased and its results and graft survival continue to improve, correct diagnosis of rejection with exact grading gains of importance. Pancreas rejection is frequent and early treatment is essential to organ survival. Most pancreas rejections are asymptomatic and specificity of laboratory markers is low, therefore percutaneous pancreas biopsy might be a helpful diagnostic method.
Methods: We analyzed frequency and results of all performed pancreas biopsies in our centre (n=75) in patients having simultaneous pancreas and kidney transplantation (SPK) or pancreas after kidney transplantation (PAK) between the years 2000 and 2007 (n=225). All but 5 biopsies have been performed CT-guided with a 20 Gauge biopsy needle.
Results: Between 2000 and 2007 in a total of n=75 (33.3%) recipients a PTx biopsy has been performed. The median time of the biopsy after transplantation was 69 days (IQR 36-50). Histological examination showed in n=21 (28%) signs of rejection, in n=30 (40%) no signs of rejection. In n=24 (32%) the biopsy sample was not representative. Results had strong influence on the further therapy (e.g. initiation of anti-rejection therapy or reduction of calcineurin-inhibitor dosage (CNI) due to CNI-associated toxicity).
Conclusion: In cases of unclear PTx malfunction PTx biopsy is a useful tool to discriminate between different causes of decreased transplant function (e.g. rejection, CNI-toxicity, pancreatitis) and to administer a specific therapy if necessary. The risk of biopsy associated complications can be reduced to a minimum as described, although risk of non-representative biopsy is given. We conclude that CT-guided pancreas transplant biopsy in cases of impaired PTx function is a safe and easy method and its results have high impact on further treatment regimen.

P-972 A REVIEW OF FACTORS INFLUENCING EARLY POST-TRANSPLANT EVENTS IN A NATIONAL SIMULTANEOUS PANCREAS & KIDNEY TRANSPLANT PROGRAMME

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Aim: To identify factors that influence post-transplant events and outcome after pancreas transplantation and select modifiable factors in order to minimise adverse events.
Methods: 108 pancreas transplants were performed in Scotland between 2000 and 2008 (98 SPK, 7 PAK, and 2 PA). Immunosuppression was tacrolimus, mycophenolate mofetil and prednisolone. After July 2004 patients were also given basiliximab induction therapy (n=62). The outcome measures were pancreas and kidney graft survival. We identified 36 donor and recipient related variables and assessed the correlation between these variables and the outcome.
Findings: Mean recipient age was 40.6y (16-61) and 57% were male. Mean follow-up was for 52 months (1-103 months). Of the 98 SPK recipients, 8 kidneys failed (4 with a failed pancreas) and 19 pancreata failed (4 with a failed kidney). The risk of pancreas graft failure was increased when (1) the recipient waited longer than the mean of 230d (p=0.09), (2) the donor was older than the mean age of 30y (p=0.04), (3) transplantation from a donor who died following an intra-cerebral event (p=0.06). The risk of failure of the kidney or pancreas was increased when there was high HLA mismatching (122 or 222) (p=0.04). There were more out-of-region donor organs transplanted than local organs after Jul 2004 (19.4% v 43.5%, p=0.01) Insulin independence at discharge was 10% higher after introduction of basiliximab despite the donor age increasing by a mean of 5 years and the waiting time increasing by a mean of 39 days.
Conclusion: In pancreas transplantation minimisation of waiting time should be a priority for the allocation process. Donor age and cause of death should be considered as risk factors informing patient selection. Highly HLA mismatched transplants should be carefully monitored with attention to immunosuppression.

P-973 PANCREATA FROM PEDIATRIC DONORS RESTORE INSULIN INDEPENDENCE IN ADULT IDDM RECIPIENTS

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Context: The use of pediatric donors can increase the number of donors available for pancreas transplantation.
Aim: To verify if pancreas transplantation from pediatric donors is effective as transplantation from adult donors to restore metabolic control in type 1 diabetic patients.
Methods: 13 IDDM patients received pancreas transplants from pediatric donors (age between 12 and 17 years). They got pancreas from May 2004 to April 2008, 8 with systemic-venous and 5 with portal-venous graft drainage. Pancreas functionality has been evaluated by measurement of HgbA1 values before transplantation and 1 year after the operation; plasma glucose and insulin values are available from oral glucose tolerance test (OGTT) on 2 patients 4 months after the operation.
Results: Donor mean weight is 59 (range 42 to 75) kg and mean BMI is 20,9 (range 17,9 to 23,4). After 1 year, patients survival rate is 92%, while pancreas graft survival is 57,1%, 40% for portal and 66,7% for systemic drainage. Two patients with portal drainage developed graft thrombosis and one interrupted immunosuppressive therapy because of the onset of Moskowitz syndrome. Two patients with systemic drainage had an acute rejection episode and one developed graft thrombosis. 1 year after the operation mean HgbA1 was 4,9 (range 4,6 to 5,4) %; during OGTT mean basal glucose was 81,9mg/dl and mean basal insulin was 9,1mU/ml, at 120 minutes mean glucose was 88,3mg/dl and mean insulin was 42,4mU/ml.
Conclusion: These preliminary results show that pediatric pancreas transplantation can restore metabolic control in IDDM patients.

P-974 APPLICATION OF THE RAT SEGMENTAL INTESTINE FOR FETAL PANCREAS AND LIVER TRANSPLANTATION

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Application of the rat segmental intestine for fetal pancreas and liver transplantation
Both pancreas and liver transplantation are limited by the shortage of donor organs. One strategy to overcome the donor shortage is to transplant xenogeneic tissues, such as fetal pancreatic and hepatic tissues that have a capacity for expansion post-implantation. It is thought that the small intestine may provide a scaffold for organ regeneration. Here we investigated whether fetal pancreatic and hepatic tissues could be transplanted into the segmental intestine in rats. Fetal pancreas and liver from embryos of the "firefly" luciferase transgenic Lewis rat (MHC haplotype: RT1l), embryonic day 14.5 and 15.5, were transplanted into wild-type Lewis rats. The recipient rats of fetal pancreas transplantation were injected streptozotocin (STZ) to be induced diabetes mellitus. As a scaffold for organ development, rat small intestinal segments were utilized after the removal of mucosa, and fetal pancreases were grafted into the luminal surface through the stoma. Because a luciferase-based assay requires cellular ATP and luciferase-derived photons are well-correlated with cellular viability, the survival of transplanted fetal pancreas and liver was monitored by luciferase-derived photons. And blood glucose levels of recipient rat transplanted fetal pancreas were measured. Transplanted fetal pancreas and liver-derived photons were stably observed for one month, suggesting that transplanted fetal pancreatic and hepatic tissues survived. Moreover, blood supply to transplanted tissue from the intestine was maintained.

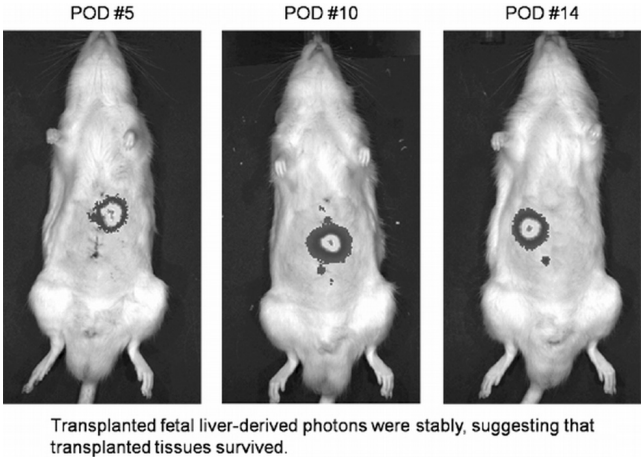

Figure 1. Luminescence from transplanted fetal livers.

We speculated that the segmental intestine could support the development of pancreatic and hepatic tissues and this strategy might have an advantage of being transplantable with blood vessels even if organ developed in the segmental intestine. In addition, this procedure allows the easy surgical removal just in case of cancer development.

P-975 IMPROVED PANCREAS-ALONE TRANSPLANTATION SURVIVAL WITH ORGANS REMOVED FROM TRAUMATIC DONORS

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Context: Pancreas alone transplantation in IDDM patients between 2004 and 2008.
Aim: To verify a difference in survival of pancreata obtained from traumatic and non-traumatic donors.
Methods: Thirty-five IDDM patients received pancreas transplants: 24 pancreas-alone transplantations (PA) and 11 pancreas-after-kidney (PAK). All of them received the whole organ with enteric diversion of exocrine secretion, 9 with portal-venous and 26 with systemic-venous graft drainage. In 2004, immunosuppression therapy was prednisone, mycophenolate mofetil, ATG (Antithymocyte globulin) and cyclosporin A, while in 2005-2008 it was prednisone, mycophenolate mofetil, ATG and tacrolimus.
Results: Donor mean age was 26 years (range 11-46), mean weight was 67 kg (range 42 to 90) and mean BMI was 23 (17.5 to 27.7).
In the group of patients transplanted in 2004, 12 were PA and 2 were PAK transplantations: after one year, pancreas graft survival was 42%. Twelve received pancreata from traumatic-death donors (mean age 24 years, range 15 to 36) while the other 2 from non-traumatic donors (37 and 46 years). The first group has a 1-year graft survival of 50% while the second group of 0%: log rank is 0.169.
From 2005-2008, 12 were PA and 9 were PAK transplantations with a 60,5% graft survival after one year. Fourteen of these 21 patients received pancreata from traumatic-death donors (mean age 22 years, range 12-35) while the other 7 from non-traumatic donors (mean age 33 years, range 11-40). The first group has a 1-year graft survival of 76.6% while the second group of 28.57%: log rank is 0.021.
Conclusion: These results show that pancreata removed from donors dead for trauma allowed an increase of 1-year survival rate.

P-976 HIGH C-PEPTIDE LEVELS IN CANDIDATES TO PANCREAS TRANSPLANTATION

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Background: Pancreas transplants (PTx) are rarely performed in patients with high C-peptide levels.
Material and methods: Between May 1996 and February 2009 288 PTx were performed C-peptide levels were measured before and after PTx in all recipients. Based on a cut-off level 1 ng/ml, patients were classified as having low ($<$1 ng/ml) (Low C-P) or high ($\geq$1 ng/ml) (High C-P) levels. There were 20 High C-P patients and 268 Low C-P patients. Mean BMI, mean duration of diabetes from onset to PTx and mean daily insulin requirements were similar in the two groups. Mean age at onset of diabetes mellitus was 14.1$\pm$0.5 years in Low C-P vs 22.6$\pm$2.6 years in High C-P ($p<0.0001$). Mean age at PTx was 38.7$\pm$0.5 years in Low C-P vs 43.8$\pm$1.2 years in High C-P (p=0.003). There was no difference in either the technique used for PTx or donor characteristics. The same quadruple immunosuppressive regimen was used in both groups.
Results: Delayed grafts function and relaparatomy rate were similar in the two groups. Ten pancreas grafts were lost due to thrombosis (3.7%) in Low C-P as compared with none in High C-P; 18 (6.7%) additional pancreas grafts in Low C-P and 2 (10.0%) in High C-P developed non-occlusive thrombosis (p=NS). There was no significant difference in the incidence of infection and early rejection between the two groups. One-year patient, kidney and pancreas survival rates were: 95%, 90% and 85% and in Low C-P vs. 95%, 100% and 90% in High C-P (P=NS); five-year figures were: 93%, 84% and 77% in Low C-P vs 95%, 92% and 79% in High C-P.
Conclusion: Our experience shows that good PTx results can be achieved in patients with high levels of C-peptide.

P-977 PANCREAS LOSS AFTER SIMULTANEOUS KIDNEY-PANCREAS TRANSPLANTATION: RISK FACTORS AND RENAL IMPACT

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Purpose: Simultaneous Kidney-Pancreas (SKP) transplantation is a complicated surgery with a high rate of pancreas graft loss. Causes are not well understood but presumed to be surgical complications. Immunologic hypothesis is difficult to prove. We herein analyze pancreas loss risk factors in our cohort of transplanted patients.
Methods: We conducted a longitudinal study of all patients transplanted of SKP at our university hospital center. Transplantation details were obtained retrospectively through chart analysis. Patients were also followed-up prospectively and a glomerular filtration rate (GFR) measurement was systematically done by Chrome-EDTA clearance (Cr-EDTA) at 12 months after transplantation.
Results: From January 2004 to December 2008, 51 patients received SKP transplantation. Recipient age was 41 (25-56) years. M/F ratio was 25/26. The majority (71%) of patients were already on hemodialysis. No patient was on peritoneal dialysis. Pancreas cold ischemia time (CIT) was 10.5 (6.7-18) hrs.
Of the 51 transplanted patients, 12 patients (15%) lost the pancreas, all in the first month after the transplantation, mainly from thrombosis (8 cases), but also from hemorrhagic shock (2 cases) and from unknown causes (2 cases). Mean pancreas CIT was similar between the 2 groups (10.5 hrs). Biopsy-proven acute renal rejection was more frequent in pancreas loss group (25% vs. 15%), and serum creatinin values were higher (147$\pm$21 vs. 112$\pm$25 μM) on the last follow-up.
Measured GFR (Cr-EDTA) at one year after transplantation was 65 (45-98) ml/min/1.73 m^2 in the group of patients that lost their pancreas graft vs. 83 (38-92) ml/min/1.73 m^2 in the other group.
Conclusion: The pancreas graft loss after SKP transplantation seems to be associated with more frequent acute rejection episodes and worse long-term kidney graft function.

P-978 THE INFLUENCE OF FUNGAL INFECTIONS ON ALLOGRAFTS FUNCTION IN DIABETIC RECIPIENTS

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The aim of the study was to evaluate the influence of fungal infections on early and late function of allografts as well as process of acute rejection.
Materials and methods: The group of 1301 organ transplant recipients: liver (LTx), kidney (KTx), pancreas + kidney (SPkTx) treated in Hospital-Lindley'a Campus at Warsaw Medical University in 2003-2006 were studied. The group of 213 patients with diabetes mellitus were carefully analyzed and divided into three groups: 1. type 1 diabetes patients with KTx or SPKTx, 2. type 2 diabetes patients with KTx or LTx transplants, 3.posttransplant diabetes recipients.
The following clinical samples were examined: blood, urine, fecal samples, throat, mouth lesions, surgical site swabs, punctuates.
Results: There were 77 patients with acute transplant rejection within the analyzed group of 213 diabetic recipients. In 54 recipients acute rejection was diagnosed on the basis of biopsy and histopathologic examination, and in 23 patients on the basis of clinical symptoms. Fungal infection was confirmed in 29 allograft recipients. Co-existence of acute transplant rejection or clinical worsening of renal function and fungal infection was observed in 17 patients.
Conclusions: 1. Direct influence of fungal infection on acute transplant rejection initiation was not confirmed in the study.
2. In the course of fungal infection clinical symptoms of renal transplant failure were present, but changes typical for acute rejection in histopathologic examination were not observed.
3. Incidence of acute rejection and than introducing adequately immunosuppression in allograft recipients induced fungal systemic infections, which were observed.

P-979 ETIOLOGICAL AGENTS OF BACTEREMIA IN THE EARLY PERIOD AFTER SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANTATION

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Bacteremia is one of the known complications in simultaneous pancreas-kidney transplantation (SPKTX)

Objective: This study aims at evaluation of the frequency of microbial isolates and their susceptibility profiles; cultured from clinical samples obtained from the blood and the tips of blood vessel catheters of 26 simultaneous pancreas-kidney (SPKTX) recipients suspected of bacteremia in the early post-transplant period.

Patients and methods: Data on microbiologic blood culture of 26 adult patients undergoing SPKTX were collected prospectively from 2001 to the end of 2006. The isolation and identification of cultured microorganisms was performed according to standard microbiological procedures and commercially available tests. Susceptibility of the strains to antibacterial agents was made by the Clinical and Laboratory Standards Institute (CLSI) guidelines.

Results: All the patients were followed prospectively for the first four weeks after surgery. From 66 clinical samples in total 23 microbial isolates: from blood samples taken from 17 recipients and the tips of blood vessel catheters from 12 recipients were cultured. The most commonly isolated were: Gram-positive bacteria (73.9%) with domination of staphylococci (64.7%): with presence of MRCNS strains (81.8%). Gram-negative bacteria comprised 17,4% of positive cultures. Yeast-like fungi comprised 8,7% of positive cultures with domination of *Candida glabrata*.

Conclusions: In conclusion in our study predominated Gram(+) bacteria 73,9% of isolates. The increased proportion of MDR bacteria and fungi to antimicrobial agents may be due to the frequent use of these agents for prophylaxis of bacterial infections in patients. MDR strains can caused severe BSI's in patients after SPKTX.

P-980 ETIOLOGICAL AGENTS OF SURGICAL SITE INFECTIONS (SSI) IN THE EARLY POST-TRANSPLANT PERIOD AFTER SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANTATION (SPKTX)

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Objective: This study aims at evaluation of the frequency of microbial isolates and their susceptibility profiles; cultured from clinical samples obtained from "surgical site" of 26 simultaneous pancreas-kidney (SPKTX) recipients suspected of surgical site infections (SSIs) in the early post – transplant period.

Patients and methods: Data on microbiologic culture of 26 adult patients undergoing SPKTX were collected prospectively from 2001 to the end of 2006. The isolation and identification of cultured microorganisms was performed according to standard microbiological procedures and commercially available tests. Susceptibility of the strains to antibacterial agents was made by the Clinical and Laboratory Standards Institute (CLSI) guidelines.

Results: All the patients were followed prospectively for the first four weeks after surgery. In total 168 microbial isolates from clinical samples from "surgical site" taken from 26 recipients were cultured. The most commonly isolated were: Gram-positive bacteria (65.5%) with domination of staphylococci (52.7%): presence of MRSA, MRCNS and enterococci (33.6%) with presence of high level aminoglycoside resistant strains – HLAR (64,9%) and vancomycin resistant strains – VRE (2,7%). Gram-negative bacteria comprised 19% of positive cultures: among them were isolated extended spectrum beta-lactamase producers – ESBL(+) and carbapenem resistant strains. Yeast-like fungi comprised 15,5% of positive cultures. In conclusion in our study predominated Gram(+) bacteria, comprising 65,5% of isolates. The increased proportion of isolation MDR bacteria to antimicrobial agents may be due to the frequent use of these agents for prophylaxis of bacterial infections in patients. MDR strains can caused severe SSI's in patients after SPKTX.

P-981 ETIOLOGICAL AGENTS OF URINARY TRACT INFECTIONS (UTI'S) IN THE EARLY POST-TRANSPLANT PERIOD AFTER SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANTATION

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Objective: Urinary Tract Infection (UTI) is a one of the common infection in simultaneous pancreas-kidney transplantation (SPKTX).

Patients and methods: The study covered 26 adult patients undergoing SPKTX transplantation between September 2001 and December 2006. All the patients were followed prospectively for urinary tract infections from the SPKTX date and during the first four weeks after surgery. Samples of urine were investigated for bacteriological cultures. The microorganisms were cultured and identified in accordance with standard bacteriological procedures. Susceptibility testing was carried out using Clinical and Laboratory Standards Institute (CLSI) procedures.

Results: Urine specimens were examined in 26 recipients (100%) during the first month after transplantation, 77 urine samples were investigated. Among the bacterial strains isolated in early period after SPKTX (n = 30), the most common were Gram-positive bacteria (53.3%) with domination of enterococci (75%) with presence of high level aminoglycoside resistant strains – HLAR (58,3%) and vancomycin resistant strains – VRE (25%). Gram-negative bacteria comprised (46,7%) of positive cultures.

Conclusions: In conclusion in our study predominated entrococci comprising 75% of Gram(+) isolates. The increased proportion of isolation MDR bacteria to antimicrobial agents may be due to the frequent use of these agents for prophylaxis of bacterial infections in patients. MDR strains can caused severe UTI's in patients after SPKTX.

P-982 A NEW SIMPLIFIED TECHNIQUE OF PANCREAS TRANSPLANTATION IN PORCINE MODEL

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Introduction: The incidence of diabetes increased steadily. At present, the only curative option is pancreas transplantation (PTx). Experimental studies are important to evaluate different aspects of PTx. Porcine models are valuable because of their resemblance to human from anatomical and physiological viewpoint. Our aim is to introduce a new simplified technique of PTx in a porcine model.

Materials and method: In landrace donor pigs (n=32), pancreas was mobilized; portal and splenic veins were prepared. The common hepatic and splenic arteries and bile duct were ligated. The proximal part of duodenum at was prepared and stapled. The third portion of the duodenum was also freed up and stapled. After systemic heparinization, pancreas was perfused through abdominal aorta with HTK. Portal and splenic veins were cut for evaluating the perfusion's sufficiency. The superior mesenteric artery and vein were prepared and stapled. Whole pancreato-duodenal graft was procured along with portal vein and 5cm of aortic jump graft. Pancreas was preserved in HTK at 4°C. In recipients, total pancreatectomy was done; IVC and aorta were prepared for vascular anastomosis in an end-to-side manner to aorta and portal vein of graft, respectively. After reperfusion of pancreas the duodenodoudenostomy was performed end to side.

Results: The median cold and warm ischemia time were 10hrs (9-14) and 50min (35-80),respectively. One pig with 80 min warm ischemia had an arterial variation leading to longer operation time. The hemodynamic status of all pigs was stable throughout the operation. The median follow-up period was 7d (4-10). There were no major intra- and postoperative complications.

Conclusion: By using one aortic jump graft there was no need for additional arterial reconstruction resulting in a short back-table and warm ischemia time. End-to-side portocaval and duodenoduodenal anastomses make this model of PTx more feasible, providing a reproducible experimental model.

Pediatric transplantation

P-983 LONG-TERM OUTCOME OF INTENSIVE INITIAL IMMUNOSUPPRESSION PROTOCOL IN PAEDIATRIC DECEASED DONOR RENAL TRANSPLANTATION

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Purpose: To report the long-term outcome of deceased donor kidney transplantation in children with emphasis on the use of an intensive initial immunosuppression protocol using R-ATG as antibody induction.
Materials & methods: Between January 1991 and December 1997, 82 deceased donor kidney transplantations were performed in 75 paediatric recipients.

Table 1. Donor and recipient characteristics

Varable	No.	%
Recipient	75	
Male	43	57
Female	32	43
Number of grafts	82	
Recipient <20 kg	22	27
Recipient >20 kg	60	73
First graft	65	79
Pre-emptive	19	29
Dialysis	46	71
Second graft	14	17
Third graft	3	4

Variable	Mean	Range
Recipient age	12.9 years	3–18 years
Donor age	25.9 years	7–53 years
Follow-up period	12.6 years	0.47–16.47 years
Cold ischemia time	22 hours	11–52 hours
HLA mismatch	2.80, SD 1.13	

All the patients received quadruple immunosuppression with steroid, cyclosporine, azathioprine and antibody induction using rabbit anti-thymocyte globulin (R-ATG-Fresenius®). Cytomegalovirus (CMV) prophylaxis was given to patients that were seropositive for CMV and those that received grafts from CMV seropositive donors. All the patients received antifungal & pneumocystis carinii prophylaxis.
Results: Actual 1, 5 & 10 year patient survival rates were 99%, 97% & 94% respectively; only one patient (1.2%) developed post-transplant lymphoproliferative disorder (PTLD). The causes of death were cardiac (*n*=3), sepsis (*n*=1), complication post bone marrow transplant (*n*=1) and unknown (*n*=1). Actual 1, 5, & 10 year overall graft survival rates were 84%, 71% & 50% respectively and the actual immunological graft survival rates were 91%, 78% & 63% respectively. The causes of graft failure were acute rejection (*n*=12; early-5 & late-7), chronic allograft nephropathy[1] (*n*=10), recurrence of primary disease (*n*=9), graft thrombosis[1] (*n*=5), death with functioning graft[1] (*n*=1) and unknown (*n*=9). [[1]Non-immunological causes of graft loss censored to arrive at the immunological graft survival rate].
Conclusions: The use of an intensive initial immunosuppression protocol with R-ATG as antibody induction is safe and effective in paediatric recipients of deceased donor kidneys with excellent immunological graft survival without an increase in PTLD or other neoplasms over a minimum 10-year follow up. Improvement of results in the future depends on prevention of cardiac related deaths, elimination of technical failure, development of more specific and less nephrotoxic immunosuppression and improving adherence to the regimen.

P-984 POST-OPERATIVE HAEMODYNAMICS FOLLOWING RENAL TRANSPLANTATION ARE NOT COMPROMISED BY LARGE DONORS IN LOW WEIGHT PAEDIATRIC RECIPIENTS

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Objectives: Renal transplantation in low weight children conventionally requires a graft well matched to recipient size. The low rate of organ donation from paediatric donors has prompted interest in the use of adult sized grafts. Such transplants are challenging and potentially complicated by graft hypoperfusion. It is imperative that graft perfusion is maintained using an adequate intravascular volume and perfusion pressure. This study examined the perioperative changes in haemodynamic parameters of recipients of size matched and mismatched renal transplants.
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 systolic blood pressure (SBP) at reperfusion, one hour post perfusion and on day 1; central venous pressure (CVP) at reperfusion and 1 hour post perfusion; and recipient body weight on the first three post-operative days. Secondary outcomes were volumes of infused fluid and the need for ionotropic/vasopressor therapy in the first 48 hours.
Results: Twenty-three recipients weight less than 20kg. 12 patients had 'low' donor:recipient weight ratios and 11 'high' ratios about the median value (4). Table 1 illustrates the comparable haemodynamic parameters in each group.

Comparison of groups based on donor:recipient weight ratio

	Size:weight ratio <4 (n=12)	Size:weight ratio >4 (n=11)	P value
Systolic BP at reperfusion (mmHg)	107±13	110±26	0.93
Systolic BP at one hour (mmHg)	101±11	102±19	0.19
Systolic BP at 24 hours (mmHg)	112±14	111±14	0.35
CVP at reperfusion	13±3	13±3	0.61
CVP 1 hour post reperfusion	12±4	12±2	0.17
Bodyweight day 1 (kg)	17.4±4	16±3.2	0.62
Bodyweight day 2 (kg)	17.5±4	16.7±3.1	0.73
Bodyweight day 3 (kg)	17.7±4	16.7±3.2	0.83

Figures are expressed as mean ± SD.

Conclusion: Low weight paediatric recipients of renal allografts have comparable post-operative cardiovascular parameters irrespective of graft size. Furthermore, the requirements for fluid and vasoactive therapy is equivalent to maintain such parameters.

P-985 FEVER IN PEDIATIC LIVER TRANSPLANT RECIPIENTS: WHAT DO YOU DO?

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Background: The fever symptom in the pediatric population after a liver transplant indicates a variety of things and creates fears and doubts. In our experience, it takes place more frequently in younger children at the time of the transplant and even more within the first year of the transplant. The immunosuppressive therapy has been massively used in this timeframe. Family members of children undergoing a transplant receive education to not underestimate and immediately report to the Center of reference.
Goals of Project Action: The goal of this project was to create a team and nursing protocol for an appropriate approach:
– to quickly identify the etiology and set the right therapy
– to prevent mayor complication;
– to assure a best quality of life for the patient
Interventions: Paediatric patient contacting the Transplant Centre reporting fever for more than 24 hours undergoes a number of blood tests and consults, after a global and thorough nursing assessment at the time of admission. After the general assessment following the indication of the protocol, the child undergoes the other following steps. The process ends with a meeting with the all the team,
Outcomes: We identify criticalities and how to treat them, to guarantee to the patient the best level of care based on the needs of the children. Up until now we have established this approach for 80 children: 16 of them required a hospital admission, while for 4 of them the Day Hospital and outpatient regimen was deemed appropriate. 14 out of 20 had an infection as etiology of the fever symptom and 6 a rejection. Following a pathway in compliance with our protocol, the etiology diagnosis took place within the 72 hours from the onset of symptoms, this guarantees a timely, dedicated and specific therapeutic plan.

P-986 COGNITIVE ABILITIES, QUALITY OF LIFE AND PSYCHOSOCIAL BURDEN IN LIVER-TRANSPLANTED CHILDREN AND THEIR FAMILIES. THE PROJECT LIVE!®

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For children and adolescents there is a risk to develop serious developmental problems and secondary comorbidities before and after transplantation. The project Live!® aims at establishing a comprehensive psychosocial medical care for liver-transplanted children and adolescents as well as their families.
By 2007, 169 families were assessed. Results concerning quality of life (KIDSCREEN-52), cognitive abilities (Wechsler Intelligence Scale for Children, Kaufman-Assessment Battery for Children, and a computer-assissted neuropsychological test system for children), psychopathology (Schedule for Af-

fective Disorders and Schizophrenia for School Aged Children), and burden of the families (Impact on Family Scale) will be presented.
At the time of transplantation, the mean age of the children was 2.1±3 years. On average, they were examined 5.8±3.7 years after transplantation. The major indication was biliary atresia (56%); 40% of the patients received a living donation. Quality of life in children after transplantation is in the normal range. However, 40% of the sample show psychiatric disorders. Cognitive abilities are significantly below average. Accordingly, families with liver-transplanted children report high psychological strain. Achievement in the cognitive tests is negatively correlated with the pre-operative duration of illness. Children who received a living donation perform better in measures of cognitive abilities. Compliance problems were stated by 18% of the parents.
Results indicate that there is an urgent need for psychological support for these families and in addition, there is a strong demand for early developmental screening for children with liver transplantation to enhance integration in school and their further working life. With regard to the strong interrelation of pre-operative illness duration and reduced cognitive capacity, transplant centers should aim at reducing waiting time for these children as much as possible.

P-987 CAN CHILDREN CATCH-UP GROWTH AFTER LIVING DONOR LIVER TRANSPLANTATION?

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Purpose: We aimed to investigate various factors which may have effects on growth of children after living donor liver transplantation (LDLT).
Patients & methods: Data was obtained from medical records of pediatric cohort patients who received LDLT between 1990 & 2007, with a survival of more than 1 year. Growth was assessed by serial height and weight measurements.Standardized height and weight scores (SD scores) were calculated for each patient at the pre-operative time (baseline), 1, 2, 3, 5, 10 and 15 years after LDLT. Effects of several variables were examined using univariate and multivariate analyses.
Results: 318 patients met the inclusion criteria with a mean follow of 10.08±4.64 years and a mean age of 4.21±4.64 years, of which 212 were female. The baseline SD scores for height and weight were -1.63 and -1.22, respectively. The height SD improved significantly to -0.52 after the first year of LDLT and weight SD improved markedly to 0.15 after 3 years. Changes in height and weight SD scores are shown below. The baseline height SD and renal impairment were determinants for initial height spurt while baseline weight SD and young age were determinants for weight gain. Late growth retardation was related to complications that cause graft dysfunction.
Conclusions: Most children can recover their lost height and weight within 1 year after LDLT. Height shows 3 phases, initial rapid growth, stationary course and lastly downhill phase while weight shows 2 phases, initial overshooting followed by gradual decrease. Baseline height SD and preoperative renal impairment are determinants for the initial height spurt and baseline weight SD and young age are determinants for weight gain. Late growth retardation is related to graft dysfunction especially at puberty time when the graft could not fulfill requirments.

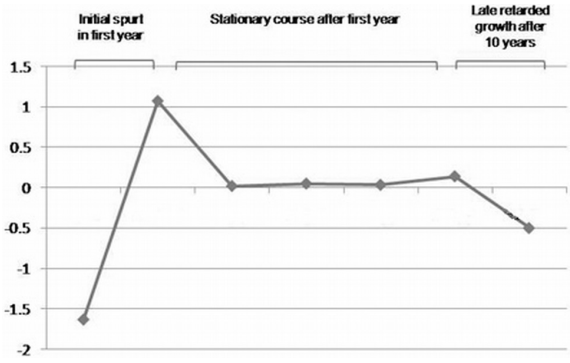

Figure 1. Patterns of changes in height SD over time.

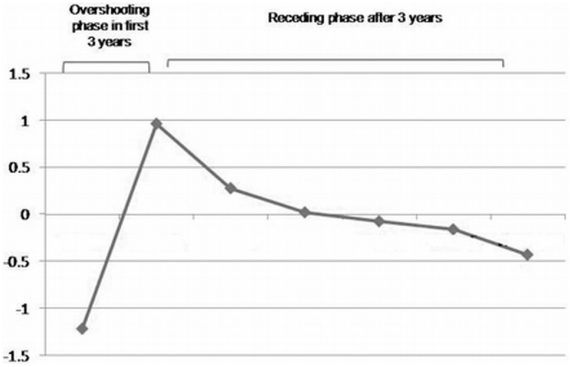

Figure 2. Patterns of weight SD changes over time.

P-988 LIVER TRANSPLANTATION FOR CRIGLER-NAJJAR SYNDROME TYPE 1: LONG TERM RESULTS

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Introduction: Crigler-Najjar sindrome type 1 (CNS1) is a metabolic disorders characterized by an unconjugated hyperbilirubinemia resulting from complete lack of hepatic bilirubin UDP-glucoronyltransferase activity. Hepatocytes transplantation failed to reduce bilirubin to normal level and to eliminate the need for phototherapy. Liver transplantation (LTx) is an established treatment for such a patient. We report our experience with LTx for CNS1 over a period of 11 years.
Methods: Between October 1997 and December 2008 we performed LTx in 4 children (median age 10,6 year, range 2,6- 11,8) affected by a CNS1. All the patient were on daily phototherapy (range 8-18 hours) with a median level of bilirubin of 27,4 mg/dl (range 20 – 28). A whole liver graft and 3 split graft were used. Biliary reconsruction was by a Roux en Y hepaticojejunostomy in the recipient of a whole liver graft and by a duct to duct anastomosis in the recipient of an extended right or left lateral segment split liver grafts.Immunosuppression was with cyclosporine and steroids in one patient and with tacrolimus and steroids in the other 3.
Results: All the children had an uneventful post operative course. After LTx bilirubin levels normalized and children eliminate the need for phototherapy. The child on cyclosporin was swicthed to tacrolimus two months after LTx for an acute cellular steroid resistant rejection. Another child, two years after LTx developed an HCV related chronic active hepatitis (HAI 8/18) with positive HCV RNA and negative anti HCV antibodies. With a median follow up of 6,6 years (range 1,93 – 10,9 years) all the patients are alive with a functioning graft with normal level of bilirubin.
Conclusion: Liver transplantation confirmed to be the therapy of choice for patient affected by CNSI with excellent long term results.

P-989 LIVER TRANSPLANTATION FOR BILIARY ATRESIA: OUTCOME AT A HIGH VOLUME CENTER

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Introduction: Biliary atresia (BA) is the main indication for liver transplantation (LTX) among children. We reviewed the results of LTx for BA at high volume center.
Methods: From October 1997 to December 2008, 194 children (median age 0,9 years range 0,2-16,8; median weight 8 kg range 4–44) underwent LTx for BA. A left lateral segment (LLS) graft from split liver was used in 158 (81%) children; a whole liver in 29 (15%) and an extended right (ER) or a full left (FL) graft in 7 (4%) children.
Results: Median waiting time was 53 days (range 0-347) and no child died on the waiting list. With a median follow up of 6,6 years (range 0,3 – 11,4) the 1 and 5 year patient/graft survival was 93/85% and 93/83%. Re-LTx rate was 12,7% mainly due to hepatic artery thrombosis HAT (7%), chronic rejection (2%) and portal vein thrombosis (2%).No statistically significant difference was found regarding patient/graft survival using different type of graft. At 1 and 5 year patient/graft survival was 93/83% and 93/80% for the whole size graft, 94/86% and 93/85% for the LLS graft, 86/71% and 86/71% for the ER or FL graft. At least an episode of acute rejection occurred in 54 (28%) children. Chronic rejection (CR)developed in 39 (20%) children but was cause of graft loss in only 4 (2%). HAT occurred in 15 patients (8%). Biliary complications occurred more often among the recipients of a split liver graft.
Conclusion: LTx confirms to be an effective treatment for children affected by BA with good long term results. Use of split graft allowed to safely transplant also small children with no mortality on the waiting list. CR represented the cause of graft loss only in a very few cases (2%).

P-990 GENETIC RISK AND THROMBOTIC EVENTS AFTER LIVER TRANSPLANTATION IN CHILDREN

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Background and aim: Thrombosis remains a cause of morbidity and mortality after Liver Transplant (LT). Thrombophilic genetic risk is has high as 5% in our population.
The aim of this study was to evaluate the correlation in between genetic thrombotic risk in recipients and donors and thrombotic events after LT.
Methods: Retrospective study, descriptive, with exploratory arm. The universe were children submitted to LT in our Centre and the organ donors in between the years 2000 and 2008. Genetic risk of thrombosis was defined as the presence of MTHFR-C677T homozygous; Factor V Leiden or Prothrombin mutations (homozygous or heterozygous), in donors and recipients. Thrombotic events were as described: Portal Vein, Hepatic Veins and Hepatic Artery thrombosis per patient. Two groups were created: A – children without thrombotic events; B – children with thrombosis. Age, sex, LT indication, and genetic mutations of both donors and recipients were analyzed using *Fisher, Chi Square and Odds ratio* statistical tests.
Results: 72 children were enrolled in our study (median age 4 years). 15 children (21%) were included in Group A (median age 4,9 Years) and 57 (79%) in Group B (median age 4 years).
A total of 42 children (58%) and 41 (57%) donors were studied for genetic risk for thrombosis. In 10 cases (children and donor) no study was performed.
In group A 12% of the donors had thrombotic risk versus 50% in Group B (p 0.03, Odds ratio 6.77). When analysing recipients, genetic risk was present in 13% of group A and 36.4% of group B (p 0.17). No differences were found concerning age and sex.
Conclusions: In this specific population, thrombophilia associated genetic mutations in donors (not in recipients) increased the risk for developing thrombotic events in paediatric recipients.

P-991 ASCITES AND GASTROINTESTINAL BLEEDING IN CHILDREN LISTED FOR LIVER TRANSPLANTATION

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Aims: To analyze the incidence and severity of ascites and haemorrhage in paediatric advanced liver disease.
Methods: Review of 63 consecutive children (excluding 8 non-cirrhotic metabolic defects and tumors) listed for liver transplantation (LT) between 1/2007-2/2009. Median follow-up after listing was 75 days, age median=1.7 years. Diagnosis was acute liver failure (ALF) in 4, biliary atresia (BA) in 31 (49%), other chronic liver disease (OCLD) in 28. PELD/MELD was <13 in n=31 (49%), 13-22 in 14 (22%) and ≥ 23 in 18 (28.4%).
Results: 1) Ascites developed in 35 (55.5%), haemorrhage occurred in 24 (38%); both affected 19 children (30%).
2) Ascites: affected all ALF, 61%BA and 43%OCLD. Incidence was 22.5% in PELD<13 group, and 87.5% in PELD≥ 13. Children with ascites showed (significant) lower albumin and sodium, and higher bilirrubin and INR compared to non-ascitic patients. Among children with ascites, 25% showed Na<130 mEq/L, 54% had fever/SIRS and 28.5% a marked bout of AST/ALT. Treatment was spironolactone (100%), furosemide (n=22; 63%), plasma/albumin (n=18; 51%), terlipressin (n=10; 28%), paracentesis (n=6; 17%), dialysis/hemofiltration (n=2; 5%)
3) Haemorrhage: occurred in 25% ALF, 35% BA, 42% OCLD; incidence was 22.5% in PELD<13 and 53% in PELD≥ 13. Albumin was lower and INR higher compared to children without bleeding. Treatment was ranitidine/omeprazole (all), plasma/clotting factors (45%), somatostatin (41%), endoscopy (21%), hemodynamic support (21%). Propranolol was used in 25%, aimed to prevent further episodes.
4) All 6 deaths in the waiting list occurred in children with both ascites and haemorrhage.
5) LT was performed in 43 children (23 had ascites). Post-LT graft- and patient-survival was 73% and 91.1% (ascites) compared to 90% and 95% (non-ascitic), differences not reaching statistical significance.
Conclusions: Ascites and bleeding related to more severe analytical disturbances of liver function. Risk of mortality is increased in affected LT candidates, but no influence was found on post-LT outcome.

P-992 EBV-ASSOCIATED PTLD ... IF YOU SEEK, YOU WILL FIND!

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Posttransplant lymphoproliferative disorder (PTLD) is estimated to occur in1-5% of renal transplant recipients. Histopathological pictures ranges from lymphohyperplasia to true lymphoma and Epstein-Barr virus (EBV) infection represents the main risk factor.
We describe a 5-years old kidney-transplant recipient, who developed an intrarenal lymphoplasmacellular hyperplasia (pre-PTLD), but achieved the complete remission after Rituximab therapy.
The boy was transplanted at the age of 3 because of ESRD in Prune-Belly syndrome. Immunosuppressive therapy included daclizumab, steroids, FK506 and mofetil-micofenolate. The boy was EBV-negative. From posttransplant week 12th, he presented a high-level blood EBV-DNA positivity, without clinical or biochemical signs of EBV-infection. Immunosuppression was then withdrawn. By posttransplant month 12th, renal function was normal (serum creatinine 45 umol/L) and EBV-DNAaemia was 1083 copies/10^4 lymphomonocytes, but protocol biopsy revealed a severe lymphomonocytes infiltration with positive EBV-in situ hybridization, compatible with pre-PTLD EBV-associated plasmacellular hyperplasia. The boy underwent Rituximab therapy (2 doses of 375 mg/mq), with stable negative EBV-DNAaemia and normalization of the histological picture in the control biopsy performed 3 months later.
In the literature, primary renal PTLD is extremely rare and lately diagnosed. Our case confirms that Rituximab may be effective as first-line therapy of EBV-associated PTLD, even in early and localized forms. Furthermore, it underlines the helpfulness of protocol biopsy as a tool to identify early non-immunological renal lesions, among which PTLD represents an increasing cause of reduced survival not only of the graft, but also of the patient.

P-993 ACUTE AND CHRONIC LESIONS AT 6 MONTHS AND 1 YEAR PROTOCOL BIOPSIES ARE INDEPENDENT MARKERS OF LONG TERM RENAL GRAFT FUNCTION

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Renal biopsy represents the gold-standard in the diagnosis of acute renal graft dysfunction, but its role in the follow up of the well-functioning kidney is still debated. We carried out a retrospective analysis of the histological data of 365 protocol biopsies performed in 166 paediatric patients (M/F 92/74, age 13.8 ± 6.6 years, mid follow up 41 months) at post transplant month 6th, 12th, 24th and 60th in 110, 123, 90 and 42 patients, respectively. Histological results were correlated with clinical and biochemical data. Acute lesions (Banff97 t1-3,v1-3,g1-3,i1-3) were seen in 6th and 12th month-biopsies (14% and 4%, respectively), with a higher prevalence in patients undergoing CyA*vs*FK506 (p 0.002) and AZA*vs*MMF (p 0.03) immunosuppressive regimens. Chronic lesions occurred in 21%, 32%, 47.8% and 69% of patients at 6th, 12th, 24th, 60th month respectively and were significantly correlated with blood CyA at 2 hours (p 0.01), triglycerides (p 0.03) and cholesterol (p 0.01) levels. Chronic lesions in the 6th and 12th month biopsy significantly correlated with 2 and 5-years posttransplant graft function, independently by renal function punctual value at the time of the biopsy. Chronic lesions or creatinine clearance did not correlate with the other studied variables, such as acute rejection episodes, HLA-mismatch, ischaemia times, hypertension, proteinuria, anaemia, glycaemia, lipid profile. Our results confirm the usefulness of 6th and 12th months-protocol biopsy to identify subclinic acute and chronic lesions that predict a long-term renal function deterioration.

P-994 URINARY TRACT INFECTIONS IN PEDIATRIC RENAL TRANSPLANT RECIPIENTS; A SINGLE CENTER STUDY

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Purpose: Urinary tract infections (UTIs) remain a common cause of morbidity in children with renal transplant. We conducted a study at our center to see the frequency of UTIs, causative micro-organisms, association of UTIs with urinary tract corrective surgery and the effect of UTIs on graft function (as measured by serum creatinine level).
Methods/Materials: At Shifa International Hospitals, Islamabad, Pakistan, 15 renal transplants were done between August, 2002 to April, 2008 in children (male-9,female-6) with mean age of 11.47 years (range 6-16 yrs), and median follow up of 53 months (range 10-78 months). 7/15 patients underwent pre-

transplant surgery including nephroureterectomy, augmentation cystoplasty and Mitrofanoff procedure.
Results: Among 15 patients, 9 patients (60%) suffered 40 episodes of UTIs (range 1-11 episodes per patient) with recurrent UTIs in 6 patients and a single episode of UTI in 3 patients. Six patients suffered no UTI. Among 40 UTIs, 29 episodes (73%) occurred in patients who underwent corrective surgery with more than a half (n=17/29) occurring in patients on self catheterization via continent catheterizable stoma. E.coli was the most common organism (42.5%) followed by Enterococcus (17.5%), Staphylococcus (10%), Enterobacter (7.5%), Proteus (5%), Pseudomonas (5%), Streptococcus (5%), Klebsiella (2.5%), Acinetobacter (2.5%) and Aeromonas (2.5%). After excluding 1 patient who failed graft secondary to chronic allograft nephropathy, there was no significant difference between mean serum creatinine of patients with urinary tract infections (1.75mg/dl) as compared to patients with no UTI (1.37mg/dl), p-value (0.7). Transient rise in creatinine with the UTI which reversed with the treatment was observed in most patients.
Conclusion: Urinary tract infections were observed in 60% cases with no significant graft dysfunction. UTIs were more common in patients who underwent corrective urological surgery especially the patients with continent catheterizable stoma on self catheterization.
KEY WORDS: urinary tract, infections, pediartric, renal transplant.

P-995 PEDIATRIC LIVER TRANSPLANTATION IN AN ADULT LIVER TRANSPLANT PROGRAM: IS IT RELEVANT?

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The aim of this study was to review the results of pediatric LT in an originally adult LT center.
Patients and methods: Between January 1991 and February 2008, a total of 928 liver transplantations were performed; 129 (13.9%) of whom were done in 124 pediatric patients including 63 males and 66 females with a mean age and a mean body weight of 29 months (range: 68 days – 16 years) and 11kg (range:5-55) respectively. Types of grafts were 42 whole cadaveric livers, 74 left lateral sections, 8 left lobes, 4 right lobes and 1 monosegment (segment 2). Regarding partial livers, 44 were split liver grafts, 35 were living donor grafts and 8 reduced-size grafts. Biliary anastomoses were bilio-enteric in 94 cases and duct-to-duct in 32 cases.
Results: One, 5, 10 and 15 year patient and graft survival was 87%, 85%, 85% and 85% and 83.5%, 81.1%, 81.1% and 77.2% respectively. During the last 5 years (50 LT), patient and graft overall survival was 96%. Overall graft survival was significantly better for whole (88%) and living donor grafts (88.5%) compared to split (72.7%) and reduced-size (50%) grafts. Surgical complications included 1 graft primary nonfunction, 18 (14%) abdominal bleeding, 2 hepatic artery thrombosis (1.5%) with successful surgical revascularization in one, 15 (11.6%) portal vein thrombosis, 45 (34.8%) biliary complications. In total, 70 (54.2%) patients needed surgical revision. Five (3.8%) children underwent retransplantation for portal vein thrombosis (n=2), chronic rejection (n=2) and biliary complication (n=1). None of the patients who had a living donor graft had retransplantation.
Conclusions: Outcome of pediatric recipients in our series favourably compares with results of the literature emphasizing the relevancy of performing pediatric LT in an adult large volume center.

P-996 OUTCOME OF LIVER TRANSPLANTATION IN CHILDREN WEIGHTING LESS THAN 10 KILOGRAMS WITH REFERENCE TO SURGICAL COMPLICATIONS: THE LYON EXPERIENCE

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Liver transplantation (LT) in small children is often more challenging technically because of the small vascular structures compared to older recipients. The aim of this study was to review the results of small children LT focusing on surgical complications.
Patients and methods: Between January 1991 and February 2008, a total of 928 liver transplantations were performed; 59 (6.4%) of whom were done in 56 pediatric patients weighing less than 10 kilograms. Mean age and body weight were 13.5 months (2.3- 46.3) and 8 kg (5-10) respectively. The main indication for LT was biliary atresia (74.6%). Types of grafts were 5 whole cadaveric livers, 53 left lateral sections, and 1 monosegment (2). Partial livers were 27 split-liver, 24 living donor and 2 reduced-size grafts.
Results: Mean follow up was 5.5 years (range 2 months-16 years). One, 5 and 10 patient and graft survival was 85.7%, 80.8% and 80.8% and 79.5%, 76.8% and 76.8% respectively. During the last 5 years (19 LT), patient and graft overall survival was 95%. Three (5.4%) children underwent retransplantation for portal vein thrombosis (n=2) and chronic rejection (n=1). Vascular complications comprised 1 (1.7%) hepatic artery thrombosis and 12 (20%) portal vein thromboses. Portal vein thrombosis was significantly more frequent in patients with biliary atresia as compared to others pathologies (27% vs 0%). Early and late biliary complications were encountered in 30 cases (51%). Abdominal bleeding occurred in 12 patients (20%) and bowel perforation in 13 patients (22%). A total of 41 patients (69.5%) required at least one reoperation.
Conclusions: Despite a higher morbidity rate, small pediatric recipients had comparable survival compared to older recipients. Portal vein thrombosis represented the major vascular complication in children having LT for biliary atresia.

P-997 LIVER TRANSPLANTATION FOR PRIMARY SCLEROSING CHOLANGITIS IN CHILDREN: A SINGLE CENTER EXPERIENCE

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Objective: The purpose of this study was to analyze the results of liver transplantation (LTx) for Primary Sclerosing Cholangitis (PSC) in paediatric recipients.
Methods: We reviewed our series of 348 isolated primary pediatric liver transplants performed between October 1997 and January 2009.
Results: PSC was the indication in 8 (2.2%) children (median age 4.36 years, 0.53 –16.87). 3 children were diagnosed in neonatal period; 4 patient were transplanted before the age of 2 years. The LTx was indicated in 2 patients for liver failure associated to portal hypertension and gastroesophageal bleeding, in 1 for a biliary stricture not treatable by a biliary stent placement, in 3 for progressive cholestasis with jaundice and intractable pruritus, in 2 for a progressive worsening of liver function up to a Pediatric End-Stage Liver Disease (PELD) score of 30 and 25 respectively. Median PELD score at the time of listing was 17 (10-30). In 2 cases PSC was associated with hitiocytosis X. Median waiting time between diagnosis and transplantation was 17.8 months (4.3-77.4). No patient had evidence of inflammatory bowel disease (IBD) before LTx. 6 children received a left lateral segment split graft, 2 a whole graft. Median follow up was 25.3 months (2.5-117.6). All the patients received a tacrolimus-steroids based immunosuppression. 3 children developed an acute rejection, 1 a mild histological chronic rejection. The 1,3 and 5 year actuarial patient survival was 100%. A child developed an histological recurrence of PSC in his allograft and a mild IBD 8 months post LTx. All children at last follow up were alive and in good condition and their liver tests were in a normal range.
Conclusion: According our experience LTx provided good patient and graft survival rates in paediatric recipients, including infants with end-stage PSC.

P-998 RATIONALE FOR NEORAL C0 AND C2 MONITORING IN INFANTS IN THE EARLY POST LIVER TRANSPLANTATION PERIOD

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The objective of the study was to examine CSA trough (C0) and 2-hour post dose (C2) levels in infants undergoing liver transplantation (LT) in order to present a general justification for Neoral C2.
Patients and methods: Seventeen infants below 2 years of age who received CSA microemulsion (Neoral®) were included in the study. The main indication for LT was biliary atresia in 82% of cases. C0 and C2 were measured every day during the first week, thrice a week during the second and twice a week thereafter. CSA doses were monitored with C0. Poor CSA absorption was defined by a C2/C0 ratio below 3. Children were separated into 2 groups whether they experienced acute rejection (AR) during 3 month-follow-up (group 1, n=11) or did not (group 2, n=7).
Results: Patient and graft survivals were 94% and biopsy-proven AR rate was 65% at 3 month post-LT. Important interindividual variability of C0 and C2 and no correlation between C0 and C2 were demonstrated (r2 = 0.137). Poor CSA absorption was noted in 41%, 35%, 24%, 12%, 12% on day 3, 7, 14, 21 and 28 respectively. Interindividual variability of CSA metabolism (rapid or delayed drug clearance) that is influenced by liver function was also noted. Mean CSA doses, C0, C2 and C2/C0 ratios did not differ significantly between groups.
Conclusion: CSA exposure cannot be estimated by single C0 or C2 determinations in the early post-transplant period. C2 as a marker of poor absorption is useful, but does not reveal delayed or rapid clearance of the drug, undetected without C0. We suggest the use of both C0 and C2 monitoring, and AUC monitoring on an individual basis during at least the first 2 weeks post-LT.

P-999 RENAL TRANSPLANTATION TO CHILDREN WITH DIFFERENT ORIGINATED LOWER URINARY TRACT DYSFUNCTION: A SINGLE-CENTER EXPERIENCE

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Renal transplantation in patients with lower urinary tract dysfunction (LUTD) of various origins is a challenging issue in the field of pediatric transplantation.
Aim: We report Gazi University, Transplantation Center experience to evaluate patient and graft survivals as well as the risks of the surgery and immunosuppressive therapy
Patients and methods: Videourodynamic tests were performed to all patients preoperatively as well as postoperatively if required.Among 55 pediatric transplantation recipients, 7 displayed severe LUTD. The cause of urologic disorders were neurogenic bladder (n=3) and urethral valves (n=4). Clean intermittent catheterization (CIC) was needed in three patients to empty the bladder. *E. coli* (n=4) was the most frequent organism, *K. pneumoniae* (n=2), *P. aeruginosa* (n=1) yield in urine culture. None of patient 6 had pretransplantation augmentation. Only one patient who has VUR+neurogenic bladder has augmentation operation during transplantation. Three out of 7 patients received kidneys from cadaveric and 4 from living donors. All patients were treated with calcineurin-based triple immunosuppressive therapy.
Results: The mean age at transplantation was 10,7±3,8 years old (4-17 years old). The median follow-up after transplantation was 15 months (8 to 124 months). Three patients who all have neurogenic urine bladder had recurrent symptomatic urinary tract infections. Totally 3 BKVAN have seen in this group. One of the graft was lost due to BKAVA and other two has normal graft functions. None of the recipients had urine leak after transplantation.
Conclusion: Severe LUTD carried high risks for the grafted kidney. Although renal transplantation is a safe and effective treatment option, severe LUTD therefore underlying urologic diseases should be followed up very closely than other transplantation patients. While surgery and follow-up is more complicated in such patients group, patient's compliance and experience of transplantation team have significant impacts on outcomes.

P-1000 OUTCOME OF URETERAL STENT PLACEMENT AT PEDIATRIC KIDNEY TRANSPLANTATION: SINGLE CENTER EXPERIENCE

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Ureteral Double J stent (DJS) placement at kidney transplantation may reduce stenosis or leakage (S/L) complication rates. However, DJS placement may also increase risk for early urinary tract infection (early UTI; < 3 months after transplant). In children, the usefulness of DJS placement is not well defined.
Material and methods: We analyzed retrospective data from children transplanted at Gazi University Transplantation Center and Pediatric Nephrology, Ankara. At our center, DJS placement decision is given by transplantation surgery team during operation. Routinely DJS placements have been performed routinely to all recipients in the operation. Removal of the DJS occurs 6 week after transplantation. Immunosuppressive regiment consists of steroids, calsineurin inhibitors and mycophenolat. In cadaver recipients, ATG 3mg/kg was used at the time of DGF onset.
Results: Among 55 transplants from 1996 to 2008, early UTI (n=3) was seen in 5.4%, stenosis (n=1) in 1.8% and no leakage. Seventeen were from cadaver and 38 from living donor.Mean DJS removal time is 6±0,5weeks. Early UTI was seen in 3 recipients with PUV+neurogenic bladder (n=2) and meningomycell+neurogenic bladder (n=1). All 3 recipients, who have early UTI, were performing clean intermittent catheterization (CIC) after transplantation for adequate emptying of the bladder. In our study group, spontaneous stent migration (n=2) was the only the complications. We have not seen any crusting, breakage, hematuria, or stone formation. Early UTI was seen only 3 patients who have neurogenic bladder type complicated urine outflow system. CIC and augmentation (n=2-PUV+neurogenic bladder) increased the odds ratio for early UTI.
Conclusion: We saw that, DJS placement was not a significant risk factor for early UTI and also has protective effect for leakage and stenosis.Regardless of DJS placement, when the recipient had complicated urological outflow problems, infection is becoming long term hurtle. DJR and stenosis may need further investigation.

P-1001 BONE MINERAL DENSITY IN RENAL RECIPIENTS: A FOLLOW UP STUDY IN CHILDREN AND ADOLESCENTS

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Although renal transplantation (Tx) is considered to be the treatment of choice for patients with chronic renal failure (CRF), decreased bone mineral density was still observed in children after Tx, due to pre-existing metabolic bone disease and administration of immunosuppression.
There are not so many studies which longitudinally evaluated skeletal changes, using DXA technique, in renal transplanted children and adolescents.
The aim of this study was to analyze the changes in BMD in renal transplant recipients.
Patients
17 renal transplant (Tx) patients (4 girls, 13 boys),The mean period since Tx was 54 months (range 1.2 -9.1 years). Immunosupression included cyclosporine, tacrolimus, azathyoprine, micophenolate mophetil (MMF)and steroids.
Methods: Serum calcium, phosphate, creatinine, total alkaline phosphatase were determined by an automated Olympus AU 2700 analyzer. Intact parathyroid hormone (PTH) was measured by two-site immuno-radiometric assay. Bone mineral density (BMD; g/cm^2) at the lumbar spine, proximal femur, distal third of radius and total body was measured by DXA Lunar Prodigy densitometer (GE Lunar, Madison, WI).
Results: Baseline and control values of serum calcium and phosphorus were inside the reference values in all patients. Baseline PTH was increased in 1 child. At the first appointment 14 patients had creatinine clearance (CCL) below 88 ml/min. At the control appointment 3 patients increased CCL. Comparison between baseline and control measurement showed the increase of BMD in spine, femur and total body. Mean Z scores were negative in spine and total body at the first measurement. Significant increase of spine Z-score was found at the second measurement ($p<0.0001$), while the total body Z-score was unchanged. BMD in distal radius significantly decreased.
Conclusion: Bone loss due to renal failure, could not be fully recovered after successful Tx. Cortical bone loss could be associated with Hyperparathyroidism.

P-1002 THE CLINICAL IMPACT OF PROTOCOL BIOPSIES AFTER KIDNEY TRANSPLANTATION IN CHILDREN

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Protocol biopsies (PB) of renal transplants are seldom performed in paediatric patients. The purpose of this study was to clarify to what extent PB provides information for clinical interventions.
Six months after renal transplantation (RTx), protocol biopsies were performed in 57 children between 2 and 17 years of age, receiving different immunosuppressive regimens. Renal function was accessed 6 months and 1 and 2 years after RTx.
Biopsies revealed no pathological changes in 32/58 (55%) children. In this subgroup, mean glomerular filtration rate (GFR) decreased from 71±20 to 62±16 ml/min/1.73m^2 ($p<0.001$, paired t-test) in the first 12 months after biopsy. Six out of 57 patients presented with borderline findings on histology. Mean GFR remained stable (65±18 vs. 69±18ml/min/1,73m^2, p=0.07) after increase of the calcineurin-inhibitor (CNI) dosage. Eleven of 57 children showed rejection Grade Ia (Banff classification); mean GFR remained unchanged (61±20 vs. 53±12ml/min/1,73m^2, p=0.1). All 11 patients were treated with 6 iv-prednisolone pulses. In 5/11 patients, cyclosporine A was replaced by tacrolimus. Three of 57 patients showed interstitial fibrosis and tubular atrophy and necrosis (IFTAN). In these 3 patients GFR remained stable (72±14 vs. 64±6ml/min/1,73m^2, p=0.2). One child presented with poly-

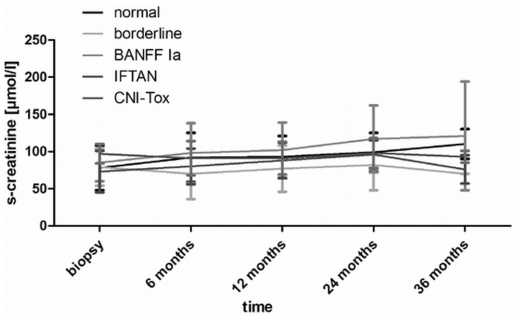

Figure 1

omavirus nephropathy. Immunosuppression was reduced and GFR increased from 48 to 76ml/min/1,73m^2 after 6 months and remained stable thereafter. Four of 58 patients showed CNI toxicity. In those patients GFR was low but stable (50±10 vs. 56±13 ml/min/1,73m^2, p=0.5), after reduction of CNI-dose. In summary, protocol-biopsy-driven interventions such as changes of immunosuppressive therapy helped to stabilize GFR.

P-1003 GANCICLOVIR-VALGANCICLOVIR PROPHYLAXIS FOR 6 MONTHS AFTER LIVER TRANSPLANTATION IN CHILDREN

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Aims: In a series of children undergoing liver transplantation (OLT) we analyzed the results of a protocol consisting of: 1) antiviral prophylaxis during 6 months, 2)surveillance of EBV infection,3) antiviral treatment of infected patients, and 4)individualized reduction of tacrolimus.
Methods: Patients: 27 consecutive children with primary OLT in 2007 (follow-up 8-21 months)
Prior to OLT IgGVCA: negative in 16, positive in 9 patients.
Prophylaxis: ganciclovir 5 mg/kg every 12 hours during 1 month followed by valganciclovir 520 mg/m^2 every 12 h for 5 months.
Sequential clinical checkups plus EBV quantitation were done at 1-3 months intervals
EBV viral load was assessed by real time PCR (AffigemeEBVTrender). High viral load was set at $>2.6\times10^4$ copies/ml.
Children displaying high EBV load were treated with valganciclovir. Tacrolimus was decreased to <5 ng/ml in selected patients.
Results: EBV infection was detected in 23 children (92%)
Primary infection: affected 15/16 (94%), 11 started within 6 months after OLT. 73% of infected displayed high viral load. One patient was symptomatic (urticaria a frigore,mild pneumonitis, high alkaline phosphatase). All infected patients continued/ restarted valganciclovir, and tacrolimus was reduced in 6 out of 11 showing high viremia. None developed PTLD.
Reactivation: occurred in 8/9 (89%), all <6 months after OLT. High viral load was found in 3/8 (37%). One patient had symptoms (bone marrow aplasia, probably related to nonA-nonB fulminant hepatitis for which he underwent OLT). They received valganciclovir, reduction of tacrolimus in 2 cases, rituximab in 1 case. None developed PTLD. The patient with aplasia died with a mixed EBV,CMV and aspergillus infection.
Conclusions: In 25 children with antiviral prophylaxis during 6 months, EBV infection was detected in 92%, 61% of them displaying high viral load. There were no cases of PTLD using valganciclovir, combined with reduced tacrolimus in 8/14 showing high viremia.

P-1004 TWO COMPARATIVE CASES OF FULMINANT HEPATIC FAILURE CAUSED BY EB VIRUS INFECTION – A PITFALL OF PEDIATRIC LIVER TRANSPLANTATION

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It is well known that the outcome of pediatric liver transplantation for fulminant hepatic failure has poor prognosis compared to that of adult. We report two comparative course of hepatic failure in children who suffered from acute hemophagocytic burst of EB virus. Case1 was 4-year-old girl who had a flu-like syndrome 3 days ago. She manifested hyper-bilirubinemia (>8mg/dl), coagulopathy (prothrombin time <8%) and third grade encephalopathy. She was diagnosed as acute fluminant hepatitis and encephalopathy recognized to be irreversible, therefore, urgent living-donor liver transplantation was carried out. Serum AST/ALT levels rose up over 4000 IU/L and hepatitis supposed to be sustained after transplantation. Real time PCR analysis of her blood samples on admission revealed over 1.6×10^5 copies EBV DNA. Most expanded clone was Natural killer cell (CD56+). After that, transient recovery of liver function was obtained by anti-tumor chemotherapy (VP-16, CyA, dexamethasone), but she died of developing multiple organ failure after 2 months. Case2 was 12 years old boy with abrupt jaundice following common cold like symptoms. He manifested hyper-bilirubinemia (>18mg/dl), coagulopathy (prothrombin time <40%) and second grade encephalopathy. Real time PCR revealed over 2.6×10^5 copies EBV DNA in his blood samples on admission. Natural killer cell mainly propagated in his blood samples. Therefore, urgent liver transplantation was suspended and chemotherapy (VP-16, CyA, methylpredonisolon) was started. After aforementioned chemotherapy, he recovered from fulminant hepatic failure. Liver is vulnerable to injuries by EBV-infected PBMC clone same as bone marrow, thus, acute worsening of EBV infection often diagnosed as fulminant hepatic failure. In pediatrics with acute hepatic failure, whether hyper prolifration of EBV is occurring or not may be crucial to decide the indication of urgent liver transplantation.

P-1005 MYCOPHENOLATE ACID PHARMACOKINETIC STUDY IN CHILDREN AFTER LIVER TRANSPLANTATION

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Mycophenolate mofetil (MMF) is a prodrug of mycophenolic acid (MPA) which inhibits lymphocyte proliferation. Since very few pharmacokinetic data have been reported, optimal doses of MMF still need to be determined in children after liver transplantation (LT), whereas a dose of 600 mg/m^2] bid was found to be efficient in renal transplant children. The aim of this study is to describe the pharmacokinetic of MPA in children after LT in order to optimize MMF dosing regimen.
Patients and methods: Seven children (age 8.3±4.3 years) receiving tacrolimus (n=5) or ciclosporine (n=2) associated with prednisone in 5, were included in the study. MMF was initiated 0.2 to 80.5 months after LT because of renal dysfunction in 2 and rejection in 5. Blood samples were collected before and 0.5, 1, 2, 4, 6, 8 hours following MMF intake. MPA was assayed in plasma using a HPLC method. MPA $AUC_{0\text{-}12}$ was calculated using the linear trapezoidal rule. MMF dose was adjusted to reach a target MPA $AUC_{0\text{-}12}$ of about 45 mg.h/L such as recommended in adults LT.
Results: MMF was initiated at a mean dose of 515±183 mg/m^2 bid. MPA AUC was below 30 mg.h/L in all children but one. One to 4 dose adjustments per patient were required to obtain an efficient AUC. Mean AUC normalized to 600 mg/m^2 was 33.8±18.5 mg.h/L. AUC remained low despite an increase of 100% in MMF dose in 2 children treated with Rifampin for severe pruritus.
Conclusion: Assuming that MPA exhibits linear pharmacokinetics, the dose required to achieve a target AUC of about 45 mg.h/L in pediatric liver recipients would be 800 mg/m^2 bid. Because Rifampin is a potent inducer of MPA, an important increase in MMF doses is required when both drugs are co-administered.

P-1006 LONG-TERM OUTCOME OF PEDIATRIC LIVER TRANSPLANT RECIPIENTS WHO SURVIVE INTO ADULTHOOD

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Aim: The aim of the present study was to describe the long-term outcome of children who underwent LT during childhood, and who are now adults.
Methods: Eighteen recipients from 120 children were identified, who underwent LT between 1987 and 2005. The mean age of the patients was 23.3 years (range, 19-30), and they had undergone LT at a mean age of 9.5 years (range, 2-15).
Results: Indication for LT was biliary atresia (BA) (n=4), metabolic diseases (n=6), autoimmune hepatitis (n=3), cholestatic liver disease other than BA (n=5). Mean follow after LT was 13.8 years (range, 7-20). The mean height was 163.6 cm (range, 122-182), and the mean BMI was 20.1 (range, 18-24). Initial immunosuppressive regimen consisted in cyclosporine in association with azathioprine (AZA) and corticosteroids (CS) (n=14), or tacrolimus in association with AZA and CS or mycophenolate mofetil (MMF) (n=4). Immunosuppressive regimen at the ultimate follow-up included tacrolimus (n=14) in combination with MMF (n=8), or ciclosporine (n=4) in combination with AZA (n=2) or CS (n=2). Liver function tests were normal for 9 patients (50%). Liver biopsy was performed in 14 patients after a mean delay of 12 years after LT, and 7 was normal, 4 disclosed mild rejection and 3 disclosed chronic rejection. The median GFR was 85 mL/min per 1.73m^2 (range 12 to 117). Five patients (23%) presented with severe renal impairment (calculated GFR < 30 mL/min per 1.73m^2), from whom 3 reached end-stage renal disease.
Conclusion: The long term outcome of patients who underwent LT in childhood is encouraging. Two major points probably need further attention: (1) liver biopsy seems to be important even in the case of normal liver function tests and (2) renal function must be closely monitored to encourage calcineurin inhibitors sparing strategies.

P-1007 LIVING DONOR LIVER TRANSPLANTATION WITH SEGMENT 2 MONOSUBSEGMENTAL GRAFT FOR NEONATES WEIGHTING LESS THAN 3 KILOGRAM

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Purpose: Living donor liver transplantation (LDLT) for neonates has various technical difficulties in harvesting and implanting of the graft.
Methods: We describe two neonatal patients weighting less than 3 kilogram with fulminant liver failure who underwent emergency LDLT with segment 2 (S2) monosubsegment graft.
Results: Case 1: The patient is a 17-day-old girl with cryptogenic fulminant hepatitis. Emergency LDLT from her father was performed at 2.6kg. Donor S2 was carefully resected after removal of segment 3 using intraoperative Doppler and contrast-enhanced ultrasonography. S2 monosubsegment graft partially reduced *ex vivo* was 95g. A temporary portocaval shunt was made by using recipient patent umbilical vein before total hepatectomy. Portal reconstruction was also used with recipient umbilical vein. Hepatic arterial reconstruction was enormously difficult. Finally, the graft was pulled toward caudal and left hepatic artery (LHA) of the graft was reversed from dorsal and anastomosed to recipient proper hepatic artery (PHA). Biliary reconstruction was made by hepaticojejunostomy. Primary abdominal closure was successful. Postoperative course was satisfactory except cytomegalovirus infection and the patient shows normal growth for 4 months after LDLT. Case 2: The patient is a 27-day-old boy with neonatal hemochromatosis. Emergency LDLT from his father was performed at 2.8kg. S2 monosubsegment graft resected in the same way from the donor was 93g. A temporary portocaval shunt was made by using recipient right portal vein. Portal reconstruction was used with recipient umbilical portion of left portal vein. Hepatic arterial reconstruction was made between recipient PHA-gastroduodenal artery branch and graft LHA. Biliary reconstruction was made by hepaticojejunostomy. Primary abdominal closure was successful. Postoperative course was uneventful and the patient has grown up well for 3 months after LDLT.
Conclusion: LDLT with S2 monosubsegment graft is a useful and alternative option for neonates.

Tissue injury & preservation

P-1008 LONG TERM PRESERVATION OF ARTERIES – IMMERSION IN ANHYDRIC SODIUM CHLORIDE

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Arterial allografts have been largely replaced by artificial grafts. However, in case of infection at the site of teflon implantation or a-v fistula for hemodialysis allografts become grafts of choice. A method for long-term preservation of arterial allografts is desperately needed.
Aim: To establish a method of successful preservation of arteries for months with unchanged morphology and low allogeneic reactivity.
Methods: Fragments of rat aorta were preserved in anhydric NaCl powder and stored 4°C for 12 months and transplanted for 10-12 months.
Results: Aorta-aorta and aorta-ivc grafts pulsated 12 months after transplantation. H/E and trichrome staining showed preserved anatomical structure. There was not thrombosis, only some thickening of neo-intima. No differences between preserved transplanted and control syngeneic aortae stained for CD 31, CD 54, RECA-1 were observed. Electron microscopy revealed normal structure of elastin fibers, appearance of fibroblasts between elastin bundles and single endothelial-like cells. There was only slight infiltration of ED1, OX 6 and W3/13 cells around the allograft.
Conclusions: Transplanted aortae patent for 12 months and with perfectly preserved anatomical and molecular structure make preservation in pulverized NaCl a novel method for use of arterial allograft as av shunts and in infected ischemic areas.

P-1009 SHORT TERM MULTIDRUG DONOR PRECONDITIONING REDUCES LIVER PRESERVATION AND REPERFUSION INJURY

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Various inflammatory changes occur in the graft during cold liver storage and reperfusion, which are critical steps before liver transplantation. This initial tissue injury can lead to primary liver graft dysfunction (PLGD). The donor organ preconditioning (DOP) is an additive approach for donor liver protection and enhanced liver graft function after transplantation. We evolved an animal model in rats for a short term multidrug donor preconditioning (MDDP) in an ex vivo blood cell-free isolated liver reperfusion model. Perfusion was performed with freshly prepared Krebs Henseleit bicarbonate (KHB) buffer saturated with carbogen. Throughout the reperfusion samples of the effluent fluid were collected after 1, 30 and 60min. At the end of cold storage and after postischemic reperfusion, liver tissue was sampled for histology, immunohistochemistry and Western blot analysis. MDDP protects liver from cold I/R injury through multiple pathways. The results of the present study showed that MDDP could decrease MDA concentration, suggesting that MDDP also inhibits ROS formation and the release of proinflammatory cytokines after I/R injury, and attenuates apoptosis and neutrophil infiltration in liver. The MDDP is an additive pharmacological and surgical approach, which could be effective to reduce primary organ dysfunction after cold liver storage.

P-1010 AMIODARONE PRETREATMENT OF ORGAN DONORS EXERTS ANTI-OXIDATIVE PROTECTION BUT INDUCES EXCRETORY DYSFUNCTION IN LIVER PRESERVATION AND REPERFUSION

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Background: Continuous organ shortage necessitates the use of marginal organs from donors with various diseases including arrhythmia associated cardiac failure. One of the most frequently used anti-arrhythmic drugs is amiodarone (AM), which is given in particular in emergency situations. Apart from its anti-arrhythmic actions AM provides anti-oxidative properties in cardiomyocytes. Thus, we were interested whether AM donor pretreatment affects organ quality and function of livers procured for preservation and transplantation.
Material and methods: Donor rats were pretreated with AM (5mg/kg body weight) 10min before flushout of the liver with 4°C cold HTK solution (n=8). Livers were then stored for 24h at 4°C before ex situ reperfusion with 37°C Krebs Henseleit solution for 60min in a non-recirculating system. At the end of reperfusion tissue samples were taken for histology and Western blot analysis. Animals with vehicle only (0.9% NaCl) served as ischemic/reperfusion (I/R) controls (n=8). Additionally livers of untreated animals (n=8) not subjected to 24h cold ischemia served as sham controls.
Results: AM pretreatment effectively attenuated lipid peroxidation, stress protein expression and apoptotic cell death. This was indicated by an AM-mediated reduction of malondialdehyde, heme oxygenase-1 and caspase-3 activation. However, AM treatment also induced mitochondrial damage and hepatocellular excretory dysfunction, as indicated by a significantly increased GLDH concentration in the effluate and a decreased bile production.
Conclusions: AM donor pretreatment exerts anti-oxidative actions in liver preservation and reperfusion. However, this protective AM action is counteracted by an induction of mitochondrial damage and hepatocellular dysfunction. Accordingly, AM pretreatment of donors for anti-arrhythmic therapy should be performed with caution.

P-1011 INDUCIBLE NITRIC OXIDE SYNTHASE-DERIVED NITRIC OXIDE REGULATES METALLOPROTEINASE-9 ACTIVITY AND LEUKOCYTE MIGRATION IN LIVER ISCHEMIA AND REPERFUSION INJURY

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Metalloproteinase-9 (MMP-9) mediates leukocyte migration in hepatic ischemia/reperfusion injury (IRI). This study tests the relevance of inducible nitric oxide synthase (iNOS)-derived nitric oxide (NO) upon regulation of MMP-9 activity in liver IRI.
Methods and results: iNOS knockout mice (-/-, KO) and matched wild-type (WT) controls were submitted to partial warm liver ischemia for 90 minutes followed by reperfusion. iNOS -/- mice showed significantly less liver damage,

as evidenced by the reduced transaminase levels (sALT, U/L: 1,368±1,240 vs. 18,810±4,317; $p<0.001$; and sAST, U/L: 1,587±828 vs. 9,293±1,166; $p<0.001$, n=6/gr) at 6h post-IRI. Moreover, improvement in liver function in iNOS -/- mice was associated with significantly better histological preservation as compared to damaged WT control livers. iNOS -/- livers showed significantly lower numbers of Ly-6G neutrophils (2.3±0.6 vs. 19.3±1.5, $p<0.001$; n=6/gr), CD3 lymphocytes (4.0±1.0 vs. 8.3±0.6, $p<0.003$; n=6/gr), and Mac-1 leukocytes (2.7±0.6 vs. 21.7±3.1, $p<0.001$; n=6/gr). The amount of active MMP-9 (ug/g) was significantly depressed in iNOS -/- deficient livers (0.042±0.009 vs. 1.289±0.091, $p<0.0008$; n=6/gr) at 6h post-IRI. MMP-9+ leukocytes were markedly reduced in iNOS -/- livers after IRI (3.3±1.5 vs. 35.3±5.1, $p<0.001$; n=6/gr). Confocal microscopy revealed that Mac-1 macrophages co-expressed MMP-9 and iNOS, while Ly-6G neutrophils were positive for MMP-9 but were virtually negative for iNOS in damaged WT livers. Interestingly, exposure of isolated murine neutrophils and macrophages to exogenous NO (DETANO) significantly up-regulated MMP-9 activity in both cell types. Moreover, using Transwell Migration Chambers, we observed that macrophage-derived NO was capable of promoting neutrophil migration (25.8±2.9 vs. 67.98±11.04, $p<0.01$; n=4/gr), which was disrupted in the presence of a selective MMP-9 inhibitor.
Conclusion: Our novel data strongly supports the view that MMP-9, by facilitating leukocyte migration, is a key mediator of iNOS-derived NO induced liver IRI.

P-1012 GLYCINE PRETREATMENT AMELIORATES LIVER INJURY AFTER PARTIAL HEPATECTOMY IN THE RAT

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Background: In contrast to organ procurements from brain-dead donors, living donor liver transplantation allows the pre-treatment of donors with substances that might improve graft quality and are possibly also advantageous for the donor. The aim of our study was to analyze the effects of pre-treatments with a-tocopherol (vitamin E), the flavonoid silibinin and/or the amino acid L-glycine on the donor in a rat model.
Methods: Male Wistar rats were pre-treated with L-glycine (5% in chow, 5 days), a-tocopherol (100 mg/kg b.w. by gavage, 3 days) and/or silibinin (100 mg/kg b.w., i.p., 5 days). Thereafter, 90% partial hepatectomy was performed without portal vein clamping.
Results: Glycine pre-treatment markedly decreased transaminase release (AST, 12 h: glycine 1292±192 U/l, control 2311±556 U/l, $p < 0.05$; ALT, 12 h: glycine 1013±278 U/l, control 2038±500 U/l, $p < 0.05$), serum ALP activity and serum bilirubin levels ($p<0.05$). Prothrombin time was reduced, and histologically, liver injury was also decreased in the glycine group. Silibinin pre-treatment was less advantageous and pre-treatment with a-tocopherol at this very high dose showed some adverse effects. Combined, i.e. triple pre-treatment was less advantageous than glycine alone. Liver resection induced HIF-1a accumulation and HIF-1a accumulation was also decreased by glycine pretreatment.
Conclusion: The decrease of liver injury and improvement of liver function after pre-treatment with glycine suggests that glycine pre-treatment might be beneficial for living liver donors as well as for patients subjected to partial hepatectomy for other reasons.

P-1013 RAPAMYCIN INDUCED TUBULAR VACUOLIZATION: A NEW REPORT OF RAPAMYCIN NEPHROTOXICITY IN KIDNEY TRANSPLANT

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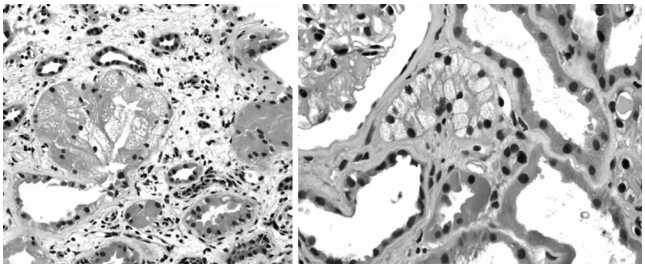
Rapamycin (Rapa) is an immunosuppressive agent that is increasingly used to replace calcineurin inhibitors (CNI) in case of CNI severe adverse effects (SAE) or CNI withdrawal/avoidance protocols. There is limited experience with Rapa clinically and pathologically at this time. Rapa has been reported to cause tubular injury, specifically, intratubular amorphous eosinophilic cast material, influx of histiocytes, and multinucleated giant cells. In this study, we report a severe isometric cytoplasmic vacuolization of the proximal tubules after Rapa therapy in two of our kidney transplant (ktx) patients.
The first patient (Pt #1) was HCV+, 30 year old (yo) African American male who had ESRD with unknown etiology. He received a 44 yo, HCV+ deceased donor (DD) kidney. The second patient (Pt #2) was a 62 yo white female with ESRD due to unknown etiology. She received a 62 yo old DD kidney. Both pts received Simulect for induction and were initially placed on tacrolimus, mycophenolic acid (MPA) and prednisone triple immunosuppression therapy. Both pts were switched to Rapa at 1 month and 5 month post transplant respectively due to new onset hyperglycemia and elevated serum creatinine levels (Pt #1, 2.3 mg/dl and Pt #2, 2.1 mg/dl). Both pts presented to our clinic with acute renal failure: Pt #1, 5 years and Pt #2, 5 months post ktx. Biopsy of transplanted kidney in both pts showed widespread severe isometric tubular cytoplasmic vacuolization and arterial hyalinosis.



Acute renal insufficiency improved after discontinuation of Rapa.
In these case reports, we introduce a new morphological appearance of tubular toxicity caused by Rapa. Isometric cytoplasmic vacuolization of the renal tubules, similar to that seen in CNI induced tubular toxicity and severe arterial hyalinosis can occur as early as two months or after long term rapamycin therapy.

P-1015 DIFFERING EFFECT OF HYPERBARIC OXYGEN THERAPY ON CYTOKINE EXPRESSION IN COLD STORED HEART AND LIVER TISSUES

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Background: Ischemia-reperfusion injury (IRI) remains a major stumbling block in organ transplantation. A number of studies have demonstrated that hyperbaric oxygen (HBO) therapy influences IRI and consequential acute cellular rejection. This study aimed to compare the levels of cytokine expression between cold stored heart and liver tissues under HBO and room air
Methods: 6-0 hearts and 50 livers were procured from male Lewis rats and submerged in cold (4°C) Histidine-Tryptophan-Ketoglutarate solution. Specimens were stored for periods of 4, 12, 16, 20, and 24 hours. 50% of organs were stored in room air, and 50% under 2.5 atmosphere absolute HBO. The levels of cytokine expression in the tissues were measured using multiplex assays.
Results: Tumor necrosis factor α (TNFα) was up-regulated in heart but down-regulated in liver tissues under HBO conditions. Anti-inflammatory cytokine, interleukin-6 (IL-6), was up-regulated for both hearts and livers under HBO (P=0.07). Interleukin-1α (IL-1α) and Interleukin-1β (IL-1β) had decreased expression in livers but increased expression in hearts stored under HBO.
Conclusion: This study demonstrates that the effect of HBO cold storage may be different depending upon organ type. These may represent important mechanisms by which HBO treatment impacts IRI in clinical settings. Further studies are needed to fully characterize the role of HBO therapy on the inflammatory aspects of IRI in liver tissues.

P-1016 DIFFERENCES BETWEEN LEVELS OF P-SELECTIN EXPRESSION IN COLD STORAGE OF KIDNEYS IN UNIVERSITY OF WISCONSIN AND HISTIDINE-TRYPTOPHAN-KETOGLUTARATE SOLUTIONS

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Background: The differences and efficacy of standard preservation solutions in kidney transplantation, University of Wisconsin (UW) and Histidine-Tryptophan-Ketoglutarate (HTK), are a matter of discourse in recent clinical studies. P-Selectins represent glycoproteins expressed on endothelial cells and platelets responsible for capture and transient adhesion of leucocytes to vascular endothelium, and activated platelets to leucocytes and endothelium, during ischemic-reperfusion injury (IRI) in kidneys. This study aimed to compare the levels of P-selectin expression between cold stored kidney tissues in UW and HTK solutions
Methods: Thirty kidneys were procured from male Lewis rats and stored in

cold (4°C) solutions for periods of 4, 12, 16, 20, and 24 hours. Group 1 (n=15) kidneys were stored in UW solution, and group 2 (n=15) kidneys were submerged in HTK solution. At the end of each time interval the kidneys underwent preparation and levels of P-Selectin expression in the tissues were measured using western blotting and readings quantified with a densitometer
Result: At all time intervals, P-Selectin expression was consistently down regulated, to statistically significant degree, in kidney tissues cold stored in UW solution as compared to HTK (P= 0.004)
Conclusion: The study demonstrates that UW solution offers a significant benefit, in terms of down-regulating P-Selectin expression, during cold storage. Consequentially, accumulation of neutrophils and propagation of IRI, in transplanted kidneys would be expected to be lower when stored in UW. Further studies are required to fully characterize the differences between these two most common solutions in kidney transplantation.

P-1017 MEASUREMENTS OF OXYGEN TENSION: AN IMPLICATION FOR STATIC ORGAN STORAGE IN TRANSPLANTATION

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Introduction: Optimizing organ storage prior to transplantation is critical to graft function and survival after implantation. The best storage environments minimize hypoxic tissue injury; little is known about which storage container is superior.
Methods: HTK and UW and three receptacles–a polypropylene cup (PC), a Ziploc bag (ZB), and a dialysis bag (DB) were chosen for the experiments. Six distinct trials were performed in the following combinations: HTK/ PC; UW/PC; HTK/ ZB; UW/ZB; HTK/ DB; UW/ DB. A probe designed to measure oxygen tension was placed into each solution and corresponding receptacle. Measurements were taken at 0, 4, 12, 16, 20 and 24 hours. At each time point two measurements were taken and a mean value was used for statistical analysis.
Results: Mean oxygen concentration after 24 hours was significantly higher in UW (106.4%) than HTK (100.6%) solution (p-value <0.01). On the other hand, mean concentration was 110.0%, 106.4% and 97.7% in PC, DB and ZB, respectively (p-value 0.01). When compared combined effect of solution and container, UW solution in PC retained highest concentration of oxygen 117.8% (p-value <0.001). The linear regression model showed that using HTK solution instead of UW will decrease oxygen concentration by 8.3% and using ZB or DB instead of PC will decrease oxygen concentration by 12.3% or 3.6% respectively.
Conclusion: We identified that UW solution in a PC demonstrated the best oxygen tension over time. These findings suggest that this solution-container combination may aid in amelioration of hypoxic injury associated with organ static storage. Further studies are warranted to address effects of additional factors such as optimal storage temperature, pressure and role of organ perfusion during storage.

P-1018 DIFFERENTIAL SCANNING CALORIMETRY, AS A NEW METHOD TO MEASURE THE STRUCTURAL INJURY DURING INTESTINAL AUTOTRANSPLANTATION

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The aim of the present work was to compare the conventional histology and Differential Scanning Calorimetry (DSC) method by measuring structural changes in bowel following experimental intestinal autotransplantation.
Small bowel has been stored in cold University of Wisconsin solution for 1 (GI), 2 (GII), 3 (GIII), and 6 hours (GIV) in Wistar rats (n=20). Reperfusion lasted 3 hours in all groups. Bowel biopsies were collected after laparotomy, at the end of the ischemia and reperfusion periods. Tissue damage evaluated on hematoxylin/eosin-stained sections and they were analyzed by quantitatively. Thermal consequences of structural changes of mucosa, muscular layer and total intestinal wall were detected by DSC.
In GI histological findings were corresponded to an injury grade 2, showing minor clefting with the villus epithelium adjacent to the crypts intact. In GII the injury was grade 2 also. In GIII showed grade 3 injury with epithelial lifting and villus tip denudation. In GIV injury was serious (grade 5), characterized by severe destruction in mucosal thickness, denudation of villi and lesion in crypts, which was further deteriorated by the end of the reperfusion. These changes were significant by quantitative analysis ($p<0.05$). According to DSC data, in GI the transition temperature (Tm) stained in control level in mucosa, but the calorimetric enthalpy decreased by 30%. In GII it was half of the control one. In GIII-GIV Tm significantly decreased in mucosa ($p<0.05$), but unchanged in muscle and in the total intestinal wall. Calorimetric enthalpy decreased less than in GI or GII.
In present work DSC showed more exact results about bowel structural changes in the mucosa and in the muscular layer than conventional histology following autotransplantation. (Supported by OTKA PD77474, Bolyai Scholarship of the Hungarian Academic of Science)

P-1019 INFLUENCE OF SIROLIMUS ON CYCLOSPORINE-INDUCED PANCREATIC BETA-CELL DYSFUNCTION

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Background: Sirolimus (SRL) is a promising immunosuppressive agent that is replacing calcineurin inhibitors. This study was performed to investigate the effect of SRL on cyclosporine (CsA)-induced pancreatic injury in rats.
Methods: Three separate studies were preformed. First, diabetogenic effect of SRL was evaluated with three different doses (0.15, 0.3 and 0.6 mg/kg). Second, rats were treated with SRL (0.3 mg/kg) with or without CsA (15 mg/kg) for 4 weeks. Third, rats were treated with CsA for 4 weeks, and then switched to SRL for 4 weeks. The effect of SRL on CsA-induced pancreatic injury was evaluated by an intraperitoneal glucose tolerance test, plasma insulin concentration, HbA1c level, HOMA-R index, immunohistochemistry of insulin, and pancreatic b islet cell mass.
Results: SRL treatment increased blood glucose levels in a dose-dependent manner. The combined treatment with SRL and CsA markedly increased blood glucose concentration, HbA1c level, HOMA-R index and decreased plasma insulin concentration, immunoreactivity of insulin and pancreatic b islet cell mass compared with rats treated with CsA. CsA withdrawal for 4 weeks improved pancreatic b-cell function and structure. However, conversion from CsA to SRL further increased blood glucose levels compared with the rats converted from vehicle to SRL.
Conclusions: The results of our study demonstrate that SRL is diabetogenic and aggravates CsA-induced pancreatic injury.

P-1020 ORAL ADSORBENT AST-120 DECREASE THE CHRONIC CYCLOSPORIN NEPHROTOXICITY BY DECREASING OXIDATIVE STRESS

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Background: AST-120 (Kremezin®) is widely used in chronic kidney disease, but the effect of AST-120 on the progression of chronic allograft nephropathy is undetermined. Our aim is to evaluat the effects of AST-120 on the chronic cyclosporine nephropathy.
Materials and methods: Adult Sprague-Dawley rats were treated daily for 4 weeks with vehicle (olive oil, 1 ml/kg), CsA (15 mg/kg), AST-120 (5% in diet) and both CsA and AST-120. The effect of AST-120 on CsA-induced renal injury was evaluated with renal function, histopathology and measuring oxidative stress with urinary 8-OHdG excretion and 8-OHdG expression in renal tissues. We measured serum indoxyl sulfate levels, a marker of uremic toxins by HPLC.
Results: Creatinine clearance in the CsA group were lower than VH group ($P < 0.05$), but concomitant treatment of AST-120 and CsA significantly increased creatinine clerance (0.27 ± 0.05 vs 0.38 ± 0.10 ml/min/100g, $p<0.05$). In addition, AST-120 attenuates interstitial fibrosis, macrophage infiltration and apoptotic cell death in the CsA treated rat kidney. Quantitative analysis revealed that CsA induced marked upregulation of βig-h3 (fivefold) and caspase-3 protein (twofold), whereas there were reduced significantly by concomitant treatment of AST-120. The urinary 8-OHdG concentrations and intrarenal 8-OHDG expression were significantly increased in the CsA group, but AST-120 treatment decreased these markers of oxidative stress. The concentration of indoxyl sulfate significantly increased in CsA treated rats compared to VH group ($p < 0.001$), AST-120 reduced the serum concentration of Indoxyl sulfate in CsA treated rats (5.87 ± 1.65 g/dL versus 0.87 ± 0.16 g/dL, $p<0.05$).
Conclusions: Oral adsorbent AST-120 plays a protective effect on the chronic CsA nephrotoxicity, and these effects may be mediated by decreasing indoxyl sulfate, which is now being recognized as a mediator of oxidative stress.

P-1021 REPERFUSION INJURY TO STEATOTIC RAT LIVERS AFTER TRANSPLANTATION CAN BE ATTENUATED WITH A MODIFIED HTK SOLUTION

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Background: Ischemia/reperfusion injury (IRI) is still an obstacle especially in

fatty livers. Most recently a modified histidine-tryptophan-ketoglutarate (HTK) solution, Custodiol-N, has been developed. This solution contains N-acetyl-histidine as buffer, the amino acids aspartate, glycine, alanine, and arginine to limit ischemic injury and to improve reperfusion and the iron chelators deferoxamine and LK 614 to inhibit cold-induced cell injury. This study was designed to test the effects of Custodiol-N on IRI to fatty livers in a rat liver transplantation model.
Methods: Moderate steatosis was induced by a single dose of ethanol (8 g/kg BW) to female Sprague-Dawley (SD) donor rats 20h before organ harvest. Livers were harvested and cold stored at 4°C for 8 hours with either HTK solution or Custodiol-N before transplantation. Serum transaminases and histology were compared at 1h, 8h and 24h after reperfusion (n=8 animals per group). Survival was compared after 7 days.
Results: Custodiol-N significantly improved permanent survival from 12.5% in controls to 87.5% after 7 days. Further, Custodiol-N decreased the release of AST, ALT and LDH to up to 25% (e.g. AST after 24h 14456±11493 vs. 4584±2340) of controls ($p<0.05$). These results were confirmed by histology.
Conclusions: These results clearly demonstrate that Custodiol-N is superior to the traditional HTK solution in experimental fatty liver transplantation.

P-1022 ENHANCING THE PRESERVATION CONDITION OF ISCHAEMICALLY DAMAGED KIDNEYS: THE ROLE OF A SHORT PERIOD OF NORMOTHERMIC PRESERVATION

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Introduction: Enhancing the preservation condition of ischaemically damaged kidneys by including a short period of normothermic preservation (NP) after hypothermic machine preservation (HMP) may reduce the level of ischaemia reperfusion (I/R) injury and improve graft function. This study assessed the role of a short period of NP in a porcine autotransplant model of donation after cardiac death (DCD) donor kidneys.
Methods: Kidneys were subjected to 35 minutes of warm ischaemia then preserved by HMP for 22h or 20h followed by 2h of NP using autologous blood. Kidneys were then re-implanted, a contralateral nephrectomy performed and renal function measured over 10 days.
Results: Post-transplant, 4/6 animals survived in the NP group compared to 5/6 in the HMP group (P=1.00). Creatinine (Cr) levels fell below 250$_{\mu}$mol/L in the 4 surviving animals in the NP group compared to 2/5 of the HMP group (P = 0.608). There was no significant difference in the level of peak Cr [HMP;1736±866, NP;1553±516$_{\mu}$mol/L; P=>0.05]. There was no difference in plasma levels of IL-6, TNFα or protein carbonyl post transplantation between the groups (P = >0.05). Levels of lipid peroxidation were significantly lower 60 minutes post transplant in the NP group (NP; 477.5±118.0, HMP; 671.1±99.4; P = 0.026).
Conclusion: A short period of NP after HMP did not have any deleterious effects on post transplant renal function. There was no additional benefit in graft survival or function however there appeared to be some reduction in the level of I/R injury in the acute post transplant phase. NP has the potential to be used a devise to allow pre-transplant modification of organs and ameliorate I/R injury.

P-1023 MACHINE PERFUSION OF KIDNEYS FROM HEART BEATING DONORS FROM EMILIA-ROMAGNA REGION. A PILOT STUDY

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Purpose: Machine perfusion of kidneys retrieved from cadaveric donors can reduce the incidence of delayed graft function (DGF) and primary non function, improving graft survival. Aim of the study was to assess the feasibility of using kidney perfusion machine devices in Emilia-Romagna region (ERR).
Methods: From September to December 2008 15 consecutive heart beating cadaveric donors (6 M, 9 F) were enrolled. Mean donor age was 57 years (18-72), mean donor serum creatinine was 0.79 mg/dl (0.2-1.3). Eleven donors (73%) met the expanded donor criteria (ECD): 8 because older than 60, 4 of whom were also hypertensive, and 3 for hypertension. In 8 donors a biopsy was done with a mean score of 3.5 (Karpinski). LifePort™ devices were used by one expert surgeon. Mean perfusion time was 10.4 hours. During the enrollement 4 further surgeons were trained.
Result: Out of 30 retrieved kidneys, 4 were not perfused due to difficulties in the artery incannulation for atherosclerotic lesions. Three of the 26 perfused kidneys were discharged: 1 for diffuse atherosclerotic lesion, 2 for lesions following the biopsy. 23 kidneys were transplanted (18 single kidney, 2 double kidney, 1 kidney-liver transplant). Seven patients (30%) showed DGF. Mean number of dialysis sessions was 2.2. All patients recovered renal function except one who underwent transplantectomy. One patient died for heart failure with a functioning graft.
Conclusion: This study showed that the use of kidney perfusion devices is feasible and safe. No kidney was lost for issues related to the procedure. The incidence and the short period of DGF, considered the high percentage of ECD donors in our study, suggest that these devices are useful in preventing/reducing the ischemia-reperfusion injury and might display their benefit especially when cold ischemia time is prolonged.

P-1024 DANSHEN IMPROVES HEPATIC MICROPERFUSION AFTER WARM ISCHEMIA IN RAT

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Background: Danshen, a potent antioxidant, has been used to treat a variety of ischemic diseases. Since oxidative stress plays the pivotal role in the pathophysiology of reperfusion injury, this study was designed to investigate the effects of Danshen on liver after warm ischemia.
Methods: Sprague-Dawley rats (230-250g) were given 1.5 ml Danshen (1.5g Danshen/ml; i.v.) 10 min before 90 min of warm ischemia to the left liver lobe. Controls were given Ringer's solution. Transaminases, histology, *in vivo* microscopy (IVM), and immunohistochemistry were performed to index liver injury and to compare the expression of tumor necrosis factor-alpha (TNF-α), superoxide dismutase (SOD) and inducible nitric oxide synthase (iNOS) after reperfusion. One-way analysis of variance (ANOVA) or Fisher's exact test were used as appropriate. Results are presented as mean ± SEM.
Results: Danshen decreased ALT, AST, and LDH at 2 hrs and 6 hrs after reperfusion by 40-55% and 58-70%, respectively ($p<0.05$). Further, the expression of TNF-α was reduced by 33% of controls while expression of iNOS and SOD increased to 136% and 139%, respectively ($p<0.05$). Danshen markedly improved hepatic microperfusion in both sinusoids and venules ($p<0.05$) while both phagocytic activity of Kupffer cells and the leukocyte-endothelium interaction were significantly reduced.
Conclusion: This study demonstrates that Danshen decreases liver injury after warm ischemia via mechanisms including hepatic microcirculation and Kupffer cells.

P-1025 REDUCED GLUTATHIONE AS ANTIOXIDANT IN COMMERCIALLY AVAILABLE PRESERVATION SOLUTIONS: FABLE OR FACT?

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Reduced glutathione (GSH) -a radical scavenger- is added to organ preservation solutions such as UW, KPS-1 and Celsior in order to reduce reactive oxygen species (ROS) generated during ischemia/reperfusion injury. Nevertheless, at the time of clinical use UW does not contain GSH anymore, because of its rapid conversion into oxidized glutathione (GSSG). This has not been reported for KPS-1 and Celsior. Therefore, we have determined in UW, KPS-1 and Celsior i) the amount of GSH and ii) the time-frame of oxidation of GSH.
Methods: Total amount of glutathione GSHt (GSH + GSSG) and GSSG were determined in different bags of UW (n=6), KPS-1 (n=6) and Celsior (n=4) at 4°C. The half-life of GSH was determined by adding 2mmol/l GSH to each preservation solution and free thiols were subsequently measured using the recycling test, at 4°C at different points of time.

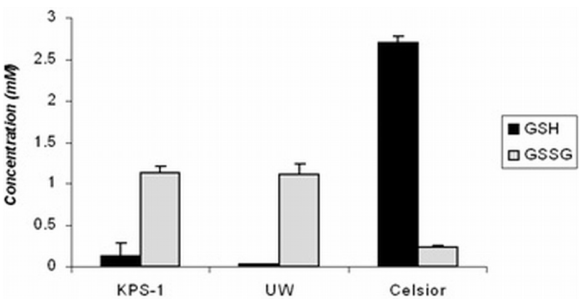
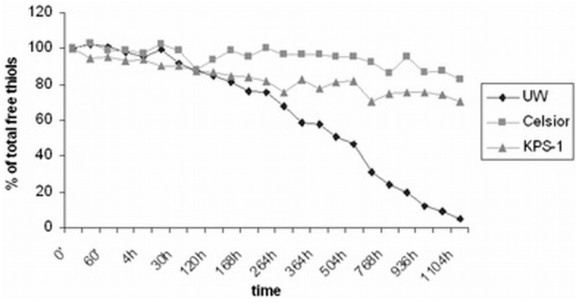


Figure 1. GSH and GSSG in KPS-1, UW and Celsior.

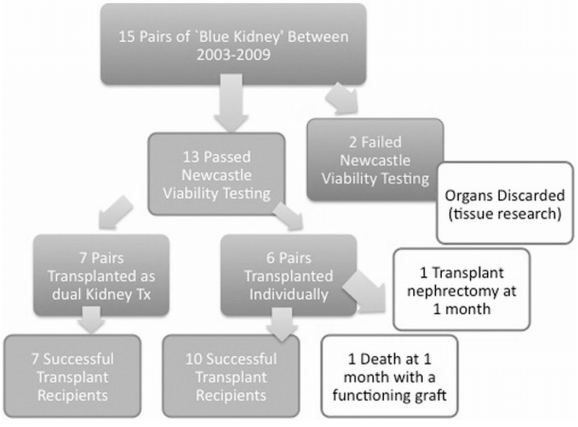


Results: GSHt concentration is approximately 2 mmol/l in all 3 solutions. KPS-1 and UW do no longer contain GSH. By contrast, Celsior contains 1.76 mmol/l GSH (80% of GSHt). Forty-two days after adding GSH, its concentration dropped to 5% in UW, by contrast to 74% and 87% in KPS-1 and Celsior respectively. Half-life of GSH in UW is 18 days.
Conclusion: Addition of GSH at the time of *production* of UW and KPS-1 seems not justified since all GSH will be oxidized by the time of clinical use. GSH appears to be more stable in Celsior. Mannitol might act as a stabilisator of GSH in KPS-1 and Celsior. However, even in Celsior GSH has already been oxidized long before expiry date. We recommend i) GSH to be added to preservation solutions *directly* before clinical use and ii) more potent stabilizing agent than mannitol to be added to preservation solutions.

P-1026 POOR PERFUSION OF RETRIEVED KIDNEYS FROM NON-HEART-BEATING DONORS – THE IMPACT OF MACHINE PERFUSION

Christopher Ray[1], Aditya Kanwar[1], Susan Stamp[2], Soroush Sohrabi[1], Mohamed-Saleem Noormohamed[1], Alex Navarro[1], Noel Carter[3], Anne Cunningham[3], Brian Shenton[2], David Talbot[1]. *[1]Liver and Renal Transplant Unit, Freeman Hospital, Newcastle Upon Tyne, United Kingdom; [2]Surgical and Reproductive Sciences, University of Newcastle-Upon-Tyne, Newcastle Upon Tyne, United Kingdom; [3]Institute of Pharmacy, Health and Wellbeing, University of Sunderland, Sunderland, United Kingdom*

Aims: To highlight the efficiency of hypothermic machine perfusion in salvaging organs that would otherwise have been discarded.
Methods: A retrospective search of the units' non-heart-beating database was conducted. The donor records between January 2003 and January 2009 were searched for reports of kidneys appearing blue, mottled or ill-perfused at retrieval. Maastricht category II and III included.
The data for Newcastle viability testing was examined and the outcome of each organ traced, via the local database and hospital records. The primary end points were passing the viability testing, subsequent transplantation and success rate.
Results: There were 15 cases of kidneys reported as blue at retrieval. These were all subjected to Newcastle viability testing. A perfusion flow index was calculated and GST samples measured at hourly intervals for 4 hours. 2 pairs of kidneys failed to pass viability testing. Of the 13 pairs that passed, 7 were successfully transplanted as dual transplants. The remaining 6 pairs were implanted as single grafts. Of these 12 single grafts, one patient died at one month with a functioning graft and one patient underwent transplant nephrectomy at 1 month secondary to renal vein thrombosis.



The others transplants were all successful.
Conclusion: By perfusing the whole organ effectively, machine perfusion converts what would traditionally have been deemed marginal or unusable organs into successful transplants.

P-1027 ESTABLISHING A BRAIN DEATH DONOR MODEL IN PIGS

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Introduction: Several factors influencing organ quality and recipient survival after multiorgan donation and transplantation are still unknown and difficult to investigate in humans. Therefore the need for an animal model that imitates human conditions might be useful not only to be able to monitor pathomechanisms of brain death and biochemical cascades in the organisms after brain death but also to be able to investigate novel strategies to ameliorate organ quality and functionality after multiorgan donation. Therefore the aim of this study was to establish a brain death donor model in pigs.
Methods: 15 pigs were used for these experiments. Brain death was induced by inserting a catheter into the intracranial space after trepanation of the skull and augmenting intracranial pressure until brain stem herniation occurred. Intracranial pressure was monitored continuously and after 60 min brain death diagnostics was performed by a neurologist including EEG examination and clinical examination. Donor care was performed according to standard guidelines and after 24 h of brain death and intensive care multiorgan donation was performed.
Results: All 15 animals showed typical signs of brain death such as diabetes insipidus, hypertensive and hypotensive periods and tachycardia. All symptoms could be treated using standard medication. After 24 h hours of brain death successful multiorgan donation was performed. After organ retrieval, abdominal and thoracic organs could be analysed for tissue damage and organ quality.
Discussion: According to standard guidelines brain death diagnostic was performed, 0 line EEG occurred in all animals 60 min after brain death induction. Using this method, a suitable brain death donor model could be establish that will enable us not only to investigate in detail effects and pathophysiology after occurrence of brain death but also to evaluate new strategies to ameliorate organ quality and even to enlarge the donor pool for multiorgan donation.

P-1028 AUTOANTIBODIES AGAINST APOLIPOPROTEIN H (B2GPI) IN RENAL TRANSPLANT PATIENTS

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The immune system intervenes in a significant way in the genesis of the transplant vasculopathy by the presence of diverse autoantiboides related to the vascular damage.
The aim of this study was to determine the effect of the presence of autoantibodies anti-B2GPI (blocking blood coagulation) upon diverse clinical parameters in a population of kidney transplanted patients.
Levels of autoantibodies anti-B2GPI of classes IgA, IgM and IgG were analyzed by ELISA in a cohort of 176 kidney transplanted patients and a control group of 80 healthy subjects. We collected several data concerning the cardiovascular status of the patients, like age, sex, D.M., CTN confirmed by biopsy, ischemic cardiopathy, proteinuria, MDRD, cholesterol, triglycerides, HCV infection and systolic/diastolic arterial pressure.
The proportion of patients presenting high levels of anti-B2GPI autoantibodies of classes IgG and IgM does not differ significantly from the one found in the control group, whereas the difference becomes significant for the case of anti-B2GPI IgA autoantibodies ($p<0.05$) (see the table below).

Differences in autoantibodies against Apolipoprotein H (B2GPI) between controls and transplanted patients

Antibody	Control group	Transplanted patients
Anti-B2GPI IgG	0,79%	5/176 (2,84%)
Anti-B2GPI IgM	0,84%	2/176 (1,14%)
Anti-B2GPI IgA	0,90%	35/176 (19,88%)

In a multivariate analysis, the only clinical data associated factor with high levels of anti-B2GPI IgA autoantibodies was the presence of proteinuria.
In summary, levels of anti-B2GPI IgA autoantibodies are elevated in renal transplant patients and seems to be associated with proteinuria. These results deserves further investigation.

P-1029 PROTECTIVE EFFECT OF PARENTERAL VITAMIN E ON ISCHEMIA-REPERFUSION RENAL INJURY IN RABBITS

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To evaluate the effect of parenteral vitamin E on renal ischemia-reperfusion injury, 20 German rabbits weighting 1.5-1.9 kg were selected and divided into 2 case and control groups. Each group contained 5 male and 5 female rabbits. Intravenous vitamin E is administered to case group five minutes before left renal artery clamping and the same volume of normal saline was injected to control group. Ischemia was maintained for 60 minutes. After 48 hours nephrectomy was performed and kidneys were sent to pathology laboratory. Histopathologic sections were evaluated by the pathologist and graded by the extent of tissue injury to normal, mild and mode rate to severe injury. Histopathologic evaluation of the sections revealed that in control group 50% of sections had signs of moderate to severe injury and 50% categorized as mild injury whereas 50% of case group sections developed no sign of ischemia-reperfusion injury and 50% developed mild injury (p value=0.033). There is also no significant correlation was found between sex and the extent of cell injury (p value=0.99). In conclusion, Parenteral injection of vitamin E significantly protects cells against ischemia reperfusion injury.

P-1030 PORCINE MODEL OF EXTRA-CORPOREAL MEMBRANE OXYGENATION (ECMO) IN THE UNCONTROLLED NON-HEART BEATING DONOR; THE EFFECT ON RENAL VIABILITY

Christopher Ray[1], Aditya Kanwar[1], Mohamed-Saleem Noormohamed[1], Soroush Sohrabi[1], Stephen Ray[1], Alex Navarro[1], Susan Stamp[1], Hugh Wyrley-Birch[2], Noel Carter[3], Anne Cunningham[3], Brian Shenton[2], Jon Smith[1], Steven White[1], David Talbot[1]. *[1]Liver and Renal Transplant Unit, Freeman Hospital, Newcastle Upon Tyne, United Kingdom; [2]Surgical and Reproductive Sciences, University of Newcastle-Upon-Tyne, Newcastle Upon Tyne, United Kingdom; [3]Institute of Pharmacy, Health and Wellbeing, Sunderland University, Sunderland, United Kingdom*

Aims: We sought to compare the effect of ECMO on organ viability, with our current standard; intravascular flush and intra-peritoneal cooling.
Methods: Using cross-Yorkshire-landrace pigs (n=11), we studied 2 groups. Under general anaesthetic, an initial laparotomy for probe placement and cannulation was performed. All animals were euthanased, and subjected to 30mins of warm ischaemia. In the 'Cooling' group (n=5), thrombolysis and intravascular flush was administered, with peritoneal cooling over a 2-hour period. In the 'ECMO' group (n=6), thrombolysis was administered, then a primed extra-corporeal oxygenation circuit was commenced after 30mins of cardiac standstill. The abdominal organs were perfused with oxygenated normothermic blood for 2hours.
After this 2-hour period, the abdomen was re-opened, iced and organs retrieved. Throughout the period of intervention microdialysis catheters in the solid organs measured ischaemic markers.
The kidneys underwent viability testing on cold machine perfusion (Lifeport) for 2-hours. Thereafter they were each re-perfused on an ex-vivo oxygenation circuit to simulate transplantation and re-animation. The circuit was purpose built and allowed further assessment of viability.
Results: During re-animation on the ex-vivo circuit, oxygen consumption, as an indicator of metabolic acitivity and damage, was calculated. Ischaemic damage and oxygen debt appeared to result in polyuria and high oxygen consumption.
Significant difference in 02-consumption reached at 2-hrs in the short-CIT group (Mann-Whitney-U z= -2.1; $p<0.05$). Microdialysis samples of tissue biochemistry look set to confirm this, but at the time of writing are still under analysis (the experiments only being completed a week henceforth).
Other results pending are biochemical analysis of glutathione-S-transferase, electron microscopy of tissues and gene-chip analysis.
Conclusion: Final summary conclusions are too early to be drawn at this stage given the bulk of data under analysis. Definitive answers will be attained and updated well in advance of presentation dates.

P-1031 GENDER AS PREDISPOSING FACTOR TO LIVER REGENERATION BY HEPATIC PROGENITOR CELLS PROLIFERATION AND STELLATE CELL ACTIVATION IN A MURINE MODEL OF ACUTE LIVER INJURY

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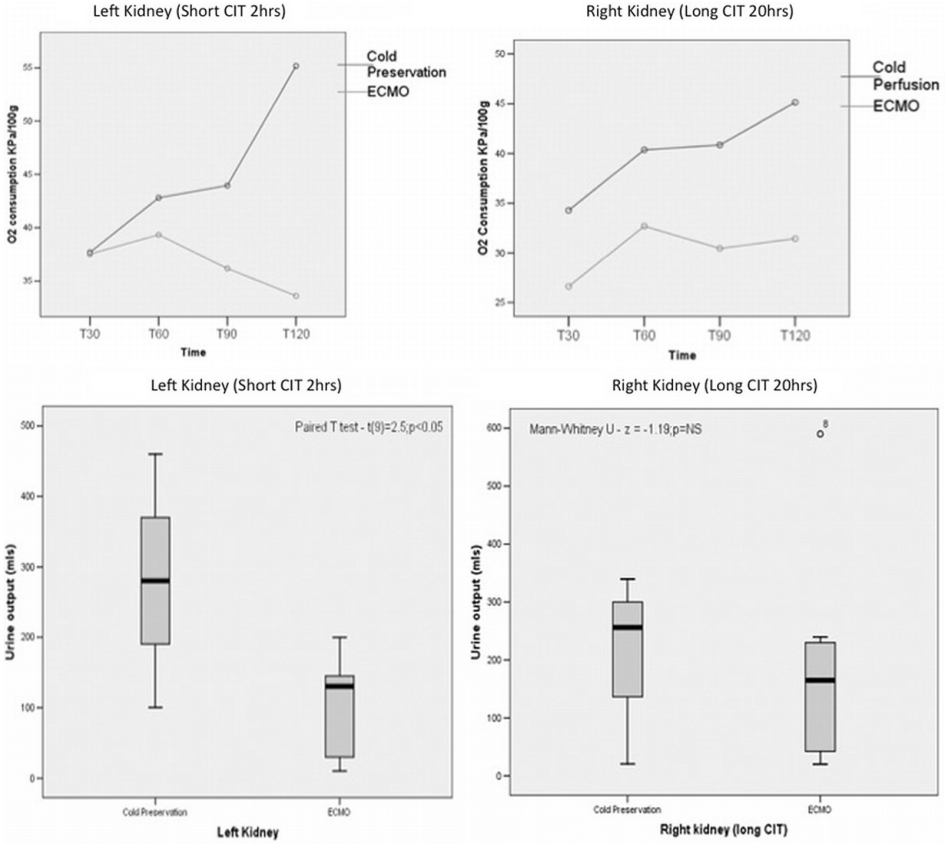
Purpose: It's known a substantial difference between gender in incidence of



Abstract P-1030 – Figure 1

acute and chronic liver disease. The aim of this study was to evaluate liver regeneration due to hepatic progenitor cells (PCs) proliferation and hepatic stellate activation in a murine model of acute liver injury.
Materials/Methods: The acute liver damage was induced in groups of males and females BALB/c mice aging 8 weeks by CCl4 administration (0.75ml/kg) associated or not with Monocrotaline (50mg/kg). The male (groups1-4) and females (groups5-8) animals were sacrificed at 24h (groups1, 3, 5, 7) or 8 days (group2, 4, 6, 8) after CCl4administration. To evaluate the liver damage, biohumoral (total and fractional bilirubin, ALT, AST, GGT), histological (haematoxylin-eosin and Masson-trichromic stains) and immunohistochemical markers (cytokeratin, αSMA) have been considered.
Results: After 24h and 8 days since CCl4 administration, in male groups not significant difference was seen in relation to administration of Monocrotaline. The damage at 24h was characterized by centrolobular necrosis, at 8 days by areas referable to activated macrophages and initial deposit of collagen. In female groups sacrificed at 24h, damage was similar although the necrosis was less defined. After 8 days activated macrophages were not visible and in Group6 (treated with Monocrotaline) remained limited areas of necrosis. Expression of αSMA was similar in all groups, while those of cytokeratin was higher in the female group treated with Monocrotaline and sacrificed at 8 days after damage.
Conclusions: Histology evaluation shown a substantial difference between genders as in PCs proliferation but similar activation of stellate cells and collagen deposition. The histological difference between gender is not reflected in a statistically significant difference in the values of blood markers considered.

P-1032 IS A LOW K^+ ORGAN PRESERVATION SOLUTION BETTER FOR VASCULAR ENDOTHELIUM?

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Purpose: To evaluate a novel organ preservation solution with low K^+ concentration using aortic ring baths in a rodent Non-Heart Beating Donor model.
Methods: In Non-heart beating rats, after an hour of primary warm ischemia abdominal aorta was flushed with streptokinase (3500 IU). This was followed by intra-arterial cooling with a mixture of cold HTK (20 ml) and heparin (200U). Aorta was dissected out and 3-5mms thoracic aortic sections were cold stored (24hrs) in three different preservation solutions. Normal saline was used as a control. Of the three preservation solutions, one was the standard kidney preservation solution (KPS1, K^+25mmol/l). The other two contained low K^+ levels. One was a KPS1 variant (SK-5, K^+5mmol/l), and the other was a non-renal Organ Preservation Solution (nrOPS, K^+6mmol/l). After cold storage the aortic rings were stretched between two points, one containing a pressure transducer probe. The rings were then immersed in 10mls of Krebs-Henseleit solution and gassed with carbogen (95% Air/5%CO_2) at 37°C and 7.4±0.5 pH. Graduated doses of phenylepherine and acetylcholine were added to measure the contraction and endothelium dependant relaxation. Contraction/relaxation profiles of the solutions were compared using ANOVA (with Bonferroni).
Results: 10 male wistar rats provided aortic rings to allow simultaneous comparisons between solutions. The maximal mean contraction was higher for SK-5 (71%) and KPS1 (73%) in comparison to nrOPS (25%) ($p<0.05$) and control (5%) ($p<0.001$). Overall relaxation (endothelial dependant) was significantly different within the groups; $F(3,27)=9.353$; $p<0.001$. SK5 produced a superior relaxation profile (end relaxation 20.2%) ($p<0.05$) as opposed to either nrOPS (end relaxation 1.5%) or control (end relaxation -6.9%). KPS1 had a relaxation profile in between SK5 and nrOPS, but it wasn't significantly different.
Conclusion: Therefore endothelial function would appear to be slightly better with SK5 as opposed to more standard K^+ levels in normal KPS1.

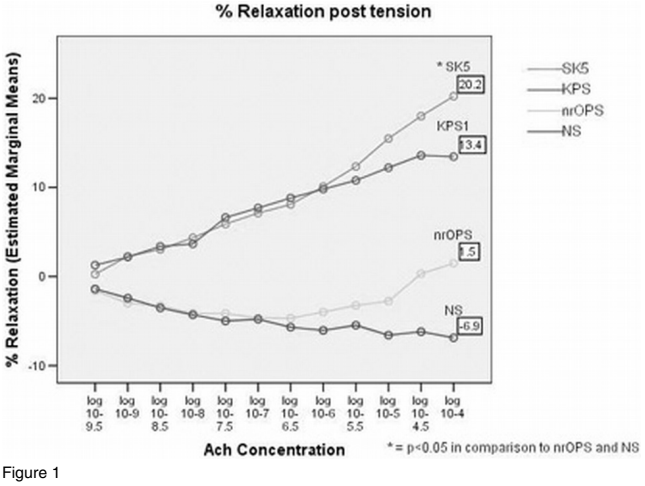

Figure 1

P-1033 DEFINING THE LIMITS OF WARM ISCHAEMIA IN A PORCINE MODEL – PRELIMINARY REPORT

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Purpose: Prolonged warm ischaemia of the donor kidney has significant adverse effects in transplantation, however, the limits of critical warm ischaemia (WI) is unknown. This study aimed to assess the biochemical effects and limits of WI using Microdialysis markers and serum creatinine in a porcine model.
Methods: The left renal artery of 14 female wild-white pigs (45-75 kg) was clamped for 60, 90, 120 and 180 minutes. Left renal urine output was verified by t-tube ureterostomy. A right nephrectomy was performed on day 7 after repeating the WI simulation for the same duration. A microdialysis probe was inserted in the cortex 30 minutes before clamping. Microdialysis samples collected via Microdialysis catheter (CMA 63, Sweden) at 15 minutes intervals before, during and after clamping. Samples were analysed for glucose, pyruvate, lactate and glycerol concentrations (CMA 600 Analyser, Lab Model, Sweden). Serum creatinine was monitored and recovery of left kidney was defined as the serum creatinine concentration returning to within +50% of baseline by 4 weeks.
Results: Left kidney produced urine for all WI times. Glucose concentrations fell with WI time becoming minimal at 45-60 minutes. After reperfusion all kidneys, regardless of WIT began to utilise glucose after 45 minutes.

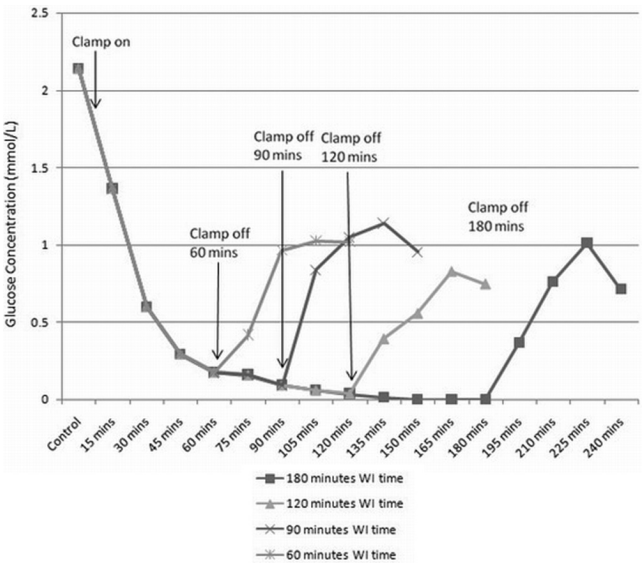
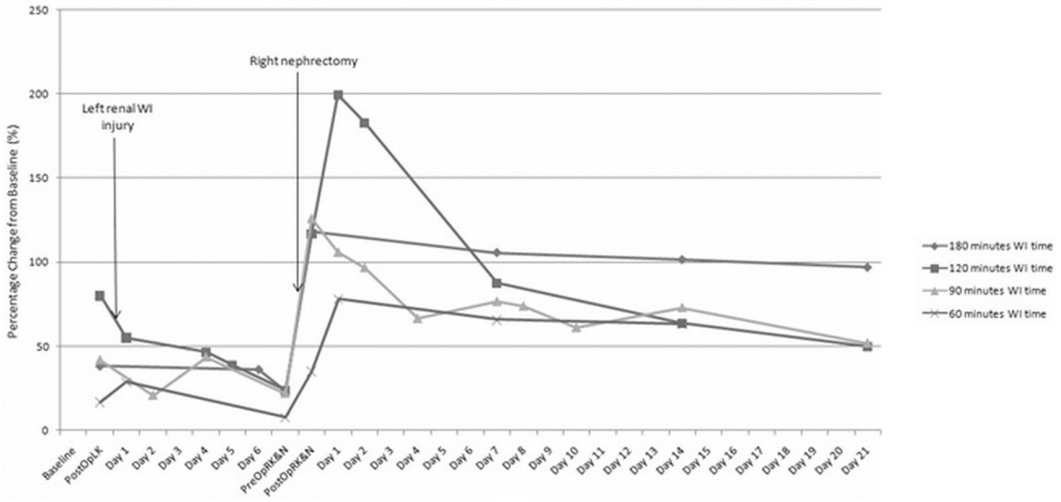


Figure 1. Microdialysis: Mean glucose concentration.

Glycerol concentration and lactate/pyruvate ratio increased with WI time and decreased during reperfusion (not shown).
For kidneys exposed to 60, 90, 120 minutes of WIT, the kidneys recovered within 4 weeks after injury but not in those exposed to 180 minutes of WIT.
Conclusion: Cell metabolic activity evidenced by glucose utilisation was present even after 180 minutes of renal WI. Serum Creatinine recovered to within +50% of baseline up to 120 minutes of renal WI, but not after 180 minutes. Urine output and biochemical markers were not diagnostic of failure to recover.

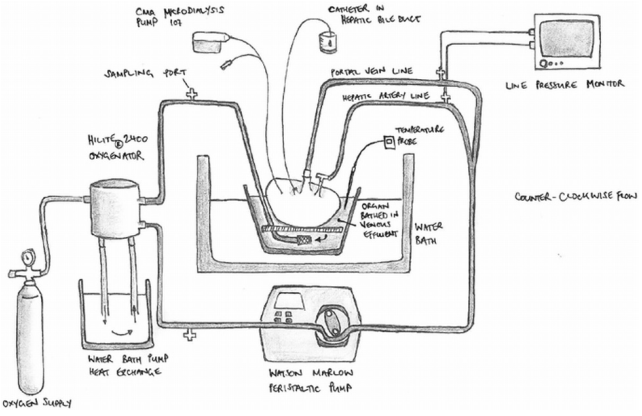


Abstract P-1033 – Figure 2. Percentage change in mean serum creatinine from baseline.

P-1034 A SIMPLIFIED CIRCUIT DESIGN FOR OXYGENATED SANGUINOUS PERFUSION OF THE NON-HEART-BEATING DONOR LIVER, KIDNEY AND PANCREAS

Christopher Ray[1], Aditya Kanwar[1], Mohamed-Saleem Noormohamed[1], Soroush Sohrabi[1], Stephen Ray[1], Alex Navarro[1], Susan Stamp[2], Noel Carter[3], Anne Cunningham[3], Brian Shenton[2], Jon Smith[1], Steven White[1], David Talbot[1]. *[1]Liver and Renal Transplant Unit, Freeman Hospital, Newcastle Upon Tyne, United Kingdom; [2]Surgical and Reproductive Sciences, University of Newcastle-Upon-Tyne, Newcastle Upon Tyne, United Kingdom; [3]Institute of Pharmacy, Health and Wellbeing, University of Sunderland, Sunderland, United Kingdom*

Aims: We designed a simplified closed-circuit construct to re-animate liver, kidney and pancreas to simulate re-animation and allow for comparative viability testing.
Methods: We designed a novel circuit that can be quickly adapted for normothermic sanguinous perfusion of the liver, kidney or pancreas.



This was used as a transplant surrogate for organs and to allow viability testing. A closed system was employed, thereby negating the need for a reservoir, and as such simplifying both the design and operation of the circuit.
Pulsatile flow was delivered to the organs at physiological rates. Pressure changes were recorded as markers of vascular resistance and organ health. The organs were perfused with a mixture of whole blood and RS-I (Aqix©) solution in a ratio of 1:5 respectively, with the addition of heparin.
Simple changes in connectors and exclusion of the second organ inflow limb (for hepatic perfusion) allows for perfusion of various organs with disparate vessel calibres.
Sampling ports were used to collect blood for ABG analysis. Microdialysis catheters were inserted into the organs to capture real-time markers of ischaemia.

Kidneys (n=22)			Liver (n=11)	
	Short Cold Ischaemic Time (2hrs) n=11	Long Cold Ischaemic Time (20hrs) n=11		Short Cold Ischaemic Time (30mins)
Mean Urine Output (ml)	**168** (Range 10 - 460)	**233** (Range 20 - 590)	Mean Bile Output (ml)	**1.15** (Range 0 - 7.5)
	Sign test; p-value < 0.05			
Oxygen Consumption (kPa/100g)	**39.5**	**36.0**	Oxygen Consumption (kPa/100g)	**4.9** (Range 2.6 - 7.1)
	Paired t-test; p-value; NS			

Serum markers of ischaemic damage (GST) and markers of metabolic activity in the liver (lidocaine:MEGX) and pancreas (glucose:insulin) were measured. Urine output and bile production were also recorded.
Results: Evidence of cellular metabolic activity was present in all the organs studied, despite a 30min period of absolute warm ischaemia and 2 hours of 'relative' warm ischaemia.
Conclusion: The circuit is a simple design that allows sanguinous organ re-animation and viability testing. We present a streamlined design that is easily re-produced and readily adaptable for re-perfusion of kidneys, liver and pancreas.

P-1035 ORGAN DONATION IN SWITZERLAND: IMPACT OF THE NEW LAW ON TRANSPORTS AND COLD ISCHEMIA TIME

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Swisstransplant, Bern, Switzerland

Background: On July 2007 the new transplantation law came into force. The principal item of this new law is the change from center-oriented to patient-oriented national allocations of organs. Aim of the present study is to analyse the impact of the new law on transports and cold ischemia time (CIT).
Patients and methods: Between 01/07/2006 and 30/06/2008 a total of 168 brain-dead donors were analysed. The results were examined for total period, as well also for the 12 months before (period A) and after (period B) the transplantation law came into effect.
Results: There was a non significant increase in the number of brain-dead donors in period B, compared to period A. Donor characteristics, as well as detection area were similar in both time periods. A clear increase of the frequency of organ transportation from 63% in period A to 82% in period B could be observed. Despite this fact, CIT was not affected significantly for the total collective, as well as for the different organs. A higher incidence of organ transports by helicopter lead to an increase of the transportation costs.
Conclusions: It can therefore be concluded that the new transplantation law in Switzerland has no negative effects with respect to the duration of CIT of all organs. However, the frequency of organ transportation has increased.

Late Breaking

LBP-1 FETAL LIVER DERIVED MESENCHYMAL STEM CELLS AUGMENT FETAL HEPATOCYTES ENGRAFTMENT

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Background: One impediment to successful hepatocyte transplantation is the extremely poor engraftment of cells after transplantation. If hepatocyte transplantation is to be a viable therapeutic alternative to liver transplantation, significant liver parenchyma repopulation is required. Mesenchymal stem cells (MSC) produce high levels of various growth factors, cytokines, metalloproteinases and have immunomodulatory effects. We hypothesized that co-transplantation of MSC with hepatocytes can augment engraftment after transplantation. We investigated the ability of human fetal liver MSC (hFLMSC CD166+/CD73+/CD44+/CD45–) to augment engraftment of phenotypically and functionally well characterized human fetal hepatocytes (hFH)
Methods: 2×10^6 hFH (passage 6) were either transplanted alone or co-transplanted with GFP-transduced hFLMSC in passages P6-P8 (1:1 ratio) into the spleen of C57BL/6 nude mice with liver injury caused by the chemical retrorsine
Results: After 4 weeks, engraftment of cells was detected by fluorescence in situ hybridization using a human-specific DNA probe. Significantly higher numbers of cell colonies expressing human specific CK8, 18, 19, c-Met, AFP and human- nuclear antigen, - mitochondrial antigen, -hepatocyte-specific antigen and -albumin expressing cells were present in the livers of recipient animals co-transplanted with hFLMSC as compared to those without. Furthermore, increased human specific hepatocyte nuclear factor 4alpha and 1beta and cytochrome CYP3A4 and CYP3A7 mRNA expression was demonstrated by RT-PCR in these animals. In addition, significantly increased amounts of human albumin and human α1AT levels were detected. Importantly, hFLMSC did not transdifferentiate into hepatocytes
Conclusion: Thus, our study reports the generation of a novel strategy for liver repopulation and thereby advances clinical applications of liver cell therapy.

LBP-2 HLA ALLO-IMMUNIZATION AND PREDICTIVE VALUE OF FLOWCYTOMETRIC PLATELETS CROSS MATCHING IN ACUTE LEUKEMIA PATIENTS

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Purpose: The incidence of refractoriness to platelet transfusion in patients with acute leukemia must be evaluated. Also, the prevalence of HLA allo-immunization in those patients and assessment of the predictive value of flow-cytometric platelet cross matching should be determined.
Patients and methods: We included 39 patients with acute leukemia and 39 donors with the mean age of 30.26±19.67 years. All patients were received transfusions in the form of packed RBCs, and platelet concentrates. We performed flowcytometric platelet cross-matching, HLA class I typing by SSP for patients and CDC for donors. Screening of HLA class I antibodies by ELISA before transfusion and 3-4 weeks post transfusion in all transfusions was performed. Multivariate analysis was done for the 78 transfusion events to detect which variable, of the clinical factors, HLA allo-immunization and platelet cross-matching, can predict transfusion response more than others.
Results: The difference between good and poor transfusion responses, regarding the presence of HLA allo-immunization and flowcytometric platelet cross-matching, were statistically significant (P=0.01 and P= 0.017), respectively. When HLA matched platelets were used, in 2 or more antigens, transfused cross-matched platelets were associated with good response in 90.9% of transfusion events. When transfused platelets were not HLA matched, transfused cross-matched platelets were associated with good response in only 53.8% of transfusion events. The difference in the prediction role of cross-matched platelets on transfusion response between using HLA matched and non-matched platelets was statistically significant (P= 0.05).
Conclusions: Both clinical factors and HLA allo-immunization are present in large number of patients. Platelet cross-matching is the most predictor for transfusion response. Flowcytometric platelet cross-matching is better than HLA matching in prediction of transfusion response especially in absence of clinical factors and HLA allo-immunization.

LBP-3 IN VITRO RECONSTITUTION OF HUMAN KIDNEY STRUCUTES FOR RENAL FAILURE

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Introduction and objectives: Increasing demand and donor shortage make kidney transplant challenging. Recent advances in cell-based therapies have provided potential opportunities to alleviate the current challenges of donor shortage. In this study, we investigated whether human kidney structures could be pre-formed in vitro for subsequent implantation in vivo to maximize tissue forming efficiency.
Methods: Primary human renal cells were isolated from unused donor kidneys using enzymatic digestion methods. Renal cells were grown, expanded, characterized using cell specific antibodies as immunofluorescence and Western-Blot. The ability of these cells to migrate was analyzed using different growth factors. To form kidney structures, single renal cells were placed in three-dimensional neutralized type I collagen culture system. Histomorphological and ultra structural analyses were performed using cell specific markers that identify proximal and distal tubules and collecting ducts. These 3D cultures were implanted in nude rats to evaluate cell survival.
Results: Human primary renal cells were effectively isolated and expanded in culture. The cells retained their phenotypic characteristics and also migration function. Single renal cells placed in a three-dimensional culture environment began to proliferate and form structures that resemble renal tubules. Histologically, these structures showed phenotypic resemblance to native kidney structures. The reconstituted tubules stained positively for proximal and distal tubular markers, and Western-Blot showed the expression of specific proteins for proximal and distal tubules. E-cadherin, N-cadherin and Na-K ATPase staining confirmed polarization of the cells present in the tubules. Cells in three dimensional cultures survive in vivo.
Conclusions: These findings show that single human renal cells grown in a three-dimensional culture system are able to generate kidney structures. The cells constituting these structures maintained the expression of renal cell specific markers. This system may ultimately be developed into an efficient cell-based therapy for patients with end stage renal disease.

LBP-4 LOCAL TREATMENT WITH SELECTIN BLOCKER PROLONGS RAT HIND LIMB ALLOGRAFT SURVIVAL

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Background: New strategies are warranted to especially overcome skin rejection after composite tissue allotransplantation. We therefore analyzed the expression of E-+P-selectin in skin of human hand allografts and the effect of efomycine-M, a special inhibitor of selectins, in a rat limb transplant model.
Methods: 150 skin biopsies from three bilateral hand transplants were assessed by H&E-histology and immunohistochemistry (anti-E-+P-selectin-antibody). Efomycine-M was investigated for its local effect on skin rejection in an orthotopic rat hind limb allotransplant model (BN-LEW). Animals received either efomycine-M alone (5mg/kg/weekly s.c. into the graft) or in combination with 50 days of systemic immunosuppression (ALS 0.5ml pod0+3 and tacrolimus 0.3mg/kg/day). Efomycine M was continued until pod 100. Untreated animals and animals receiving ALS+tacrolimus alone served as controls. Skin rejection was assessed by inspection and H&E-histology.
Results: E-and P-Selectin expression in the vascular endothelium were significantly upregulated and correlated well with severity of rejection in human hand allografts. In the experimental trial animals rejected on pod 61±1 (grade III) after weaning systemic tacrolimus treatment on pod 50. Histology showed necrosis and massive infiltration of lymphocytes in all tissues by then. Additional treatment with local efomycine-M resulted in long term (150 days) allograft survival. Histology on day 150 showed a lymphocytic infiltrate in the dermis and a dermal-epidermal interphase reaction consistent with rejection grade 2. Animals receiving Efomycine-M alone revealed grade III rejection by day 9±1, which was similar to untreated animals.
Conclusions: Selectins are upregulated upon skin rejection after human hand transplantation. Local administration of a selectin blocker results in significant prolongation of graft survival after total withdrawl of systemic immunosuppression, but doesn't prevent chronic rejection in a rat limb-transplant-model.

LBP-5 EARLY AND INTERMEDIATE OUTCOMES AFTER LUNG TRANSPLANTATION USING LUNG DONATION AFTER CARDIAC DEATH

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Purpose: Organ donation after cardiac death (DCD) has the potential to alleviate some of the shortage of suitable lungs for transplantation. There are currently only limited data describing outcomes following DCD lung transplantation. This study aims to describe the early and intermediate outcomes following DCD lung transplantation in Canada.
Methods/Materials: Data were collected from donors and recipients involved in DCD lung transplantation between June 2006 and December 2008. We describe our lung DCD protocol, donor characteristics and the occurrence of post-transplant events including primary graft dysfunction (PGD), bronchial complications, acute rejection (AR), bronchiolitis obliterans syndrome (BOS), and survival.
Results: Successful multi-organ controlled DCD increased from 4 donors in 2006 to 26 in 2008. Utilization rates of lungs among DCD donors were 0% in 2006, 11% in 2007 and 27% in 2008. Thirteen DCD donors were evaluated on site by the lung transplant team and lungs from 9 donors were ultimately used for 10 recipients. Thirty-day mortality was 0%. Severe PGD requiring ECMO occurred in 1 patient. Median ICU stay was 3.5 days (2-21) and hospital stay was 25 days (9-47). AR occurred in 2 patients and none of the patients have developed early BOS. Nine (90%) patients are alive at a median of 270 days (47-798) with good performance status and lung function. One patient died of sepsis 17 months after transplantation.
Conclusion: DCD has steadily increased in Canada since 2006. The use of controlled DCD lungs for transplantation is associated with very acceptable early and intermediate clinical outcomes.

LBP-6 DONOR-DERIVED DISEASE TRANSMISSION EVENTS IN THE UNITED STATES IN 2008: A REPORT FROM THE OPTN AD HOC DISEASE TRANSMISSION ADVISORY COMMITTEE (DTAC)

M. G. Ison, S. Covington, K. Taylor, E. Blumberg, K. Carney, J. Cutler, M. DiMaio, M. Green, R. Hasz, B. Kubak, T. Pruett, L. Teperman, B. Vasudev, M. Nalesnik. *OPTN/UNOS Ad Hoc Diseases Transmission Advisory Committee, UNOS, Richmond, VA, USA*

Background: Donor-derived disease transmission is increasingly recognized as a source of morbidity and mortality among transplant recipients. Policy 4.0 of the OPTN currently requires reporting of donor-derived events.
Methods: All potential donor-derived transmission events (PDDTE) that were reported to UNOS from 1/1/08 – 12/31/08 were reviewed by the DTAC. These events were categorized as to the likelihood of being donor-derived and outcomes were assessed.
Results: There were 84 reports of PDDTE reported to UNOS to date in 2008. There were 30 reports of malignancy PDDTE with 2 recipients with confirmed transmission and no deaths (table 1). There were 50 reports of infectious PDDTE with 19 recipients with confirmed transmission and 5 attributable deaths (table 2). There were 4 reports of other PDDTE with 3 affected recipients and 1 attributable death. Many of the cases remain under investigation so documented transmission and deaths may increase.

Table 1. Potential donor-derived malignencies transmissions reported to OPTN

Disease	# of Donor Reports	# of Recipients with Confirmd Transmission	# of DDD-Attributable Recipient Deaths
Renal cell carcinoma	18	0	0
Prostate cancer	3	1	0
Adenocarcinoma	1	0	0
Brain cancer-spindle cell	1	0	0
Breast	1	0	0
Colon cancer	1	0	0
Dermatofibrosarcoma protuberans	1	0	0
Liposarcoma	1	1	0
Melanoma	1	0	0
Non-Hodgkins lymphoma	1	0	0
Thyroid cancer	1	0	0
Totals	30	2	0

Conclusions: PDDTE continue to be reported as required by OPTN policy. There are increased numbers of reports suggesting under-reporting. Renal cell carcinoma remains the most frequently reported malignancy and bacterial infections were the most commonly reported infection. One case of HCV transmission from a sero - donor was documented. DTAC will continue to review common features of transmission events to advise on policy changes to minimize the risk of transmission of donor-derived disease. Enhanced donor screening and communication about donor and recipient conditions may facilitate prevention and early recognition of a PDDTE.

Table 2. Potential donor-derived infectious diseases transmissions reported to OPTN

Disease	# of Donor Reports	# of Recipients with Confirmd Transmission	# of DDD-Attributable Recipient Deaths
Bacteria†	7	4	2
HCV‡	7	3	0
HIV‡	5	0	1
TB	4	0	0
West Nile	4	1	0
Chagas	3	1	0
Babesiosis	2	2	0
Candida spp.	2	2	0
Histoplasmosis	2	0	0
Syphilis	2	1	0
Ehrlichia	1	0	0
HTLV	1	0	0
LCMV	1	2	2
Lyme disease	1	2	0
Mycobacteria avium-complex	1	0	0
PIV-3	1	0	0
Rabies	1	0	0
Schistosomiasis	1	0	0
Strongyloides	1	1	0
Viral encephalitis	1	0	0
Total	46+4§	19	5

† *Serratia*, *Pseudomonas*, GPC, VRE, bacterial emboli, *Veillonella*, *Enterococcus*.
‡ All but one case false + NAT; 1 case HCV with 3 transmissions; 1 case HIV with post-transplant acquisition of HIV.
§ 4 Expected transmissions: 2 CMV (1 neg serology); 1 toxoplasmosis; 1 EBV.

LBP-7 DEFINING THE SUCCESS OF LIVER TRANSPLANTATION: A PROPOSAL FOR A QUALITY PERFORMANCE INDICATOR FOR LIVER TRANSPLANT PROGRAMS

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Usual methods of providing survival data on liver transplant patients focus on either waiting list mortality or post-transplantation survival. Since these two concepts are strongly related, combined pre- and post-transplantation survival figures would allow optimal assessment of the quality performance of different liver transplant programs.
This study presents a relatively simple and uniformly applicable view on assessing the outcome of patients listed for liver transplantation, combining pre- and post-transplant survival figures.
All 538 patients having spent any time on the waiting time for liver transplantation in the Netherlands between September 2004 and December 2006 are included in this study.
Of 333 patients removed from the waiting list during the study period, 252 were transplanted, 46 died, 23 were removed due to contra-indications, and 12 patients improved. The death rate per patient year on the waiting list was either 7.7% or 11.0%, dependent on whether those patients who had to be removed from the waiting list due to contra-indications were included. Mean waiting time for removal from the waiting list was 0.85 years.
The expected value for pre-transplantation mortality was $0.85 \times 11.0\% = 9.4\%$.
One year post-transplantation patient and graft survival were 87.7% and 80.0% respectively.
Transplantation success, defined as the chance to survive up to transplantation and one year thereafter, without re-transplantation, was estimated at $90.6\% \times 80.0\% = 72.5\%$.
Conclusion: This study presents a combined method of presenting pre- and post-transplantation survival data, allowing for quality assessment of the performance of different liver transplant programs.

LBP-8 STEROID WITHDRAWAL FOLLOWING RENAL TRANSPLANTATION INCREASES THE RISK OF ACUTE REJECTION BUT IMPROVES CARDIOVASCULAR RISK FACTORS: A META-ANALYSIS

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The morbidity related to long-term steroid therapy has led to interest in with-

drawal of steroids from immunosuppressant regimens following renal transplantation. A number of recent trials have provided longer term information regarding the risks and benefits of steroid avoidance or withdrawal (SAW).
Methods: Literature searches were performed using Medline, Embase, the Cochrane Library and the Transplant Library from the CET. All trials comparing maintenance steroids with complete avoidance or withdrawal of steroids were included. Studies were assessed for methodological quality. Meta-analysis of extracted data was performed using the statistical software R. All data are reported as summary effect (relative risk (RR) or weighted mean difference (WMD)) and 95% confidence intervals (CI).
Results: 117 publications from 34 studies met the inclusion criteria (5,472 patients). Only 14 of the studies were rated as good quality. SAW regimens increased the risk of acute rejection over maintenance steroids (RR 1.56, CI 1.31-1.87, P<0.0001). This effect was independent of time of withdrawal and concomitant immunosuppression. No differences in corticosteroid resistant acute rejection, patient survival or graft survival were observed. Serum creatinine was increased and creatinine clearance reduced with SAW (serum creatinine WMD 4.42 μmol/L, CI 1.70-6.16, P=0.0006, clearance WMD -3.36 ml/min, CI -4.96 - -1.76, P<0.0001). Cardiovascular risk factors including incidence of hypertension (RR 0.91, CI 0.85-0.97, P=0.003), new onset diabetes (RR 0.53, CI 0.41-0.70, P<0.0001) and hypercholesterolemia (RR 0.76, CI 0.66-0.87, P<0.0001) were reduced with SAW.
Conclusion: Despite an increase in the risk of acute rejection with SAW protocols, there is only a small effect on graft function with no measurable impact on graft or patient survival. However there are significant benefits in cardiovascular risk profiles following SAW which may lead to a longer-term reduction in cardiovascular events.

LBP-9 IMPACT OF PROTEINURIA ON GRAFT SURVIVAL AFTER CONVERSION TO SIROLIMUS IN RENAL (RT) AND SIMULTANEOUS KINDEY-PANCREAS TRANSPLANTS (SPK)

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[1]Medicine-Nephrology Section, CEMIC, Buenos Aires, Argentina; [2]Pathology, CEMIC, Buenos Aires, Argentina

Purpose: Our purposes were to determine the impact of proteinuria on graft survival after conversion to Sirolimus from a CNI-based regimen and to analyse the progression of proteinuria after conversion, also the impact of conversion on graft histology, renal function, acute rejection and patient and graft survival.
Methods: 93 patients, 86 RT and 7 SPK recipients were converted to Sirolimus in our unit between 01/2001 and 11/2008. We collected demographic data, laboratory values, AR episodes, BP control and use of ACEI/ARBs at baseline and 6,12 and 24 months after conversion.We analyse the impact of proteinuria as a binary categorical variable with a cut-off value of 500 mg/day on graft survival in univariate and multivariate regression model.
Results: Baseline data are presented in Table 1 and Table 2.

Table 1

Data	Mean ± SD
Age	44. 18±10.4
Creatinine	1.76±0.52
GFR	50.6±19.0
Proteinuria	0 (0-302) median (25-75)
Follow up (months)	42.12±24.61
Time to conversion (months)	25.77 (7.45-74.80) median (25-75)
SBP	126.38±14.32
DBP	76.±28.9

Baseline values.

Table 2

Data		n (%)
CNI	CSA	43 (47)
	TAC	49 (53)
Proteinuria >500 mg/d	yes	14 (15)
Biopsy prior to conversion	yes	68 (74)
Reason for Conversion	CAN (confirmed)	64 (71)
	Cancer	7 (7.7)
	CNI Toxicity	7 (7.7)
	TMA	3 (3.3)
	Other	4 (4.4)

Baseline values.

Proteinuria >500 mg/day predicted graft survival in the univariate analysis (Figure 1) and also after adjustment in the multivariate model (p= 0.025).
Proteinuria increased after conversion (p<0.001) despite an increase use of ACEi/ARB (p<0.001). BP, creatinine and GFR remained stable. Acute rejection rates were 5.6%, 6.7% and 7.6% at 6, 12 and 24 months respectively. Over 42 months of follow up, Graft and patient survival were 90% and 95% respectively. 16/68 patients had baseline and follow up biopsies at 12 or 24 months. 6/16 had FSGS lesions at baseline. 9/14 had FSGS lesions at 24 months (p<0.016). IFTA at baseline of 6-25% was present in 50% of patients, at 12 and 24 months was not different from baseline.
Conclusions: Proteinuria > than 500mg/day at baseline has a negative impact on graft survival after conversion to SRL from CNI-based therapy. Proteinuria increases after conversion. FSGS lesions also increases on follow up biopsies. Conversion remains a safe procedure with excellent patient and graft survival.

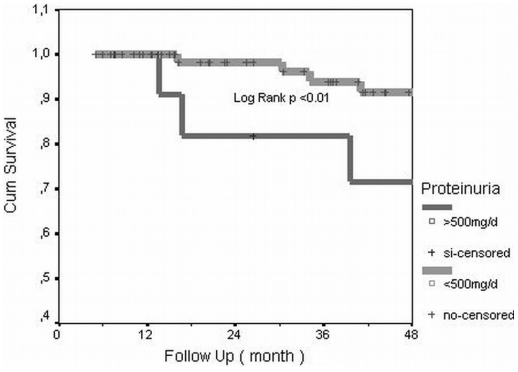

Figure 1. Survival functions.

LBP-10 SIROLIMUS CONVERSION TO ACHIEVE CALCINEURIN-INHIBITOR-FREE, STEROID-FREE IMMUNOSUPPRESSION

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Background: Calcineurin inhibitors (CNI) cyclosporine and tacrolimus are still the cornerstone of immunosuppressive therapy for the prevention of acute rejection (AR) after kidney transplantation. However, a steroid- and CNI-free regimen (using sirolimus) would presumably minimise metabolic and cardiovascular complications along with avoidance of nephrotoxicity. This being not always successful, we attempted to identify the markers of failure for conversion from CNIs to sirolimus-based regimen.
Patients & methods: Indications for conversion to sirolimus plus mycophenolate mofetil (MMF) and steroids [n=101]: gout [n=1], paranoid delusions [n=2], hyperacute rejection [n=1], cancer [n=7], biopsy-proven chronic allograft nephropathy [n =12], biopsy-proven CNI toxicity/ischemia [n=10], fall in creatinine clearance [n=66], acute tubular necrosis [n=4].
Results: At 6 months following successful conversion 71% patients were steroid-free. Based on biochemical and clinical response, 3 groups were identified:
Group 1 [n=61]: successful conversion. Had fall in serum creatinine from mean of 246μmol/L to 195μmol/L following conversion [p<0.05] whereas mean proteinuria changed from 0.8 gm/day to 0.9gm/day [p = not significant].
Group 2 [n=20]: converted back to previous immunosuppression due to complications. Following conversion mean serum creatinine decreased from 318μmol/L to 216μmol/L [p = not significant] whilst total amount of 24-hr proteinuria increased from mean 0.7gm to of 1.5gm [p<0.05]. Two patients developed steroid responsive AR.
Group 3 [n=22]: failed conversion. Following conversion, mean proteinuria increased from 1.9 gm/day to 3.2 gm/24 hr [p<0.05].
Markers of failure for conversion:
– Proteinuria >1 gm/24 hr: 66% failed conversion,
– Creatinine >300 mmol/L: 62% failed conversion,
– MMF ≥ 1.5 gm/day: 80%, failed conversion,
– MMF ≥1.5 gm/day + Sirolimus >5 mg/day: 90% failed conversion.
Conclusions: Sirolimus-based immunosuppression is worth considering in patients with chronic graft nephropathy. Serum creatinine >300 μmol/L and proteinuria >0.8 gm/day is a contraindication to conversion.

LBP-11 STUDY THE PREVALENCE OF ADENOVIRUS INFECTION IN HSCT DONORS AND RECIPIENTS

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Background: Adenovirus infection is one of the viral causes of postoperative morbidity for ability to establish a latent infection in lymphoid cell in soft and

solid organ transplant recipients and cause of mortality for significant role in late onset hemorrhagic cystitis in hematopoietic stem cell transplant (HSCT) patients.
Objectives: In this investigation the prevalence and role of adenoviral infection in HSCT clinical syndromes were studied by molecular methods pre and post-HSCT conditions.
Materials and methods: In a retrospective and cohort study, 349 plasma samples of 92 HSCT donors and recipients were included. One EDTA-treated blood sample was collected from any donors and recipients pre-transplantation. Also for 3 months (one sample per-month) the blood samples were collected from HSCT patients. The prevalence of adenovirus DNA infection was analyzed by a qualitative in house PCR method.
Results: Adenovirus genome was diagnosed in 16 of 92 (17.4%)HSCT recipient's pre to post-transplantation. The 25 of 349 plasma samples of transplant patients were adenovirus DNA infected. Significant correlation was diagnosed between adenoviral infection with the questionnaire data of HSCT patients and donors.
Conclusion: For high prevalence of adenovirus infection in HSCT donors and recipient's pre and post-transplantation, accurate detection and monitoring of this viral infection in pre and post-HSCT periods is need.

LBP-12 PRE TO POST-HSCT DONOR AND RECIPIENT RELATIONSHIPS INFECTED WITH HBV AND HCV GENOMES

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Background: patients undergoing hematopoietic stem cell transplant (HSCT) are at risk of blood-borne hepatitis vial infections such as hepatitis B virus (HBV) and hepatitis C virus (HCV).These viruses may transmit form donors (D) to recipients (R) via transplantation and/or transfusion.
Objectives: In this research the relationships which may occur between donor and recipient who infected with HBV and HCV genomes pre to post-transplant were studied
Materials and methods: In a cohort and retrospective study, the molecular prevalence of HBV and HCV infections in transplant donors and patients were analyzed in EDTA treated blood samples were collected from 53 BMT donors and recipients pre and post transplantation by PCR and RT-PCR methods, respectively.
Results: The pattern of comparing pre-HSCT D/R relationships with post-transplant condition that may infect with HBV and HCV are presented as follow: in D+/R+ condition 3 HBV infected patients was R-(Post-HSCT) and 1 HBV infected patients were R+(Post-HSCT). In D-/R- condition 1 HCV infected patients was R+ (Post-HSCT) and 10 HCV infected patients were R-(Post-HSCT). But D+/R- and D-/R+ relationships were not diagnosed in HBV and/or HCV infected patients post-transplantation.
Conclusion: Different pattern of D/R relationships separately for HBV and HCV infections were diagnosed. Also the high prevalence of both HBV and HCV post-transplant negative patients (R-) announced the low rate of pre to post-HSCT transmission of these viral infections form donors to recipients.

LBP-13 STUDY THE DIFFERENT PATTERN OF HCMV gB GENOTYPES IN CLINICAL OUTCOME OF BONE MARROW TRANSPLANT PATIENTS

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Background and objectives: Different genotypes of human cytomegalovirus (HCMV) glycoprotein B (gB) producing gene may influence the different pattern of HCMV in Bone marrow Transplant (BMT) recipients. So in this investigation the prevalence and role of different HCMV-UL55 genotypes in multiple post transplant clinical presentations were studied.
Materials and methods: In this cohort and retrospective study blood (plasma and Buffy coat) and urine samples were collected for 6 years from 110 BMT patients pre-transplantation and followed weekly for 100 days post-transplantation. HCMV-UL55-nested-PCR method was optimized and used for detection and genotyping of HCMV infection in collected samples of BMT recipients. The prevalence of HCMV UL55 genotypes were analyzed by RFLP method for all UL55-nested PCR positive sample.
Results: UL55-nested-PCR positive results were diagnosed in plasma 3540/4950 (71.5%), Buffy coat 3634/4950 (73.4%) and urine 3292/4950 (66.5%) samples of BMT patients. Also mean of 25% of transplant donors were infected totally with HCMV infection. The decline pattern of the prevalence of UL55 genotypes in plasma, Buffy coat and Urine samples were as followed, respectively: gB2>gB3> gB1> gB4, gB2> gB1> gB3> gB4 and gB2> gB3> gB1> gB4. The gB gene variations that may influence the pathogencity of HCVM in transplant patients.
Conclusion: Detection of gB2 UL55 genotype in the most clinical samples of BMT patients and also diagnosis of significant association between different genotypes of HCMV-UL55 strains with clinical outcome of transplant patients compared with the result of another HCMV researchers, announced the need of completed studies focused on the pattern variation of HCMV-UL55 genotype in clinical complications of BMT recipients.

LBP-14 EFFECT OF FK506 ON ENDOPLASMIC RETICULUM (ER)–MEDIATED APOPTOSIS OF JURKAT CELLS

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Two major apoptotic pathways are dead receptor pathway and mitochondrial pathway. And third apoptotic pathway is endoplasmic reticulum (ER) mediated apoptosis. We examined the effects of FK506 on ER mediated apoptosis of Jurkat cells. We observed cell viability, measurement of H_2O_2 generation, intracellular accumulations of Ca^{2+} and NO, and western blottings of ER stress mediated apoptotic pathway proteins, such as phospho-PERK, PERK, CHOP, Grp78, Grp94, Bcl-2, and Bak proteins. 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, FK506 treated Jurkat T cells increased the sub G0/G1 phase, nuclear fragmentation and activations of 3 and 12 caspases. FK506 also increased NO production through induction of iNOS and H_2O_2. Reactive oxygen species induced by FK506 resulted in the modulation of Bak protein expression and mitochondrial dysfunction through ER stress mediated pathway. FK506 induced ER mediated apoptosis in Juekat T cells were identified.

LBP-15 BORTEZOMIB AFFECTS THE FUNCTION OF HUMAN B CELLS: POSSIBLE IMPLICATIONS FOR DESENSITIZATION PROTOCOLS

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The proteasome inhibitor bortezomib is a potent inducer of apoptosis in malignant as well as non-malignant human plasma cells. For that reason, bortezomib has recently come to attention to the transplantation community for the treatment of humoral rejection. Since bortezomib targets the proteasome, it is likely that, besides plasma cells, it also affects other cell types, such as activated human B cells. To this end, we have tested the ability of bortezomib to block activated peripheral B cell immunoglobulin production, as well as B cell proliferation.
We added bortezomib in graded concentrations to isolated human B cells that were activated by either anti-CD40 mAb with IL-2, IL-10, IL-21 and CpG ODN-2006, or with Staphylococcus aureus with supernatant of activated T cells. We tested culture supernatants for IgM and IgG levels by ELISA at day 6 and proliferation by 3H-TdR incorporation at day 7.
Bortezomib completely abrogated IgM and IgG production as well as proliferation in a dose dependent fashion. Complete inhibition was already observed at a concentration of 1.0 ng/mL. Additionally, when added to B cells that were already activated for 2 days, bortezomib completely inhibited IgM and IgG production as well as proliferation, albeit at slightly higher doses. We observed that bortezomib induced inhibition of immunoglobulin production and proliferation with both activation protocols, indicating that this is a general effect of bortezomib on B cells.
We conclude that bortezomib, in addition to its effects on plasma cells, is a profound inhibitor of activated human peripheral B cells. This finding suggests that, when bortezomib is used for desensitization or for the treatment of humoral rejections, there is no need for additional anti-B cell therapy, such as anti-CD20 mAb treatment.

LBP-16 THE EFFECT OF CYCLOSPORINE AND TACROLIMUS ON REGENERATION OF THE RENAL TUBULES

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The incidence of acute tubular necrosis following renal transplantation is about 15-30%. The recovery of renal allograft function is dependent on regeneration of the renal tubules. Although cyclosporine and tacrolimus are known to be nephrotoxic at higher levels, the effect of these drugs on regeneration of the renal tubules has not been documented previously. The aim of this study was to investigate the effect of cyclosporine and tacrolimus on regeneration of the renal tubules.
Long Evans rats were subjected to 90 minutes of normothermic ischaemia of the right kidney. The animals were treated with saline, cyclosporine (5mg/kg twice daily) or tacrolimus (0.2mg/kg twice daily). Groups of animals (n = 10) were sacrificed at 0, 6, 12, 24, 48, 72 and 96 hours postoperatively. Both kidneys were removed and used to measure the mitotic index and Ki labelling index in the cortex and medulla.
There was a significant increase in the mitotic index and Ki labelling index in the control group (saline) at 24 hours and reached a peak at 48 hours (MI = 11.1/hpf; Ki = 26.4%). The Ki labelling index was higher in the cyclosporine treated animals at 48 hours (33.0% vs 26.4%), at 72 hours (21.4% vs 14.7%) and at 96 hours (22.2% vs 16.5%) compared to the control group.
These studies suggest that cyclosporine enhances the regeneration of the renal tubules following ischaemia to the kidney.

LBP-17 THE USE OF EVEROLIMUS AS A RENAL SPARING AGENT IN CARDIOPULMONARY TRANSPLANT PATIENTS WITH ESTABLISHED RENAL DYSFUNCTION

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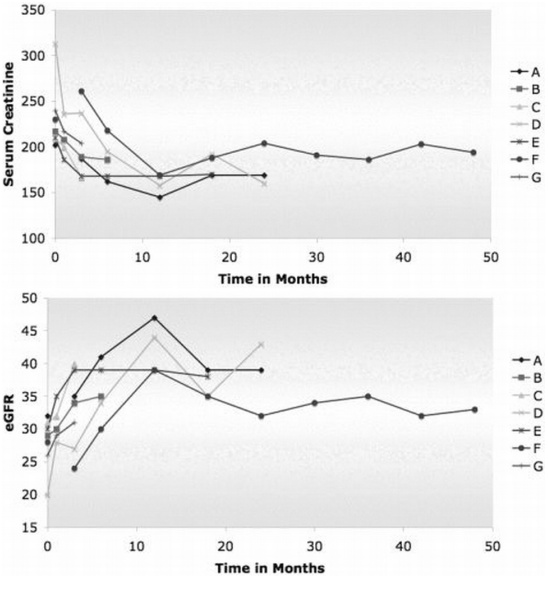
Introduction: The chronic nephrotoxic effects from calcineurin inhibitors (CNIs) are a common clinical complication after cardiopulmonary transplantation. The 10-year rate of developing chronic renal failure (CRF) in these patients is 20%. The reduction of CNIs may improve renal dysfunction. However reducing CNIs requires an alternative agent, which is renal sparing without loss of immunosuppressive efficacy. The proliferation signal inhibitors e.g. everolimus, have the potential to facilitate reduction in CNI dosing.
Methods: A retrospective study was conducted on our 7 male patients receiving everolimus with reduced dose CNI. Their baseline creatinine and eGFR were collected pre-commencement of everolimus. After the introduction of everolimus, serum creatinine and eGFR levels were collected at 1, 3 and 6 months, and at 6 monthly intervals thereafter depending on length of treatment. During this period patients were initially started on 0.75mg b.i.d of everolimus with trough levels maintained between 3-8ng/mL. CNIs were initially reduced according to renal function, following this there was a progressive CNI reduction by 25% until achieving trough levels between 50-100ng/mL.
Results: The ages of the patients ranged from 46-58. The average creatinine and eGFR pre-everolimus was 232μmol/L and 28mls/min (CKD4) respectively. The minimum length of time on everolimus was 3 months up to a maximum of 48 months. The average creatinine and eGFR post everolimus was 179μmol/L and 37mls/min (CKD3B) an average percentage decrease in creatinine of 21% (p=0.003 Wilcoxon signed-rank).



Conclusion: The observed data from this small sample demonstrates a convincing improvement in renal function. Even though this study consist of a small number of patients it offers compelling evidence for the further investigation of everolimus as a renal sparing immunosuppressant used in combination with CNIs.

LBP-18 "INTRA-BROAD ANTIGEN" AND "INTRA-BROAD ANTIGEN" HLA ANTIBODIES IN KIDNEY TRANSPLANT CANDIDATES

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In renal transplantation donor-recipient HLA-matching is classically performed considering "broad" antigens of the HLA-A, B and DR loci. On the contrary sensitized patients showed production of antibodies against all HLA class I and II molecules.
In 350 HLA antibody positive renal transplant candidates, we characterized detected antibodies using FlowPRA/LABScreen Single Antigens beads. We also investigated production of antibodies specific for an other "split" or an other allele of patient own HLA molecule, that is "intra-broad antigen" (IBA) or "intra-allele" (IA) antibodies. The epitope specificity of IBA-/IA-antibodies was analyzed comparing amino acid sequences of patient's HLA molecules to those of the HLA alleles corresponding to IBA-/IA-antibodies, using an online database.
Forty patients (11%) produced IBA-antibodies. Sixteen HLA class I IBA-antibodies (anti-A23, -A24, -B38, -B44, -B45, -B49, -B52) and 33 HLA class II IBA-antibodies (anti-DQ5, -DQ6, -DQ8, -DQ9, -DR11, -DR12, -DR13, -DR14, -DR16, -DR52, DR51) were found.
The potential immunizing epitope was exactly defined for all the HLA class I IBA-antibodies (67S, 82-83LR, 116L, 144K, 156D/Q, 283H) and for 18 HLA class II IBA-antibodies (6C, 57A, 58E, 60S, 67F, 70D, 71R, 87F, 112Y, 185I). It is important to underline that the trans-membrane 283H epitope determined production of inefficacious intra-A9 antibodies in 4 patients.
Eleven patients (3%) had IA-antibodies specific for HLA class I and/or class II molecules (intra-A*01, -A*30, -B*44, -DRB1*01, -DRB1*08, -DRB1*14, -DRB3*02). In all these patients the immunizing epitope was identified (77D, 97I, 156D and 57S, 70D, 71E, 112Y, 164F for class I and class II IA-antibodies respectively). Five of these patients had IA-antibodies due to recognition of an "allele mismatch" of the previous graft.
Our data strongly confirm the epitope specificity of HLA alloantibodies and underline the need to adopt a "structural" HLA matching in kidney transplantation of sensitized patients.

LBP-19 COMBINED KIR/HLA GENOTYPING INDICATES A ROLE FOR ALLOREACTIVE NATURAL KILLER CELLS IN KIDNEY TRANSPLANTATION

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Although it is widely accepted that Natural Killer (NK) cells play a role in the rejection of hematopoietic grafts, it is unclear whether NK cells are also involved in solid organ transplantation. As NK cell allorecognition is mediated by the interaction – or lack thereof – of Killer Immunoglobulin Receptors (KIR) with HLA class I, we determined the KIR and HLA genotypes of recipients and the HLA genotypes of donors of HLA-DR compatible kidney allografts (n=421). In transplantations fully compatible for HLA-A, HLA-B and HLA-DR (n=137), in which a role for T cells is minimised, mismatches between donor and recipient HLA that could be detected through recipient KIR were associated with an approximately 25% reduction in long-term graft survival (p=0.04). Multivariate Cox regression analysis considering risk factors that are known to influence transplant outcome confirmed the effect of KIR ligand mismatching as an independent risk factor on HLA-A/B/DR-matched transplantations (HR 2.3, range 1.0-5.1, p=0.04). This finding supports a role for NK cells in kidney transplantation, and suggests that suppression of NK cell activity could improve the survival of 'fully' matched kidney grafts in which NK alloreactivity is predicted based on KIR and HLA typing.

LBP-20 MECHANICAL CIRCULATORY ASSIST FOR RIGHT VENTRICULAR FAILURE FOLLOWING HEART TRANSPLANTATION: RVAD OR ECMO?

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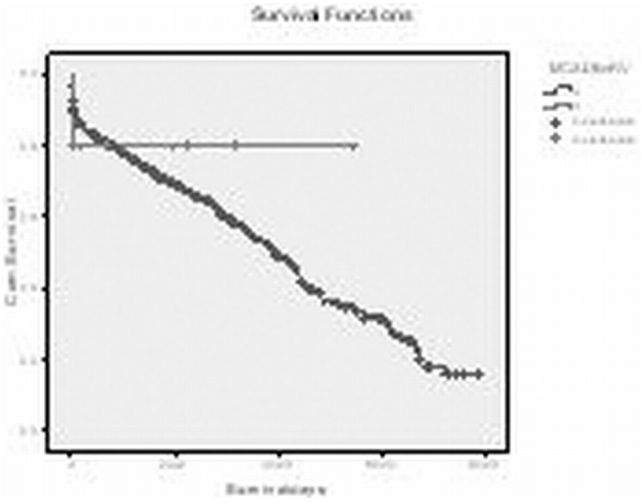
Introduction: Primary graft failure and right ventricular failure (RVF) is potentially a catastrophic complication following heart transplantation. Occasionally pharmacologic therapy may prove insufficient, and a mechanical circulatory support (MCS) is required. It is, however, debatable whether a right ventricular assist device (RVAD) or modern form of veno-arterial extra-corporeal membrane oxygenator (ECMO) may provide optimum circulatory "off-loading and support" for RVF.
Methods: A retrospective review of the case records of all patients who underwent heart transplantation between 1987 and 2008 was performed to determine the occurrence of post-transplant RVF, the types of MCS and outcomes. Statistical analysis was performed using SPSS v15.
Results: Out of a total of 463 heart transplants, seventeen patients (3.6%) required MCS for RVF, including 11 males (64.7%) and 6 females (35.3%); pre-transplant diagnoses were ICM (n=3), DCM (n=10), and other (n=4). There were 14 RVAD (11 Biomedicus, 3 Centrimag) and 3 ECMO (Centrimag). Patients receiving MCS for RVF were significantly younger ($p<0.005$), with longer ischemia time ($p<0.05$). An intra-aortic balloon pump was inserted in all patients requiring MCS. The median duration on MCS was 5 days (4 hrs-13 days). Re-exploration for bleeding was required in 7 patients with RVAD and 2 patients on ECMO. No device-related complications were recorded. The wean rate from MCS was 50% for RVAD, but was 100% for ECMO. Subject to successful weaning from MCS, we found no significant difference in long-term survival in patients with or without MCS for RVF. (figure 1)



Conclusion: In our limited experience, ECMO using Centrimag provided satisfactory outcome for RVF following heart transplantation, with acceptable complication rate. It is most likely due to optimum off-loading of the RV, leading to gradual return of cardiac physiological function.

LBP-21 LOCALISED IMMUNE-PRIVILEGE IN PANCREATIC ISLET TRANSPLANTATION

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Purpose: Chronic systemic immunosuppression is a major limiting factor in pancreatic islet transplantation. Our study sought to explore the potential of cell based immune-modulation as an alternative to immunosuppressive drug therapy. Human amniotic epithelial cells (AEC) possess innate anti-inflammatory and immunosuppressive properties which were utilised to create localised immune-privilege in an *in vitro* islet cell culture system.
Methods: Cellular constructs composed of human islets and AEC (islet:AEC) were bio-engineered under defined culture conditions. Insulin secretory capacity was validated by glucose challenge and immuno-modulatory potential characterised using a peripheral blood lymphocyte (PBL) proliferation assay. Results were compared to control constructs composed of islets or AECs cultured alone.
Results: Sustained, physiologically appropriate insulin secretion was observed in both control islets and those co-cultured with AECs. Activation of resting PBL proliferation occurred on exposure to human islets alone but this response was significantly ($p<0.05$) attenuated by the presence of AECs. Mitogen (phytohaemagglutinin, 5mg/ml)-induced PBL proliferation was sustained on contact with isolated islets but abrogated by both the AEC and islet:AEC constructs.
Conclusions: These data suggest that transplanted islets may benefit from the immune-privilege status conferred on them as a consequence of their close proximity to human AECs.

LBP-22 INCIDENCE AND SECURITY OF BIOLOGICAL AGENTS IN KIDNEY TRANSPLANT PATIENTS (KT)

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Individualization of the immunological risk and the acceptance of grafts with expanded criteria lead us to a greater use of biological agents. With the aim of knowing the exact frequency in its use and their security profile we reviewed our experience
Patients and methods: We analyzed the use of biological agents in 613 adult KT patients (2004-2009). Infectious complications and tumor incidence were evaluated. Cytomegalovirus (CMV) prophylaxis was administered with valganciclovir in seronegative receptors/+donors and ganciclovir iv when receiving Thymoglobulin. All patients received trimethoprim-sulfamethoxazole.
Results: Of a total of 613 KT (51.9±13.2 yr), 258 receptors (42%) received biological agents: anti-CD25 Basiliximab (Bxb) 147 patients (58.6±10.9 yr; 104M/43F); anti CD25 Daclizumab (Dzb) 69 (62±8.9 yr; 55M/14F); 37 patients TMG (45±12.1 yr; 17M/20F); and Rtb 5 (36.7±10.4 yr; sex 3M/2F). The average follow-up period was: 29.2±14.4 months (rank: 3-63m). The average age of TmG was fewer than those who received anti-CD20 ($p< 0.000$). Any remarkable adverse effects were not detected following their administration. With Bxb, 81 infectious episodes in 63 patients were registered (42.9%; 9 pneumonias, 8 CMV diseases) and 3 cancers; with Dzb 43 infections in 35 patients (52.2%; 6 pneumonia, 7 CMV) and 4 cancers; with TmG 1 breast carcinoma, and 17 infectious complications in 14 patients (37.8%; 3 CMV) and in the Rtb group a same patient presented colon adenocarcinoma and pneumonia. The CMV seronegative patients (IgG-) who developed CMV were 4;2;1 and 0, respectively (3% in every group).
Conclusions: Four of 10 KT received biological agents, who turned out to be well tolerated. The infectious complication rate affected to 44% without clear differences between treatment groups. The CMV disease incidence using anti-CD25 (5% with Basiliximab and 10% with Daclizumab) was not inferior to that observed with Thymoglobulin (8%).

LBP-23 NEW TOOL FOR INTRAOPERATIVE ASSESSMENT OF RENAL VASCULATURE AFTER REVASCULARIZATION OF A TRANSPLANTED KIDNEY

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Background: Intraoperative assessment of the flow of renal artery and vein after reconstruction is a crucial matter in kidney transplantation. Conventional Doppler ultrasound detects only blood flow in limited area. Here we report a newly developed device which not only non-invasively visualizes the condition of perfusion of whole allograft at one time from any angle, but also clearly detects the state of anastomosis of renal vessels.
Method: In 6 kidney transplantations, after revascularization of the kidney grafts, perfusion was assessed qualitatively by using a PDE system. Before scanning, 2 mg of indocyanine green (ICG) was injected intravenously into the patient. Then, about 20 seconds after the injection, perfusion was scanned by the CCD camera for a couple of minutes.
Results: In all patients, PDE system depicted condition of blood flow of whole allograft at one time from any angle, and detected the state of anastomosis. In one patient, non-perfused area was detected by PDE, and subsequently re-anastomosis was conducted. No ICG-associated side effects were observed.
Conclusion: The near-infrared camera system, PDE system will provide opportunity for intraoperative assessment of vasculatures of renal allograft.

LBP-24 OBJECTIVE AND SUBJECTIVE DIFFERENCES IN QUALITY OF LIFE FOR THREE MODALITIES OF RENAL REPLACEMENT THERAPY OVER TIME

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Background: Renal transplantation (TX) is a life-enhancing procedure with excellent outcomes. Hence QoL assessment is important in a holistic assessment of outcomes among the modalities of renal replacement therapy (RRT).

Purpose: Observational study comparing the evaluation of QoL of haemodialysis (HD), peritroneal dialysis (PD) and transplant (TX) patients over time, and to determine factors of change.
Methods and Materials: EuroQol_5D, a validated health related (5-domains each with 3 states,) generic questionnaire, was used to assess mobility, self care, activity, pain and anxiety over time. Patients were interviewed on the ward, clinics or HD units. Objective (UK Time Trade Off Value set) scores were derived from the selection of statements from each of the 5 domains. Subjective scores were obtained using a visual analog scale. Demographic information was also obtained for subgroup analysis.
Results: 228 patients undertook 268 QoL assessments. Tx patients had the best QoL score (0.72) followed by PD (0.6) and then HD (0.48) patients. There was no significant difference between the objective and subjective QoL scores amongst the TX and PD patients. The subjective scores of HD patients were significantly higher than the objective score for after 24 months on dialysis. TX patients were younger and better educated. Only 39% of Tx patients were employed even after 24 months post-transplant. Changes in QoL over time is shown in Figure 1.

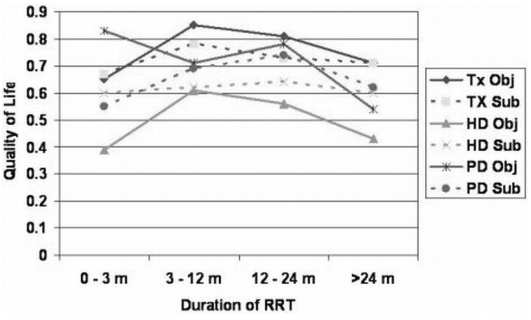

Figure 1. Quality of life over time: RRT modalities.

Conclusion: QoL improved among TX patients but declined slightly over time. The statistically higher subjective score among the stable HD cohort suggests that HD maybe an acceptable long-term alternative to TX for some patients.The QoL among older patients after undergoing TX may be poorer between 6 and 24 months post Tx; as they may miss the social interaction of HD. Low employment rate after Tx is a concern.

LBP-25 BK TRANSPLANT NEPHROPATHY SUCCESSFULLY TREATED WITH LEFLUNOMIDE

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Purpose: BK viremia and nephritis are increasing problems in renal transplant recipients. The treatment of BKV nephritis (BKVN) consists of reduction in immunosuppressive therapy and antiviral therapy with cidofovir or leflunomide or a combination of both. Leflunomide has immunosuppressive effect and also antiviral activity. Addition of leflunomide may be associated with better outcome.
Methods: 7 KT patients with biopsy proven BKVN (histological pattern B) were treated with leflunomide and reduction of immunosuppression. All patients were monitored with serial determination of viral load in blood and graft function.
Results: BKVN was confirmed at 15 months (3-27) after kidney transplantation, at that time median serum creatinine concentration was 2.9 mg/dL (1.9 ~ 3.7). 12.5 months (7~17) later of leflunomide treatment, median serum creatinine was 2.3 mg/dL and no graft loss was found.
Conclusion: We consider it most likely that leflunomide and reduction of immunosuppression was crucial to treatment for BKVN. Further issues that arise from this cases include the optimal dose and duration of leflunomide therapy.

LBP-26 FACTORS INFLUENCING COMORBIDITY SCORE IN YOUNG RENAL TRANSPLANT RECIPIENTS

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Despite the improvement in patient and allograft survival rates in renal transplant population, multiple comorbidities that develop during the follow-up period is still an important problem. Charlson Comorbidity Index (CCI) is a valid index of determination of comorbidities in many disease conditions. There is little data about the clinical associates of CCI in young transplant patients. We tried to investigate the factors affecting comorbidities in a population of young and diabetes free renal transplant recipients.
107 young and diabetes free renal transplant recipients (71 male, 32 female; mean age 34.4±17.7) with a functioning allograft more than one year were included in our study. Demographic and biochemical parameters, fetuin, osteopontin and 25-hydroxyvitamin D levels, presence of insulin resistance with homeastasis model assesment (HOMA-IR), determination of nutritional status with subjective global assesment (SGA) and CCI of these patients were recorded. According to CCI there were 36 (47%) patients with at least one comorbidity (16 (21.1%) patients with one, 13 (17.1%) with two, 3 (3.9%) patients with three and 3 (3.9%) patients with four comorbidities). Among clinical and laboratory parameters, prior hemodialysis duration, SGA score, uric acid and osteopontin levels and biopsy proven chronic allograft nephropathy was found to be positively correlated whereas albumin and mean arterial pressure was negatively correlated with comorbidities. In multivariant analysis only uric acid (OR= 1.48, *p* 0.046) and dialysis duration (OR= 1.02, *p*=0.009) correlated with comorbidities.
Duration of prior dialysis and high uric acid levels were among the strongest factors related with comorbidities in young renal transplant patients. Early planning of transplantation and good metabolic control will help to reduce comorbidity in young transplant patients.

LBP-27 MALE SEXUAL FUNCTION IN PATIENTS RECEIVING DIFFERENT TYPES OF RENAL REPLACEMENT THERAPY IN COMPARISON WITH HEALTHY MEN: PRELIMINARY RESULTS

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There are limited studies correlating possible sexual functional alterations related to the mode of renal replacement therapy among end stage renal disease (ESRD). In this study we performed a cross-sectional observational study to assess sexual function scores and biochemical variables that may have impact on male erectile dysfunction (ED) in ESRD patients.
A total of 100 ESRD patients and 50 healthy men were recruited to the present cross-sectional study. The study was consisted of 53 renal transplantation (group I, mean age 39.01±7.68 years, mean post-transplant duration 97.72±10.35 months) and 47 hemodialysis (HD) (group II, mean age 38.72±9.12 years, mean ESRD duration 89.13±8.65 months). All groups were evaluated with following scales; International Index of Erectile Function (IIEF) 5 and Short Form (SF)-36 questionnaires, Beck Depression Inventory (BDI).
Total IIEF-5 scores of men in groups I, II and III were (19.54±4.59, 16.48±5.91 and 22.56±3.44 respectively). The mean total IIEF-5 score of control group was higher than group I and II. ($p<0.001$). Post transplant group's mean total IIEF-5 score was also higher than hemodialysis (HD) group ($p<0.05$). Group I and II significantly differed from control group in terms of presence of ED (IIEF score 21) [(n=28, 52.8%), (n=33, 70.2%), (n=12, 24%) respectively ($p<0.001$)] whereas there was no significant difference between group I and II. Physiological health domain of SF-36 was significantly better in healthy controls ($p<0.001$). Erectile dysfunction score was negatively correlated with BDI ($r= -0.368$, $p<0.001$); whereas positively correlated with SF-36 ($r=0.495$, $p<0.001$) in all patient groups.
Lower sexual function and lower quality of life scores in patients with ESRD compared with healthy controls. It is worth mentioning that mode of renal replacement therapy may have no impact on erectile dysfunction.

LBP-28 FACTORS ASSOCIATED WITH INSULIN RESISTANCE AFTER LONG TERM RENAL TRANSPLANTATION

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Insulin resistance (IR) is an early and very strong predictor of post-transplant diabetes mellitus as well as an important cardiovascular risk factors even in the absence of hyperglycemia. Patients after renal transplantation are insulin resistant compared to a control group with similar demographic characteristics. The aim of the study was to determine the frequency of IR in renal allograft patients without glucose disorders, to correlate IR indexes with the doses of immunosuppressive medications and other risk factors such as age, obesity and antihypertensive therapy used.
One hundred and six patients who received a kidney transplant at Baskent University Hospital between 1992 and 2006 were enrolled the study. IR was diagnosed when HOMA-IR is equally or up to 2.5. The prevalence of IR in our patients was 53.8% (n: 57), Waist-hip ratio and creatinine clearance was higher in IR patients (respectively p=0,001, p=0,037). HOMA-IR was correlated age, waist-hip ratio, body mass index (BMI) (respectively r=0,272, p=0,005, r=0,330,p=0,001, r=228,p=0,019). The waist-hip ratio was positively associated with HOMA-IR after multivariate analysis (beta=0,238, p=0,022). HOMA-IR level was 2,9±1,3, 2,4±1,5 and 3,1±1,8 in patients used cyclosporine A (CsA), sirolimus, tacrolimus ($p>0.005$). In patients used CsA, HOMA-IR was correlated with age, waist-hip ratio, and BMI (respectively r =0,328, p=0,048,

r=0,421, p=0,010, r=0,402, p=0,014). it was correlated with BMI in patients used sirolimus (r=0,479, p=0,006), and waist-hip ratio (r=0,443, p=0,006) in patients used tacrolimus. BMI was associated with HOMA-IR in all groups in multivariate analysis (respectively beta=-0,421, p=0,012, beta=0,379, p=0.023, beta= 0,529, p=0.007).
Our results indicate that abdominal waist-hip ratio is a major determinant of IR after renal transplantation. Even in the absence of hyperglycemia, renal transplant patients may have IR. If obesity is prevented, the long term patients and graft survival may be better than now.

LBP-29 COMPARISON OF 5 YEARS FOLLOW-UP OF PREEMPTIVE AND NON-PREEMPTIVE RENAL TRANSPLANT RECIPIENTS

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End-stage chronic renal disease (ESCRD) is a severe health problem with high mortality and morbidity rates and growing incidence both in our country and in the world. Preemptive renal transplantation is an important treatment modality for preventing dialysis-related comorbidities.
Specially in the studies of the last 15 years, preemptive transplantation has better outcomes than non-preemptive transplantation. Low infection and hypertension and less acute rejection episodes rates in preemptive transplant patients may be the main reasons for these results.
In our study, we compared the 5 year outcomes of 37 preemptive and 67 non-preemptive renal transplant patients and aimed to find out the differences of preemptive and non-preemptive transplantation according to adverse effects, complications, comorbidities, laboratory parameters, clinical symptomes, and both graft and patient survival.
In the study, preemptive patients were named as group 1 and non-preemptives as group 2. According to our statistical analysis, 3 (8,1%) of group 1 and 5 of group 2 (7,95%) patients had graft loss, whereas 1 (2,7%) of group1 and 1 (1,6%) of group 2 patients died respectively. No significant statistical differences were found for graft and patient survival between two groups at the end of 5 years (p=0,36 and p=1,00 respectively).
In the comparison for the complications, 4 (10,8%) of group 1 patients had serious infection whereas 20 (31,7%) of group 2 patients had infection which was statistically significant (p=0,02).
Hypertension rates of two groups were also significantly different with 67,6% in group 1 and 85,4% in group 2 (p=0,03).
There were no differences for other complications between groups.
As a result, preemptive renal transplantation, when compared ton onpreemptive renal transplantation, has lower complication rates. Further long-term studies may be more helpful for evaluating graft and patient survival rates.

LBP-30 THE CASE OF ISCHEMICALLY DAMAGED KIDNEYS REHABILITATION BY NORMOTHERMIC EXTRACORPORAL PERFUSION WITH LEUCOCYTES DEPLETION

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Background: Due to the organ shortage the potential of donor after cardiac death is actual issue. Organ removal is allowed only from brain death and uncontrolled donors after cardiac death in Russia. Ischemic-reperfusion injury is relevant for non-heart beating donation. We suggested the critical role of leucocutes in microvasculature blocking in donors kidneys.The subscribed protocol targets reparing kidneys by restoring energy resources and removal of activated leucocytes from kidney microcirculation.
Materials and method: The uncontrolled kidney donor's age was 47 y.o. The warm ischemic time was 52 minutes. The perfusion of abdominal organ was operated through femoral access and the creating of perfusion contour which included portable pump machine, oxygenator line, portable oxygen supply, and leucocytes depletion filer (6L/min). The perfusat was presented as a modificated donor blood (24°C temperature) including 25000 ME heparin, 1,5 mln ME streptokinase, 400 ml perfluorocarbonic emulsion. The start perfusion parameters were 500 ml/min volume, pressure 60 mm Hg with increasing till 1200 ml/min, 120 mm Hg, oxygen supply 500 ml/min, pCO_2 120 mm Hg, pO_2 425 mm Hg. The leucocytes number was 18×10^9 per ml^3 at the time of start perfusion and 4×10^9 per ml^3 to the finish. The procurement was performed during normothermic perfusion time and was finished by cold preservation flushing. Both kidneys were tested by pump perfusion machine and successfully transplanted to old patients. The diuresis has recommenced to the end of first week in both recipients, the common time of delayed grafts function was 3 weeks, the serum creatinin levels were 190 and 215 mmol/l to the end of 2hd month after transplantation.
Conclusion: Normothermic abdominal hemoperfusion with leucocytes depletion from circulating donor's blood is challenging protocol because it is allowed to rehabilitate kidneys after one-hour warm ischemic time.

LBP-31 PROOF OF CONCEPT STUDY: CARDIAC OUTPUT INCREASES AFTER RENAL TRANSPLANTATION – A PRELIMINARY REPORT

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Background: A major problem of kidney transplant is early post transplant deaths from cardiac causes (around 50%). We hypothesised that the extra work to increase cardiac output (CO) to perfuse the newly transplanted kidney may tip the balance against survival in patients with poor cardiac reserve.
Aim: To demonstrate an increase in CO after a kidney transplant.
Method: Prospective study of living donor recipients without cardiac comorbidity or fluid retention. Echocardiographic determinations of CO was performed by a cardiologist, blinded to the transplant status of the recipient, within two weeks before and repeated between 6 to 8 weeks after transplantation. The post transplant delay was judged to be a suitable time to achieve cardiovascular stability. Two tailed paired t-test was used to detect significant difference.
Results: There were 7 recipients, 4 males and 3 females, with mean age of 38.5 yrs and weight of 67.2 kg.

Details of the 7 patients

Patients	Status	Sex	Age Yr	Weight Kg	CO before Tx	CO after Tx	Difference
1 – NH	PD	M	34	68	4.7	5.28	0.58
2 – WB	PE	M	31	71.6	4.8	6.18	1.38
3 – NN	PE	F	51	81.4	4.3	4.76	0.45
4 – AH	HD	M	36	72.5	5.7	6.5	0.80
5 – HG	PE	F	29	53.8	3.9	4.98	1.08
6 – WL	PE	F	42	48.9	3.8	3.7	-0.1
7 – HT	PE	M	52	74.5	4.47	4.47	0
Mean (SD) of values of all 7 patients		4M/3F	38.5 (8.8)	67.2 (11.7)	4.53 (0.64)	5.13 (0.97)	0.6 (0.54)

CO = cardiac output; PE = Pre-emptive Tx, HD/PD = haemo/peritoneal dialysis

The mean CO prior to transplantation was 4.53 l/min and their CO at 6 to 8 weeks post transplant was 5.12. The mean increase of 0.6l/min was statistically significant (p=0.026).
Conclusion: Power calculations indicated a 40% chance of significant statistical difference in the pre-and post-transplant CO of 0.6 ml/min at alpha level of 0.05 and a sample size of 7. Increase in CO may explain our ability to eliminate early cardiac deaths in our programme by meticulous cardiac screening. We now need to a) increase the number of patients sampled, b) to compare the ability to increase cardiac output post transplant for different patient cohorts and c) to see if inability to increase in CO correlates with early graft failure in addition to early post transplant death.

LBP-32 DESENSITIZATION WITHOUT INTRAVENOUS IMMUNOGLOBULIN FOR LIVING DONOR KIDNEY TRANSPLANTATION IN T-CELL FLOW CYTOMETRY CROSS-MATCH POSITIVE PATIENTS – A PRELIMINARY STUDY

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Background: Kidney transplantation in human leukocyte antigen (HLA) cross-match positive patients had been a contraindication for kidney transplantation (KT). Recently, several pre-transplant desensitization protocols using rituximab, plasmapheresis or intravenous immunoglobulin (IVIG) have been reported as an effective regimen in the high risk group. However, the desensitization protocol has not been standardized. In this preliminary study we evaluated the feasibility of our desensitization protocol using plasmapheresis and rituximab without IVIG for living donor KT in the recipients with T-cell flow cytometry cross-match (FCXM) positive recipients.
Patients and Methods: We enrolled end-stage renal disease patients who had negative complement-depedent cytotoxicity cross-match but positive T-cell FCXM. Desensitization protocol was pre-transplant plasmapheresis (3 to 4 times) with or without single dose rituximab (500mg) at pre-transplant 7~10 days. Prior to living donor KT, negative conversion of T-cell FCXM was required.
Results: Seven patients underwent desensitization treatment with 3 to 5 times of plasmapheresis with 1-plasma volume exchange each. Single dose rituximab was administered prior to plasmapheresis in 3 patients. Five patients who showed negative T-cell FCXM after plasmapheresis, underwent living donor KT. In one patient refractory to conversion regimen, donor was changed to another with ABO-incompatible (AB→O) and positive T-cell FCXM. This pa-

tient underwent another session of plasmapheresis with rituximab administration, and showed negative in T-cell FCXM, and 1:2 in anti-A (IgM)/1:1 in anti-B (IgM) titer. Finally, living donor KT was performed in 6 patients including one with ABO-incompatible relation. Median follow-up duration was 10.5 months (range 2∼15). There was no episode of acute antibody-mediated or cellular rejection.
Conclusion: Although this study is preliminary short-term follow-up, desensitization protocol using plasmapheresis without IVIG in T-cell FCXM positive recipients reveals as a feasible strategy in living donor kidney transplantation.

LBP-33 REPLICATION OF HUMAN POLYOMAVIRUS BK BEFORE AND AFTER KIDNEY TRANSPLANTATION

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Reactivation of BK human Polyomavirus (BKV) from latent infection may be one of the main causes of BKV-nephritis in kidney transplant recipients.
Purpose: Since October 2007 we prospectively investigated a) the prevalence of BKV replication in immunocompetent patients (ptI+) in waiting list for kidney transplant and b) the change in prevalence and viral load in plasma (viraemia) and urine (viruria) of renal transplant immunosuppressed patients (ptI-).
Materials and methods: BKV replication of 105 patients on the waiting list for kidney transplantation (66 M,39 F) was assessed by qualitative PCR of plasma (T-1). Of these, 36 underwent cadaveric kidney transplantation; immunosuppression included tacrolimus/cyclosporine, mycophenolate mofetil and steroids. BKV load was measured by quantitative PCR on plasma and urine samples in these patients at the time of transplant (T0), at 3 (T1) and 6 months (T2) post transplantation.
Results: Overall, BKV viraemia was detected before transplantation in only 14.2% (15/105) of ptI+ patients (BKV+), while the occurrence of viral replication increased progressively up to 52% (19/36) 6 months after transplantation in ptI- subjects. Interestingly, 8 out of 19 BKV+ (42%) was already positive before transplant at T-1 (group A), while 11 (58%) were BKV- at T-1 (group B). Plasma and urine viral loads showed a progressive increase in the number of copies reaching the maximum value at T2, with viruria always preceding the detection of viraemia.
Conclusions: Time from kidney transplant and the immunosuppressive state seem to have a role in BKV replication in the post transplant period. PCR on urine heralds the following appearance of viraemia. Pre-transplant latent infection does not seem to be the most relevant risk factor while latent viral infection of the donor could be a significant and unrecognized risk factor for the development of post-transplant active infection.

LBP-34 ATORVASTATIN (ATO) ADMINISTERED BEFORE AS WELL AS AFTER ISCHEMIA ALLEVIATES ISCHEMIC ACUTE RENAL FAILURE (iARF)

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Introduction and aims: Ischemia-reperfusion injury (I/R) causes glomerular capillaries endothelial dysfunction and nephron epithelium necrosis leading to iARF with activation of inflammatory reaction mediated by increased cytokines and adhesion molecules expression as well as reactive oxygen species synthesis and neutrophils activation. In consequence, the long-term kidney failure may develop next.
Statins with proofed pleiotropic function can prevent inflammatory reaction and potentially alleviate ischemic ARF. The aim of this study was to assess the best schema of ATO therapy in periischemic period and sense of postischemic administration.
Methods: 14 days after right nephrectomy, I/R was induced in 40 male Sprague-Dawley rats by 45-minute clamping of left renal vascular pedicle. ATO by oral gavage was administered: 5mg/kg body weight (bw) twice daily for 4 days before ischemia (group 1) or 7 days after (group 3). Rats of the control groups (2 and 4) were given respectively vehicle. Creatinine clearance (Cr_{Cl}; ml/min/kg bw) and fractional excretion of sodium (FE_{Na}; %) were estimated 48 hours and 7 days after I/R.
Results: As shown in table (means±SD), 48 hours after I/R, Cr_{Cl} was significantly higher, whilst FE_{Na} lower in group 1 and 3 in comparison to controls. 7 days after I/R Cr_{Cl} was significantly higher in rats of group 3.

ATO 2×5mg/kg		Before I/R (group 1)	Control (group 2)	*P*	After I/R (group 3)	Control (group 4)	*P*
N		10	10		10	10	
48h	Cr_{Cl}	1,31±0,80	0,27±0,20	*<0,005*	0,48±0,30	0,17±0,20	*<0,05*
	FE_{Na}	2,54±3,77	7,49±7,03	*<0,05*	7,63±7,0	16,56±10,45	*<0,05*
7d	Cr_{Cl}	2,46±1,02	2,42±0,47	*NS*	2,59±0,55	1,56±0,79	*<0,005*
	FE_{Na}	0,17±0,16	0,14±0,08	*NS*	0,10±0,06	0,13±0,10	*NS*

U Mann-Whitney test.

Conclusions: Atorvastatin given during reperfusion only effectively alleviates ischemic acute renal failure like administered before I/R. These findings point at validity of statin therapy of clinical incidences of ARF where pretreatment is impossible as well as in kidney transplant recipients management.

LBP-35 MEDICAL AND NON-MEDICAL DETERMINANTS OF DELAYED ACCESS TO THE KIDNEY TRANSPLANTATION WAITING LIST

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Eligibility criteria for kidney transplantation diverge among centres, although factors associated with poor access to the waiting list are well-known. In our centre we develop active attempts to manage several of those risk factors in order to allow a later access to the waiting list. For this purpose, we evaluated 129 patients currently on list in our centre in April 2009 and evaluated medical and non-medical factors that determined delayed access to the wait list. Eighty patients were male (62%), 81 Caucasians (62.7%), average age 46.1±19.7 years, 9 diabetics (0,06%) and 112 treated with haemodialysis (86.8%). Thirty-five patients (27.1%) were placed on list more than 6 months after the first consultation, 22 (17%) after one year and 15 (11.6%) more than 18 months after the first visit. Using logistic regression, registration in the waiting list more than 6 months after the first visit was associated with the presence of coronary artery disease (CAD) (p=0.037), valvular disease (p=0.022), hypertension (p=0.047) and chronic hepatitis B (HBV) infection (0.046). Registration at 12 months was associated with the presence of CAD (p= 0.038), valvular disease (p=0.016) and HBV infection (p=0.004) and at 18 months only CAD (p=0.003) and HBV infection (p=0.001) determined delayed access to the waiting list. Non-medical factors (race and distance from our department) were not associated with delayed access.
In conclusion, in our centre, the presence of CAD and chronic HBV infection were the most important predictors determining delayed access to the kidney transplant waiting list.

LBP-36 TESTICULAR PAIN AND SWELLING FOLLOWING LAPAROSCOPIC DONOR NEPHRECTOMY (LDN) FOR LIVING DONOR RENAL TRANSPLANT

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Laparoscopic donor nephrectomy (LDN) is now a well-established method for the procurement of kidneys from living donors. Since the introduction of LDN in our centre in February 2005, approximately one-third of all nephrectomies have been performed using this approach. At present in our centre, LDN is only offered to donors suitable for left nephrectomy. Our aim was to investigate the incidence of testicular pain and swelling following LDN.
54 left-sided LDNs were performed in our centre between February 2005 and December 2008, 25 of which were in men. A transperitoneal totally laparoscopic approach was used in all cases. An equal number of consecutive male donors who received left-sided open donor nephrectomy (ODN) were identified as a control cohort. A retrospective structured interview was conducted and data collected on testicular pain, swelling and numbness, as well as urinary symptoms and sexual dysfunction.
Data was acquired from 25 of 25 (100%) LDN and 25 of 25 (100%) ODN patients. Of 25 LDN patients, 11 (44%) experienced testicular pain and/or swelling. In most instances pain was of immediate onset, mild to moderate in severity, lasted for a few days to several weeks and was associated with testicular swelling (10 of 11). One donor had testicular swelling alone. Testicular pain or swelling was not apparent in those who had received ODN, with only 2 of 25 (8%) experiencing mild testicular pain, one with swelling. Testicular pain and swelling following LDN was not associated with any urinary symptoms or sexual dysfunction.
Testicular pain and swelling following laparoscopic living donor nephrectomy

appears to be a common problem but is under-reported in the literature. Further investigation is required into the causation of these symptoms.

LBP-37 EFFICACY AND SAFETY OF CINACALCET IN RENAL TRANSPLANT PATIENTS WITH SHPT AND ADVANCED CKD (STAGES 3B AND 4)

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Introduction: Cinacalcet has been successfully used in dialysis patients for the treatment of SHPT, where effectively suppresses PTH without causing hypercalcemia and hyperphosphatemia. Also it has demonstrated efficacy in post-transplant hypercalcemic SHPT, however it remains unclear it's indication in CKD patients, pre-dialysis or pos-transplantation. Our aim was to review the efficacy and safety of cinacalcet in renal transplant patients (RTP) with SHPT and CKD 3b-4.
Patients and methods: Retrospective review of all RTP treated with Cinacalcet in our centre (Sep/06 to Dec/08). Demographic, clinical, analytical and treatment (immunosuppressive and concomitant) data were collected. Patients were divided in two groups by their estimated GFR at baseline; Group A) MDRD $\geq$ 45 ml/min·1.73m^2, Group B) MDRD 15-45 ml/min·1.73m^2 (CKD 3B and 4).
Results: 25 patients were included in the analysis (Group A, n=15; Group B, n=10). Cinacalcet was initiated a mean of 51.1$\pm$54.5 m pos-transplant, and follow-up was of 12.9$\pm$8.01 m. The initial and final dose of Cinacalcet were 30 and 39,2$\pm$19,5 mg/day, respectively. Comparative of clinical data and analytical results between two groups, and baseline and end of follow-up, are showed in Table 1. Cinacalcet was efficacy improving iPTH and Calcium control in two groups. There were no differences in BP or hypotensive medications between baseline and end of follow-up. There were no symptomatic nor sever hypocalcemic or hiperphosphoremic episodes. Cinacalcet was withdrawn in 2 patients due to drug related adverse events.

	Baseline			End of follow-up		P value (Basal vs end fu)	
	Group A (MDRD ≥ 45)	Group B (MDRD <45)	P value (A vs B)	Group A	Group B	Group A	Group B
Age (years)	51,1 ± 13,4	53,2 ± 13,3	0,690	-	-	-	-
Hemodialysis (months)	39,7 ± 27,4	43,7 ± 28,1	0,747	-	-	-	-
Cold time (h)	16,1 ± 3,4	18,0 ± 4,6	0,166	-	-	-	-
Donor age (years)	31,4 ± 14,5	54,8 ± 16,9	0,001	-	-	-	-
Tx - Cinacalcet (months)	49,4 ± 49,9	53,3 ± 60,2	0,860	-	-	-	-
Cr (mg/dL)	1,17 ± 0,29	2,15 ± 0,74	<0,001	1,16±0,22	2,24±0,71	0,089	0,666
MDRD (mL/min*1.73m²)	65,8 ± 18,6	32,7 ± 8,1	<0,001	66,7±16,8	31,1±8,3	0,318	0,483
i-PTH (pg/mL)	303 ± 141	415 ± 201	0,141	227±105	257±151	0,002	0,016
Calcium (mg/dL)	11,2 ± 0,8	10,5 ± 0,7	0,036	9,5±1,0	9,8±0,6	<0,001	0,002
Phosphorus (mg/dL)	2,6 ± 0,5	3,2 ± 0,9	0,048	2,7±0,5	3,6±1,09	0,179	0,079
Alkaline phosphatase	93,9±67,8	88,5±42,2	0,073	93,1±38,6	85,3±44,6	0,860	0,848
Cholesterol (mg/dL)	174±38	176±27	0,595	160±26	168±24	0,098	0,404

Conclusions: In our experience, Cinacalcet is effective, safe and well tolerated in RTP with hypercalcemic HPT and adequate renal function, and in RTP with SHPT and advanced CKD (MDRD $<$ 45 ml/min·1.73m^2).

LBP-38 TUBERCULOSIS IN RENAL TRANSPLANT RECIPIENTS

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Purpose: Renal transplant recipients have a high risk of opportunistic infections. Tuberculosis (TB) is more prevalent in this group compared to normal population, and results in high morbidity and mortality. In this retrospective study we aimed to explore the prevalence and clinical manifestations of TB in renal transplant patients.
Materials and methods: We retrospectively analyzed pediatric and adult renal transplant recipients data in our center between 1992 and 2009.
Results: The prevalence of TB was 3.2 percent. Five patients received kidney from living-donor related and four from cadaveric donors. Cadaveric-donor patients received anti thymocyte globulin (ATG) for induction, and four patients received pulse steroid for acute rejection. The median duration of time between transplantation and TB was 21 (1-150) months, and between induction/pulse therapy and infection 5 (1-100) months. The immunosuppressive protocols included prednisolone and cyclosporine/rapamycine with or without mycophenolate mofetil/ azathiopurine.
The major symptoms were fever (%77), cough (%66), and abdominal pain (%22). Extrapulmonary TB with intestinal (2/9), pericardial (1/9), lymph node (1/9) and cerebral (1/9) involvements developed in 5 patients.The diagnosis was made by one of the methods: (1) demonstration of acid-fast bacilli or cultivation of *Mycobacterium tuberculosis* at specimens (7/9); (2) histological evidence of caseating granuloma (3/9); (3) response to anti-TB treatment in patients with clinical and radiological findings of highly suggestive TB, but without any microbiologic or pathologic confirmation (1/9). All patients received quartet of anti-TB therapy for a median duration of 9 months. One patient died at second month of therapy because of dissemination of TB, and one patient returned to hemodialysis because of chronic allograft nephropathy.
Conclusion: The prevalence of TB was high in our renal transplant patients. The quartet of antiTB treatment including rifampicin resulted in success in majority of patients.

LBP-39 KIDNEY TRANSPLANTATION UTILIZING EXPANDED CRITERIA DONORS

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Purpose: According to The United Network for Organ Sharing (UNOS) approximately 15% of potential cadaveric donors fulfil the criteria of Expanded criteria donors. 39% of these donors are declined because of different reasons. The main reason why to utilize kidneys from ECD is general known shortage of organs available for transplantation. On the other hand, utilizing ECD is associated with higher propability of DGF, rejection and worse long term outcome. The purpose of our work was to evaluate the short-term outcomes in the group of patients – recipients of ECD kidney (group A) and compare them with recipients of standard – non ECD graft (group B)
Methods: We have evaluated the group of 28 patients, which underwent renal transplantation from the "marginal" donor. We were evaluating histology in zero biopsy (according to Remuzzi score system), cold ischaemia time, frequency of DGF and creatinine level in the discharge day and six months after operation. The control group consisted of 28 recipients of standard kidney.
Results: The average Remuzzi score in the A vs B group was 2,89/12 vs. 1,46/12, average cold ischaemia time was 19 hrs 22 min vs.16 hrs 49 min, primary graft function was reported in 17 vs. 20 pts, DGF in 11 vs. 8 pts. The average creatinine level in the discharge day was157,5 umol/l vs. 119 umol/l (p=0.11), six months after operation 126 umol/l vs. 108 umol/l (p=0,14). The number of biopsy proven acute rejections was the same in both groups 7 vs.7.
Conclusion: By evaluating of our results in short period of time we didn't find statisticaly relevant difference in observed parameters between recipients of kidney from ECD and recipients of standard (non ECD) graft.

LBP-40 DOES ROUTINE COAGULATION SCREENING PREDICT THE RISK OF BLEEDING AFTER RENAL TRANSPLANT BIOPSY?

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Introduction: Coagulation testing is widely performed before renal transplant biopsy on assumption of predicting the risk of post biopsy bleeding. We investigated the clinical usefulness of this assumption.
Material and method: Platelet count (PC), prothrombin time (PT) and activated partial thromboplastin time (aPTT) in all patients undergoing ultrasound-guided renal transplant trucut biopsy were retrospectively reviewed while results of patients not biopsied served as control. Test results during early ($<$6 week) and late ($>$6 week) post-transplant period were noted and correlated with bleeding complications. Results outside reference range (PC $<$ 150$\times$10^9/l; PT $>$14 s; aPTT $>$35 s) were treated as abnormal.
Results: Of 408 patients transplanted over 6-yr study period, 325 consecutive biopsies were performed on 197 (48%) patients. Of these, 211 (65%) early and 114 (35%) late biopsies were performed in 151 and 85 patients respectively while 42 (10%) had biopsy in both periods. Tests were abnormal in 19% during the early and 18% in the late period (no significant difference from control group). Fourteen (4.5%) episodes of significant hematuria were recorded, 9 (4 in 1 patient) in early and 5 in late period. Seven episodes (4 in early and 3 in late phase) were associated with normal coagulation tests. Of 6 patients with early phase complications, 5 were on haemodialysis for delayed graft function (DGF) while one had acute rejection. The coagulation abnormalities as well as clinical characteristics such as age, sex, blood pressure, number of passes, number and length of cores did not influence bleeding after biopsy.
Conclusion: Post transplant biopsy bleeding occurs in patients with both abnormal and normal coagulation. Indiscriminate coagulation screening is not a useful predictor of bleeding although it is still recommended in patients undergoing haemodialysis for DGF.

LBP-41 THE PROCESS OF ESTABLISHING LAPAROSCOPIC DONOR NEPHRECTOMY PROGRAMME: LIVERPOOL EXPERIENCE

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Background: A reduction in morbidity associated with live donor nephrectomy confers social and economic benefits. The stakes being high, it is imperative that highest standards of safety are ensured when a new procedure is introduced in a unit. We report the process of introduction of hand-assisted laparoscopic donor nephrectomy (LDN) programme in Liverpool.
Methods: Two consultant surgeons initiated the programme over a period of 3 years. In the first phase, a total of 16 weeks were spent in six centres outside United Kingdom, observing nephrectomy by total laparoscopic or hand-assisted approach (both trans-peritoneal and extra-peritoneal) and working on anaesthetised pig models (n=6). An initial series of 27 cases was carried out by both consultant surgeons assisting each other, first 12 cases were mentored by the visiting expert. First 23 cases were performed via hand-assisted extra-peritoneal approach followed by further 4 cases by trans-peritoneal total laparoscopic approach. In addition, 6 nephrectomies were carried out for non-functioning kidneys, including 5 for polycystic kidneys.
Results: Audit data showed median in-hospital stay 5 days (range 3–6 days) for LDN which was same as for open procedure (range 4-10 days). Three right donor kidneys (all hand-assisted extra-peritoneal) and 24 left kidneys were retrieved. Mean blood loss for open procedure was 283 ml versus 58 ml for the LDN group. In the hand-assisted extra-peritoneal group, one patient developed delayed graft function, and another developed adhesive bowel obstruction needing laparotomy. No graft loss was reported in our study group.
Conclusion: A careful and planned introduction of a laparoscopic approach to live donor nephrectomy gives good results without compromising patient safety. In initial learning phase, the option of hand-assisted approach allows direct handling of tissues and hence easier haemostatic control compared to total laparoscopic procedure.

LBP-42 THYROID DYSFUNCTION AND THYROID CANCER IN RENAL TRANSPLANT RECIPIENTS: A SINGLE CENTER EXPERIENCE

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Purpose: The prevalence of thyroid neoplasm in the renal transplant population has not been widely published and little has been written about recommendations for thyroid cancer screening in transplant patients. The aim of this study was to investigate the incidence of the thyroid cancer after renal transplantation, and to evaluate changes in thyroid hormone levels.
Materials and methods: 122 renal allograft recipients followed in our center from October 1989 to April 2007 were investigated. All patients were evaluated for changes in thyroid hormone levels and underwent thyroid ultrasonography to examine the gland. Totally 72 nodules were detected, and fine-needle aspiration biopsy (FNAB) performed under ultrasonography guidance (US-guided) for all nodules greater than 1 cm diameter, and for those 8-10 mm diameter with calcifications.
Results: One-hundred-eighty patients (88.5%) had normal thyroid function. Subclinical hypothyroidism was diagnosed in two patients, whereas ten patients had subclinical thyrotoxicosis, and low T3 syndrome was diagnosed in two patients. The thyroid volume was 14.2±7.2 ml. The goiter was diagnosed in majority of subjects (91.8%). Thyroid nodules (n:72) were detected by sonography in fourty-nine recipients (single nodule in 30, multiple in 19 cases). The biopsy samples (n:96) were cytologically interpreted as benign (87. 5%), suspicious (8.3%), and inadequate for diagnosis (4.1%). All patients with suspicious cytology underwent surgery, and histological examination confirmed the diagnosis of papillary thyroid carcinoma in one (0.8%).
Conclusion: Because of high incidence of thyroid dysfunction in transplant patients, screening of thyroid function should be a part of follow-up. Our results suggest that although frequency of nodules seemed to be increased in kidney transplant patients, the prevalence of thyroid cancer was not higher than seen in normal population.

LBP-43 UROLOGICAL COMPLICATIONS AFTER RENAL TRANSPLANTATION – ENDOUROLOGICAL TREATMENT OF URETERAL STENOSIS

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Introduction: The urological complications after renal transplantation is estimated between 4 to 8%, being the ureteral stenosis (US) the most frequent one (2-7,5%). These complications can me managed endoscopically or surgically.
The main purpose of this study was to achieve the US endourological treatment success rates.
Methods: Retrospective study of all kidney transplanted patients of the Santo António's Kidney Transplant Department (SAKTD), complicated with US, that were treated between 2002 and 2008.
Results: Since 2002 in SAKTD, 575 kidney transplants were performed, 82 of which were of live donors.
24 of these patients, 83% men, with 43,9±15 years, were diagnosed with US. It's a 4,2% complication rate. 20 of those were located in the vesicoureteral junction (VUJ) and only 4 were located in the ureteropelvic junction (UPJ).
Acute renal failure with hidronefrosis of the kidney graft 19,75±24,5 months (1 to 72 months) after transplant, was the most frequent clinic manifestation.
An endourological treatment was initially performed in 19 patients, and in others an open surgical procedure was made. 79% of the endourological technique consisted in percutaneous balloon dilatation of the US, and in 21% an antegrade ureteral stent placement.
The overall success rate of the endourological complication management was 53%.
An open surgical procedure was always performed when endourological treatment failure happened.
Conclusions: In this study the US complication rate was of 4,2%, and the majority of them appeared during the first years (19,75±24,5 months), and affected principally (83%) the distal ureter (VUJ).
In our institution the preferable initial therapeutic management of the US is endourological, performed in 79% of patients, with 53% success rate. When an endourological procedure fails or when a pielography shows an old and extensive US, a classical open surgical procedure is made. We can affirm that in selected cases, the initial endourological management of US is safe and successful.

LBP-44 RESULTS OF OVERSEAS KIDNEY TRANSPLANTATION IN AZERBAIJAN

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Introduction: Despite the improvement of results of graft and patient survival in kidney transplantation many aspects of it remains unsolved. Our purpose was to study results of the kidney transplantation in Azerbaijanian patients at the different neighbouring countries.
Methods: We retrospectively reviewed the clinical outcomes of previously kidney transplanted patients in the outside of Azerbaijan.We identified 108 patients, who underwent kidney transplantation outside of the Azerbaijan between June, 2000 and July, 2008. All patients were Azerbaijanian citizen. 93 were transplanted in different transplant centres at Iran, 3 were transplanted in Pakistan, 6 were transplanted in Turkey, 6 were transplanted in Russia. All patients had organs from the living donors, while 58 patients were male, 50 patients were female patients. Mean age of the patients were 42±11.3 years. While in 35 patients primary cause of chronic renal failure (CRF)was glomerulonephritis, in 30 patients was pyelonephritis, in 11 patients was diabetes, in 9 patients was hypertonia, remaining 21 patients CRF was unknown aetiology. Induction immunosuppressive therapy was available in 56/102 patients. Remaining patients' data is not well documented.
Results: Complications were mainly infectious.In one patient had wound side gas gangrene which manifested with septic shock and died as a result of multiple organ failure. At last follow-up, mean serum creatinine level was 1.45±0.24 mg/dl, episodes of acute rejection had occurred in 31/102. 12/102 grafts failed due to acute rejection and 80/102 were alive.
Conclusions: Kidney functions and graft survival were not good after overseas kidney transplantation. Although, improper follow up was a main factor, other problems like incomplete preoperative preparation, states of donor organs condition had great impact on postoperative complication and graft survival.

LBP-45 BORTEZOMIB ALONE DOES NOT DECREASE DSA LEVELS IN SENSITIZED KIDNEY TRANSPLANT RECIPIENTS

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Context: The presence of donor specific antibodies (DSA) after kidney transplantation is associated with an increased risk of acute humoral rejection, of transplant glomerulopathy and hence a deleterious influence on the graft prognosis. Bortezomib, an inhibitor of the proteasome, used in the treatment of myelome, may be a drug of choice l to decrease DSA levels in sensitized kidney transplant recipients.
Patients and methods: Four renal transplants recipients with a biopsy proven subacute antibody-mediated rejection (SAMR) and the presence of DSA at a significant level (>2000 MFI) were treated with Bortezomib (4 doses of 1.3 mg/m^2 at day 1, 4, 8, 11). Anti-viral prophylaxis was initiated and pursued during 6 months. DSA levels, serum creatinine, proteinuria, haemoglobin, platelets counts were monitored at days 0, 4, 11, 21, and 40. Changes in plasmocytoïd cells and B lymphocytes subsets as well as specific antibody titers against various infectious agents (such as anti-HSV and HBV) were studied. Adverse events and infectious episodes were recorded during the whole follow-up (12 weeks).
Results: DSA levels remained stable between day0 and Day40 in all four kidney recipients: 4994 to 4111; 2483 to 2530; 2302 to 2779; 3060 to 3031 MFI respectively. Serum creatinine remained unchanged in all patients. None presented thrombopenia or peripheral neuropathy. They all presented a major asthenia during the treatment and thereafter during one month. Two of them experienced a severe conjunctivitis. There were no significant changes in plasmocytoïds cells, B lymphocyte subsets and specific antibody titers against infectious agents.
Conclusion: Bortezomib alone does not decrease DSA levels in sensitized kidney transplant recipients. Except for fatigue and conjunctivitis, tolerance was acceptable. These data strongly suggest that bortezomib used alone is not useful in sensitized kidney transplant recipients.

LBP-46 DONOR AGE AND P-GLYCOPROTEIN (ABCB1, MDR1) ARE ASSOCIATED WITH CHRONIC HISTOLOGICAL DAMAGE PROGRESSION IN RENAL ALLOGRAFTS

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Background: The complementary impact of donor kidney quality, allograft rejection and calcineurin inhibitor nephroxicity on the progression of histological damage of renal allografts is not well studied. Moreover, the determinants of individual susceptibility to calcineurin inhibitor nephrotoxicity are not known.
Methods: In a prospective cohort of 252 adult renal allograft recipients, treated with the combination of tacrolimus, mycophenolate mofetil and corticosteroids, 744 renal allograft biopsies were obtained regularly from time of transplantation to 3 years thereafter. The determinants of the histological evolution were assessed, including tacrolimus exposure, renal P-glycoprotein (ABCB1) expression and polymorphisms in *CYP3A4*, *CYP3A5* and *ABCB1* genes.
Results: Within the first 3 years after transplantation a progressive increase in interstitial fibrosis and tubular atrophy, glomerulosclerosis and vascular intimal thickening was noted (all $P<0.001$). Higher donor age ($P<0.001$), absence of P-glycoprotein expression at the apical membrane of tubular epithelial cells ($P<0.05$) and combined donor-recipient homozygosity for the *C3435T* variant in *ABCB1* ($P<0.001$) were associated with increased susceptibility to chronic allograft damage and progression of lesions suggestive of calcineurin inhibitor nephrotoxicity, independent of graft quality at implantation ($P<0.05$). These effects of donor age and *ABCB1* polymorphisms were reflected in graft functional evolution (respectively $P<0.001$ and $P<0.05$) but not in early graft survival, which was mainly determined by acute T-cell mediated rejection ($P<0.05$).
Conclusion: The effects of higher donor age reach beyond the quality of the allograft at implantation and continue to be important for the histological evolution in the post-transplantation period. *ABCB1* genotype and renal tubular epithelial expression of P-glycoprotein determine susceptibility to chronic tubulointerstitial damage of transplanted kidneys, independent of donor age. Kidneys from older donors and kidneys with absent or dysfunctional P-glycoprotein may benefit most from a calcineurin inhibitor-free immunosuppressive regimen.

LBP-48 INFECTION – A SIGNIFICANT CLINICAL AND ECONOMIC BURDEN FOLLOWING RENAL TRANSPLANTATION

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Introduction: Infectious complications are known to be the cause of significant morbidity and mortality after renal transplantation. We present an audit of infection rate and outcome for patient and graft in our unit.
Methods: Admissions to the transplant unit were analysed prospectively over a 12 month period. Reasons for admission were documented, and, if due to infection, aetiology established, whether renal function was affected, as well as mortality. Immunosuppression consisted of basiliximab induction with tacrolimus/MMF maintenance.
Results: A total of 183 patients (107 male, 76 female; mean age 47.55 $\pm$ SD 14.9 yrs) had 331 admissions over the 12 months. 21% (69 episodes in 54 patients) of admissions, and the commonest cause, were attributable to infection. 13.3% patients who were admitted for reasons other than infection experienced an infection during their admission. 40% of newly transplanted patients experienced an infection before discharge. 61.5% of all infective episodes resulted from a UTI and 10% had septicaemia. CMV syndrome was treated in 8 patients. 63% patients experienced deterioration in kidney function due to infection (AKIN criteria). 78% had full recovery of function but 16% patients only had partial recovery, 1 patient needed to start long-term dialysis and 2 patients died. Length of stay was 15 days for patients with infection and 6 days for those without.
Conclusion: Bacterial infections were the predominant cause of admission post-transplantation with significant serious consequences in a minority of patients. Peri/post-operative UTI remains a challenging problem. There may be a case for antimicrobial prophylaxis to reduce the burden of infection in patients, with its increased admission rate and economic costs as has previously been suggested.
1. Fox et al (Am J Med 1990, 89: 255-274).

LBP-49 A FAST AND SAFE LIVING-DONOR "FINGER-ASSISTED" NEPHRECTOMY TECHNIQUE: RESULTS OF 359 CASES

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Objective: To determine operative parameters and complications, using finger assisted donor nephrectomy.
Methods: 359 consecutive live donor procedures, performed between October 2000 and November 2008. Patient demographics, intra-operative parameters and post-operative complications.
Results: Mean donor age was 44.2$\pm$12.3 years (range, 21-75 years). Average body mass index of 28.2$\pm$5.3 (range, 17.1-44.9). 23 patients (6%) have right-sided donor nephrectomies and 41 donors (11%) have multiple renal arteries. Median incision length was 6.8cm (range, 3.5-15cm). Average operative time was 117 minutes (range, 50-265 minutes). Median blood loss of 109mL (range, 20-500mL) and an average warm ischaemia time of 4.5minutes (range, 1.5-10 minutes). Four patients (1%) required peri-operative blood transfusions. There were no other intra-operative complications, and there were no donor deaths. Thirteen patients (4%) developed minor post-operative complications, including two incisional hernia, over a median follow-up period of 19 months (range, 2-97 months).
Description of finger assisted nephrectomy technique: The patient is positioned in the lateral-decubitus position. 4.0 cm transverse incision is made anterior to the 11th rib. All muscle layers and the lumbodorsal fascia are cut. Two Dever retractors are positioned superiorly and medially. Dissection of the ureter and peri-urethral tissue is performed to obtain 10-12cm of ureter. A long right-angled dissector with a diathermy extension, is used to free capsular adhesions. The renal artery and vein are isolated. The gonadal and lumbar veins are dissected, Liga-clipped and divided. Five thousand units of heparin are administered intra-venously. The ureter, renal artery and vein are individually divided using the ETS-FLEX endoscopic articulating linear vascular cutter (Ethicon Inc.),followed by removal of the kidney. The wound is closed in three muscle layers, followed by sub-cuticular skin closure.
Conclusion: This technique can result in a smaller incision length whilst maintaining patient safety, and has few post-operative complications.

LBP-50 THERAPY WITH CINACALCET IN KIDNEY TRANSPLANTED PATIENTS WITH SECONDARY HYPERPARATHYROIDISM: EFFICACY AND SAFETY

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It exists a high rate of secondary Hyperparatiroidism in kidney transplant, being

the most frequent cause of hypercalcaemia post-transplant. Both factors are relevant in the morbid-mortality.
Objective: To determine the safety and efficacy of Cinacalcet in transplanted patients with hypercalcaemia and/or secondary Hyperparatiroidism. To check his safety in terms of stability of renal function, immunosupresor levels and the absence of adverse reactions.
Patients and methods: Transverse, retrospective and observational study in 26 kidney transplanted patients in treatment with Cinacalcet (30 mg/day). No patient presented concomitant treatment with D vitamin, phosphorus binders or calcium. Cinacalcet dose during the analyzed time did not get modified, except for one patient whose dose was raised to 60 mgs/day.
Immunosupressor treatment with anticalcineurins, mycophenolate mofetil and corticoids. We analyzed PTHi, calcium, phosphorus, creatinine, dose and levels of immunosuppressants basal and to 3, 6 and 12 months after the start of the treatment with Cinacalcet.
Results: A total of 26 patients were included (17 males and 9 women), with a mean age of 52±12,81 years
Statistically significant differences were found in the level of calcium and ionic calcium to the 3, 6 and 12 months and in the phosphorus to 3 months. There were no significant differences in the l phosphorus to 6 and 12 months. The treatment with Cinacalcet does not seem to have a negative effects on the renal function.

Time	Before Cinacalcet	3 Months	P T0-P3	6 Months	P T0-P6	12 Months	P T0-P12
PTHi (pg/ml)	314±407	314±129	NS	165±102	NS	231.50±132	NS
Ca (mg/dl)	10.49±0.49	9.37±0.76	0.015	9.76±0.57	0.006	8.92±0.59	0.006
P (mg/dl)	2.37±0.41	2.80±0.57	<0.05	2.48±0.44	NS	2.54±0.46	NS
Cr (mg/dl)	1.63±0.54	1.73±0.66	NS	1.68±0.46	NS	1.56±0.34	NS
Ionic calcium	1.37±0,007	1,24±0.09	0.001	1.25±0.08	0.000	1.19±0.07	0.001

Conclusions: Cinacalcet seems a good alternative for hyperparatiroidism treatment of the transplanted patients.
It is well tolerated in low dose and it is efficacious in the control of the hypercalcaemia.
Even though we did not detect significant differences in PTH levels, a higher dose will be probable more effective, as other studies demonstrate.
The renal function does not get modified with this type of treatment.

LBP-51 PROGNOSTIC VALUE OF INTRAOPERATIVE RENAL TISSUE OXYGENATION MEASUREMENT ON EARLY RENAL TRANSPLANT FUNCTION

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Purpose: Kidney transplants from living donors have a higher survival rate than cadaveric kidneys probably due to shorter ischemia time. We hypothesized that intraoperative kidney oxygenation (kox) predicts postoperative transplant function.
Methods: We measured kox (microvascular hemoglobin oxygen saturation in %) by reflectance spectrophotometry and microcirculatory kidney perfusion by laser Doppler flowmetry (O2C™, Lea, Germany) 5 and 30 min after kidney reperfusion on the surface of the transplant in 53 renal transplant patients.
Results: Kox improved 30 min after reperfusion compared to 5 min (from 67 to 71%, $p<0.05$) probably due to higher oxygen extraction shortly after reperfusion. Kox correlated with mean arterial blood pressure and central venous pH ($p<0.01$). Most importantly, kox was significantly higher in kidneys from living compared to cadaver donors (74 vs. 63%) and in kidneys with good as opposed to those with poor postoperative function (71 vs. 45%). Finally, kox correlated positively with cold ischemia time and postoperative creatinine clearance and negatively with plasma creatinine, need for hemodialysis and hospital length of stay.
Conclusion: The intraoperative measurement of tissue oxygenation in kidney transplants is predictive of early postoperative kidney function. Further studies should look at the effects of therapeutic maneuvers aimed at improving kidney oxygenation intraoperatively.

LBP-52 BIASED EXPANSION OF MEMORY-TYPE CD8+ T CELLS AS A CAUSE OF ACUTE REJECTION UPON IMMUNOSUPPRESSION WITHDRAWAL IN A TOLERANCE PILOT TRIAL IN LIVER TRANSPLANTION

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Background: Peritransplant T cell depletion was suggested to favour tolerance induction in organ transplantation. In a pilot trial in liver transplantation (LT), we used high doses anti-thymocyte globulins (ATG) induction therapy followed by Sirolimus and investigated whether such regimen would allow early immunosuppression (IS) withdrawal.
Methods: Patients received 3.75 mg/kg ATG/day from day 1 to 5, followed by Sirolimus. In these patients, we monitored the phenotype of circulating lymphocytes, interleukin (IL)-7 serum levels, interferon (IFN)- g and IL-17 mRNA accumulation in mixed leucocyte reaction (MLR) and intra-graft IFN-g mRNA and IL-17 expression by qPCR and immunohistochemistry respectively.
Results: Ten patients were included. In all, ATG therapy induced a profound $CD4^+$ and $CD8^+$ T cells depletion. $CD4^+$ T cells remained low for more than 12 months, while $CD8^+$ T cells, mostly of memory phenotype (T_{EMRA}, $CCR7^-CD45RA^+$), recovered and expanded from month 2. After ATG administration, increased IL-7 serum levels were measured, peaking at day 25. In the first 3 patients, attempts of IS discontinuation at days 140, 206 and 124 were followed by reversible acute rejection (AR), 140, 40 and 39 after withdrawal. At AR, significant levels of IFN- g and IL-17 mRNA were measured in MLR between recipient T-cells and donor spleen cells. Consistently, high levels of IFN-g mRNA and IL-17 were measured within rejecting liver grafts. Immunostaining revealed significant $CD8^+$ T cells infiltrates at the time of acute rejection while double staining indicated that these cells participate to IL-17 production.
Conclusions: Lymphopenia-induced IL-7 production following ATG induction might lead to preferential expansion of memory-type $CD8^+$ T-cells, potentially responsible for AR after IS withdrawal through IFN- g and IL-17 secretion.

LBP-53 SURVIVAL BEFORE AND AFTER THE INTRODUCTION OF MELD IN BRAZILIAN PATIENTS ON THE WAITING LIST FOR LIVER TRANSPLANTATION

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To examine whether the official implantation of Model for End-Stage Liver Disease (MELD) as a criteria for organ allocation we studied risk factors for patients' deaths and the accuracy of MELD score as a predictor for death.
Methods: Patients on the waiting list for liver transplantation were divided into two Periods depending on if they were on the waiting list before (Period 1) or after (Period 2) the MELD introduction in Brazil.To study survival of the patients in each period Kaplan Meir and long-rank tests were used. Predictive factors were identified in the univariate analysis and multivariade analysis,using Cox regression method. Receiver Operating Characteristic (ROC curve) was used to analyze CTP (Child-Pugh-Turcotte) and MELD accuracy.
Results: Two hundred and ninety-five patients in Period 1 were analyzed, and 240 in Period 2. In Period 1, survival in 3,6,9- months and 1 year were 95.6%,90.5%, 84.9% and 69.6% respectively and in Period 2, 95.7%, 92.1%, 85.3% and 83.3%, respectively. It can be seen that no statistical differences between the two periods were found (log-rank: $\chi^2=2.35$; GL=1; P=0.125). Multivariable analysis shows CTP,MELD-Na, and albumin levels, besides Spontaneous Bacterial Peritonitis (SBP), the independent factors related to survival in Period 1. In period 2, CTP, creatinine levels, INR, besides SBP were the independent factors. ROC curve for CTP was 0.676 and MELD was 0.644 (P=0.377) in Period 1. In Period 2, ROC curve for CTP was 0.680 and for MELD was 0.718 (P=0.411).
Conclusion: Patients' survival on the waiting list for liver transplantation did not change 1 year after the introduction of MELD. Although SBP was not an objective data, it would be considered as an important factor related to survival of these patients.

LBP-54 COMPARISON OF FIVE SCORES TO PREDICT MORTALITY IN BRAZILIAN CIRRHOTIC PATIENTS IN WAITING LIST FOR LIVER TRANSPLANTATION

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To evaluate the accuracy of 5 scores for mortality prediction in cirrhotic patients on a waiting list for liver transplantation in two different periods, in Brazil, one-year before (Period 1) and after (Period 2) official adoption of the Model for End-Stage Liver Disease (MELD).
Methods: Patients on a waitlist for liver transplantation at Clinics Hospital – State University of Campinas (UNICAMP), Sao Paulo, from July1st, 2005 to June 30th, 2007, were studied. The data were analyzed into two periods according to how long they were on the list, before or after official MELD score use in Brazil. Period 1 was considered from the begin of the study until June, 30th, 2006, after which MELD score was implanted. So, period 2 corresponds to the rest of reported time. Univariable and multivariable models were constructed to examine predictive factors of mortality. Receiver Operating Characteristic (ROC curve) was used to compare Child-Turcotte-Pugh (CTP), MELD estimation, MELD-Na, Delta MELD e Delta MELD- Na.
Results: Two hundred and ninety-five patients in Period 1 were studied, and 240 in Period 2. The results were: CHILD C ($P<0.001$), Na $\leq$130 (P=0.002) and creatinine 1.2-1.5 (P=0.028) all which are independent factors for mortality prediction in Period 1 and CHILD C (P=0.001), creatinine $>$1.5 ($P<0.001$) and INR 1.8-2.3 (P=0.008) in Period 2. In Period 1, ROC curves for CTP, MELD, MELD–Na, DELTA MELD and DELTA MELD- Na were respectively 0.676, 0.644, 0.734, 0.794 and 0.767. In period 2, ROC curves for CTP, MELD, MELD-Na, DELTA MELD and DELTA MELD-Na were respectively 0.680, 0.718, 0.786, 0.835, and 0.821.
Conclusion: Delta MELD and Delta -MELD Na showed a better accuracy to predict mortality in patients on the waiting list for liver transplantation than the others scores.

LBP-55 HOW CAN WE TREAT A PATIENT WITH LIVER CIRRHOSIS (HCV), HEPATOCELLULAR CARCINOMA (HCC) AND SYCHRONOUS COLON CANCER?

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Purpose: The co-existence of liver cirrhosis with HCC and colon cancer (Ca) is a rare clinical condition with if only few references in the pertinent literature. Our aim is to present the way we treated a similar clinical case in our institution.
Materials and methods: A 46-year-old male was diagnosed with 3.5cm HCC at segment VII, relating to his chronic HCV. He underwent laparoscopic evaluation and liver appearance and biopsy from the left lobe matched to the Child B/C liver cirrhosis. As he fulfilled Milan criteria, suggested a liver transplantation (OLTx) and proceeded to pre-OLTx assessment. During protocol colonoscopy, an ulcerative sigmoid colon-Ca was found. He successfully completed his pre-OLTx assessment and listed. He underwent an OLTx 3 weeks later. OLTx and his post-transplant course was uneventful and discharged home on day 11, with immunosuppression regime of Everolimus, Myfortic and Prezolon. Two months after his transplant, underwent a sigmoidectomy and a month later he commenced chemotherapy for his colon-Ca (6 cycles of FolFox).
Conclusion: We chose to proceed first to OLTx for the following reasons: first, if the patient after sigmoidectomy needed chemiotherapy, he won't be able to receive any with cirrhotic liver and second, after sigmoidectomy the patient was more likely to develop a de-compensated liver cirrhosis and not be able for further treatment. The way we treated this patient, he was able to have chemotherapy immediately after colon resection with a good functioning liver. One year after his OLTx, patient is in excellent condition free of his disease with a perfect graft function, with low doses of immunosuppression. HCV-RNA remains negative.

LBP-56 ORTHOTOPIC LIVER TRANSPLANTATION FOR PRIMARY SCLEROSING CHOLANGITIS

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Primary sclerosing cholangitis (PSC) is a rare, chronic cholestatic liver disease of uncertain etiology characterized by the destruction of the intrahepatic and extrahepatic bile ducts through inflammation and fibrosis. This development of inflammation and fibrosis leads to biliary complications including cirrhosis. They are also at risk for the development of cholangiocarcinoma (CCA) and those with IBD for colon carcinnoma. Due to the unknown pathogenesis there are currently no effective therapies known to halt progression. This survey focuses on OLT as an succesful approach for patients with PSC.
Medical records of patients who underwent OLT since 01/1999 have been reviewed for PSC. Actuarial patient and graft survival was determined at 1,2 and 5 years. The incidence and outcome of patients with CCA, recurrence of PSC and post transplant CCA was determined. Furthermore we assesed the median follow-up, re-transplantation and immunosuppression.
Eight patients underwent OLT for PSC in our department. Four patients had associated IBD (Colitis ulcerosa), these were all men. One patient underwent several times biliary tract endoscopy. Seven patients received single grafts, one patient needed retransplantation due to arterial thrombosis within the early postoperative course. This patient received initally a split graft, whereas the rest reiceived full size grafts. In every OLT we performed a Roux-Y-reconstruction after resection of the common bile duct. Every patient received Tacrolimus as immunosuppression throughout the follow-up-period. The 1-, 2- and 5-year survival rate were n=6/8, 6/8 and 5/8, whereas graft survival was n=5/8, 5/8 and 4/8. Recurrence of the PSC was found in none patient, also no patient is known to suffer from CCA. One patient underwent total colectomy due to symptomatic colitis.
Liver Transplantation provides excellent patient and graft survival for patients suffering from PSC due to low recurrence rates of PSC and low malignancies in the graft.

LBP-57 PORTAL VEIN THROMBOSIS (PVT) IN LIVER TRANSPLANTATION AND SURGICAL TECHNIQUE USED IN PATIENTS THAT THROMBECTOMY WAS NOT POSSIBLE

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To demonstrate technical options for portal vein reconstruction in patients with PVT grade II and III in which thrombectomy was not possible.
Material and methods: We analyzed, retrospectively, 420 patients submmited to liver transplantation from September 1991 to March 2009. The PVT was diagnosed and classified as intra-operative in grade I ($<$50% of PVT), grade II ($>$ 50% of PVT), grade III (complete PVT and proximal part of superior mesenteric vein = VMS) and grade IV (Full PVT and parts of VMS).
Results: There were 26 cases of PVT grade I (6.19%), three cases of PVT grade II (0.71%) and one case of PVT in grade III (0.24%). In all cases of PVT the grade I thrombectomy was effective, but in three cases of PVT grade II and in one case PVT of grade III was insufficient to thrombectomy (0.95%), requiring different techniques for portal vein reconstruction. The types of reconstructions were: two cases of anastomosis of the portal vein of the donor liver graft with the iliac vein in the recipient VMS; a case of anastomosis of the portal vein with the donor's vein splenorenal collateral and another with left gastric varicose vein. The methods of image used (with Doppler ultrasound and computed tomography) were insensitive method to diagnose PVT preoperatively. The survival rate in the sample was 75% and for patients with PVT with grade I thrombectomy effective and without PVT were 73.8%.
Conclusions: We conclude that the technical options with or without the use of venous grafts are feasible in the portal venous reconstruction, the imaging methods were not sensitive in the preoperative diagnosis of PVT and patients without or with PVT have similar mortality rates.

LBP-58 LACK OF HEPATIC ARTERIAL PERFUSION IS AGGRAVATING THE INITIAL DAMAGE CAUSED BY FOCAL HEPATIC OUTFLOW OBSTRUCTION AND IMPAIRING THE SPONTANEOUS RECOVERY PROCESS

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Purpose: We previously observed that after right median hepatic vein ligation (RHMV-L)+partial hepatectomy in rats, the outflow obstructed territory can recover spontaneously via the formation of vascularised sinusoidal canals (VSC). We hypothesized now, that the initial damage, the recovery process and the formation of VSC are dependent on hepatic arterial perfusion.
Methods/Materials: Male Lew rats were subjected to RMHV-L +/- additional dearterialization (ligation of hepatic artery) and +/- additional denervation (arterialized versus non-arterialized syngeneic liver transplantation). Analysis included liver damage (extent of necrosis (macroscopy, morphometry), liver enzymes, histology), hepatic microcirculation (OPS: sinusoidal diameter, VSC), liver regeneration (BrdU-PI) and vascular remodelling (Laminin, vW).
Results: RHMV-L primarily blocked blood flow in the obstructed zone (OZ),

leading to clear demarcation. All sinusoids dilated in OZ and border zone (BZ). Within 24hrs confluent necrosis was observed in the OZ with viable portal islands. Within POW1, VSC in BZ with visible blood flow and normal sinusoidal structure developed. Furthermore, necrotic areas were resorbed and gradually replaced via hepatocyte proliferation mainly in the BZ and in the viable portal islands leading to a full parenchymal recovery. Additional dearterialization led to a full necrosis of the OZ without any viable portal islands. At POW4 only single large draining VSC without any surrounding sinusoids were found. The necrotic area decreased over time via hepatocyte proliferation in BZ, but did only lead to full recovery in 1/6 animals. Additional denervation further aggravated the extent of damage and slowed down the recovery process. Denervation, but preservation of arterial perfusion led to a slightly reduced outcome compared to RHMV-L only.
Conclusion: Lack of hepatic arterial perfusion is associated with severer initial damage and impairment of spontaneous recovery from hepatic focal outflow obstruction.

LBP-59 IMPACT AND EXPERIENCE ONE YEAR AFTER MELD IMPLEMENTATION – SINGLE-CENTER RESULTS IN GERMANY

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Background: On December 16, 2006 the EUROTRANSPLANT-Organisation implementated the Model for Endstage Liver Disease (MELD)-Score as a new allocation system for patients on the liver transplantation waiting list. One year after implementation of the new allocation system the impact on the early-postoperative outcome shall be analysed.
Patients and methods: All patients undergoing orthotopic liver transplantation (OLT) at our hospital from 2006/01 to 2007/12 were reviewed. The total was divided into period A from 2006/01 to 2006/12/16 (pre-MELD) with 42 patients and period B from 2006/12/16 to 2007/12 (first year after MELD)
Results: In the MELD-era the median MELD-Score (except high urgency (HU)-patients) at the time of OLT increased [16,3 points (period A)/22,41 (B); p=0,007). The median time on the waiting list for OLT (except HU-patients) decreased [12,10 months (A)/7,97 (B); p=0,1] just like the waiting list mortality [18,4% (A)/10,4% (B); p=0,015]. The median postoperative hospitalization on the intensive care unit [16,78 days (A)/25,13 (B); p=0,094] and the time of general hospitalization increased [30,29 days (A)/43,39 days (B); p=0,016] As the 90-days-mortality remains the same, especially the percentage of postoperative infections increased significantly [26% (A)/50% (B); p=0,018].
Conclusions: In the first year after implementation of the MELD-Score the new allocation system benefited sicker patients compared to the era before MELD, which resulted for them in a shorter waiting time until OLT. There is no increase in 90-days-mortality, but in the time of hospitalization and in the percentage of postoperative infections. Especially patients with HCC benefited from the new allocation system due to their adjusted match MELD, which results in a higher probability of timely OLT.

LBP-60 REMNANT LIVER REGENERATION AND SPLEEN VOLUME CHANGES AFTER LIVING LIVER DONATION: INFLUENCE OF THE MIDDLE HEPATIC VEIN

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Background and objectives: Graft harvest with or without the middle hepatic vein affects venous return and function of the remaining liver. The aims of this study are to compare the remnant liver volume and spleen changes in the donors of different types of graft harvest and to evaluate the influence of resection with or without the middle hepatic vein on the remnant liver volume regeneration, spleen volume change and serum total bilirubin.
Patients and methods: A total of 165 donors were grouped according to the type of graft harvest: 88 donors underwent left lateral segmentectomy (LLS), 10 donors underwent extend left lateral segmentectomy or left lobectomy (LL), and 67 donors underwent right lobectomy (RL). Groups LLS and LL were later combined as group LH (left hepatectomy, n=98). The total liver volume (LV) and spleen volume (S1) before graft harvest, graft weight (GW), regenerated liver volume (LV_{6m}) and spleen volume (S2) six months post-donation were calculated.
Results: There were no significant differences in the regenerated liver volume 6 months post-operation (LV_{6m}) and recovery ratio (LV_{6m}/LV x 100%) among the different groups, albeit significant smaller LV_{6m} in both groups compared with the initial liver volume was noted. Post-operative spleen volume (S2), average spleen ratio (S2/S1) and spleen change ratio were significantly larger and higher in group RL than in group LH. A significant increase in spleen volume was noted in both groups 6 months after graft harvest. A significantly higher TB in group RL (4.1±1.7 mg/dL, range: 1.4-8.5 mg/dL) was noted compared to that of group LH (1.6±1.0 mg/dL, range: 0.7-6.2 mg/dL).
Conclusion: There was a significant increase in the regenerated remnant liver and splenic volumes 6 months post-operation in all types of hepatectomy following living donor hepatectomy.

LBP-61 HIGH AND DIFFERENT MOLECULAR PREVALENCE OF HBV, HCV, AND ESPECIALLY HGV INFECTIONS IN ORTHOTROPIC LIVER TRANSPLANTATION PATIENTS

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Background: Orthotropic liver transplantation is the final therapeutic protocol in some of liver injuries, dysfunctions, and malignancies which introduced by different and multiple criteria including hepatitis viral infections. Between hepatitis viruses the role of HBV and HCV infections in serious liver clinical complications were confirmed. But the knowledge about relationships between liver malfunction and HGV infection are mostly unknown and need have completed study.
Objectives: In this research the prevalence of HBV, HCV, and HGV infections were determined by PCR-based molecular methods in orthotropic liver transplantation patients.
Material and methods: In this cross sectional study the 173 EDTA-treated blood samples were collected from 77 orthotropic liver transplant recipients post-transplantation. A qualitative PCR protocol was used for determination of HBV infection in transplant patients. All liver transplant plasma samples were analyzed for HCV and HGV infections by an in-house-RT-PCR-protocol.
Results: HBV-DNA was diagnosed in 71 of 173 (41%) samples in 30 of 77 (38.96%) transplant patients, respectively. The HCV-RNA was detected post-transplant in 23 of 173 (13.3%) samples in 7 of 77 (9.1%) patients, respectively. Thirty and three of 173 (19.1%) plasma samples in 12 of 77 (15.6%) liver transplant patients were infected by HGV genome.
Conclusion: Detection of different prevalence of HBV, HCV, and HGV infections and also especially high distribution of HGV-RNAmia in orthotropic liver transplant recipients, announced repeatedly the possible role of HGV infection in liver clinical complication and dysfunctions.

LBP-62 PROLONGED COLD ISCHEMIA LEADS TO HMGB-1 RELEASE, BUT DOES NOT INTERFERE WITH SPONTANEOUS LIVER GRAFT ACCEPTANCE

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Aim: According to "Danger signal theory", cellular injury leads to the release of alarmins (eg.HMGB-1). Alarmins act as inflammatory mediators and activate adaptive immunity.
Therefore, we wondered whether prolonged cold ischemia (CI) leads to the release of HMGB1, which in return interfere with spontaneous liver graft acceptance (SLGA).
Method and material: CI dependent release of HMGB-1 (Western-Blot) and liver enzymes was assessed in the effluent of explanted livers of Brown-Norway (BN) rats (n=6), cold preserved in saline for 24h.
Interference with SLGA was tested by subjecting BN livers to 1hr, 6hr, 8hr, 9hr and 10hr (n=6 in each group) CI in saline before transplantation into Lew-recipients. After sacrifice on POD30 or spontaneous death, grafts were evaluated by histology.
Result: CI in saline caused severe injury to explanted liver starting between 8h and 9h CI as indicated by massive release of HMGB-1 and liver enzymes into the effluent. In contrast to our hypothesis, transplantation of liver subjected to CI of 9 and more hours did not lead to lethal rejection (lymphocytic infiltrate extending heavily into the liver parenchyma) but to the death of recipients within 24h postoperatively due to severe IRI.
Livers subjected to 8h of CI or less were all spontaneously accepted by Lew-recipients (lymphocytic infiltrate mostly limited to expanded portal tract), and underwent the typical postoperative course with a period of weight loss (max 20%, POD3-5) and severe, but transient jaundice (POD13.3±1.4).
Conclusion: HMGB1 was only released after prolonged CI of the liver and served as a marker of lethal organ damage, following the same kinetic as the enzymes. In contradiction to the danger theory, CI for less than 8 hours did not interfere with postoperative recovery or SLGA, whereas prolonged preservation caused lethal IRI.

LBP-63 NON-INVASIVE ASSESSMENT OF SEVERE FIBROSIS IN PATIENTS TRANSPLANTED FOR NON-HCV RELATED LIVER DISEASES

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Purpose: To assess the efficacy of TE, biochemical tests, and more complex scores in determining severe fibrosis (F≥3) after LT in non-HCV patients. Moreover, we assessed the diagnostic value of the ActiTest for predicting moderate to severe inflammation (A≥2).
Methods: One hundred seven patients transplanted for non-HCV related liver diseases [HBV infection (n=24), alcohol-related liver disease (n=22), autoimmune-related liver disease (n=14), and other etiologies (n=47)] who underwent liver biopsy, TE and blood tests on the same day were included in the study.
Results: The optimal TE cut-off values were 5.0 kPa for F≥1, 7.3 kPa for F≥2, 9.9 kPa for F≥3 and 12.6 kPa for F=4, respectively. The corresponding area under the receiver operating curves (AUROCs) for F≥1, F≥2, F≥3, and F=4 were 0.86, 0.85, 0.88 and 0.97, respectively. Univariate analysis identified the following significant variables for predicting F≥3: INR (p=0.01), total bilirubin (p=0.005), AST (p<0.0001), ALT (p=0.007), AP (p=0.004), GGT (p=0.0007), total protein (p=0.01), albumin (p=0.03), cholesterol (p=0.01), gamma globulin (p=0.0005), haptoglobin (p=0.02), alpha 2 macroglobulin (p=0.01), hyaluronic acid (p=0.01), TE value (p<0.0001). Independent predictors of severe fibrosis were cholesterol (p=0.03), AST (p=0.03), ALT (p=0.02), GGT (p=0.04), total protein (p=0.04), haptoglobin (p=0.03) and TE value (p=0.002). Results from multiparameter scores revealed a significant difference between patients with F0-F2 and F≥3 [APRI (p<0.0001), Benlloch score (p=0.01), Fibrotest (p=0.0006), Hepascore (p<0.0001), Fib4 (p=0.0005), Lok score (p=0.02), Fibroindex (p=0.001)].
For the ActiTest, optimal cut-off value was 0.45 for prediction of A≥2 with corresponding AUROC curve of 0.69 indicating a lower performance as compared to results from studies in viral liver disease.
Conclusion: Transient elastography as well as multiparameter scores can be reliably used for predicting F≥3 in non-HCV transplant recipients.

LBP-64 HEPATITIS C (HCV) – 3 STUDY: DAY-90 PROTOCOL BIOPSY (PB) GRADE (G) IS A SURROGATE MARKER FOR SEVERE HCV RECURRENCE (SHCVR), ON PB, AT YEARS 1 AND 2 POST LIVER TRANSPLANTATION (OLT).

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Assess efficacy of steroid (P)-free immunosuppression (IS) using daclizumab (DAC), tacrolimus (TAC) and mycophenolate mofetil (MMF) to minimize acute rejection (AR) and SHCVR.
Methods: Prospective, multicenter study (n=18) on 312 adults (Pts) HCV-OLT randomized (1:1:2) to 3 IS arms (see Results). Laboratory/graft biopsies done when indicated or PB: days (d) 90/365/730. AR graded by Banff schema; HCVR staged by Batts classification. Endpoints: AR (G ≥2 + RAI ≥4) and/or SHCVR (Stage [S] ≥2 or G ≥3, anytime). Significant statistics: p≤0.05
Results: Arm 1 (n=80): TAC+P; Arm 2 (n=79): TAC+P+MMF; Arm 3 (n=153): DAC(3 doses, d 1, 3 and 8) + TAC + MMF. All data (intention to treat; central pathologist) reported, at 2 years, for arms 1,2 and 3 *respectively*. Graft and Pt survivals: 79%, 78%, 84% (NS) and, 83%, 81%, 87% (NS). AR-free rates: 86%, 87%, 86% (NS). HCVR-free incidences: 33%, 27% and 34% (NS). Arm analyzes showed S ≥3 fibrosis in 33%, 28% and, 19% (NS). More SHCVR noted, between years 1-2, in arms 1 and 2. In Pts with no S ≥3 HCVR in year 1, freedom of S ≥3 at year 2 is superior in arm 3 (75%, 85% and 93%, p<0.01). Differences persist for arms 1 + 2 (P) vs. 3 (P-free): 80% vs. 93% (p<0.01) and, for arms 1 (no-MMF) vs. 2 + 3 (MMF): 75% vs. 90% (p<0.01). Day-90 G showed a prognostic value - for higher inflammation (G 2-4) - on the degree of fibrosis (S) at years 1 and 2 (table).
Conclusions: Two-year follow up completion suggests HCVR, *apparently*, not affected by IS. However, progression rate to S ≥3, during year 2, is favorably influenced by MMF, particularly on P-free regimen. Day-90 PB showed that G (2-4) is an indicator for SHCVR at years 1 *and* 2 with consequent direct therapeutic implications. Longer-term follow up is critical to confirm these findings on HCVR.

Day-90 grade impact on years 1 and 2 stage

Level	N	Grade 0–1	Grade 2–4	p value
Stage 0–1, Year 1	86	73 (54%)	13 (23%)	
Stage 2, Year 1	66	47 (35%)	19 (34%)	
Stage 3–4, Year 1	39	15 (11%)	24 (43%)	
Total	191	135	56	<0.0001
Stage 0–1, Year 2	48	42 (40%)	6 (14%)	
Stage 2, Year 2	62	41 (40%)	21 (50%)	
Stage 3–4, Year 2	36	21 (20%)	15 (36%)	
Total	146	104	42	<0.005

LBP-65 PREVALENCE OF BONE MINERAL DENSITY LOSS IN CYSTIC FIBROSIS PATIENTS WITH PROGRESSIVE LUNG DISEASE

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Objective: In cystic fibrosis patients (CF) bone loss is caused by various reasons, such as 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. Only an early and adequate osteoporosis therapy (Biphosponate/calcium/vitD therapy) in osteopenic or osteoporotic CF can prevent them from bone fractures.
Methods and results: In a prospective study we analysed clinical data, bone radiographs and dual-energy X-ray absorptiometries (DXA) of all 18 CF patients (9 f/9 m; age: 28.8±9.9 range: 16 – 44 years ; BMI: 17.3±1.9), who were lung transplanted at our institute between 04/08-04/09 (CFTX).
Mean time from CFTX to first DXA was 19.4±10.8 days. 11 CF (61.1%) had osteoporosis, 6 CF (33.3%) had osteopenia and only 1 CF (5.6%) had normal perioperative bone mineral densitiy.

Bone mineral density

	Normal	Osteopenia	Osteoporosis
Femur	n=1 (5,6%)	n=7 (38,9%)	n=10 (55,6%)
LWS	n=1 (5,6%)	n=6 (33,3%)	n=11 (61,1%)

Hypercyphosis and scoliosis was detected in 16 pts (88%). 2 CF (11.1%) had bone fractures of the thoracic spine. Parathyroid hormone (PTH) was elevated in 5 CF (27.8%) during the observation time, osteocalcin in 1 CF (5.6%) and 25-Hydroxyvitamin D was in all CF in a normal range. Mean perioperative creatinine clearance in CFTX was 132.8 ml/min.
Conclusion: The prevalence of osteoporosis in CF admitted to lung transplantation (LuTX) is very high. A high bone fracture rate especially, if these patients are exposed to corticoids and immunosuppressive therapy can be expected within the first postoperative year.
We therefore conclude, that: 1. All CF should be screened for osteoporosis;
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 incidence of osteoporosis and vertebral column fractures within the first year after LuTX.

LBP-66 THROUGH MOTHERS' EYES: THE LIVED EXPERIENCE OF CARING FOR A CHILD WHO HAS RECOVERED FROM LIVER TRANSPLANTATION

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Paediatric liver transplantation commenced in New Zealand in July 2001. Each year six to eight New Zealand children receive a liver transplant.
Care of post transplantation children following discharge is monitored in outpatient clinics and hospital settings. The long term implications of caring for a child recovering from a life-threatening condition to relative normalcy are largely unobserved.
Mothers, whose children had undergone a liver transplant more than one year ago, were the participants in this research. Mothers are the most common primary caregiver of children.
A Heideggerian hermeneutic phenomenological approach, informed by the work of van Manen (1990) was used. Three mothers were interviewed to reveal the meanings of the phenomenon - what is the meaning of lived experience of mothers in caring for their child following liver transplantation?
Analysis and interpretation indicated that stress was a consistent feature. Ruddick's (1983) concepts of maternal thinking were utilised to draw together the emerging themes. The absolute capacity for attentive love was the central theme. An essential theme arising from the analysis was the concept of survival relating to unique features of liver transplantation and the potential consequences of liver rejection and failure.

The findings identified the need for good support for families of children following transplantation; assistance in the establishment of maternal coping strategies and regular feedback on the children's progress acknowledging the role and care provided by mothers. Health professionals may develop new understandings of the dynamic and evolving issues arising out of the provision of care by mothers, including a greater empathy and understanding of the experiences of mothers in their roles of caring. The findings provide glimpses of the life of children who have recovered from a liver transplant.

LBP-67 MICROSURGICAL FREE TISSUE TRANPLANTATION AS A VALUABLE PROCEDURE IN FOOT RECONSTRUCTION

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Purpose: Owing to the limited soft tissue donor sites in the foot area, the use of microsurgical tissue transplants is frequently becoming mandatory in this area, especially in cases of massive defects due to the common motor vehicle accidents. In this study, we tried to evaluate foot defects according to their size, shape and site and to determine the general and specific parameters of free tissue transplantation to the foot area in concomitance with the patients needs.
Materials and methods: Eleven patients were included in this study. For each patient, complete history was taken, general and local examination, photographic documentation, laboratory investigations, imaging and other investigations were performed. Free flap transplants were applied in all cases as follows: Latissimus dorsi flap in five cases, Rectus abdominis flap in three cases, Scapular flap in one case, Gracilis flap in one case and Radial forearm flap in one case.
Results: Nine flaps survived. No infection or donor site complications were recorded. Every patient had the optimum free flap as regards the defect size, site, depth, condition, shape, donor site availability and the recipient vessels' condition.
Conclusion: The study of the optimum free tissue transplant for foot reconstruction in relation to the present defect and the patient condition is crucial to have significant results.