POSTERS

IMMUNOSUPPRESSION / IMMUNOLOGY

P01 ANTIBODY MEDIATED REJECTION IN VASCULARIZED COMPOSITE ALLOTRANSPLANTATION

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Introduction: Clinical relevance of antibody-mediated rejection (AMR) in vascularized composite allotransplantation (VCA) remains unknown. While C4d deposition and presence of donor specific antibodies (DSA) have been previously described, the phenotype, clinical symptoms and treatment requirement and options have not been reported.
Patients: Two male patients presented with edematous hands and forearms and described a sensation of tension without any exanthema typical for a rejection episode at nine and three years after bilateral forearm and unilateral hand transplantation, respectively.
Results: Punch-skin biopsies revealed rejection grade Banff II-III in both patients. Immunhistochemical analysis identified large aggregates of lymphocytes with an architecture resembling lymph nodes. CD20 staining identified the center of the aggregates almost entirely consisted of B-lymphocytes. DSAs (Luminex) were found at high levels in both patients for the first time since transplantation. Based on the predominance of B-cells and DSAs with lack of response to conventional treatment with steroids and Tacrolimus dose increase, Rituximab was given at 375 mg/m^2 BSA. In response, clinical symptoms disappeared and biopsies showed normal skin with absence of B-cells. DSAs were negative at 3 months after rituximab.
Conclusion: We herein report the first cases of a B-cell driven rejection with presence of DSAs in VCA at nine and three years after forearm and hand transplantation, Rituximab therapy successfully reversed the event in both cases.

P02 DSA CLEARANCE AND FUNCTIONAL RECOVERY OF A KIDNEY TRANSPLANT FROM SEVERE ACUTE HUMORAL REJECTION UNDER A COMBINED TREATMENT WITH ECULIZUMAB AND BELATACEPT

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We report a 58 year old female which underwent renal transplantation in our center. C*omplement-dependent cytotoxicity (*CDC) cross-match was negative. Due to historic panel reactive antibodies of 100%, therapeutic plasma exchange (TPE) was performed once before and after transplantation. A more sensitive AMS ELISA X-match excluded donor specific antibodies (DSA) on day 1. Initial therapy included thymoglobulin, tacrolimus, MMF and steroids. A biopsy was performed 3 days after tx, demonstrating acute tubular necrosis (ATN), C4d negative. Seven days later, a second biopsy showed type 2 humoral rejection, strongly C4d positive. DSA against HLA class I A2, B12 and B15 were detected. Thymoglobulin was continued, steroid pulses, rituximab and 7 consecutive immunoadsorptions (IA) were initiated. Humoral rejection with high C4d positivity persisted.

On day 21, weekly eculizumab. Serological complement analysis performed immediately before the first dose showed no signs of activation. A sequence of daily TPE with supplemental eculizumab was started 7 days later, without success (DSA+ rejection). The anuric patient was dismissed, weekly eculizumab therapy was continued. Signs of thrombotic microangiopathy in follow up biopsies led to IS switch to cyclosporine and finally to belatacept (5 mg/kg bw every 2 weeks). Following initiation of belatacept urine production started to increase. Three months (mo) after onset of eculizumab and 1 mo after belatacept start, DSA were below detection levels. Eculizumab levels were measured by ELISA in serum and urine samples to exclude proteinuria associated loss. Five mo after transplantation and 4 mo after start of eculizumab, dialysis therapy was discontinued and creatinine levels began to decline.

P04 FOLLOW-UP DATA FROM HERAKLES STUDY AT MONTH 24: MAINTAINED SUPERIOR RENAL FUNCTION IN PATIENTS ON AN EVEROLIMUS-BASED CALCINEURIN INHIBITOR FREE REGIMEN COMPARED TO STANDARD CYCLOSPORINE/ MYCOPHENOLATE AND LOW CYCLOSPORINE/EVEROLIMUS

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Aim: To follow up (FU) on renal function (RF) at month (Mo)24 post renal transplantation (Tx) on 3 different immunosuppressive regimens with different calcineurin inhibitor (CNI) exposure.
Methods: 802 patients (pts) were included in this 1 year, prospective, open-label, randomized active-controlled multi-center study. After induction with basiliximab all pts received cyclosporine A (CsA), enteric-coated mycophenolate sodium (EC-MPS) and steroids. 3Mo post Tx 499 pts were randomized 1:1:1 to either a) continue standard (STD) CsA (100–180 ng/ml) with EC-MPS (n = 166), b) convert to a CNI-free regimen with everolimus (EVE;5–10 ng/ml) and EC-MPS (n = 171) or c) convert to CNI-low regimen with EVE (3–8 ng/ml) and reduced CsA (50–75 ng/ml) (n = 162). All pts continued on steroids. Mo24 FU visit was performed by 131 (95.6%) STD, 132 (95.7%) CNI-free and 125 (92.6%) CNI-low pts. RF as primary endpoint was calculated as Glomerular Filtration Rate (cGFR; Nankivell).
Results: CsA trough levels: 99 $\pm$ 32 ng/ml in STD, 83 $\pm$ 34 ng/ml in CNI-low pts. EVE trough levels: 6.7 $\pm$ 3.1 ng/ml in CNI-free, 6.2 $\pm$ 2.3 ng/ml in CNI-low pts. RF was similar at randomization 3Mo post Tx and had significantly improved at Mo12 by +5.6 mL/min/1.73 m2 (95%CI:[+2.9;+8.3]; $P < 0.001$) in favour of the CNI-free regimen and remained significantly improved by +4.8 mL/min/1.73 m2 (95%CI:[+1.0;+8.6]) in favour of the CNI-free regimen at Mo24 (ITT; $P = 0.014$).
Conclusion: Reduced CsA in combination with EVE did not result in better RF compared to STD therapy with EC-MPS. However, CNI-free regimen lead to better RF maintained for 2 years, confirming previous reports.

P05 TACROLIMUS - GENERIC OR ORIGINAL, IS THERE A DIFFERENCE?

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Purpose of review: To provide an overview of currently available data about the use of original or generic Tacrolimus for immunosuppression in solid organ transplantation.
Recent findings: Tacrolimus is a basic immunosuppressive agent and is used in many immunosupressive regimens after solid organ transplantation. Tacrolimus was launched in Germany in 1995 as Prograf®. The first generic of this calcineurin inhibitor (CNI), Tacrolimus HEXAL®, has been available in Germany since March 2010 as hard capsules for oral administration. The marketing authorisation was granted in the framework of the EU decentralized procedure based on proof of bioequivalence in healthy volunteers by the European Medicines Agency (EMA). From an economic point of view substitution of the original product with a generic is understandably favored. Still concerns about safety and efficacy of generic tacrolimus in patients exist. In the last few years quite a few studies on this topic have been published, most of them hardly noticed by the transplant community. More than 1000 transplant patients have been observed so far, who received a generic, most frequently the Sandoz/HEXAL product, either as a substitute or as the primary drug (Table).
Summary: The research data demonstrate bioequivalence between the generic and the original formulation of Tacrolimus. Given the comparable safety and efficacy profile shown in most studies and the cost savings recognized, conversion from brand-name tacrolimus to generic tacrolimus should be encouraged. Even when used critically, the available clinical data support the use of the generic form of tacrolimus.

P06 DOSE/TIME-DEPENDENT MODULATION OF THE ENDOTHELIAL FUNCTION THROUGH INDUCTION AGENTS: NON-DEPLETING VS. DEPLETING AGENTS

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Objective: Polyclonal-antithymocyte-globulins (ATGs) and anti-CD25 antibodies are agents employed for induction of immunosuppression in solid organ transplantation. We aimed to investigate the effect of different regimens of immunosuppressive induction agents upon transendothelial-migration of peripheral blood mononuclear cells (PBMC).
Methods: Human microvascular endothelial-cells were either activated or not and further treated with 25 or 125 μg/ml ATG (Thymoglobulin©,Sanofi-Aventis, Germany) for 2 h or 24 h, or with 5 μg/ml Basiliximab (Simulect©,Novartis, Germany) for 2 h or 24 h. PBMC were either activated or not and further treated with 25 or 125 μg/ml ATG or with 5 μg/ml Basiliximab for 2 h and then used for transendothelial-migration-assays.
Results: Prophylactic 24 h administration of ATG/Basiliximab to naïve endothelial-cells without PBMC treatment reduced transendothelial-migration. Prophylactic 24 h administration of ATG/ Basiliximab to naïve endothelial-cells after PBMC treatment with the same agents reduced the transendothelial-migration after 24 h. In both cases no effect could be observed after 2 h treatment. Basiliximab, though not ATG, showed a reduction of transmigration after 2 h treatment of PBMCs without naïve EC treatment.
Conclusion: Immunosuppressive induction agents can modulate the endothelial activity in a dose and time dependant manner. Our results suggest that administration of induction agents over longer time periods could provide a potential benefit regarding endothelial immunomodulation.

P07 COMPREHENSIVE ANALYSIS OF GENETIC VARIANTS INFLUENCING PLASMA LEVEL OF TACROLIMUS IN KIDNEY TRANSPLANTATION

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Background: The immunosuppressant drug tacrolimus exhibits high interindividual pharmacokinetic variation mainly due to variant genotype of cytochrome P450 (CYP) 3A5. The aim of this study was to analyse if further single nucleotide polymorphisms (SNPs) in genes contributing to the regulation of the CYP3A locus, contribute to tacrolimus dose/trough ratios.
Methods: A cohort of 189 patients, receiving tacrolimus after kidney transplantation, was genotyped for *CYP3A5*3* (rs776746), *CYP3A4*22* (rs35599367) and recently identified SNPs in peroxisome proliferator activated receptor alpha (*PPARα*) (rs4253728), P450 oxidoreductase (*POR*28)* (rs1057868) and in pregnane X receptor encoding gene *NR1L2* (rs2276707).
Results: Statistical analysis using the Jonckheere Terpstra test showed that *CYP3A5*3* ($P < 0.001$) as well as *CYP3A4*22* ($P = 0.025$) genotypes are significantly correlated with dose/trough levels of tacrolimus. No significant results were observed for *POR*28* ($P = 0.592$) and *PPARα* ($P = 0.325$). Additionally, significant associations of NR1L2 with dose/trough levels ($P = 0.010$) were confirmed. Univariate analysis of variance revealed that *CYP3A5*3* ($P = 0.020$) alone or in combination with *POR*28* and *NR1I2* ($P = 0.41$) has a significant impact on tacrolimus dose/trough level.
Conclusion: These results underline the high impact of *CYP3A5*3, CYP3A4*22* and CYP3A-regulating *NR1I2* genotype on tacrolimus pharmacokinetics. The presence of these genotypes lead to higher tacrolimus levels. Genotyping of patients' gDNA before tacrolimus treatment may contribute to faster optimization of immunosuppressive therapy, preventing underimmunosuppression or toxicity.

P08 EFFECTS OF RECIPIENTS' MDR1 AND CYP3A5 GENOTYPES ON TACROLIMUS DOSE REQUIREMENTS AFTER LIVER TRANSPLANTATION

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Aims: This study sought to investigate the role of SNP CYP3A5(rs776746) and MDR1(rs1045642) on pharmacokinetics of prolonged-release tacrolimus (TAC-OD).
Methods: $N = 69$ stable liver transplanted patients were converted from TAC twice daily (TAC-BID) to TAC-OD. TAC doses and trough levels were determined at regular time intervals between baseline and month 6 postconversion. Sequencing of PCR-amplified genomic DNA was used to determine the recipients' genotype. Kruskal–Wallis test was performed to compare subgroups of patients with different genotypes. *T*-test or Mann–Whitney-*U*-test was used to compare continuous data.
Results: TAC-OD doses differed significantly according to CYP3A5 genotype at week 1 ($P = 0.03$), week 2 ($P = 0.03$), month 1 ($P = 0.02$) and month 3 ($P = 0.04$). Patients with G/G-SNP required significantly lower doses of TAC-OD than those with G/A- and A/A-genotypes ($P < 0.05$ at each time point). Moreover, there was a significant difference regarding the dose requirements of TAC-OD at month 6 for MDR1 genotypes ($P = 0.02$). Patients with C/C-genotype needed to be dosed significantly higher at month 6 (4.7 ± 1.96 mg vs. 3.3 ± 1.69 mg, $P = 0.01$) than those with other genotypes.
Conclusion: The recipients' CYP3A5 and MDR1 genotypes seem to affect the function of enzymes in TAC metabolism; this may explain differences in TAC pharmacokinetics among transplant patients.

P09 INFLUENCE OF THE TACROLIMUS METABOLISM RATE ON THE RENAL FUNCTION AFTER KIDNEY TRANSPLANTATION

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Background: The calcineurin inhibitor (CNI) tacrolimus is an effective immunosuppressive drug after renal transplantation (RTx) but is often associated with an impaired renal function due to CNI nephrotoxicity. This study analyzes the impact of the tacrolimus metabolism rate on the renal function after RTx.
Methods: 407 adult patients underwent a renal transplantation between January 2007 and March 2012. 319 patients received an initial immunosuppression with basiliximab, tacrolimus, mycophenolate mofetil and prednisolone. The tacrolimus metabolism rate was expressed as the dose normalized by blood trough concentration (C/D ratio). Patients were sectioned in three groups: fast, intermediate and slow metabolizers. The renal function was collected 6, 12 and 24 months after RTx.
Results: 6 months after RTx significant lower eGFR values were found in the group of fast metabolizers (fast: 41.0 ± 14.0 vs. intermediate: 51.3 ± 17.5 and slow: 47.6 ± 19.4, $P < 0.001$). After 12 and 24 months, fast metabolizers still showed lower eGFR values compared to intermediate metabolizers ($P = 0.022$ and $P = 0.036$, respectively) and slow metabolizers (no significance). In the group of slow metabolizers significantly older recipients ($P < 0.001$) and a lower number of living transplantations were found ($P = 0.007$). Due to CNI nephrotoxicity, significantly more fast metabolizers were switched from tacrolimus to another immunosuppressive drug compared to slow metabolizers (9.0% versus 1.2%, $P = 0.03$).
Conclusions: The tacrolimus metabolism rate has a significant influence on the renal function after RTx. This analysis shows that the C/D ratio is a suitable and simple clinical tool to define patients at risk of CNI nephrotoxicity.

P10 NO ASSOCIATION BETWEEN CTLA-4 AND PDCD1 POLYMORPHISMS AND ACUTE REJECTION IN GERMAN LIVER TRANSPLANT RECIPIENTS

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Programmed cell-death 1 (PDCD1) and cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4), two important coinhibitory regulators of T-cell responses, have been demonstrated to be involved in limiting alloimmunity and in promoting tolerance induction. It has been suggested that CTLA-4 and PDCD1 inhibit T-cell activation through distinct and potentially synergistic mechanisms. An impairment of these regulatory pathways may promote the susceptibility to acute rejection after liver transplantation. Therefore we tested in our retrospective study whether four functional relevant single nucleotide polymorphisms (SNPs) in gene of PDCD1 (7146G>A, rs11568821; 7209C>T, rs41386349) and CTLA-4 (-1661A>G, rs4553808; -1722T>C, rs733618) are associated with the susceptibility to acute liver transplant rejection in a Caucasian population. The SNPs were genotyped by polymerase chain reaction allele specific restriction enzyme analysis (PCR-ASRA) in 100 liver recipients with acute rejection, 104 liver transplant recipients without acute rejectionand 100 healthy control individuals.For the selected SNPs we did not detect any significant difference in genotypic and allelic frequencies between liver transplant recipients with and without acute rejection. In conclusion, our results suggest that the tested SNPs are not involved in the susceptibility to liver transplant rejection in a Caucasian population.

P11 CAPABILITY FOR ANTIBODY DETECTION IN ELUATES OBTAINED BY IMMUNOADSORPTION (IA)

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Background: Vascular rejection is the B-cell-mediated production of immunoglobulin G (IgG) antibodies (AB) against the transplanted organ.The quick removal of AB and other plasma factors via IA remains an effective and supportive method for treating AMR, but there is no satisfactory answer when, how often and for how long treatment should be administered. Is it possible that the behaviour of the AB concentration in eluates from protein A sepharose column can give an answer?
Material and methods: A total of 30 transplant recipients (20 kidneys and 10 hearts) suffering from AMR were analysed. In total patients received 168 high-volume IA (Immunosorba, Fresenius Medical,Bad Homburg,Germany). Following methods were used for the detection of HLA- and non-HLA-AB: CDC, different ELISA, Luminex
Results: Before IA treatment HLA-AB (CDC) in sera were detected in 27% versus 39% in eluates and 46% versus 87% by using ELISA. We could not find any AB against GP in sera. In eluates, however, we could detect AB against GP: GP IIb/IIIa in 86% of all samples with titres from 1:1 to 1:32, GP Ib/IX (up to 1:32) in 76% and GP Ia/IIa with titres from 1:1 to 1:16 in 82%. Further we detected AECA against receptors AT1 and ETA in sera before IA in 22%, after IA in 10% and in eluates in 39% of all samples. The antibody titres vary from 1:1 to 1:256.
Conclusion: Our investigation pointed out, that AMR is still possible without detectable AB in serum and consolidates the hypothesis that clinical relevant non-HLA-AB and HLA-AB are partly fixed on the graft.High-volumeIAis qualified to detach fixed AB. If this hypothesis is true, the eluate as a medium for detection of these AB is more suitable than sera. The use of the eluates for antibody detection is only meaningful when antibodies are examined with titres.

P12 POLYMORPHIC VARIATIONS OF SEMAPHORIN 7A ALTER ITS FUNCTION IN THE REGULATION OF ANTIGEN PRESENTATION AND EFFECTOR IMMUNE RESPONSE

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Background: Polymorphisms of Semaphorin (Sema)7A have been associated with autoimmune diseases. In this study, the functional role of two Sema7A variants (Sema7A_R207Q & Sema7A_R461C) on immune responses was investigated.
Methods: Soluble recombinant wild-type Sema7A (Sema7A_wt) and its variants were produced. Specific assays were performed to determine the effects of Sema7A proteins on immune cell activation in terms of proliferation, phenotypic alterations, granzyme B transcript levels, and secretion of proinflammatory cytokines.
Results: T cell responses were not affected by Sema7A_wt, whereas Sema7A_R461C led to marked antigen-independent activation of T cells. Upon Sema7A_R461C stimulation, CD4 + T cells strongly proliferated and exhibited a cytotoxic phenotype with significant upregulation of granzyme B transcripts (up to 220-fold). In the presence of antigen stimulation, Sema7A_R461C had a major costimulatory effect on T cell response. Antibody blocking studies indicated that Sema7A_R461C mediated T cell activation is largely beta1 integrin dependent. Furthermore, the effect of Sema7A proteins on monocytes was investigated. Sema7A_wt, a known monocyte activator, stimulated the secretion of the proinflammatory cytokines IL-1β, IL-6, IL-8, and GM-CSF. However, both Sema7A variants caused higher IL-1β, IL-6, IL-8 and GM-CSF secretion levels and additionally induced the secretion ofIFN-g,IL-7, and IL-12. Furthermore, Sema7A_R461C, but not wild-type Sema7A or the Sema7A_R207Q variant, increased proliferation of monocytes.
Conclusion: Sema7A variants R207Q and R461C caused differential immune cell responses compared to the wild-type protein which may explain their disease association.

P13 IMPACT OF PRE-SENSITIZATION, TIME ON WAITING LIST AND HAEMODIALYSIS ON PRE-TRANSPLANT AS WELL AS OF GRAFT FUNCTION ON POST-TRANSPLANT SERUM KYNURENINE LEVEL IN KIDNEY GRAFT RECIPIENTS

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Aim: The activation of the Indoleamine 2,3-dioxygenase leads to the formation of kynurenine and other tryptophan metabolites which counterregulates immune activation resulting in restoration of immune homeostasis. But, in haemodialyzed patients these feedback mechanisms continue as indicated by elevated kynurenine concentrations. In this study we want to find out factors responsible for this elevation.
Material and methods: The pre- and post-transplant serum kynurenine levels were quantified in 307 kidney graft recipients and analysed in connection with some pre- and post-transplant variables. Statistics: analysis of variance, Scheffé's test for pairwise comparisons, Cox regression, Spearman's rank correlation, extended segmentation analysis.
Results: Pre-transplant kynurenine levels were significantly elevated (14.1 ± 5.9 nmol/ml; normal: 2.5 ± 0.4). Panel-reactive antibody (PRA) positive recipients showed higher concentrations than PRA negative patients (16.1 versus 12.9 nmol/ml), were a longer time on the waiting list and therefore a longer time on haemodialysis. The post-transplant kynurenine levels returned to normal within 3–5 days but only in patients with immediately functioning grafts. In patients with delayed graft function the kynurenine levels returned to normal not before starting graft function.
Conclusions: The necessity of haemodialysis (e.g. end-stage renal disease, DGF, non-functioning grafts) with its endothelial cell irritations leads to chronic immune activation and via IDO activation to increased tryptophan degradation followed by elevated kynurenine concentrations.

P14 PREFORMED CELLULAR ALLOREACTIVITY IS DOMINATED BY CD8 T-CELLS AND IS MORE FREQUENTLY OBSERVED IN RENAL TRANSPLANT CANDIDATES AS COMPARED TO CONTROLS

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Knowledge of the preformed donor-specific T-cell repertoire in transplant recipients prior to transplantation would allow guidance on individualized immunosuppressive drug treatment. We developed a simple flow-cytometric assay suitable for rapid use to quantify alloreactive T-cells directly from whole-blood samples. This assay is based on IFN-γ-accumulation and CD69-induction and was evaluated by testing 966 pair combinations consisting of 35 controls and 30 dialysis patients (awaiting renal transplantation). Autologous combinations served as negative controls. Additionally, 114 pairs were re-tested after 3 months.

The detection limit was 0.0081% among CD4 and 0.0143% among CD8 T-cells. Cytotoxic T–cell alloreactivity was with 17.49% more common compared to CD4 alloreactivity (7.66%) ($P < 0.0001$) and maximum frequency of alloreactive CD8 T-cells may reach 6.9%. A combined CD4 and CD8 alloreactivity was detectable in 2.69%. In dialysis-patients, CD8 T-cell alloreactivity was significantly more frequent than in healthy controls (28.74% versus 11.55% of combinations, $P < 0.0001$). Upon re-testing of 114 pair combinations, 80% with alloreactive CD8 T-cells remained positive over time.

Preformed cellular alloreactivity is dominated by CD8 T-cells and can rapidly be detected from whole blood samples. Stability of alloreactive repertoire over time indicates feasibility of this test to study the risk arising from preformed alloreactivity for graft rejection and loss of renal function after transplantation.

P15 REFRACTORY REJECTION AND POSITIVE HLA-ANTIBODIES IN A PEDIATRIC PATIENT AFTER REPEATED LIVER TRANSPLANTATIONS - EVIDENCE FOR HUMORAL REJECTION?

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Introduction: Humoral rejection is associated with hyperacute, acute and chronic rejections after liver transplantation. The diagnosis is based on deteriorating liver function, detection of HLA antibodies, B-cell-infiltrates and positive C4d-staining in liver biopsy.
Case report: A 2.5 year old boy was liver transplanted for biliary atresia at 1 year of age; repeated vascular complications required four retransplantations. After the last transplantation, cholestasis with moderately elevated liver enzymes (LFT), high GGT and high GLDH persisted, while liver function was normal. Liver biopsy showed cellular rejection without evidence for biliary obstruction. Treatment with steroids, MMF and ATG was initiated, but LFT and GGT persisted. Liver biopsy showed no sinusoidal C4d staining and no other signs of humoral rejection, but high titers of donor-specific HLA-antibody DQA2*05:05 were detected. Treatment with plasmapheresis, rituximab, IVIG and bortezomib resulted in decreased but still detectable HLA-antibody-titers with persisting LFT and GGT elevation. Liver histology now showed chronic rejection, without signs of humoral rejection but with isolated mononuclear infiltrates.
Conclusion: The diagnosis of humoral rejection after liver transplantation is difficult to establish due to unspecific diagnostic criteria and insufficient sensitivity and indeterminate significance of C4d-staining. Therefore, in refractory cellular rejection and putative humoral rejection, further therapeutic approaches targeting both components of the immune system should be discussed.

P17 DURING ACUTE CELLULAR REJECTION HLA-E IS EXPRESSED IN KIDNEY GRAFTS*

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Objective: The non-classical HLA-E molecules are restrictedly expressed under physiological conditions and display a limited polymorphism. Diametrically opposed immune functions, ranging from inhibiting natural killer cell activity to presenting alloantigens to cytotoxic T-lymphocytes are executed by HLA-E. Peptides presented by HLA-E mostly comprise signal peptides derived from other HLA proteins or certain viruses (especially CMV). Thus, the question emerges whether HLA-E plays a role as an alloantigen in renal transplantation.
Methods: HLA-E expression was examined in kidney biopsies taken from grafts with tubular atrophy ($n = 13$) or acute rejection ($n = 12$) by immunohistochemistry, using the HLA-E specific antibody MEM-E/02. Additionally, HLA-E typing of all donors and recipients was performed. Results of HLA-E-staining were associated with clinical data (e.g. biopsy-proven rejection, HLA-mismatches, CMV-status of donor/recipient or CMV-reinfection after transplantation).
Results: HLA-E expression was predominantly found in biopsies taken from grafts showing acute rejection ($P < 0.001$, Fishers exact test). It seems to be independent of HLA-E phenotype, of the number of HLA-mismatches, or other clinical parameters. Of note, HLA-E expression did not correlate to a positive CMV status or CMV-reinfection.
Conclusions: The exclusively strong HLA-E expression during acute rejection may indicate that immune reactivity towards HLA-E plays an important role in renal transplantation.

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P18 SUCCESSFUL PANCREAS/KIDNEY RE-TRANSPLANTATION BY A PATIENT WITH VERY HIGH PANEL REACTIVE ANTIBODIES. OUR DESENSITIZATION PROTOCOL.

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Introduction: The waiting time for sensitized patients is prolonged given the lack of transplants and the additional immunological barrier of this group.
Case report: A 45-years-old female underwent 2004 combined pancreas/kidney transplantation (PKTx) due to juvenile diabetes mellitus type 1. She experienced repetitive rejections with consequent function loss of both transplanted organs, requiring a transplant-nephrectomy six years later.

By PRA-titer higher as 90%, she enrolled a desensitization protocol, which included a single-dose of the B-cell depleting agent Rituximab, followed by five repetitive plasmapheresis/immunabsorption treatments and intravenous substitution of immunoglobulin (IVIG) in 14-day rythmus. There were eight cycles required, until a cross-match proofed acceptable (PRA-titer <50%). The patient underwent preoperatively an additional plasmapheresis. Induction was performed with 1000 mg prednisolon and administration of weight-adapted thymoglobulin within the first four days. The basic immunosuppressive medication consisted of prednisolon, tacrolimus and mycophenolatmofetil. The postoperative course was uneventful.
Discussion: Preoperative treatment is essential for sensitized patients. There are no prospective and randomized trials comparing all suggested desensitization protocols. The main columns of every approach are plasmapheresis and high-dose IVIG, which seem to have a strong immunomodulatory effect.
Conclusion: PKTx in patients with high PRA is feasible and can be performed successfully under novel desensitization protocols.

THORACIC ORGANS

P21 TUMOR INCIDENCE IN HEART TRANSPLANT RECIPIENTS RECEIVING CYCLOSPRIN A OR TACROLIMUS AS MAINTENANCE THERAPY

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Background: Heart transplant (HTx) recipients are at an increased risk of developing tumors and administration of the calcineurin (CNI)-inhibitors cyclosporine (CSA) or tacrolimus (TAC) may contribute to this risk. We compared tumor incidence rates in HTx patients receiving either CSA or TAC as maintenance immunosuppressive therapy.
Methods: We included 145 patients into this retrospective data analysis. All patients were transplanted between 2003 and 2007 and were followed up until 2011. Group A ($n = 25$) received CSA and group B ($n = 120$) TAC as maintenance therapy. Those patients who died within the first postoperative year were excluded from data analysis.
Results: The two study groups were comparable with respect to sex, year of transplantation and primary and concomitant diagnoses. Group A was, however, significantly older compared to group B (58.8 ± 11.4 years vs. 49.1 ± 13.0 years; $P = 0.01$) and so was the donor age of group A (43.2 ± 11.2 years vs. 37.0 ± 11.7 years; $P = 0.02$). Mean follow-up was 60.7 ± 19.3 months in group A and 59.8 ± 18.1 months in group B ($P = 0.813$). In total, 16 tumors were diagnosed in 15 patients (5 patients in group A and 10 patients in group B). In age-adjusted Cox regression analysis, tumor-free survival did not differ in the CSA group compared to the TAC group (relative risk = 1.22 (95% CI: 0.39–3.78; $P = 0.730$). Moreover, age-adjusted overall survival was comparable between groups (relative risk for the CSA group = 1.89 (95% CI: 0.52–6.80; $P = 0.332$).
Conclusions: Our data indicate that tumor incidence does not significantly differ in patients receiving CSA or TAC as maintenance therapy.

P22 THREE-YEAR FOLLOW-UP RESULTS IN HEART TRANSPLANT RECIPIENTS RECEIVING TACROLIMUS RETARD (ADVAGRAF®)

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Objectives: Tacrolimus retard (Advagraf®,ADV) is a new oral formulation of tacrolimus. It is given once daily, whereas tacrolimus (Prograf®,PRO) is administered twice daily. We have recently presented data indicating that in heart transplant recipients ADV is as safe as PRO within the first 6 postoperative months. Here, we present our 3-year follow-up data.
Methods: We compared 3-year clinical outcomes in 11 patients receiving ADV and 11 patients receiving PRO. The primary endpoint was a composite of death and drug discontinuation. Secondary endpoints were biopsy-proven rejections and safety parameters determined on the basis of laboratory evaluations.
Results: In the ADV and PRO group, the primary endpoint was reached by 18.2% and 36.4% of patients, respectively ($P = 0.399$). In detail, 3-year survival was 90.0% and 70.0%, respectively ($P = 0.291$), whereas freedom from drug discontinuation was 90.9% and 90.9%, respectively ($P = 0.973$). Freedom from biopsy-proven rejections was 90.0% and 70.1%, respectively ($P = 0.299$). In the surviving patients, postoperative GFR values improved to a similar extent in both study groups (ADV group: from 44.1 ± 21.5 to 62.4 ± 25.2 ml/min/m^2; PRO group: from 56.0 ± 25.0 to 75.0 ± 10.7 ml/min/m^2, $P = 0.550$). During follow-up, mean tacrolimus trough levels were significantly lower in the ADV group compared to the PRO group ($P = 0.017$). In the ADV group, levels were below the target range (5.0–8.0 μg/l) at the end of the follow-up period. Liver function, C-reactive protein concentrations and haematological parameters were comparable between groups.
Conclusion: This small follow-up study suggests lower tacrolimus trough levels but similar clinical outcomes in the ADV group compared to the PRO group.

P23 TUMOR INCIDENCE IN HEART TRANSPLANT RECIPIENTS RECEIVING SIROLIMUS OR EVEROLIMUS AS MAINTENANCE THERAPY

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Background: Immunosuppressive therapy may contribute to the increased tumor risk in heart transplant (HTx) recipients. However, the mTOR-inhibitor sirolimus (SRL) is also known to suppress tumor development.
Methods: We compared tumor incidence and overall survival in HTx patients receiving either SRL or the mTOR inhibitor everolimus (EVL) in combination with a CNI-inhibitor as maintenance immunosuppressive therapy. We included 67 patients receiving SRL and 163 patients receiving EVL into this retrospective data analysis. Data were assessed during the period of mTOR inhibitor administration and during a similar follow-up period.
Results: The total follow-up period did not differ between the SRL and EVL group (48.7 ± 32.0 months vs. 44.5 ± 24.0 months; $P = 0.343$). Moreover, the two groups were comparable with respect to sex and age at transplantation. However, compared to the SRL group, the prevalence of previous myocardial infarction (34.4% vs. 17.9%) and arterial hypertension (36.8% vs. 13.4%) was significantly higher and the time period until conversion (76.1 ± 59.2 months vs. 48.8 ± 57.7 months) was significantly shorter in the EVL group. In total, 15 tumors were diagnosed (5 patients in the SRL group and 10 patients in the EVL group). In covariate-adjusted Cox regression analysis, tumor-free survival did not differ in the SRL group compared to the EVL group (relative risk = 2.02 (95% CI: 0.64–6.33; $P = 0.229$). Moreover, covariate-adjusted overall survival was comparable between groups (relative risk for the SRL group = 3.05 (95% CI: 0.63–14.7; $P = 0.165$).
Conclusions: Our data indicate that during a follow-up of 4 years tumor incidence does not significantly differ between patients receiving SRL and EVL.

P24 CLINICAL OUTCOME IN HEART TRANSPLANT RECIPIENTS WITH CHRONIC KIDNEY DISEASE RECEIVING THYMOGLOBIN FOR INDUCTION THERAPY

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Background: In heart transplant (HTx) recipients with pre-existing chronic kidney disease (CKD), calcineurin inhibitor-free induction therapy with thymoglobin may be an option to prevent drug-induced nephrotoxicity.
Methods: We followed two groups of HTx recipients for up to one year. Group A ($n = 16$) suffered from CKD stages III-IV and received thymoglobin for induction therapy. Group B ($n = 16$) had preserved kidney function and received standard immunosuppressive therapy. We assessed survival rates, freedom from biopsy-proven rejection, freedom from cytomegalovirus (CMV) infection, other infections, kidney function and haematological parameters.
Results: Age, sex, body mass index and diagnosis were comparable between the two groups ($P > 0.05$). One-year survival estimates in group A and B were 81.3% and 75.0%, respectively ($P = 0.724$). Freedom from biopsy-proven rejection in group A and B was 100% and 85.9%, respectively ($P = 0.148$). Freedom from CMV infection was 100% (group A) and 87.5% (group B; $P = 0.171$). During follow-up, 11 other infections occurred in group A and 16 in group B ($P = 0.189$). In the surviving patients, mean GFR values increased non-significantly by 2.5 ml/min/m^2 in group A (from 30 to 32.5 ml/min/m^2), whereas mean GFR values decreased non-significantly by 7.5 ml/min/m^2 (from 77.5 to 70.5 ml/min/m^2) in group B until the end of the follow-up period. During follow-up, white blood counts were significantly higher in group B compared to group A.
Conclusions: Our data indicate that thymoglobin for induction therapy may be a treatment option in HTx recipients with pre-existing CKD.

P25 IMPACT OF EXTRACORPORAL PHOTOPHERESIS IN HEART TRANSPLANT RECIPIENTS WITH DIFFERENT IMMUNE STATUS

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Objective: Immunmodulatory effects of extracorporal photopheresis (ECP) in heart transplant recipients (HTxR) with different immune status are still missing. Thus, we measured regulatory CD4$^+$ T cells (Tregs) and dendritic cells (DCs) in HTxR treated with ECP for prophylaxis of rejection (PRX), to treat acute rejection (AR) or to treat chronic rejection (CR).
Methods: HTxR were treated monthly 3 times with ECP: PRX-group ($n = 5$) at month 4 after HTx; AR-group ($n = 7$) at time of biopsy proven rejection and 2 times thereafter; CR-group ($n = 4$) monthly at time of angiographic proven diagnosis of allograft vasculopathy at two times afterwards. Peripheral blood was analyzed each time before ECP therapy to assess Tregs and myeloid and plasmocytoid (m and p) DCs by FACS. Blood samples before ECP treatment and one month after the last ECP therapy were compared (%±SD).
Results: In the PRX-group pDC levels decreased from 28 ± 25.4% to 15.2 ± 9.2% ($P = 0.10$), while mDC levels increased from 58.7 ± 26.0% to 68.7 ± 12.2%, respectively ($P = 0.23$). Whereas Tregs increased from 6.3 ± 3.5% to 7.2 ± 2.6% ($P = 0.46$).

In the AR-group both m and pDCs increased from 56.6 ± 21.1% to 68.5 ± 10.4% and 4.2 ± 3.9% to 14.2 ± 5.7%, respectively ($P = 0.05$). Tregs did not change before and after ECP (6.8 ± 4.25% to 6.2 ± 2.0%).

Whereas Tregs expression in the CR-group with 4.8 ± 0.8% prior to ECP and 7.3 ± 3.7% after ECP (p).
Conclusion: We showed that ECP therapy had different effects on Tregs and DCs in HTxR with different immune status. Further clinical studies are needed to identify the optimal time point and duration of ECP therapy depending on the indication after HTx.

P26 PIRFENIDONE: A POTENTIAL THERAPY FOR PROGRESSIVE LUNG ALLOGRAFT DYSFUNCTION?

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Background: Chronic lung allograft dysfunction (CLAD) is one of the major factors limiting graft function after lung transplantation (LuTx). No effective medical treatment is available but animal experiments with pirfenidone have shown some promise. The aim of this case report was to evaluate pirfenidone in a LuTx recipient with progressive CLAD.
Methods: Descriptive data analysis was performed prospectively based on lung function testing, functional outcome and quality of life valuation.
Results: Our case is a 56-year-old female LuTx recipient who underwent LuTx in 2009 due to idiopathic pulmonary fibrosis accompanied by pulmonary hypertension. In 2011 the patient was diagnosed with bronchiolitis obliterans syndrome (BOS) stage 1 (A0/B0). As the patient rapidly progressed to BOS stage 2 and a therapy with azithromycine, montelucast and i.v. steroids as well as a fundoplication were unsuccessful we started a pirfenidone treatment in October 2011. Forced Expiratory Volume in 1 Second (FEV1), Forced Vital Capacity (FVC) and Total Lung Capacity (TLC) before the start of pirfenidone were 1.09 l (51%pred.), 2.21 l (84%pred.) and 4.24 l (95%pred.), respectively. Follow-up pulmonary function tests after three months revealed a FEV1 of 1.26 l (59%pred.), a FVC of 2.23 l (85%pred.) and a TLC of 4.49 l (101%pred.) as well as after six months a FEV1 of 1.30 l (61%pred.), a FVC of 2.54 l (100% pred.) and a TLC of 4.53 l (102%pred.), correspondingly. The distance covered in 6 minutes before the treatment was 510 m and during therapy after three months 590 m and after six months 580 m, respectively. According to the Short Form-36 Health Questionnaire the patient was found to have a good quality of life throughout the conduct of the treatment. Laboratory evaluations including monthly renal- and liver function tests, CMV- and infection screening as well as tacrolimus blood levels showed no change during the administration of pirfenidone.
Conclusion: Pirfenidone was well tolerated and the patient continued the treatment on stable dosage and remained on BOS stage 2 under therapy. Our case suggests that the use of pirfenidone after LuTx is safe. The therapeutic potential of pirfenidone in LuTx recipients should be investigated in future controlled trials.

P27 BILATERAL VERSUS SINGLE LUNG TRANSPLANTATION FOR IDIOPATHIC PULMONARY FIBROSIS

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Objectives: It is unknown if uni - or bilateral lung transplantation (LTX) is the optimal treatment for usual interstitial pneumonia (UIP). The aim of this study was therefore to review our single centre experience and compare uni (ULTx) - versus bilateral LTX (BLTx).
Methods: A total of 137 patients underwent LTX at our institution from 2002 to 2011. Out of these 58 patients presented with UIP (56.9%) and form the focus of this study. Mean age of patients was 54 $\pm$ 10 years and 69% of our patients were male.
Results: Thirty-nine patients received single LTX and 19 patients bilateral sequential LTX. Cold ischemia time was 288 $\pm$ 64 min in ULTx and 317 $\pm$ 68 min in BLTx ($P = 0.03$). Warm ischemia time was 56.7 $\pm$ 12.1 ULTx and 46.4 $\pm$ 8.7 BLTx ($P < 0.01$) Intraoperative course was uneventful except for seven patients who needed ECMO support. Three patients had pre-LTx respiratory failure requiring mechanical ventilation and were supported by ECMO. More PBC (3.2 $\pm$ 3.8 vs. 10.3 $\pm$ 11.6; $P < 0.01$) and FFP (2.8 $\pm$ 4.1 vs. 8.1 $\pm$ 11; $P < 0.01$) was used in BLTx.

Elevated PA pressure over 40 mmHg was identified as predictor of early mortality in multivariate analysis. As predictor for long term survival in cox regression analysis was postoperative ECMO support and over 10 PBC in first 72 h. Actuarial survival at 1 and 5 years was 65.6% and 55.3%, respectively and no significant difference was observed between groups (70.6% and 54.3%).
Conclusion: LTX is a safe and curative treatment for UIP. Uni-lateral LX seems can be considered as effective as bilateral LTX.

P28 AV-VALVE SURGERY IN HEART TRANSPLANT RECIPIENTS

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Background: Improved long-term outcome after orthotopic heart transplantation (HTx) leads to a growing number of valvular diseases late after HTx. Tricuspid regurgitation is the most frequent valvular heart disease after HTx. Nevertheless, there is a small group of patients who develop post-transplant mitral valve disease. We report on nonretransplant surgical results of both groups.
Methods: 9 patients (8 male/1 female) presented with massive tricuspid regurgitation (mean interval between HTx and valve surgery 4.8 years), 5 patients (4 male/ 1 female) developed severe mitral valve insufficiency after HTx (mean interval between HTx and valve surgery 5.5 years). Among these 14 patients 7 patients underwent valve replacement (TKR $n = 4$; MKR $n = 3$). 5 patients had tricuspid valve repair, 2 patients underwent mitral valve repair, 1 of these via minimally invasive approach.
Results: The mean ICU stay was 2.5 days. 2 patients who initially had mitral valve repair were readmitted because of recurrent mitral insufficiency for mitral valve replacement. All patients undergoing mitral valve surgery are long-term survivors. Out of the tricuspid valve surgery patient one died in the long-term follow-up because of malignancy.
Conclusions: According to our results surgery of atrioventricular valves after HTx is a safe and effective therapeutic approach with good long-term results. Long-term immunosuppression may possibly influence the results after mitral valve repair. Minimally invasive approach may reduce the surgical trauma in this special patient group.

P29 HU FAILURE VS. VAD FAILURE: EFFICACY AND SAFETY OF TREATMENT CONCEPTS FOR TERMINAL HEART FAILURE IN THE CURRENT ERA

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Introduction: Decision making for either strategy is crucial for prognosis with increasing waiting time and superimposable indications for HU listing and VAD implantation.
Methods: Retrospective analysis of charts of all pts. listed HU or supported with a VAD system as a bridge to transplant initially.
Results: From 11/2005 until 08/2012 765 pts. (81% male) have been listed "HU" or received a VAD initially. The diagnosis ICM was more common in the VAD group (274/50% vs. 66/34%). Age distribution (HU/VAD) (49.5/47.0 yrs), ischemic times (197/227 min) and donor age (39.9/36.8 yrs) where similar. Waiting times for Tx have been longer in the VAD group (59/422 days).
Conclusion: VAD patients had long support times, a higher mortality risk and lower transplant rates. 1-year survival after HTX was poorer. Patient selection was biased with more advanced stages of disease in the VAD group. An optimized selection using Score systems and early decision making may improve results. Prospective studies are needed in this matter.

P30 THE IMPACT OF DONOR AND RECIPIENT PARAMETERS ON THE OUTCOME OF HEART TRANSPLANTATION IN GERMANY

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Due to organ shortage in heart-transplantation (HT) grafts were used from donors with substantial risk factors increasingly. However, it is discussed controversially which donor characteristics may be detrimental for the outcome of HT. Therefore, we evaluated the combined impact of recipient and donor related factors in HT on patient survival by multivariate analyses in a nationwide multicenter study.
Methods: A database was created from data on hearts donated and transplanted in Germany between 2006 and 2008 as provided by Deutsche Stiftung Organtransplantation and BQS-Institute. Multivariate Cox regression was conducted ($n = 774$, recipient age $\geq$18 years; significance level 5%, risk ratio [95%-CI])
Results: Patient survival was significantly decreased by donor-age (1.026 [1.014–1.039] per year), Troponin >0.1 ng/ml (2.006 [1.426–2.823]), ischemia time (1.188 [1.033–1.366] per hour), recipient-age (1.017 [1.003–1.032] per year) and in recipients with pulmonary resistance $\geq$320 dyn*s*cm^{-5} (1.723 [1.090–2.723]) or with complex previous heart surgery (1.750 [1.260–2.430]). Hypotensive periods or catecholamine administration in donors were without impact.
Conclusion: After proper donor selection the survival after HT was limited by advancing donor- and recipient age, increasing ischemia times and other recipient related problems (e.g. pulmonary hypertension, previous complex heart surgery).

P31 PROCALCITONIN (PCT) IN COMBINATION WITH HIGHLY SENSITIVE CARDIAC TROPONIN T (HS-CTNT) TO DETECT PATIENTS AT RISK AFTER HEART TRANSPLANTION (HTX)

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Objective: PCT and C-reactive protein are established markers of inflammation. As we could confirm in a former study, however, PCT is not suitable to

detect an acute rejection after htx. In combination with the new hs-cTnT it may be useful for an early identification of patients at risk after transplant.
Methods: In heart transplant recipients daily blood samples for PCT- and hs-cTnT-measurement were taken until postoperative day 7. At the same time CRP and leucocytes were determined.
Results: Between 10/2010 and 06/2013 32 patients underwent htx in our department.

In 17 patients (53.1%) all postoperative PCT-values were less than 10 ng/ml (group A). Postoperative peak-levels between 10 and 50 ng/ml could be found in 9 patients (28.1%) (B) and > 50 ng/ml in 6 patients (18.8%) (C). However, the incidence of systemic, bacterial infections was comparable between all 3 groups.

Thirty-day-mortality was 7.6% in group A, 11.1% in B and 33.3% in C.

Consistently, we found postoperative peak PCT-levels of 55.8 ± 28.7 ng/ml in non-survivors, compared to 20.4 ± 11.2 ng/ml in survivors. Those peak PCT levels in survivors preceded those of non-survivors (postoperative day 1.7 vs. 2.8).

The postoperative peak of hs-cTnT was also significantly higher in deceased patients with 20476 pg/ml compared to 5387 pg/ml in survivors.
Conclusions: PCT, mostly used as a marker of systemic inflammation, seems to be a useful parameter to predict an adverse outcome after htx. In combination with hs-cTnT, it may support the posttransplant management with regard to detection of complications before their clinical appearance.

P32 A COMPARISON OF CARDIAC TROPONIN I AND CREATINE KINASE-MB FOR SELECTION OF HEART DONORS AND AS PREDICTORS OF GRAFT FAILURE

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Objectives: Donor selection remains a critical yet poorly standardized aspect of heart transplantation (HTx). In an effort to predict which donor hearts will yield the most successful recipient outcomes, many transplant centers have started using cardiac serum markers of myocardial cell injury to help determine whether to use a potential graft. The aim of this study was to evaluate cardiac troponin I (cTnI) and creatine kinase (CK)-MB as predictors of graft failure after HTx.
Methods: cTnI and CK-MB serum concentrations were measured in samples collected immediately before pericardium opening from 131 consecutive brain-dead multiple-organ donors. The donors were retrospectively divided into 2 groups: group I (n = 103) donors of graft with good function, group II (n = 28) donors of graft with impaired function after HTx.
Results: The estimated left ventricular ejection fraction on the initial donor echocardiogram was similar in both groups (66% ± 12% vs. 62% ± 11%; P = 0.11), as were the mean allograft cold ischemic times (203 ± 49 min vs. 197 ± 50 min; P = 0.57). There were no correlations between cTnI and CK-MB. The cTnI level was significantly higher in group II (0.60 ± 0.85 ng/mL vs. 0.22 ± 0.41 ng/mL; P = 0.001). The CK-MB level was similar in both groups (23 ± 24 U/L vs. 24 ± 36 U/L; P = 0.86). One or both markers were elevated in 45 donors (44%) in group I and in 21 donors (75%) in group II (P = 0.005). CK-MB was elevated in 41 donors (40%) in group I and in 11 donors (40%) in group II (P = 0.98). In contrast, cTnI was elevated in 33 donors (32%) in group I and in 18 donors (64%) in group II (P = 0.004).
Conclusions: Elevated cTnI serum concentration in donors was independent prognostic marker of impaired graft function after HTx. cTnI is superior to CK-MB for the prediction of impending graft failure. Its use as additional parameter may improve heart donor selection.

P33 MONITORING THE CYTOMEGALOVIRUS-SPECIFIC CELLULAR IMMUNITY IN LUNG TRANSPLANT RECIPIENTS: A COMPARATIVE ANALYSIS OF TWO ASSAY SYSTEMS

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Objective: Monitoring the cellular immunity for Cytomegalovirus (CMV) in organ transplant recipients is a promising tool to support prevention strategies for posttransplant CMV infection or reactivation. Commercially available *in vitro* test systems differ substantially in their capacity to stimulate subpopulations of T-lymphocytes. We compared two assays for CMV immune monitoring in respect of their clinical practicability and significance.
Methods: Blood samples of 30 lung transplant recipients were examined before transplantation and over a period of six months afterwards with T-Track® CMV (Lophius Biosciences GmbH, Regensburg) and QuantiFERON®-CMV (Cellestis GmbH, Darmstadt). The T-Track® CMV is based on ELISpot-technology, allowing quantification of interferon-gamma (IFNγ) secreting CD4 + and CD8 + T-cells after specific stimulation. Contrarily, the QuantiFERON®-CMV assay is restricted to detection of IFNγ secreted by CD8 + T-lymphocytes with ELISA. The data are evaluated in the context of transplant outcome and determination of viral load in plasma by qPCR.
Results and Conclusion: Both approaches provide similar results while exhibiting certain advantages and limitations. Early during immune suppressive therapy, QuantiFERON®-CMV generates often indeterminate results as depletion of T-cells is not taken into account. Although T-Track® CMV circumvents this drawback by applying a constant number of cells, a comparatively large volume of blood is required. The benefits of both assays to assess the individual risk of CMV disease will be discussed.

P34 TREATMENT OF ASYMPTOMATIC CMV DNA POSITIVE INFECTIONS IN HEART TRANSPLANT RECIPIENTS WITH CMV HYPERIMMUNOGLOBULIN MONOTHERAPY (CYTOTECT©)

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Background: Heart transplant (HTX) recipients often develop CMV infection with positive CMV DNA. Antiviral medication induces complications such as renal failure and neutropenia. The aim of our study was it to analyze the value of CMV-hyperimmunoglobuline (IVIG) (Cytotect©) monotherapy in HTX recipients with positive CMV DNA proof without clinical symptoms.
Methods: In 01 - 12/ 2012 15 HTX recipients transplanted 2008–2012 with positive baseline DNA without clinical symptoms where initially treated with IVIG monotherapy (50 ml/1 i. v. infusion initially). The median follow up was 3 - 10 months.
Results: Nine patients (60%) developed a negative CMV DNA test without further recurrence. 5 patients (33%) initially had a negative result of CMV DNA but developed a recurrence of positive CMV DNA within 6 weeks. One patient required -IVIG- therapy three times to reach a stable negative result of CMV DNA. No patient died. The course of creatinine, BUN, GFR, bilirubine, GOT, GPT, AP, blood count and CRP was similar to baseline laboratory results. Only one adverse event (Allergy) occurred during follow up.
Conclusion: IVIG therapy, is efficient to achieve CMV DNA negative result s in initially CMV DNA positive patients without the use of valgancyclovir/ganciclovir especially in patients with neutropenia or renal dysfunction. Repeated treatment in case of recurrence is possible. The safety profile is acceptable with very low adverse event rate and stability of laboratory values during follow up. Projected prospective investigations will evaluate this treatment strategy further.

P35 SUCCESSFUL TREATMENT OF EPSTEIN-BARR VIRUS (EBV) INFECTION WITH RITUXIMAB IN POST LUNG TRANSPLANT PATIENT WITH PREVIOUS B-CELL LYMPHOMA: A CASE REPORT

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Background: Immunosuppression due to lung transplantation (LTX) is associated with high risk for EBV infection or reactivation with a potential development of post-transplant lymphoproliferative disease. EBV infection may also cause premature loss of graft function. Treatment of EBV remains difficult. Reduction of immunosuppression combined with antiviral agents is often not successful.
Abstract: We present a 36-year-old male LTX patient admitted with acute impairment of lung function (FEV1 1.8 l) presumably due to pneumonia. He suffered successfully through a B-cell Non-Hodgkin lymphoma in 2006 and has since been in complete remission. The bronchoscopy and chest x-ray were without pathological findings. Despite antibiotic therapy for pneumonia, the patient's clinical condition declined. EBV-DNA was found in blood with >150.000 copies/ml. Immunosuppression was reduced, but EBV-load further increased. Due to the history of CNS-Lymphoma we decided for single shot treatment with the anti-CD20 monoclonal antibody rituximab (115 mg/m^2). Shortly thereafter, lung function improved, EBV-DNA-load declined and the patient improved that he could be discharged. One month later, the patient presents in good condition with good lung function (FEV1 2.7 l). There is currently no evidence of EBV-DNA.
Conclusion: This case suggests that treatment of EBV-infection with elimination of any EBV-DNA in transplant-patients using rituximab is an attractive option.

P36 SUCCESSFUL TREATMENT OF CEREBRAL VENTRICULAR MUCORMYCOSIS IN A HEART-LUNG TRANSPLANT RECIPIENT

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Purpose: Mucormycosis is a rare opportunistic fungal usually occurs as a pulmonary, gastrointestinal, disseminated or rhinocerebral infection. Neither a

primary ventricular cerebral mucormycosis nor a mycomycosis in a heart-lung transplant recipient have been described so far.
Case Report: We report the case of a 51-year-old patient with dilatative cardiomyopathy and consecutive fixed pulmonary hypertension received combined Heart-Lung-Transplantation in 2011.

After deterioration of a preexisting slight hemiparesis and epileptic seizures in 2012 a c*MRT* showed an *expansion of the left lateral ventricle due to a linear structure with contrast enhancement associated to the foramen monroi. Neurosurgical endoscopic fenestration of the septum pellucidum, placement of an EVD and a biopsy of the structure were performed. This* verified *the diagnosis of the cerebral mucormycosis by histopathology and PCR. Microbiological we could isolate Rhizopus arrhizus.*

Intravenous antifungal therapy with liposomal Amphotericin B and Posaconazol were initiated. *Intrathecal treatment with* Amphotericin B was not tolerated by the patient. After confirmation of the diagnosis *a neurosurgical removal of the fungal* hyphae was performed. After long term antifungal therapy the patient recovered completely without any incidence of a relapse in cMRT.
Conclusion: A cerebral ventricular mucormycosis should be considered as a differential diagnosis in transplant recipient with sudden neurological symptoms. Options for a successful treatment are intravenous Amphotericin B or Posaconazol, *intrathecal* Amphotericin B and surgical removal.

P37 DEPRESSIVE SYMPTOMS AT TIME OF WAIT LISTING ARE ASSOCIATED WITH REDUCED SURVIVAL AFTER HEART TRANSPLANTATION: RESULTS FROM THE WAITING FOR A NEW HEART STUDY

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Purpose: To evaluate depression and social isolation (<4 social contacts/month) assessed at time of listing for a heart transplant (HTx) as predictors of post HTx survival.
Methods: The focus of analyses were 124 recipients of an HTx in the Waiting for a New Heart Study, a prospective observational multisite study of 318 HTx candidates registered with Eurotransplant (ET) between 2005 and 2006. Demographic and psychosocial characteristics were assessed by questionnaires at time of listing. ET provided transplantation dates and donor characteristics, hospitals reported medical data at time of HTx and post-transplant survival.
Results: During a median follow-up of 57.6 months, 43 (34.7%) of HTx recipients had died. In univariate analyses, elevated depression and social isolation assessed at time of listing were associated with increased mortality risk after HTx. Cox proportional hazard analyses controlling for medical parameters and other factors known to influence post-HTx mortality (e.g., donor age, mechanical assist device) confirmed these results: the hazard ratio for depression was 1.09 (95% CI 1.003–1.18, $P = 0.04$); a similar marginally significant finding emerged for social isolation ($P < 0.10$).
Conclusions: Decreasing depressive symptoms and increasing social contacts among patients with advanced heart failure may help prevent poor outcomes after cardiac transplantation.

P38 REDUCTION OF OBLITERATIVE BRONCHIOLITIS (OB) BY PROLYL-HYDROXYLASE-INHIBITORS ACTIVATING HYPOXIA-INDUCIBLE TRANSCRIPTION FACTORS IN AN EXPERIMENTAL MOUSE MODEL

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Purpose: Obliterative Bronchitis (OB) is the major limiting factor for long-term survival after lung transplantation. As previously shown, donor treatment with a PHD-inhibitor activating Hypoxia-inducible transcription factors (HIFs) prevents graft injury both in an allogenic kidney and aortic allograft transplant model. The aim of this study was to investigate the effect of HIF activation with a PHD-inhibitor on the development ofOB.
Methods: Fully MHC-mismatched C57BL/6 (H2(b)) donor tracheas were orthotopically transplanted into CBA (H2(k)) recipients. Donor animals received a single dose of PHD-inhibitor 2-(1-chloro-4-hydroxyisoquinoline-3-carboxamido) acetate (ICA) (40 mg/kg i.p.) or vehicle 4 h before transplantation ($n = 5$). Animals were harvested 30 days after transplantation and grafts were analyzed by histology, mRNA expression and immunofluorescence.
Results: Donor preconditioning withICA resulted in HIF accumulation and induction of HIF target genes: HOI, VEGF, TGFβ, and MIFα, which persisted during different times of ischemia. Vehicle treated controls showed substantial luminal obliteration on postoperative day 30 in contrast to groups pre-treated with ICA [luminal obliteration 29.2 + 5% (ICA) vs. 36.7 + 8% (control), $P < .01$]. We found significantly lower expression of TNFα, PDGFß, MCP1, E-Selectin, and ICAM1 afterICA premedication. In additionICA pretreated groups revealed decreasedT-cell,DC, and macrophage infiltration in vascular grafts ($P < .05$).
Conclusions: Pre-treatment with ICA substantially reduces Obliterative Bronchiolitis. These data suggest that activation of Hypoxia-inducible transcription factors (HIFs) and hereby adaptation to low oxygen prevents the development of OB and therefore allograft injury. Pharmaceutical inhibition of PHDs appears to be a very attractive strategy for organ preservation that deserves further clinical evaluation

P39 DEVELOPING A NOVEL XENOTRANSPLANTATION MODEL TO STUDY CHRONIC OBLITERATIVE AIRWAY DISEASE

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Background: Different animal models have been developed to study the pathogenesis and treatment of obliterative airway disease (OAD).However, these models are limited by the fact that fibroproliferative lesions are from murine origin and there is the need for a humanized model to overcome the translational gap. Here we describe a novel xenotransplantation model in rat using human bronchi.
Methods: Human bronchi were orthotopically transplanted into immunocompetent (BN) or immunodeficient (RNU; lacking T cells) ratsas tracheal graft.Grafts were harvested after 7 or 28 days post-transplantation for histological evaluation and analysis of host cellular and humoral response.
Results: In RNU group, grafts developed fibroproliferative lesions whichwere morphologically indistinguishable from human BOS. Airway epithelial vanished after transplantation due to the ischemia-reperfusion injuryat 7 daysand was recovered after 28 days in the RNU group ($P = 0.029$; 7 days vs 28 days)and identified as donor origin. Cellular host response by IFN-γ ELISPOT and anti-donor specific antibody production were significantly stronger in BN group compared to RNU group at both 7 days and 28 days.
Conclusions: Our new model using human bronchi imitates lesions and epithelial integrity of human BOS patients and is therefore suitable to study the development of that in vivo.

P40 COLLAGEN-PRODUCING HEMATOPOIETIC CELLS (FIBROCYTES) IN EXPERIMENTAL HEART TRANSPLANTATION AND THEIR REGULATION BY BASOPHILS

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Introduction: Fibrotic organ remodelling of cardiac allografts represents a major factor for progression of heart failure after the first post-transplantation year. Mechanistically, cardiac graft fibrosis presents as a complex interplay between the immune response against the graft and various collagen-producing cells. So far, it is unclear which cells contribute to production of collagen in allograft fibrosis and how basophils, as stimulators for Th2 response, influence this process.
Methods: Bm12 donor hearts were transplanted into MHC-class-II-mismatched C57BL/6J recipients and Balb/c donor hearts into completely mismatched, transiently CD4 depleted C57BL/6J mice. Graft function was assessed by palpation of the abdomen and rejection was defined as cessation of cardiac contractility. Before transplantation basophils were depleted with mAb against FcεR1, the high affinity IgE receptor.
Results: In both models, progressive allograft rejection of donor hearts with decreased organ function, severe vasculopathy and interstitial fibrosis was evident within four weeks, as demonstrated by histologic evaluation of the grafts. Allograft rejection and fibrosis was associated with increased infiltration of large numbers of $CD11b^+$ collagen-producing hematopoietic cells (fibrocytes). Furthermore, depletion of basophils resulted in a reduction of infiltrating lymphocytes as well as fibrocytes and inhibits collagen expression in allografts.
Conclusion: Our results describes for the first time the presence of collagen-producing hematopoietic cells in two chronic rejection models and demonstrates an important role of basophils following cardiac rejection and fibrotic organ remodelling.

P41 DEPLETION OF IMMUNE-MEDIATORS FROM DONOR LUNGS USING THE ORGAN CARE SYSTEM® - A POTENTIAL MECHANISM FOR IMPROVED OUTCOMES

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Purpose: Release and composition of donor-derived immune mediators (IM), triggering allorecognition and inflammation after transplantation (Tx), might be differentially affected and impinging on clinical outcome using warm perfusion of donor lungs (Organ-Care-System®, OCS) or standard cold preservation (SOC). Both, IM in preservation solutions (PS) and recipients peripheral blood (PB) were analyzed and clinical outcomes monitored.
Methods: IM were quantified at protein level by Luminex-based multiplex-technology at the end of warm preservation ($n = 13$) or cold storage ($n = 11$).
Results: In PS, concentrations of IL-6, IL-10, IL-16, IFN-g, CXCL8, CCL4, G-CS, Ang-2, PECAM-1 and PDGF-b were much higher in OCS than SOC ($P < 0.0001$). Inverse distribution was observed for basic-FGF ($P = 0.005$), indicating physiology rather than passive mechanisms causing IM distribution. Very low significance level was seen for GM-CSF ($P = 0.04$). ROC analyses revealed AUC values between 0.74 for GM-CSF and 1.0 for several factors. High concentrations in PS using OCS induced lower concentrations of IM in PB after Tx. PGD-scores were lower and mechanical ventilation shorter using OCS.
Conclusion: IM remained low in PS using SOC, whereas OCS potentially depleted them from the organ by accumulation in PS. This 'dialysis' effect had a positive impact on the clinical outcome in the OCS group.

P42 HEART TRANSPLANTATION IN A YOUNG PATIENT WITH ANOREXIA NERVOSA - A PERSPECTIVE? A CASE REPORT

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Introduction: Anorexia nervosa is considered a psychiatric contraindication for HTx. The chronic malnutrition and the possible non-absorption of immunosuppressant drugs pose a threat to the transplantation's success. The pathological body perception in anorexic patients can impede the psychological integration of the new organ, as does a questionable compliance.
Method: We present the treatment of a 20-year-old female patient with chronic Anorexia nervosa (BMI 16) with an indication for HTx. After non-acceptance by another center she presented with severely impaired hemodynamics for second opinion in our center 02/11. Underlying diagnosis was post myocarditis cardiomyopathy (PV B19 in 10/00), intermittent AVB III° and previous mitral valve replacement. HU-listing was performed after interdisciplinary discussion. A psychotherapeutic treatment was installed. No complications occurred during the transplantation process. Postoperatively, a thorough integration of the organ was enforced.
Results: An outpatient psychotherapeutic treatment was initiated. Nutritional status and physical activity level steadily improved after HTx. In the 2-year follow-up the patient appeared stable, regarding cardiac situation and weight (BMI 20). Compliance was reliable including frequent TDM results.
Conclusion: Anorexia should be still considered as a relative contraindication for HTx, however in carefully selected patients and frequent mandatory psychological treatment HTx with positive long-term outcome is feasible.

ORGAN DONATION / MARGINAL ORGANS

P46 LIVER TRANSPLANTATION FROM DONORS WITH PAST HISTORY OF MALIGNANCY: A SINGLE CENTER EXPERIENCE

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Introduction: The demand for transplantable organs exceeds donor supply. Transplantation of organs from donors with past history of malignancy is controversial, and the transmission of cancer in liver transplant recipients has not been sufficiently determined.
Patient and methods: From May 2002 until February 2013, 55 livers from donors with a past history of malignancy were transplanted at the University Hospital Essen. Donor and recipient data, type of malignancy, tumor-free interval at organ procurement and follow-up data were collected and analyzed.
Results: Ten tumor sites [genitourinary (n = 20), brain (n = 17), skin (n = 3), breast (n = 5), thyroid (n = 2), lung (n = 2), acute myeloid leukemia (n = 1), larynx (n = 1), colorectal (n = 3), liver (n = 1)] were diagnosed in the 55 donors with a history of malignancy. The majority (64%) of donors had tumor-free intervals of 5 years or less. 13 recipients died within the first 30 postoperative days, 42 patients had a median follow up of 408 days (31–2840). No recipients of organs from donors with malignancy in history developed donor-derived cancer.
Conclusion: Liver transplantation with organs from donors with a past medical history of malignancy is feasible and the risk of donor-transmitted tumor seems to be small. The careful selection of donors remains mandatory and can expand the donor pool.

P47 DEVELOPEMENT OF DONOR CRITERIA OF COMBINED PANKREAS-KIDNEY-DONATION WITHIN THE LAST 10 YEARS

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Objective: For a long time donor criteria for pancreastransplantation were constricted to young donors without any illnesses. Due to increasing organ needs donors with extended criteria are going under investigation within several research groups.
Method: Between 1/1994 and 7/2012 we analysed 478 patients with isolated or combined pancreastransplantation.
Results: During the follow up (average 92 month) patientsurvival after 1/5/10 year was 96%/ 90% and 85%. Accepted donations were divided into time groups (I: 1994–1999, II: 2000–2005, III: 2006–2012). Donorage is increasing (I: 16 years, III 47.4 years). The contingent of donors > 45 increases from 9.7% in I, 29% in II to 36% in III. BMI is rising from 22 in I to 24 in III. Percentage of the accepted organs with BMI> 25 increases: I: 9%, II: 23%, III: 28.1%. Rate of accepted organs with age> 45 and BMI> 25 increases: I: 0.6%, II 6%, III: 7.2%. Outcome at 5 years did not differ (log rank test) I: 71.7% pancreas/80.6% kidney, II: 71.5% pancreas/80.7% kidney, III: 74.8% pancreas/87.8% kidney.
Conclusion: In summery good results can be achieved with grafts of extended donor criteria. Despite greater rate of accepted organs with extended criteria graftfunction within the time groups stayed comparable well.

P48 DOUBLE LUNG TRANSPLANTATION FROM A DONOR SUPPORTED BY A LEFT VENTRICULAR ASSIST DEVICE

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Introduction: Extended donor criteria are required to meet the demands of organ shortage in thoracic transplantation. So far, patients with mechanical circulatory support systems were not considered as potential donors for thoracic organ procurement.
Case Report: The lungs of a 25-year old donor were offered to our center. Gas exchange was good and radiological and bronchoscopic findings were regular. Cause of brain death was the occlusion of the left carotid artery. The patient was ventilated for 3 days. Due to heart failure after a myocardial infarction and emergency coronary artery bypass graft surgery 6 month earlier, the donor was supported by a left ventricular assist device (LVAD). The procurement of the donor lung demanded an intricate thoracic organ preparation. Immediately before aortic cross-clamp the LVAD was deactivated by severing the driveline. The recipient was a 57 year-old male with chronic global respiratory insufficiency. The sequential bilateral lung transplantation followed standard procedures. The patient was extubated on day 2 and was discharged from hospital in good physical and mental condition on day 22 postoperatively.
Summary: This case demonstrates for the first time that patients with mechanical circulatory support systems can be regarded as suitable donors for a lung transplantation.

P50 PORCINE MODEL FOR WHOLE-BLOOD NORMOTHERMIC EXTRACORPOREAL KIDNEY PERFUSION (NEKIP) - PERFUSION AFFECT ON T-CELL FREQUENCY OR FUNCTION

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Introduction: To simulate a kidney-transplantation for immunolocical studies, non lymphcyte-depleted whole blood has to be used for NEKiP. So far, it is unclear whether perfusion alters T-cell functionality.
Methods: A porcine model for NEKiP was mounted with whole blood and pressure-controlled normothermic perfusion with continuous oxygenation in six different kidneys was studied. During a four hour perfusion (T0 to T4) we studied hourly CD4-T-cell frequency and function (INFgamma production responding to PMA-Ionomycine stimulation) via flow cytometry.
Results: All 6 kidneys were perfused over at least 2 hours sufficiently, (mean art. Pressure 90–140 mmHg) within 30 min all kidneys produced urine and a significant decrease in S-creatinine was monitored. One kidney perfusion had to be stopped due to a thromboembolic occlusion. All other kidneys were perfused over 4 hours. During NEKiP the frequency and function of the tested CD4 T-cells decreased not significantly. Frequency of CD4 T-cells: T0 vs. T4 (given% of parent; mean and SD): 40.0 $\pm$ 6.07% vs. 39.80 $\pm$ 6.78% P = n.s. Likewise T-cell function, as responding INF gamma production on PMA-stimulation, was not significantly affected: (given%-of INFgamm pos. CD4-T-cells after stimulation): 22.42 $\pm$ 9.68% vs. 25.86 $\pm$ 12.30% P = n.s.
Conclusion: T-cell frequency and functionality was not altered during whole-blood normothermic extracorporeal kidney perfusion.

P51 NEW STRATEGY FOR AB0-INCOMPATIBLE PAEDIATRIC LIVER TRANSPLANTATION

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Introduction: Blood group incompatibility is a challenge in transplant medicine, as ABO-compatibility was regarded a premise for successful liver transplantation (LT). ABO-incompatible LT may result in hyperacute rejection, thrombotic events or biliary complications. However, ABO-incompatible LT is an increasing option facing organ shortage.
Methods: We report on two infants (aged 7 and 8 months), who were transplanted due to biliary atresia. Both received a graft from their ABO-incompatible father, because no ABO-identical donor was available. Following a new invented protocol preparation for LT included isoagglutinin apheresis (IA, Glycosorb and Terumo Optia) and intravenous immunoglobulins, if ABO-antibody titers exceeded 1:16. Furthermore we adapted the immunosuppressive and anticoagulation protocols.
Results: Anti-A was markedly elevated in one patient (IgG 1:128) who received four treatments of IA before LT. In the second patient IA was not required due to low antibody titers (anti-A 1:4). Both patients were successfully transplanted with good initial and ongoing graft function, no rejection and no signs of other antibody mediated complications.
Conclusion: ABO-incompatible liver transplantation is a good option, when no ABO-compatible donor is available. The new invented protocol was sufficient to control ABO-incompatibility.

P53 INFLAMMATORY RESPONSE AFTER BRAIN DEATH IS REDUCED BY DONOR TREATMENT WITH DESMOPRESSIN (DDAVP) IN AN ALLOGENIC KIDNEY TRANSPLANTATION MODEL IN RATS

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Introduction: Organ shortage leads to augmented use of marginal organs. Therefore the development of a mechanism to counteract the negative effects

of brain death and maintain organ quality in the brain dead donor is urgently required. Desmopressin (1-deamino-8-D-arginine-vasopressin [DDAVP]), used to treat brain-death related diabetes insipidus, is associated with an improved graft survival after kidney transplantation. Hence we proofed a potential beneficial effect of DDAVP in an allogenic kidney transplantation model in rats.
Methods: After induction of brain death, donor fisher rats either received DDAVP or saline. After 6 h of brain death, kidneys were explanted, stored for 24 h at 4°C in UW solution and transplanted into allogenic lewis rats.
Results: At the time of explantation donor kidneys treated with DDAVP showed a significant reduction in the RNA expression level of the adhesion molecules ICAM, VCAM and E-Selectin. Nonetheless we detected no effect of DDAVP treatment on graft survival, kidney functions parameters, proteinuria, infiltration of inflammatory cells and renal histology (Banff score) after the complete follow up of 24 weeks
Conclusion: Donor treatment with DDAVP influences the immunogenicity of transplanted organs, which might by due to hemodynamic effects of DDAVP on organ perfusion.

P54 DUAL KIDNEY TRANSPLANTATION WITHOUT PREIMPLANTATION BIOPSY: A SINGLE CENTER EXPERIENCE

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Kidney transplants from expanded criteria donors (ECD) have become generally accepted due to the increasing organ shortage. Dual kidney transplantation (DKT) of marginal kidneys not suitable for single kidney transplantation (SKT) can further expand the donor pool. Still, DKT remains underused and potentially eligible kidneys are often discarded.

To evaluate whether DKT can be performed savely, we analysed outcomes of DKT in our center and compared them to SKT and to an ideal kidney transplantation (IKT), a living donor kidney transplantation with older donors and recipients.

We retrospectively analysed 12 DKT and 23 SKT which were matched by recipient age, HLA and ischemia time. IKT were 13 patients. The follow up period was 12 months. Quality of life (QoL) was assessed with a questionaire.

Donor age and creatinine was significantly higher in DKT compared to SKT and IKT. Duration of hospitalization was similar and no difference in renal function at discharge was observed between DKT and SKT, with a trend towards more delayed graft function in DKT. Best-creatinine in the follow-up period was not significantly different in all groups. DKT patients were significantly longer on ICU, received more blood transfusions and were re-operated more often compared to SKT and IKT. Rejection episodes were lower in DKT compared to IKT and SKT, but tacrolimus was used more frequently in DKT. QoL was not affected by DKT.

In conclusion two marginal kidneys allocated by careful recipient selection can be performed safely and successfully. Surgical complications are increased but patient and graft survival as well as renal function are comparable. Although a larger cohort and longer follow up is needed, our results suggest that DKT can be used to transplant kidneys which otherwise might have been discarded.

P55 HEPATITIS C INFECTED DONORS: KNOWLEDGE OF VIRAL-LOAD IMPROVES USE OF GRAFTS IN GERMANY

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The European *Guide to safety and quality assurance for the transplantation of organs, tissues and cells* recommends to test every donor for anti-HCV and to extend this by PCR in case of an increased risk for HIV- or HCV-window period infection (WPI). We examined in anti-HCV reactive donors (anti-HCV+) the number of organs transplanted per donor with regard to HCV-viraemia.
Methods: Out of 6426 realised German donors (2006–2010) 125 were anti-HCV+. In 39 anti-HCV+ cases an increased risk for WPI existed with HIV-PCR and HCV-PCR performed prospectively (*Increased-Risk*). In 86 anti-HCV+ cases no such increased risk existed (*Standard-Risk*). The number of organs transplanted per donor (Median [interquartile Range]) was compared between cases with HCV-Viraemia actually detectable (PCR+), undetectable (PCR-) or not investigated (noPCR).
Results: In *Increased-Risk* cases the number of organs transplanted per donor did not differ with regard to HCV-viraemia ($P = 0.511$): anti-HCV+/PCR+ 1[0–3], ($n = 24$); anti-HCV+/PCR- 1[1–2], ($n = 15$). In *Standard-Risk* cases this number differed with regard to HCV-viraemia ($P < 0.001$): anti-HCV+/PCR+ 1 [0–2] ($n = 21$); anti-HCV+/PCR- 2[1–3], ($n = 31$); anti-HCV+/noPCR 1[0–1], ($n = 34$). When viral load was reported this exceeded log4 IU/ml.
Conclusion: In Anti-HCV+ *Standard-Risk* cases knowledge about viral load may increase the number of organs transplanted. Since PCR-measurement is unavailable for such cases in most European countries at a 24 h/365 d basis alternative technologies should be considered: Recently a HCV-Antigen test was introduced with appropriate determination of viral load equivalently. Further studies are requested to investigate this option before any new recommendations may be issued.

P59 ARE MARGINAL DONORCRITERIA A RISKFACTOR FOR GRAFT THROMBOSIS IN PANCREAS-TRANSPLANTATION?

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Objective: Graft thrombosis can lead to graft loss. Multivariate analysis in former studies identify high donor-BMI or-age as a riskfactor. We investigated whether marginal donor criteria (age > 45, BMI > 25) are correlating with an accumulation of graft thrombosis.
Method: 478 Patients underwent combined or isolated pancreas transplantation between 1/1994 and 7/2012.
Results: Occurrence of thrombosis was 14% (1.8% in kidneys, 12% in pancreas) with consecutive graft failure. From 1994 - 2012 average BMI increased (1994–1999: $n = 151$/ average BMI 22; 2000–2005: $n = 166$/ average BMI 24; 2006–20012: $n = 147$/ average BMI 24.7). Average donor age increased from 1994–1999: 36.9 year, to 2000–2005: 47.8 years and 2006–2012: 47.4 years.

In the group of graft thrombosis average age was 36 years and median BMI 23. Only 23% of all graft thrombosis were found within the group donor age > 45 and 18% in the group of donor-BMI > 25. For marginal donor criteria average age was 49.3 and median BMI was 28. This group only showed 5% of the graft thrombosis.
Conclusion: We could not establish a higher graft thrombosis occurrence within the group of marginal grafts. Therefore transplantation of marginal donor organs should be considered to increase the number of donations.

P60 CONTACT BETWEEN DONOR FAMILIES AND ORGAN RECIPIENTS - EVALUATION 2010 - 2013, DSO MITTE REGION

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Background: "How can I say thank you?" People who have received a new organ, and with it a new lease on life, grapple with this question. Legal stipulations currently do not allow the release of the donor family identity. Sending an anonymous thank you letter to the donor relatives is thus the only way by which an organ recipient can convey his gratitude.
Methods: Between January 2010 and May 2013 the correspondence of 127 organ recipients and 5 donor families in the DSO Mitte region was evaluated.
Results: The letters were written on average 4.04 years after surgery (with a range of 1 month to 22 years). The authors had received a liver (53), kidney (39), lung (16), heart (17), and combined transplantations (2). In 5 cases, the donor family initiated contact to organ recipients. In 15 cases, letters could not be forwarded due to missing addresses. In 13 cases, a response was received. In 8 cases, a regular correspondence ensued.
Conclusion: Donor families often express their wish for a thank you letter, yet organ recipients take an average 4 years post surgery to send a sign. The expectation of an answer from donor families often remains unfulfilled as well. Few of them respond. If they do, a regular mail correspondence ensues in about half the cases. Very rarely, but usually vehemently, the demand is made to end anonymity stipulations as they run counter to the right of self determination of both parties. This wish can currently not be granted in Germany.

INFECTIONS AND COMPLICATIONS AFTER ORGAN TRANSPLANTATION

P63 PNEUMOCOCCAL AND HLA ANTIBODIES ARE PREDICTIVE OF KIDNEY TRANSPLANT OUTCOME

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Background: There have been concerns that immune activation after vaccination could lead to (subclinical) rejection. The aim of the present study was to define (I) if pneumococcal vaccination induced HLA antibodies using highly sensitive methods and (II) if pneumococcal/HLA antibodies were predictive of patient outcome.
Methods: Forty-nine clinically stable kidney transplant recipients were immunized with Pneumovax 23. The median interval between transplantation and vaccination was 6.5 years. In none of the patients rejection occurred within 5 years post-vaccination. Pneumococcal and HLA/MICA antibodies were determined by Luminex™ technology.
Results: While pneumococcal antibodies were significantly higher at month 1 and 15 post- vs. pre-vaccination ($P < 0.0001$ each), HLA/MICA antibodies remained unchanged. Positive Luminex™ reactions (mixed beads) were present in 63, 67 and 63% (HLA class I), 47, 47 and 55% (HLA class II) and 29, 29 and 29% (MICA) pre-vaccination, at month 1 and 15, respectively. Kaplan-Meier analysis indicated that inferior patient survival was significantly associated with high concentrations of pneumococcal antibodies pre-vaccination [hazard ratio (HR) = 3.7, $P = 0.04$] and HLA class I antibodies pre-vaccination (HR = 3.6, $P = 0.04$]. Pneumococcal and HLA class I antibodies pre-vaccination were positively correlated ($r = 0.26$, $P = 0.07$).
Conclusion: Presumably, "natural" antibody formation (without vaccination) could be a surrogate marker for decreased patient survival.

P64 LOW-DOSE CIDOFOVIR AND CONVERSION TO MTOR IN POLYOMA VIRUS-ASSOCIATED NEPHROPATHY (PVAN) - A CASE SERIES

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Rationale: Polyoma virus-associated nephropathy (PVAN) is associated with a high rate of graft loss in renal transplantation. Overall reduction in immunosuppression is a cornerstone of PVAN therapy, whereas optimum drug combination and specific antiviral therapy remain a question.
Methods: We report safety, efficacy and outcome data of a protocol consisting of single low-dose cidofovir and conversion to mTOR-based immunosuppression in an ongoing case series of patients with biopsy-proven PVAN and progressive renal functional deterioration.
Results: Results of currently 11 patients with a median follow-up of 1.4 [0.3 - 6.2] yrs. are presented. Median eGFR prior to therapy was 26.6 [9.9 - 41.5] ml/min/1.73 m^2. The protocol allowed antiviral therapy without adverse nephrotoxicity, irrespective of allograft function. Polyoma virus clearance from plasma was achieved in 82% of patients after a median of 77 [27 - 249] days. Nine patients stabilized or improved allograft function, two patients progressed to ESRD, one of which was successfully retransplanted without recurrence of PVAN.

In Conclusion, low-dose cidofovir and conversion to mTOR-based immunosuppression allows for effective virus clearance and preservation of allograft function in a high proportion of patients with PVAN and may prolong allograft survival in these patients.

P65 SEVERE APHTHOUS STOMATITIS RELATED TO HUMAN HERPES VIRUS 6 INFECTION IN A RENAL TRANSPLANT PATIENT

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The Case: A 27-year-old caucasian with end stage renal failure secondary to IgA nephropathy presented six years after renal transplantion with new onset of fever and a sore throat to his familiar physician. Immunosuppressive regime consisted of tacrolimus, mycophenolate mofetil and prednisolon. Current physical examination showed pharyngitis and tender cervical lymph nodes. In the following two days he developed coughing, severe dysphagia, and vomiting and was admitted to a general hospital. Mycophenolate mofetil was stopped. Acute allograft injury was observed and the patient was transferred to the university clinic. He developed multiple skin lesions and severe stomatitis. Chest x-ray, urinalysis and graft sonography were unremarkable. Laboratory analysis showed leukocytosis, elevated CRP, and serum creatinine (1.5 mg/dL, baseline 1 mg/dL). Procalcitonin, liver, thyroid parameters and blood cultures were negative. He also tested negative for active HIV, CMV, EBV, HSV, VZV, Parvo B19, and hepatitis infection. Human herpesvirus 6 PCR from serum revealed viremia. The patient responded to a treatment with ganciclovir.

Human herpesvirus 6 disease is usually not considered as a differential diagnosis for infections leading to unnecessary investigations, treatments and late diagnosis. Raising awareness of characteristic features is needed to help guide optimal therapy in a timely manner.

P66 ORTHOTOPIC LIVER TRANSPLANTATION IN HUMAN IMMUNODEFICIENCY VIRUS (HIV)-POSITIVE PATIENTS IN GERMANY

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Objectives: This summary evaluates the outcomes of orthotopic liver transplantation (OLT) of HIV-positive patients inGermany.
Methods: Retrospective chart analysis of HIV-positive patients, who had been liver-transplanted in Germany between July 1997 and April 2013.
Results: 41 transplantations were performed in 35 patients at 9 German transplant centres. Reasons for OLT were end-stage liver disease (ESLD) and/or liver failure due to hepatitis C (HCV) ($n = 20$), hepatitis B (HBV) ($n = 11$), multiple viral infections of the liver ($n = 2$) and Budd-Chiari-Syndrome ($n = 1$). In April 2013 20/35 (57%) of the transplanted patients were still alive and had a median survival of 75 months (IQR (interquartile range: 57–100 months). 7 patients had died in the early post-transplantation period (first 3 months) from septicaemia ($n = 5$), primary graft dysfunction ($n = 1$), and intrathoracal hemorrhage ($n = 1$), respectively. Later on 7 patients had died due septicaemia ($n = 2$), delayed graft failure ($n = 2$), recurrent HCC ($n = 2$, and renal failure ($n = 1$), respectively. HCV reinfection occurred in all patients and contributed considerably to the overall mortality.
Conclusions: Overall OLT is a feasible approach in HIV-infected patients and achieves acceptable survival rates inGermany. Nevertheless, reinfection with HCV is a major clinical challenge in HIV/HCV coinfection after OLT.

P67 ALTERED PHENOTYPE AND FUNCTIONALITY OF VARICELLA-ZOSTER VIRUS SPECIFIC CD4 T-CELLS IN PATIENTS WITH ACUTE HERPES ZOSTER

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To improve risk assessment infectious complications in immunocompromised patients, we wanted to identify immunologic parameters associated with reactivation of varicella-zoster virus (VZV).

VZV-specific T-cell- and IgG-responses were characterized in 42 immunocompromised and immunocompetent patients with acute herpes zoster and compared to 90 patients and controls without VZV-reactivation. VZV-specific CD4-T-cells were analyzed after whole blood stimulation with VZV-lysate using flow-cytometric detection of intracellular IFNγ, IL-2, and TNFα and surface molecules typical for maturation (CD127) or anergy (CTLA-4 and PD1). IgG-titers were assessed using standard ELISA.

VZV-specific CD4-T-cells of non-symptomatic immunocompetent controls showed median frequencies of 0.15% (0.03–0.29%), were predominantly triple-cytokine-positive (median 54.0% (IQR 9.8%)) and CD127-positive (96.0% (6.2%)), but had low CTLA-4- and PD1-expression. Non-symptomatic immunocompromised patients had similar T-cell-properties. In contrast, individuals with acute zoster had elevated frequencies of VZV-specific CD4-T-cells (0.48% (0.65%)) and IgG-titers. The T-cell-cytokine-profile was shifted towards IFNγ-single-positive cells and CTLA-4- and PD1-expression was significantly increased whereas CD127-expression was decreased. Interestingly, T-cells analysed >3 months after acute reactivation reverted back to the phenotype observed in non-symptomatic individuals.
Conclusion: VZV-specific CD4-T-cells in patients with acute herpes zoster are elevated in frequencies and bear typical features of anergic cells. This phenotype may be applied for monitoring infectious complications in patients at risk.

P69 IDENTIFICATION OF NEW FACTORS THAT IMPACT SUBCUTANEOUS HBIG REQUIREMENT AFTER LIVER TRANSPLANTATION

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Aims: High interindividual variability of anti-HBs consumption may be of multifactorial etiology. We therefore aimed to identify predictive parameters for sc HBIG consumption in a prospective study.
Methods: Transplanted HBV patients were switched from iv HBIG to weekly sc HBIG. According to SPC, sc doses of 500 IU/week and 1000 IU/week were initiated in 24 (55.8%) and 19 patients (44.2%) respectively. At baseline, relevant parameters were determined and repeated at day 8, 15, monthly between month 1–6, at month 9 and 12, and comprehensive body composition was assessed using a bioelectrical-impedance-analyzer.
Results: Mean body weight, BMI and waist circumference (74.9 ± 14 kg, 26.2 ± 4.9 kg/m2 and 96.9 ± 13.2 cm) measured at baseline did not significantly change during follow-up. The same was true for renal function and total protein. Pearson correlation analysis showed that anti-HBs titers were negatively associated with MDRD ($P = 0.04$), total protein ($P = 0.04$), total body water ($P = 0.007$), fat-free mass ($P = 0.005$) and muscle mass ($P = 0.01$) and positively associated with creatinine ($P = 0.03$), body weight ($P = 0.02$), BMI ($P = 0.003$), body waist ($P = 0.03$) and fat mass ($P = 0.005$).
Conclusion: This is the first study showing that body composition and renal function impact HBIG levels. Given these findings, future studies are warranted to investigate individualized HBIG schedules.

P70 ALLOGRAFT FAILURE IN AN INTESTINAL GRAFT RECIPIENT AFTER CYTOMEGALOVIRUS DISEASE WITHOUT DNAEMIA

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Case report: We report a case of a 52 year old small bowel transplant recipient, with a clinical course complicated by CMV disease. Recipient and donor were CMV-IgG positive. Ganciclovir i.v., followed by valganciclovir was used for CMV-prophylaxis for 100 days. An antilymphocytic induction therapy was performed with Alemtuzumab on days 0 and 1. Immunosuppression was continued with tacrolimus, mycophenolate mofetil, prednisolone. Six months posttransplant the patient presented with CMV tissue invasive disease of the esophagus and stomach, without presence of viremia, tested by quantitative PCR. Treatment with ganciclovir resulted in complete viral load suppression and valganciclovir was initiated for secondary prophylaxis, whereas mycophenolate mofetil and prednisolone were discontinued. Shortly afterwards candida and recurrent CMV esophagitis was diagnosed, still without viremia. Improvement was achieved with ganciclovir and caspofungin. However, during the following course the patient developed CMV tissue invasive disease of the ileal graft, with persistent absence of viremia. Antiviral coverage was extended with foscarnet and CMV immunoglobulin. Viral load declined to undetectable levels, however the patient failed to improve clinically due to occurrence of graft rejection. Despite infliximab and high dose prednisolone, graft rejection was progressive, requiring surgical explantation of the graft. This case highlights the importance of additional diagnostic tools such as endoscopy including PCR analysis of tissue samples. Extension of primary antiviral prophylaxis interval up to 6 months and prolonged retreatment in recurrent CMV disease may be useful to avoid severe CMV-related complications.

P71 BILE COLONIZATION IN LIVER TRANSPLANT PATIENTS UNDERGOING ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATICOGRAPHY (ERCP): INCIDENCE, CLINICAL RELEVANCE AND ANTIBIOTIC SUSCEPTIBILITY

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Aim: Aim of this study was to evaluate microbiological spectrum and antibiotic susceptibility of specimens found in bile of liver transplant individuals undergoing ERCP and to investigate the clinical efficacy of administered prophylactic antibiotics.
Methods: We prospectively collected bile in 80 patients who underwent ERCP after LT. Samples were analyzed for colonization and antibiotic susceptibility. During follow up, patients were clinically observed with respect to development of infectious complications.
Results: The majority of bile samples 68/80 [85%] were tested positive and 12 [15%] were tested sterile. A total of 168 microbes (98 [58.3%] gram-positive, 48 [28.6%] gram-negative and 11 [13.1%] candida albicans) were isolated. Among the isolates, 67% were sensitive to the given prophylaxis, 35% were resistant to all typically used antibiotics (ciprofloxacin, imipenem and piperacillin/combactam) and 37% were sensitive to all three antibiotics.

During follow up 15 patients showed signs of infection. In 12 of them [80%], blood cultures were positive and a total of 19 microbes were isolated. In 17 of 19 isolated specimens [89%] there was a match between blood culture and culture out of bile. In 16 of these [84%], the administered peri-ERCP antibiotic prophylaxis was ineffective. Eight of the 16 samples were gram positive, 7 were gram negative and one was found to be candida albicans. Notably, all gram positive bacteria [50%] were sensitive to vancomycin or linezolid.
Conclusion: Monitoring of bile colonization during ERCP could help to facilitate the choice of suitable antimicrobial therapy in case of infectious complications.

P72 CMV INFECTION FOLLOWING LIVER TRANSPLANTATION: PREEMPTIVE THERAPY OR PROPHYLAXIS

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Introduction: Cytomegalovirus (CMV) infections causes often infection following solid organ transplantation. The incidence and severity of CMV infection depend among others on the CMV serostatus of donor and recipient. If donor and recipient are CMV-positive (D+/ R+) a potential benefit of CMV prophylaxis in patients after liver transplantation is not yet established.
Methods: 47 recipients of liver transplants (D+/ R+, 2005–2012) were included in this retrospective study. 21 patients received oral valganciclovir for 100 days after transplantation as CMV prophylaxis. CMV infection was monitored during the first 6 months by regular analysis of CMV-DNA (PCR) and pp65 antigen
Results: A CMV infection could be detected in 4 patients, 2 developed a CMV disease (CMV pneumonia and CNS disease). 3 of these patients received no CMV prophylaxis ($P = 0.408$). 8 patients developed a graft failure. This occured more frequently among patients without CMV prophylaxis ($P = 0.044$). Patients receiving a CMV prophylaxis developed more often a leukopenia (1. month $P = 0.104$, 2. month $P = 0.057$, 3. month $P = 0.075$), regarding number of platelets, hemoglobin and creatinin there was no difference.
Conclusions: A CMV prophylaxis can minimize the risk of CMV reactivation and graft failure. But disadvantages of the prophylaxis as leukopenia should be respected.

P73 THE GENETIC SIGNATURE OF THE DONOR ORGAN INFLUENCES THE FIBROSIS PROGRESSION AFTER LIVER TRANSPLANTATION

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Background: Fibrosis progression (FP) after liver transplantation (LT) is accelerated under immunosuppression. The cirrhosis risk score (CRS) was established in 2007 from data of a genome scan and validated in caucasian patients with chronic hepatitis C in the non transplant population (Huang et al., Hepatology 2007;46:297–306). The CRS comprises allele variants in seven genes. A CRS < 0.5 is associated with a low risk to develop cirrhosis, patients with a CRS > 0.7 are at high risk.

We aimed to validate the CRS after LT in HCV positive and negative patients including recipient and donor genotypes.
Methods: Genotypes were determined from DNA of liver biopsies ($n = 245$, donor) and from peripheral blood ($n = 512$, recipient) by fluorescence resonance energy transfer. The patients were stratified into three CRS categories: < 0.5, 0.5 to 0.7, and > 0.7. All patients underwent protocol biopsy after LT. Data were correlated with clinical variables and risk factors for fibrosis.
Results: Donors with CRS values > 0.7 showed a high risk for significant fibrosis (≥ F2) in the one year protocol biopsy ($P = 0.023$). The same results were found in biopsies performed within three years after LT ($P = 0.035$). Interestingly, HCV negative patients carrying a donor CRS > 0.7 showed a significantly higher risk for fibrosis (≥ F2) in the one year protocol biopsy compared to HCV positive patients ($P = 0.007$). The predictive value of the CRS for FP was independent of known clinical risk factors. A Kaplan-Meier analysis confirmed the prognostic value of the donor CRS with respect to the recurrence of liver fibrosis in HCV-negative patients after LT ($P = 0.05$).
Conclusion: The CRS of the donor liver influences the fibrosis progression after LT, especially in HCV negative patients.

P76 RECURRENT HEPATITIS C VIRUS GENOTYPE 1 INFECTION AFTER LIVER TRANSPLANTATION - WHOM TO TREAT?

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Background: Recurrent hepatitis C virus (HCV) infection after liver transplantation (LT) is a frequent and relevant problem, especially in HCV genotype (GT) 1 infection. This analysis evaluates a large real life cohort of HCV genotype (GT) 1 patients after LT with respect to the crucial questions which patients (i) need to be treated with direct antiviral agents (DAA), (ii) are likely having a benefit of the therapy and (iii) can be treated with respect to the expected treatment-associated side effects.
Methods: We retrospectively analyzed a cohort of 106 LT patients infected with HCV GT 1. Patient survival, fibrosis, interferon (IFN)-response as well as outcome and side effects of previous antiviral therapies were assessed. Based on the data from phase III clinical trials in the non-transplant setting (REALIZE and RESPOND-2), SVR rates according to previous IFN-response and fibrosis were modeled for this cohort.
Results: Overall survival with recurrent HCV GT 1 infection is worse compared to other HCV genotypes ($P = 0.01$). Subgroup analysis showed that survival is significantly worse in HCV GT 1 patients with advanced fibrosis (^{3} F3) in the first year after LT when compared with lower fibrosis grades ($P = 0.001$). In IFN-experienced LT HCV GT 1 patients ($n = 59$) the majority showed partial and null response. Compared to dual therapy predicted SVR rates of triple therapy indicated a benefit in this cohort. Finally, clinical decision making based on the side effects of former antiviral therapies was not reliable.
Conclusions: To our knowledge this is the first detailed analysis evaluating a large real life cohort of HCV GT 1 patients after LT. Patients with recurrent HCV-associated advanced fibrosis urgently need antiviral treatment. Fibrosis and response to previous IFN-therapy should guide the clinical decision since modeled success rates of DAA therapy in LT are promising.

P79 INNOVATIVE CONSEQUENCES FOR CLINICAL PHARMACOLOGICAL APPROACH: HELP - HIERARCHICAL ELEMENTS FOR LONG-TERM PREVEILLANCE

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Background: Minimizing organ transplant (TP) injury, elder or marginal organs themselves and preexisting or upcoming comorbidities recommend implementation of clinical pharmacological expertise, still underestimated.
Concept: HELP is designed to elaborate hierarchically structured elements within the pharmacological treatment options for this vulnerable TP patient group and TP itself esp. with regard to polypharmacy. Drug drug interactions become obvious in about 38% of patients being on 4 co-dispensed drugs, up to almost 100% with 8 drugs. Synopsis of internal medicine and clinical pharmacology with daily experience in TX over a decade is the basis of the innovative attempt to present advices for further "preveillance" (prevention and surveillance) of TP. Relevant examples are documented and evidence is reviewed via updated literature.
Findings and Advices: Aftercare in transplantation (TX) involves drug management of cardiovascular diseases, organ deteriorations, immunosuppression and complications resulting in polypharmacy, but also vice versa. For each of these components first hierarchical structures within pharmacological treatment options are presented. They consistently focus on preserving the individual TP and improving long-term graft survival and cardiovascular comorbidities and metabolic risks.
Conclusion: To avoid insidious organ deterioration in TX resulting from drug therapy and polypharmacy HELP presents an innovative consequent clinical pharmacological approach that might further improve long-term survival of TP.

P80 TEXT MESSAGING MAY IMPROVE SUN PROTECTION ADHERENCE IN PEDIATRIC ORGAN TRANSPLANT RECIPIENTS

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Objectives: To evaluate the technical feasibility and acceptability of short message service (SMS) based on sun protection recommendations for adolescents after organ transplantation.
Methods: Organ transplant recipients participated in sun protection program ("HIPPOlino"), followed by sun protection recommendations sent to their mobile phones via SMS. Recommendations were tailored to the regional UV index.A questionnaire was administered to evaluate the sun protection knowledge and behavioral change.After the text messaging intervention a telephone interview was conducted.
Results: 26 (8 females, 18 males) were enrolled.19patients (6 females, 13 males) took part in the SMS intervention. 84% of the participants (16/19; 5 females, 11 males) confirmed daily receipt of sun protection recommendations. Text messages helped them to remember the most important information of the sun protection training. 52% of theadolescents(11/19; 3 females, 8 males) mentioned that both sun protection training and text messages influenced their sun protection behaviour.
Conclusions: SMS based sun protection recommendations are technically feasible and accepted by adolescent organ transplant recipients. Text messaging may be a valuable tool to support sun protective behaviour in everyday life. A national trial was initiated in Germany to further evaluate the effectiveness of this intervention to improve sun protection adherence.

P81 BK VIREMIA AND POLYOMAVIRUS NEPHROPATHY IN 352 KIDNEY TRANSPLANTS; RISK FACTORS AND POTENTIAL ROLE OF MTOR INHIBITION

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Background: Polyomavirus BK nephropathy (PyVAN) remains an important cause of early graft dysfunction and graft loss in kidney transplantation.
Methods: In this retrospective, single centre cohort study we studied the incidence and outcome of BK viral infection in 352 patients transplanted in 2008–2011.
Results: During follow-up viral replication was detected in 48 patients (13.6%); 22 patients (6.2%) had biopsy proven PyVAN.

In multivariate logistic regression analyses risk factors for BK-viremia were lack of enrolment into randomized controlled trials (RCTs), biopsy proven acute rejections, cytomegaly virus (CMV) serostatus of both donor and recipient and previous transplantation.

In patients without PyVAN reduction or switch of immunosuppression was associated with rapid viral clearance and stable graft function. In contrast, in most patients with PyVAN graft function deteriorated and 5 patients prematurely lost their allograft. Switch of immunosuppression to a low dose cyclosporine plus mTOR inhibitor based regimen in patients with PyVAN was safe, well tolerated and tended to be associated with a better short-term outcome in terms of graft function compared to reduction of existing immunosuppression alone.
Conclusions: With the lack of licensed anti-polyoma viral drugs reduction or conversion of immunosuppression remains the mainstay of therapy in patients with PyVAN. The combination of low dose cyclosporine plus mTOR inhibition appears to be safe and warrants further investigation.

P82 PROPOSAL FOR HYGIENE MANAGEMENT OF METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS (MRSA) IN ORGAN DONATION AND PROCUREMENT

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Since 2001 hygiene management in Germany is regulated by law according to the Infection Protection Act (Infektionsschutzgestz). After revision in 2011, the act highlights the legal character of guidelines published by the Robert Koch Institute. The amendment had become necessary inter alia after reality stroke expectations regarding control of MRSA in Germany: MRSA-prevalence (KISS-data from ICU's) rose from 8% in 1997 to 30% in 2003. Moreover at least 400,000 to 600,000 nosocomial infections are presupposed in annually, whereof 14,000 MRSA-infections. As this situation has impacts on organ transplantation programs, too, consequently case reports regarding the spread of MRSA via organ donation have been published. Moreover, there is evidence suggesting that the outcome of S. aureus donor-to-recipient-transmitted infection might be poor in cases of solid organ transplantation. Today, organ donation programs in Germany usually refer to respective hospital hygiene guidelines which are not specially adapted to the needs of multi-organ donations involving multiple teams arriving from different places bringing along their own equipment for organ recovery, preservation and transportation. Therefore, it is of major importance to apply standardized guidelines for hygiene management of MRSA in organ donation and transplantation programs, too. Present recommendations on hygiene management of MRSA in organ donation and procurement refer to mentioned regulations but as well take into account actual published literature. As it is generally agreed upon that the course of nosocomial infection is mostly due to transmission via contaminated hands, hygienic hand disinfection remains the most important measure in organ transplantation setting, too.

P83 PNEUMONIA IN KIDNEY AND KIDNEY-PANCREAS TRANSPLANT PATIENTS

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Introduction: Pneumonia in transplant patients is a life-threatening disease, often manifested with atypical sings.
Materials and methods: We performed a retrospective analysis of kidney and kidney-pancreas transplant patients (30 men / 20 women) [aged 59 $\pm$ 10.95 years] who were treated between 2005–2011 in our center because of pneumonia.
Results: In 32 cases remained the pathogen despite extensive diagnostic (BAL, antigen-tests, PCR) unknown. 10 cases showed typical (gram-positive cocci and gram-negative bacilli), while further four atypical pathogens (2 mycoplasma, 2 CMV). In 8 patients, only CT scan could reveal an atypical pneumonia. In 20 cases (33%) (12 men, 8 women) [aged 59 $\pm$ 10.93 years] a ICU admission was necessary because of respiratory failure. 4 patients (6.7%) [60.5 $\pm$ 7.18 years] did not survive the severe course. A statistical correlation between the time start of treatment outside the center and a more severe course was not observed.
Conclusion: Because of the high mortality rate, targeted diagnostics in a transplant center is decisive. Frequently pathogen identification fails, despite the use of different methods. An immediate broad antibiotic therapy has to be initiated already on strong suspicion of pneumonia. In our cohort "typical" and "atypical" pathogens were equal observed.

LIVING DONATION

P84 TELEMEDICAL SUPPORTED AFTER CARE IN LIVING KIDNEY RECIPIENTS - AN INNOVATIVE PROJECT-STUDY AT THE TRANSPLANTATIONCENTER FREIBURG INTERIM RESULTS OF A PROSPECTIVE ONGOING STUDY OF 50 PATIENTS

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Introduction: For the possibly longest patient and graft survival, the successful operation is a keyfactor, but also to take care for the possibly best post-operative treatment. Therefore the Transplantationscenter Freiburg initiated a project to evaluate the medical, psychosocial and economic wellbeing of living kidney recipients with a telemedical supported aftercare.
Methods: The scientific evaluation of the project „Telemedical aftercare in living kidney recipients" is designed to draw comparisons. 2x25 patients are observed, one group with telemedical support, the other group with a conventional after care as the control-group. Both groups are examined in detail at the course of their medical condition, at their adherence concerning the intake of immunosuppressive medication and also at their psychosocial and economic factors with Interviews and Questionnaires. The focus in the design of this study is a high scientific quality. Therefore the evaluation is carried out as a prospective, randomized, controlled and open project-study and the data are analyzed with inductive and descriptive statistics.
Results: Early diagnosis of acute rejections and infections, a higher life-quality and self-responsibility are expected outcomes. Also economic effects in the form of time- and cost-savings for the German health facilities and insurance companies are expected. First interim results at timepoint 3 months after transplantation confirm these expectations. Telemedical supported aftercare improves the patient's adherence significantly and reduces the frequency of unplanned hospital-readmissions. It provides a higher quality of life and an earlier return back to normal life.
Conclusions: It is validated, that the recipient's medical and psycho-social benefit is being substantially supported with telemedicine in the after care after living kidney transplantation. Further, there is a time and cost saving without any restriction in the quality of supply.

P85 DESENSITIZATION PROTOCOL IN IMMUNIZED LIVING DONOR KIDNEY TRANSPLANTATION - A SINGLE CENTER EXPERIENCE

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Objective: Due to growing waiting times for renal transplants living donor kidney (LDK) transplantation performed in the presence of donor-specific antibodies (DSA) or ABO incompatibility (ABOi) using various desensitization protocols has increased. We herein evaluated graft outcome after desensitization in comparison to immunological low risk LDK recipients at our center.
Methods: 8 patients with Luminex-detected DSA and 26 ABOi patients were successfully desensitized by anti-CD20, plasmapheresis (DSA) or immunoadsorption (ABOi) and received a LDK transplant. Graft survival and function, rejections and infectious complications were compared to LDK recipients with non donor-specific antibodies (low risk, $n = 20$) or no antibodies (no risk, $n = 37$), receiving no desensitization but similar maintenance therapy. All patients had a negative CDC crossmatch before desensitization and/or transplantation.
Results: The 1-year graft survival rate was 100% in the DSA, ABOi, low risk and 98% in the no risk group (1 graft lost due to recurrence of FSGS). Renal function at 12 months was similar in all 4 groups (creatinine: 1.8 vs 1.7 vs 1.6 vs 1.5 mg/dL; eGFR: 42 $\pm$ 10 vs 48 $\pm$ 18 vs 46 $\pm$ 16 vs 49 $\pm$ 16 in DSA, ABOi, low risk and no risk group). Incidence of acute T-cell mediated rejections did not differ (25 vs 25 vs 22 vs 20%), while antibody-mediated rejections (AMR) were only found in the DSA (2/8) and ABOi (1/26) group. 3/8 patients showed evidence of persistent DSA. 2 of those patients experienced AMR and had impaired renal function at last follow-up (creatinine 2.6 mg/dL). The incidence of BK nephropathy was more frequent in desensitized patients (5/34 vs 0/57)
Conclusions: We demonstrate favorable short-term allograft outcome in LKD transplant recipients after desensitization, if DSA can be removed. However, the intensified desensitization was associated with an increased risk of BK nephropathy.

P86 FIRST EXPERIENCE WITH ABO INCOMPATIBLE LIVING RELATED KIDNEY TRANSPLANTATION (ABOI) WITHOUT RITUXIMAB IN HAMBURG

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ABOi kidney transplantation became a successful therapeutic option for patients without a blood group compatible living donor. In 2003 Tyden et al. introduced rituximab induction in the standard treatment protocol to avoid splenectomy. As CD20-positive B-cell depletion with rituximab has no direct effect on antibody production the biological relevance of this treatment is uncertain.

In 2011 we changed our standard immunosuppressive (IS) regimen in ABOi. 5 patients were transplanted after successful bloodgroup-antibody reduction with immunoadsoprtion with basiliximab ($\pm$ single dose ATG induction (1 mg/kg bw)) followed by maintenance IS with low dose steroids, CNI and everolimus.

After a follow up of 6–18 month graft survival is 4/5. One patient lost his graft due to recurrent atypical HUS 10 month post ABOi. 4/5 patients have a very good kidney function with s-creatinine of 1.3–1.8 mg/dl. No rejection or infection with CMV or BKV occurred within the first 6–18 month in any of the patients.

In conclusion: Induction treatment with rituximab is not needed to successfully perform ABOi renal transplantation in patients with low to moderate ABOi antibody titers ($\leq$ 1:128).

P88 AB0-INCOMPATIBLE LIVING DONOR KIDNEY TRANSPLANTION AT THE TRANSPLANT CENTER OF ERLANGEN-NUREMBERG - A SINGLE CENTER EXPERIENCE OVER 7 YEARS

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Background: Blood group incompatible (iABO) living kidney donation is experiencing increasing importance due to the lack of post-mortem organ donation in Germany. At the centre of Erlangen-Nuremberg 23% of living kidney transplantation are iAB0 donated also to recipient at risk with pre-immunization or repeatedly transplanted.
Method/material: Retrospective analysis of 152 LSP-NTX in 2006–2013 with 117 (77%) blood group compatible (cAB0) donors and 35 (23%) iAB0 donors.

iAB0 recipients receive in 71% a non-relative donation, showing in 27% preformed antibodies against human leukocyte antigen (HLA) and have been repeatedly transplanted in 17% (2nd/3rd kidney transplant, after heart, liver or pancreas transplantation).

The cAB0 standard therapy is tacrolimus, mycophenolate mofetil, steroids and basiliximab.

The iAB0 recipient conditioning is preoperatively extended by rituximab four weeks before and (Glycorex-)Immunoadsorption accordingly to blood group antibody titer (target 1:4).
Results: Patient survival after 7 years is 100% in both groups. Graft graft survival is 97% in iAB0 vs. 92% in cAB0. No significant difference in eGFR between iAB0 (56 ml/min) and cAB0 (53 ml/min) at 12 months. Significantly fewer rejection episodes in the first two years in iAB0 (18%) with borderline or BANFF I acompared to cAB0 (49%) with more BANFF II and humoral rejections ($P = 0.028$). Less incidence of polyomavirus nephropathy in iAB0 compared to cAB0 (P = n.s.)
Conclusions: The iAB0 living kidney transplantation is a successful expansion of the living donor program with good function rates, significantly less rejections and less polyomavirus nephropathy. Even recipients at risk with pre-immunization or previous transplantations will have a benefit from iAB0 transplantation.

P89 HAND-ASSITED TWO-PORT RETROPERITONEOSCOPIC LIVING DONOR NEPHRECTOMY: STILL CONDEMNED TO THE LEFT SIDE?

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Objectives: Hand-assisted retroperitoneoscopic (HARS) living donor nephrectomy combines safety of hand-assistence and advantages of retroperitoneal access. To date, the feasibility has been exclusively described for left side kidney donation. HARS technique for left and right living donor nephrectomies were compared.
Methods: Retrospectively single center analysis of 47 LDN from 2010 to 2012 with a two-port HARS procedure was perfromed. Selection algorithm for donationat Zurich UniversityHospital is the kidney with the lowest glomerural filtration rate despite anatomy.
Results: 27 patients underwent right and 20 left LDN. Median follow-up was 12 months. Postoperative complication rate was 6%, one case each side.

Median length of hospital stay was 5 (IQR: 4–6) days. No conversion to open surgery became necessary. Median length of renal artery and vein was 44 mm and 50 mm respectively for left kidneys whereas 30 mm and 20 mm for right kidneys. Mean operation times were 150 minutes for left versus 125 minutes for right sided donations. There was no technical failure during and post transplantation.
Conclusion: Hand-assisted retroperitoneoscopic living donor nephrectomy is a feasible and safe procedure for both left and right kidneys.

P91 COMPARISON OF GLYCOSORB AND PROTEIN A IMMUNOADSORPTION IN AB0-INCOMPATIBLE-KIDNEY TRANSPLANTATION

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Problem: In AB0-incompatible kidney transplantation (AB0i-KT) immunoadsorption is used to reduce the AB0 antibody titer. So far it is unclear whether antigen-specific glycosorb or regenerable protein A immunoadsorption is favorable.
Methods: In our center glycosorb immunoadsorption was the standard for AB0i-KT until the end of 2011. Thereafter protein A immunoadsorption was used instead. In an explorative retrospective analysis of all AB0i-KT's from 2011 to march of 2013 we compared 4 consecutive AB0i-KT's with each device. Two sensitized patients were not included into the analysis.
Results: In all 8 patients it was possible to reduce AB0 IgG antibody titer (AT) to a minimum of 1:8 with subsequent successful transplantation. The higher the initial AT the higher was one patients treatment sessions count (TSC). (5 to 15 treatment sessions in the glycorb group and 6 to 13 in the protein A group). Titer reduction in one treatment session was higher for higher pretreatment titer. That is why for comparison a logarithmic titer scale was used (natural logarithm of initial AT: $\ln(\text{titer}_i)$). The ratio of TSC and $\ln(\text{titer}_i)$ was comparable in both treatment groups: 1.20 to 2.10 in the glycosorb group versus 1.44 to 2.34 in the protein A group.
Discussion: Both ways of immunoasorption can be used in AB0i-KT. Larger studies are necessary and should include analysis of further aspects like non AB0-immunity and cost effectiveness.

P92 DIFFERENCES BETWEEN LIVE AND DECEASED-DONOR KIDNEY TRANSPLANTATION IN A CENTRE PERFORMING PROTOCOL BIOPSIES

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Background: Live kidney transplantation (LK-tx) results in a longer transplant survival than non-living transplantation (NLK-tx).
Methods: We tested the reasons for that by analyzing retrospectively 892 renal transplant patients having participated in a protocol biopsy program (started at 2000, biopsies at 6, 12, 26 weeks) with at least 1 biopsy.
Results: 134 patients after LK-tx were compared to 758 patients after NLK-tx. Transplant failure at 10 years was seen in only 8% of LK-tx patients and 15% of NLK-tx ($P = 0.04$, death-censored Kaplan-Meier analysis); their creatinine clearance (C&G) after 6 weeks and 1 year was significantly higher (median 67 [range 23–140] vs 56[14–148]; and 60[14–131] vs 53[13–160] mL/min, resp; $P = 0.001$). Significant differences between the groups were donor age (53[29–74] vs 49[5–82] yrs, $P = 0.001$; recipient age (44[18–69] vs 51[19–76] yrs, p6 mos post-tx (32 vs 25%, ns); positive PRA, 3 vs 8% of patients, ns; PRA 6–84%, 2 vs 6%, ns; PRA >84%, 0 vs 0.9%, ns.
Conclusion: Patients after live kidney tx had a better 10-yr transplant survival and a better early and late renal function than patients after deceased-donor tx. They were younger, had a shorter length of dialysis before tx, were less often pre-transplanted, and had a shorter cold ischemia time. Patients after deceased-donor tx had younger donors and a better HLA match. The very good 10-yr transplant survival in both groups may be attributed to the participation in protocol biopsies of this cohort: On the one side, changes in the biopsies are reflected in treatment; on the other side, these patients permitting protocol biopsies probably are a positive selection of patients with a good adherence.

P93 EARLY SURGICAL COMPLICATIONS COMPROMISE LONG TERM SURVIVAL AFTER LIVING-RELATED KIDNEY TRANSPLANTATION

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Surgical complications following kidney transplantation may compromise immediate graft survival. Impairment of *long term survival* by surgical complications however has been challenged. Purpose of the study was to investigate the interrelation between complications requiring revision surgery and survival after living related kidney transplantation (LRKT).

270 LRKTs between 1995 and 2011 were analyzed. Besides graft- and patient survival and the incidence of surgical revisions, data of age, comorbidity, BMI, time on dialysis, remaining diuresis, immunosuppression and immunological prerequisites (HLA-mismatch, panel-reactive antibodies, rejections) were determined. Early graft function was monitored by means of diuresis onset and serum creatinine at 3, 6 and 12 months.

Graft survival with and without surgical revision was 95.8/86.7% (1y), 91.5/75.2% (3y) and 85.5/66.2% (5y), patient survival was 99.5/96.2 (1y), 97.2/90.4 (3y) and 93.7/85.9% (5y), respectively. Surgical revision was required in 18.9%, which impaired graft- ($P = 0.032$) and recipient survival ($P = 0.014$), and was associated with delayed graft function ($P < 0.0001$). Cox-regression confirmed the results for patient survival, which was furthermore influenced HLA-mismatch and BMI elevation, whereas HLA-DR mismatches affected graft survival.

Revision surgery impact long term patient survival following LRKT. Complication-free post-surgical results may improve long term graft function, reduce the necessity of dialysis restart and determines long term recipient survival.

P94 SEVERE ANEMIA DUE TO PARVO VIRUS B19 INFECTION IN A PATIENT AFTER LIVING DONOR KIDNEY TRANSPLANTATION - SUCCESSFUL TREATMENT USING HIGH-DOSE IMMUNOGLOBULINS

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We report about a 32 year old male patient who had undergone living donor kidney transplantation in May 2012. He had developed end-stage renal disease due to IgA nephropathy, his wife donated the organ.

Initially no complications occured, the renal function was stable represented by a medium serum creatinine level of 1.5 mg/dl. Immunosuppression consisted of our standard triple drug therapy including tacrolimus, prednisolone and mycophenolic acid.

A few months after transplantation episodes of severe anemia occured while the patient suffered from no specific symptoms. There were no signs of hemolysis nor of toxic effects of the immunosuppressive therapy. Gastrointestinal blood loss was excluded endoscopically. Parvo virus B19 was detected by PCR in the blood. A bone marrow biopsy was examined detecting a typically suppressed erythropoesis as seen in parvo virus b19 infection.

The reduction of the immunosuppressive therapy showed no success, the patient had to receive blood transfusions repeatedly. Treatment using immunoglobins also led to quick recurrance of viral load and anemia. A therapeutical approach with higher doses (90 g of immunoglobuline G) was then tried. He underwent this therapy 3 times achieving viral clearance and medium hemoglobin levels around 11 g/dl.

High-dose immunoglobine therapy showed promising results in a case of severe anemia due to parvo virus b19 infection in a kidney transplant recipient.

P95 LIVING DONOR SMALL BOWEL TRANSPLANTATION FOR HYPOGANGLIONOSIS

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Purpose: We recently performed living donor small bowel transplant (LDSBT) in three patients with hypoganglionosis. We report here the peri- and postoperative management and discuss several issues about LDSBT.
Patients: The patients were 14 (Case1), 11(Case2) and 15(Case 3) years old boy. All of them were with total parenteral nutrition associated with hypoganglionosis.
Transplantation Procedure: One third of the donor bowel was harvested. The graft vessels were connected to the recipient's infra renal aorta and inferior vena cava (Case 1), or SMA and SMV (Case 2,3)
Postoperative course: The immunosuppressive regimen consisted of daclizumab, tacrolimus, and steroids. The first patient developed liver dysfunction on POD 7, subsided spontaneously on POD 12, requiring no additional therapy. Two months after transplantation, he was weaned off TPN, tolerating oral intake with a fully functioning graft. The second patient was weaned off TPN on 3 months after transplantation with a functioning graft. He developed mild acute cellular rejection on day 111, which was successfully treated with bolus injections of steroid. The third patient encountered mild rejection at 1 year after transplantation. Subsequently intestinal perforation of graft occurred maybe due to adverse effect of steroid therapy. This was fortunately successfully managed.
Conclusion: LDSBTs were performed to the three patients with hypoganglionosis successfully. It is advisable that LDSBT would be performed before getting more serious liver dysfunction or blood access route problem. It would lead to physical and psychological improvement of quality of life.

P96 LIVING DONOR NEPHRECTOMY - A SINGLE-CENTER EXPERIENCE WITH OPEN AND LAPAROSCOPIC APPROACHES

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Introduction: Kidney transplantation is the treatment of choice for patients with end stage kidney diseases, but the average time on the waiting list is up to 6 years. Offering a standard laparoscopic donor nephrectomy technique, the number of living kidney donations increased in our institution.
Methods: In 2010 our institution introduced a fully laparoscopic donor nephrectomy technique. The aim of our study was the comparison with the open donor nephrectomy approach used before. Therefore, we analysed all patients (01/2007–12/2012), who underwent a donor nephrectomy.
Results: We performed 88 donor nephrectomies (mean age 51.1 years). 62.5% (56) of the procedures were performed as open and 37.5% (33) as laparoscopic nephrectomy. The mean operation time was slightly longer in the laparoscopic group (LG) with 196.4 minutes compared to 185.1 minutes ($P = 0.007$). The warm ischemia time in the LG was 22 seconds longer than in the open nephrectomy group ($P = 0.001$). No conversion to open surgery was necessary. In contrast to other studies the complication rate was not higher in the LG. We had to perform 2 reoperations after open nephrectomy (bleeding, ureter complications) and 1 reoperation in the laparoscopic group (wound infection). Donor creatinine 1 year after donation did not differ between the two groups.
Conclusion: We were able to show that our fully laparoscopic donor nephrectomy technique is a safe approach with favourable donor acceptance. Although we performed a complete change of our approach with an unavoidable learning curve, no higher rates of complications and no conversion to open surgery were observed. Laparoscopic donor nephrectomy might be the new standard for living kidney donation.

P98 PRE-TRANSPLANT IMMUNE STATE IS ASSOCIATED WITH ACUTE REJECTION AFTER LIVING-DONOR KIDNEY TRANSPLANTATION

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Background: Acute rejection episodes still represent a major contributing factor for development of chronic graft dysfunction. Reliable immunological parameters representing the pre-Tx immune state and hence defining the individual risk for graft rejection hold potential to enable individualization of immunosuppression in advance.
Methods: Mixed lymphocyte culture was used to determine donor- and 3rd-party alloreactivity. Soluble forms of CD25, CD30 and CD44 were detected in patients' serum by ELISA. Flow-cytometry was applied to define various lymphocyte subpopulations. Patients were grouped according to protocol and indicated biopsies within the first year post-Tx: non-rejector (NR, $n = 13$), borderline (BL, $n = 5$), acute rejector (AR, $n = 7$). In all cases immunosuppression with CNI/MMF/steroids was given.
Results: Kidney recipients suffering from AR showed significantly higher pre-Tx alloreactivities than NR ($P < 0.02$). Likewise highest levels of sCD25, sCD30 and sCD44 were observed in the former ($P = 0.030$, 0.011 and 0.002 compared to NR). Patients of the BL-group were found in between. Combination of these parameters enhanced differences seen between groups. Individuals with graft rejection showed markedly increased frequencies of $CD4^+CD28^-$ and $CD8^+CD28^-$ T-cells pre-Tx.
Conclusions: The patient's pre-Tx immune state defined by soluble serum markers and allroreactivity as well as the frequency of particular T-cell subsets seem to correlate with acute graft rejection after kidney-Tx and should be further evaluated for clinical applicability.

KIDNEY AND KIDNEY / PANCREAS

P99 HIGH-URGENCY RENAL TRANSPLANTATION: INDICATIONS AND LONG-TERM OUTCOMES

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The concept of high-urgency (HU) renal transplantation was introduced in order to offer to patients, who are not able to undergo long-term dialysis treatment, a suitable renal graft in a short period of time, overcoming this way the obstacle of the prolonged time spent on the waiting list. The goal of this study was to evaluate the patient and graft survival after HU renal transplantation and compare them to the long-term outcomes of the non high-urgency renal transplant recipients. The clinical course of 33 HU renal transplant recipients operated on at our center between 1995 and 2010 was retrospectively analyzed. The major indication for the HU renal transplantation was the imminent lack of access for either hemodialysis or peritoneal dialysis (67%). The patient survival of the study population was 67%, 56% and 56% whereas the graft survival was 47%, 35% and 35% at 5-, 10- and 15-years respectively. In the comparison between our study population and the non HU renal transplant recipients, our study population presented statistically significant ($P < 0.05$) lower patient survival rates. The HU transplant recipients also presented lower graft survival rates, but statistical significance ($P < 0.05$) was reached only in the 5-year graft survival rate.

P100 RECURRENCE OF IDIOPATHIC MEMBRANOUS NEPHROPATHY 12 YEARS AFTER KINDEY TRANSPLANTATION - SUCCESSFUL TREATMENT WITH RITUXIMAB

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Rationale: Idiopathic membranous nephropathy (IMN) recurs in 10–40% of patients after kidney transplantation and is associated with variable clinical outcome. Autoantibodies against M-type phospholipase A2 receptor (PLA2-R) are associated with recurrence of IMN after transplantation and allow for differentiation from *de novo* disease and therapeutic monitoring. The monoclonal CD20-antibody rituximab was shown effective in treating IMN. Here we report very late recurrence of IMN, 12 years after kidney transplantation, and successful treatment with rituximab.
Clinical setting: A 44 year-old male with IMN presented with progressive proteinuria up to 5000 mg/g creatinine and renal functional deterioration 12 years after 2nd kidney transplantation. Renal biopsy demonstrated recurrence of IMN with IgG, C3 and PLA2-R staining. In serum, PLA2-R autoantibodies were highly detectable.
Results: Rituximab, 375 mg/m², was administered twice within two weeks and FACS analysis confirmed B-cell depletion. Renal function stabilized and PLA2-R autoantibody titres decreased rapidly. Six months after rituximab, PLA2-R autoantibodies were no longer detectable and proteinuria continuously decreased to 800 mg/g creatinine.

In Conclusion, late recurrence of IMN after kidney transplantation may successfully be treated with rituximab. Reduction of PLA2-R autoantibody titres preceeds changes in proteinuria and may help to predict response and guide therapy in these patients.

P101 NON-INVASIVE SCREENING FOR ACUTE REJECTION IN MURINE RENAL TRANSPLANTATION USING DIFFUSION WEIGHTED MRI

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Introduction: Biopsies are often required to detect the underlying condition for deterioration of the transplant function. Here, we tested a novel substance which inhibits the MCP1/CCR2 pathway via oligonucleotides in a murine renal Tx model. The aim was 1.) to detect potential effects of this drug on acute rejection processes and 2.) show that diffusion weighted MRI (DWI) may be a valuable tool to non-invasively monitor these rejection processes.
Methods: Kidneys of Balb/c mice were transplanted onto B6. Mice were either treated with the anti-MCP1-Spiegelmer in monotherapy or in combination with subtherapeutic CsA (10 mg/kgBW). For further analysis immunohistochemistry, FACS, doppler ultrasound and diffusion-weighted MRI were used.
Results: The number of F4/80$^+$ cells was efficiently suppressed and kidney cortex perfusion measurements improved under combination therapy. The apparent diffusion coefficient (ADC) of native kidneys and syngenic allografts did not show significant differences. Allogenic allografts without treatment showed significantly lower ADC ($P < 0.001$). Under combination therapy the ADC significantly improved ($P = 0.002$).
Discussion: The novel drug based on oligonucleotide technology inhibiting the MCP1 alleviates acute rejection. Diffusion-weighted MRI may serve as a valuable tool to detect rejection processes.

P104 GLOMERULAR ENDOTHELIAL MICRORNA EXPRESSION PROFILES IN AN IN-VITRO MODEL OF ACUTE HUMORAL REJECTION

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Purpose: Acute humoral rejection (AHR) is mediated by alloantibodies against donor endothelial cells with and without complement activation. Histological and serological diagnosis remains challenging. Therefore, identification of a diagnostically useful miRNA signature for complement-mediated and complement-independent AHR is most desirable.
Methods: Human renal glomerular endothelial cells (HRGEC) were HLA-typed and treated with binding (HLA-A1) or non-binding (HLA-A2) antibody with and without addition of complement. Expression of 762 microRNAs was analyzed by Taqman Low densitiy arrays in a model for 1. complement-mediated AHR, 2. complement-independent AHR and 3. the additional effects of complement in AHR. Here we defined miRNAs as up- or down-regulated when a P value of < 0.05 in two-sided t-test.
Results: In complement-mediated AHR several microRNAs were down-regulated (miR-29b, miR-195, miR-215, miR-641) and miR-770-5p was up-regulated. In complement-independent AHR several miRNAs were up-regulated (miR-125a-5p, miR-374b#, miR-501-3p among others) and down-regulated (miR-520c-3p, miR-1201, miR-1255b). Additional effects of complement in AHR show a signature of up-regulated miRNAs (miR-554, miR-601, miR-604, miR-886-3p, miR-1255b) and down-regulated miRNAs (miR-133a, miR-423-5p, miR-502-3p).
Conclusion: With microRNA profiling in an *in-vitro* model we identified a glomerular endothelial-specific microRNA signature of complement-mediated and independent forms of AHR. These miRNA signatures will be validated for the tissue-based diagnosis of complement-mediated and independent forms of AHR. Putative target mRNAs will be identified by *in-vitro* experiments.

P105 THE TREATMENT WITH EPOETIN THETA (BIOPOIN®) IN PATIENTS WITH RENAL ANEMIA IS EFFECTIVE, SAFE AND WELL ACCEPTED

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Introduction: Biopoin® with the active ingredient Epoetin theta (rhHuEPO) is a biotechnologically produced variant of endogenous human erythropoietin.

The open-label, multicentric non-interventional study was designed to gain experience concerning the treatment efficacy, safety and patient compliance.
Methods: Between Jan to Dec 2010 158 patients (median age: 71.45 years) with renal anemia from 19 dialysis centers were readjusted to Biopoin® ($n = 30$) or switched ($n = 128$) from another rhHuEPO to Biopoin®. Data regarding the efficacy and tolerability were collected at baseline and following 2 to 4, 6 to 8 and 12 weeks of therapy. The therapeutic success was confirmed by the development of health-related quality of life (SF-36) and an improvement of the hemoglobin values in the newly with an epoetin treated patients and an at least comparable efficacy and tolerability in the patients who were switched from another epoetin to Biopoin®.
Results: During the 12 weeks of therapy the mean hemoglobin values were increased from 9.62 $\pm$ 1.75 to 11.65 $\pm$ 1.83 g/dl ($P < 0.001$) in the patients readjusted to Biopoin® ($n = 30$) and remained relatively unchanged, compared to the initial values in the switch patients ($n = 128$). The health-related quality of life has increased significantly in both patients with initiated and with change-over therapy (readjustment: $P = 0.001473$; switch: $P = 0.0002854$).

The physicians assessed the effectiveness of Biopoin® for 95.6% of the patients the tolerability for 98.7% and the acceptance for 96% as good and very good.

One adverse drug reaction was reported (rash at the whole body with strong itching similar to allergic urticaria).

Conclusion: The treatment with Biopoin® was effective, safe and well accepted by the outpatients.

P106 SURGICAL MANAGEMENT AND OUTCOME OF AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE IN PATIENTS BEFORE AND AFTER RENAL TRANSPLANTATION

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Objective: Autosomal dominant polycystic kidney disease (ADPKD) is a hereditary disorder which leads to massive kidney enlargement and subsequent renal failure. Surgical management of ADPKD in patients awaiting renal transplantation is a challenging task and controversial in terms of necessity and timing of nephrectomy. The objective of this study was to assess the surgical management and the risks of posttransplantation complications among ADPKD patients.
Patients and Methods: From 07/2000 to 03/2011, a total of 65 consecutive renal transplantations with nephrectomy were performed in 36 men and 29 women with ADPKD. Among those subjects were 6 groups: (I) unilateral nephrectomy preceding (28 patients) and (II) succeeding (2 patients) transplantation; (III- two-step (4 patients) / IV- one-step (3 patients) bilateral nephrectomy preceding transplantation; (V) bilateral nephrectomy preceding and succeeding (sandwich) transplantation; and (VI) without nephrectomy (15 patients). Demographic data and intraoperative and postoperative data were collected from patient charts. Mean follow-up was 0.6–10.8 years.
Results: There were no differences regarding background data. Overall patient and graft survival were 97% at 1 year and 92% at 5 years, respectively. Overall surgical complications, which might be associated with the time-point of nephrectomy occurred in 15.3%. None of the patients died peri-operatively.
Conclusions: Unilateral nephrectomy is an established preliminary surgical treatment before kidney transplantation. Bilateral nephrectomy before or during transplantation does not have a significant negative impact on patient and graft survival. The most complications were observed among the patients without pretransplantation nephrectomy.

P109 AUTOTRANSPLANTATION FOR THE TREATMENT OF SEVERE RENAL ARTERY STENOSIS AND ANEURYSM IN A SOLITARY KIDNEY AFTER REPEATED COILING: A CASE REPORT

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A 75-year-old male suffering from a long history of an aneurysm in the right solitary kidney and a stenosis of the lower renal artery segment was admitted to reevaluate this finding.

In this patient several percutaneous transluminal renal angioplasties with coiling had resulted in an increase of the aneurysm and the stenosis of the lower renal artery segment. The renal artery stenosis was reevaluated and a further re-angioplasty attempt was not reasonable in due to the disproportional risk of requiring dialysis and because the definite restoration of the finding probably would not be achievable. Blood pressure remained difficult to manage. Renal function decreased as a result of presumed acute renal failure. A further progression of the renal artery aneurysm and stenosis was found. Out-of-body-reconstruction of the right renal artery and autotransplantation to the right iliac fossa was performed without any complications. Renal function normalized and follow-up Doppler ultrasonography examinations showed a good perfusion of the kidney. While medical therapy and percutaneous transluminal angioplasty with stent deployment and coiling are common treatment options, surgical interventions are reserved for cases of complex stenosis and aneurysms. Autotransplantation as a complex option in the treatment of renal artery stenosis and aneurysms seems to be an adequate alternative after failure of interventional procedures and the impossibility of standard surgical techniques.

P112 6 CASES OF SUCCESSFUL DELIVERY AFTER COMBINED KIDNEY-PANCREAS TRANSPLANT: A SINGLE CENTER REPORT

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Purpose: We retrospectively analyzed six cases of successful delivery in four women after combined kidney transplant regarding graft and obstetric outcome.
Patients and Methods: A total of six babies (2 male, 4 female) were born by cesarean delivery from four combined kidney pancreas transplanted women with a mean age of 32.5 (27–36) years at transplant and 37.5 (36–40) at the delivery, in the mean 30th (26–36) week of pregnancy. Two mothers each gave birth to the second child. Immunosuppression consisted of Tacrolimus plus Azathioprine.
Results: All six babies were healthy, two out of them at preterm date underwent successful respiratory support. The maternal pancreas graft function remained stable in 5/6 cases without requirement of insulin. The kidney function remained stable in 3 cases, among them one mother with two deliveries. In one women with a serum creatinine of 2.0 mg/dL before pregnancy the creatinine increased to 3.7 mg/dL after the 2nd delivery. One women with preeclampsia and coronary heart disease was preterm delivered, severely complicated by peripartal myocardial infarction, kidney and pancreas graft loss, and postpartal CMV pneumonia. She was successfully combined kidney-pancreas re-transplanted after two years.
Conclusion: Good obstetric and stable transplant function can be achieved in pregnancy after combined kidney pancreas transplant. A careful monitoring including frequent gynecological and transplant visits, cardiac control and cautious immunosuppression avoiding antiproliferative agents is recommended.

P113 INFLUENCE OF DIALYSIS MODALITY ON OUTCOME AFTER SIMULTANEOUS PANCREAS KIDNEY TRANSPLANTATION

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Background: Peritoneal dialysis is considered to be a risk factor of post transplant graft loss due to peritoneal thickening and subsequent disturbed peritoneal function. Here, we have analyzed patients and graft survival after simultaneous pancreas kidney (sPK) transplantation.
Methods: 192 patients. who received a combined pancreas kidney transplant between January 1, 2000 and May 15, 2013 were analyzed. Prior transplantation 159 patients were treated with hemodialysis (HD) and 33 received continuous ambulatory peritoneal dialysis (CAPD).
Results: Patient survival at 1, 5 and 10 years after transplantation was 96.2, 90.4 and 87.2% for HD and 93.9, 93.9, and 93.9% for CAPD patients. Pancreas graft survival was 67.7, 61.8, 55.7 for HD and 60.6, 60.6, 60.6% for CAPD patients. Corresponding kidney graft survival was 93.7, 84.1 and 75.5% for HD and 93.9, 87.7 and 83.9% for CAPD patients. Patient-, pancreas- and kidney graft survival was similar between HD and CAPD patients. However, CAPD may result in superior long-term outcomes (beyond 5 years).
Conclusions: Our data suggests, that current policy to generally prefer HD over CAPD in patients awaiting sPK transplantation has to be reconsidered. Although peritoneal thickening may complicate surgery, CAPD may have a positive effect on long-term outcomes by yet unknown mechanisms.

P114 MANAGEMENT OF PANCREATIC FISTULA FOLLOWING PANCREAS TRANSPLANTATION

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Pancreas transplantation is associated with high postoperative morbidity with a need for relaparotomy in up to 40%. The pancreas is the source of most of the early complications.

We analyzed the incidence and management of pancreatic fistula following pancreas transplantation.
Methods: From 1/04 to 5/13 63 pancreas transplantations were performed at our center, 61 simultaneous pancreas kidney transplantations, 2 pancreas transplantations alone. The mean age was 42 years, mean duration of diabetes was 27.0 years and mean duration of dialysis was 24.6 months. All transplantations were performed using systemic-enteric drainage.
Results: The incidence of clinically relevant pancreatic fistulas (PF) was 18/63 (28.6%). 13/18 (72.2%) were treated conservatively with drainage. 5/18 (27.8%) patients underwent relaparotomy, 2 due to leak age of the enteric drain, 2 due to peritonitis and 1 with acute hemorrhage. In all but 1 cases the pancreas graft was saved.

The long-term pancreas graft survival was 47/63 (74.6%) after a mean follow-up of 64.6 months. There was no significant difference between patients with (77.8%) or without PF (77.8%).
Conclusion: Pancreatic fistula following pancreas transplantation is a common complication. Conservative treatment without relaparotomy is effective and graft survival is not reduced by occurrence of a fistula.

P115 DEMOGRAPHIC CHALLENGES OF SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANTATION (SPKT) 2005 TO 2012: A SINGLE-CENTER EXPERIENCE

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Background: SPKT is the only possibility of type 1 diabetics with terminal renal failure to get away from dialysis and substitution of insulin. Organ shortage and an ageing society are recent challenges.

Patients and Methods: We retrospectively analyzed and compared the outcome of graft- and patient survival after SPKT (165 patients) at our transplantation centre from 2005–2012, depending on the age of recipients (<40 y. vs. > 50 y.) and donors (< 16 y. vs. > 45 y.).
Results: Since 2005, the proportion of donors over 45 years rose from 10% to 50%. The number of recipients of the age of over 50 increased from 10% - 30%. The outcome of patient- and graft survival rates in older recipients show no significant differences. Results of older donor grafts show no significant differences according to patient - and kidney graft survival. Pancreas graft survival is slightly worse in older pancreas grafts.
Conclusion: Despite organ shortage and a high proportion of old organ donors and recipients, good transplantation results are achievable in an experienced transplantation centre.

P116 HYPERACUTE REJECTION OR ISCHEMIA-REPERFUSION INJURY? SCRUTINY OF AN INTRAOPERATIVE PRIMARY ALLOGRAFT NONFUNCTION OF A SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANT

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Background: Careful donor and recipient matching has made the hyperacute rejections rare. On the other hand, the organ shortage with the consequent use of extended criteria donors, including organs with preexisting damages and longer ischemia times, and sophisticated interregional logistics make the allografts more prone to ischemia-reperfusion injury (IRI). Here, we report an intraoperative primary allo-graft nonfunction of a simultaneous pancreas-kidney (SPK) transplant and undermine some rather invisible kind of such obstacles.
Case Report: A 36 year-old male recipient with type 1 diabetes mellitus and diabetic nephropathy underwent SPK using ABO-compatible organs donated after brain death. Within minutes after the reperfusion, both grafts became cyanotic and hemorrhagic. Transplant nephrectomy and pancreatectomy ensued due to the diffuse intraparenchymal hemorrhage of both grafts. Repeat cross-match and panel reactive antibodies, as well as C4d were negative. While it was not possible to histomorphologically rule out the hyperacute rejection completely, the findings were more likely compatible to an IRI. Follow-up of the fate of other organs from the same donor was unremarkable for heart, but problematic for left and right liver splits, and the contralateral kidney. Review of the Eurotransplant donor report charts showed a remote history of a stab wound injury and the consequent peritonitis in the donor: it took nearly 2 hours between the start of the cold reperfusion and the organ recovery due to dense peritoneal adhesions.
Conclusions: Although the exact mechanism of primary nonfunction could not be fully illucidated in this case report, longer warm ischemia time most likely played a significant role. In the era of organ shortage, every effort has to be made to prevent IRI, including keeping ischemia time as short as possible.

P117 METABOLIC FOLLOW-UP FOUR YEARS AFTER SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANTATION WITH PORTAL VENOUS VERSUS SYSTEMIC VENOUS DRAINAGE

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Background: The impact of the venous drainage on the outcome of simultaneous pancreas and kidney transplantation (SPK) remains controversial.
Methods: We reviewed 72 consecutive SPK from January 2005 to December 2008, including 36 transplantations with systemic venous drainage and 36 with portal venous drainage.
Results: Four weeks after transplantation and one year after transplantation patients with systemic venous drainage present a significant peripheral hyperinsulinemia in the oral glucose tolerance test (insulin in the OGTT one year after transplantation: 0 min: 16.0 $\pm$ 7.8 mU/l vs. 10.1 $\pm$ 5.4 mU/l, $P = 0.010$; 60 min: 76.5 $\pm$ 44.8 mU/l vs. 37.6 $\pm$ 30.1 mU/l, $P = 0.004$; 120 min: 51.6 $\pm$ 32.3 mU/l vs. 28.6 $\pm$ 21.3 mU/l, $P = 0.019$). At the same time they display a lightly reduced glucose tolerance. Patient survival, kidney and pancreas allograft survival as well as HbA1c, fasting c-peptide, triglyceride, cholesterol, HDL and LDL are similar in both groups. Two, three and four years after transplantation there is no significant difference between both groups at all, neither in the results of the oral glucose tolerance test nor in the metabolic parameters HbA1c, fasting c-peptide and lipids.
Conclusions: The results suggest that SPK with portal venous or systemic venous drainage can be performed with comparable short-term outcomes. The hyperinsulinemia with reduced glucose tolerance in the first year after transplantation cannot be showed in the following years.

LIVER

P118 UTILIZING A CLINICAL PATHWAY FOR LIVER TRANSPLANTATION: FIRST LESSONS LEARNT

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Introduction: Clinical pathways are a way of improving transparency, quality, patient safety and performance of treatment processes. We developed and introduced a clinical pathway for liver transplantation (LTX).
Method: In a clinical pathway, key measuring points, e.g. admission of patients, start of evaluation for transplantation or the registration with Euro Transplant were defined.

We assigned data from the clinical information system to the defined measuring points. We included all patients from 2009 to 2013 who were evaluated for LTX or/and were transplanted at our department ($n = 345$). The efficiency of the clinical pathway was analyzed and potential improvements were initiated.
Results: Analysis of the data assigned to each step of the LTX pathway revealed that several evaluations for transplantation were recorded as terminated in the financial department even though patients underwent the complete procedure. With data analysis, we found that some examinations were performed at a later time, preventing billing of these procedures for insurance policy reasons. Examinations are now planned in a timely fashion and queries with health insurance companies were settled.

We optimized the sub-process of donor and recipient evaluation. Thus, decisions about listing can be made at an earlier stage, and less evaluations are terminated. For living donors, the hospital stay for evaluation was reduced from 4 to 2 days.
Conclusion: The connection of clinical pathways with a proper analysis of treatment data allows to not only documentation of such pathways but also to optimize clinical processes, improve treatment quality, contribute to patient safety and realize possible savings.

Other clinical processes may be analyzed in this way.

P119 LIVER GRAFT PERFUSION IN CHILDREN AFTER COMBINED LIVER-KIDNEY TRANSPLANTATION VERSUS SINGLE LIVER TRANSPLANTATION - A MATCHED-PAIR ANALYSIS

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Purpose: Simultaneous combined liver-kidney transplantation (CLKT) is a rare operation in children. With most organs derived from adult donors, grafts size discrepancies are common, especially in small recipients. To evaluate the impact of the kidney graft on the liver graft perfusion we compared Doppler ultrasound measurements in pediatric CLKT before/after kidney implantation and in comparison to recipients of isolated liver grafts (LTx).
Methods: Data from all children transplanted at our hospital (1998–2011) were prospectively collected and retrospectively analyzed. Overall 464 pediatric LTx were performed, thereof 22 CLKT, 22 single LTx were matched based on age, high-urgency status, number of LTx, graft type, time period.
Results: Indications for CLKT ($n = 22$; median age 7.3(range 1.3–15.9)yrs) were primary hyperoxaluria type I ($n = 12$), ARPKD ($n = 9$) and other ($n = 1$).

Indices in CLKT recipients immediately after liver reperfusion and secondly after implantation of the kidney showed no significant difference in the median systolic peak flow 51.5(20.8–128.5) versus 49.8(25.5–151.1)cm/s or the maximum portal flow 38.6(10.3–99.6) versus 41.4(9.8–92.5)cm/s ($P = 0.8/0.534$).

Comparison of children following CLKT with the matched group of single LTx showed a trend ($P = 0.079–1$) to a higher arterial and portal blood flow after single LTx in the early postoperative course, vanishing with increasing time distance to LTx.
Conclusion: We found no significant difference in the liver graft perfusion in children following CLKT before or after kidney implantation. Children with single LTx in contrast to CLKT showed a trend to a higher liver graft perfusion immediately after LTx but similar later on.

P120 PORTAL VEIN THROMBOSIS IN LIVER TRANSPLANTATION: A SINGLE CENTER ANALYSIS

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Introduction: Portal vein thrombosis (PVT) in liver transplantation remains a serious condition. An absolute contraindication in the earlier times, PVT can nowadays be successfully managed in the majority of pts. The aim of this study was to analyze our data for the incidence of PVTs prior to LTx, describe the operative techniques and compare the outcome to the LTx patients without PVT.
Methods: We retrospectively screened our liver transplant data for portal vein thrombosis and evaluated transplant variables, the underlying condition and the outcome. Budd-Chiari syndrome was excluded.
Results: We performed $n = 277$ liver transplants in $n = 251$ pts. from 2007–2012. A total of $n = 33$ PVTs (11.9%) was detected. Underlying conditions were alcoholic (39.4%), HCV (24.2%), cryptogenic (9.1%), HBV (6.1%), drug related (6.1%), secondary biliary liver cirrhosis (3%), PSC (9.1%) and echinococcosis (3%).

The majority of the PVTs were managed by venous thrombectomies (84.9%). In $n = 3$ (9.1%) patients we used a venous jump graft and $n = 2$ pts. (6.1%) received anastomosis to varix.

90-day mortality was 9.1% in the patients with PVT and was not different from those without PVT 12.8% ($P =$ n.s.)
Conclusion: In our cohort of liver transplant patients we found a number of PVTs comparable to the existing literature. It remains a technically challenging situation. However, in most cases, PVT can be managed successfully.

P121 SURGICAL COMPLICATIONS REQUIRING EARLY REOPERATION ARE ASSOCIATED WITH POOR LONG-TERM OUTCOME AFTER LIVER TRANSPLANTATION

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Introduction: Surgical complications may have not only immediate, but also long term effects on postoperative outcomes. Here, we aimed to investigate the impact of surgical complications requiring an early reoperation on patients- and graft survival following liver transplantation.
Methods: Transplant variables, comorbidities, postoperative surgical complications and the outcome of 277 consecutive liver transplants performed from 01.2007 to 12.2012 were analyzed.
Results: 277 liver transplants were performed in $n = 251$ patients. Of these $n = 137$ (54.6%) required one or more reoperations due to complications. 1- and 2-yr mortality was significantly increased in the pts. requiring reoperations compared with those without reoperation (29.2% vs. 4.4%, $P < 0.001$; 33.6% vs. 7.9%, $P < 0.001$).

Also, graft survival rates differed significantly. 1-yr graft survival was 62.2% in the group with reoperations compared to 89.6% without reoperations ($P < 0.001$).
Conclusion: These data suggest that surgical complications after liver transplantation have a significant impact on the half-life of the transplanted livers and on the overall patient survival.

P122 PRAISE: A PROSPECTIVE, MULTI-CENTER, RANDOMIZED, DOUBLE BLINDED, PLACEBO-CONTROLLED STUDY FOR THE EVALUATION OF ILOPROST IN THE EARLY POSTOPERATIVE PERIOD AFTER LIVER TRANSPLANTATION. THE STUDY PROTOCOL.

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Background: Liver graft dysfunction can deteriorate to complete organ failure and increases perioperative morbidity and mortality after liver transplantation. Therapeutic strategies reducing the rate of graft dysfunction are of current clinical relevance. One approach is the systemic application of prostaglandins, which were demonstrated to be beneficial in reducing ischemia-reperfusion injury. Preliminary data indicate a positive effect of prostacyclin analogue iloprost on allograft viability after liver transplantation. The objective of the study is to evaluate the impact of iloprost in a multi-center trial.
Methods/Design: A prospective, double-blinded, randomized, placebo-controlled multicenter study in a total of 365 liver transplant recipients was designed to assess the effect of intravenous iloprost after liver transplantation. Primary endpoint will be the primary graft dysfunction characterized as presentation of one or more of the following criteria: ALAT or ASAT level $>$ 2000 IU/ml within the first 7 postoperative days, bilirubine $\geq$ 10 mg/dl on postoperative day 7; INR $\geq$ 1.6 on postoperative day 7 or initial non-function. Secondary endpoints are parameters of post-transplant morbidity, rates of infections, biliary complications and the graft and patient survival.
Discussion: A well-established treatment concept to avoid graft dysfunction after liver transplantation does not exist at the moment. However, liver allograft function is affected by various donor and recipient characteristics. If the data of this trial confirm prior findings, iloprost would improve the general outcome after liver transplantation.

Trial Registration: German Clinical Trials Register: DRKS00003514. Current Controlled Trials Register: ISRCTN12622749.

P123 CYBERKNIFE® RADIOSURGERY AS A POTENTIAL TOOL FOR BRIDGING TO LIVER TRANSPLANTATION IN PATIENTS WITH HEPATOCELLULAR CARCINOMA AND LIVER CIRRHOSIS

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Stereotactic radiotherapy represents a new technique within the set of bridging strategies for patients with hepatocellular carcinoma (HCC) before liver transplantation. Although local HCC progression may be effectively controlled, conventional stereotactic radiotherapy requires repeated interventions and may cause considerable comorbidity. Computer-assisted robotic guided single session radiotherapy (Cyberknife®) allows for a minimization of these disadvantages. Here, we describe our first experiences applying this technique to HCC patients.

Cyberknife® therapy was applied ten times in 8 patients between 7/2006–6/12 whose tumors fulfilled BCLC criteria for HCC an therapeutic alternatives were excluded. HBV-, HCV-, PSC- and nutritive toxic cirrhosis were underlying causes for cirrhosis (Child A/B). One patient was treated 3 times for different intrahepatic HCCs. Treatment included a CT-guided positioning of one gold fiducial and radiation, using a photon linear accelerator (6 MeV LINAC, dose rate 6 Gy/minute)Post-interventional surveillance included clinical and MRI re-examinations every 6 months.

All patients are alive. No local tumor recurrence at treated sites was detected, however overall recurrence occurred in 6 cases. Intervals until recurrence varied from 8 to 44 months. No peri-interventional complications were registered. A combination of the Cyberknife® therapy with other established therapeutic approches (TACE, RFA, surgery) was performed in 6 cases, and was not hindered by Cyberknife®therapy.

Cyberknife® radiosurgery represents an effective tool for local tumor control in HCC patients. Time to recurrence was never shorter than 8 months. The technique may serve as a new option in the arsenal of bridging therapies in HCC patients awaiting liver transplantation.

P124 APOA-I AMYLOIDOSIS CAUSES SEVERE HEPATIC INVOLVEMENT IN THE ABSENCE OF CLINICAL AND LABORATORY SIGNS OF LIVER DYSFUNCTION

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Background: Hereditary amyloidosis is often treated by liver transplantation, with the intent to eliminate the main source for the amyloidogenic protein. The lack of hepatic involvement allows to donate the explant liver to another patient in a domino fashion. Most of these cases are associated with mutations of the transthyretin gene. However several patients with amyloidosis associated with apolipoproteinA-I (ApoA-I) have been reported to have hepatic involvement. Previous cases report liver involvement to be evident by histological analysis or laboratory markers only, with an unremarkable macroscopic picture.
Case: We present a patient with p.Leu75Pro ApoA-I amyloidosis who underwent combined liver-kidney transplantation for amyloidosis associated advanced chronic kidney dieases and to slow down progression of polyneuropathy. Preoperative clinical picture and laboratory markers did not implicate hepatic dysfunction. On macroscopic inspection however, with 2130 g the liver was enlarged, with a grossly nodular surface and firm parenchyma. Histologically, liver architecture was preserved with areas of moderate/severe steatosis. Large confluent deposits of amyloid were found in a rather unique jig saw like distribution pattern, enclosing central veins, differing from the typical perisinusoidal deposition pattern of AL amyloidosis. Polarized light revealed the typical apple green birefringence and immunoreaction for ApoA-I was strong. Electron microscopy detected extracellular fibrils typical for amyloid as well as cytoplasmic accumulation of lysosomes and concentric lamellar inclusion bodies.
Conclusion: This is the first report of an ApoA-I amyloidosis case with macroscopically evident hepatic involvement.

P125 TREATMENT OF POST-TRANSPLANT OSTEOPATHY AFTER LIVER TRANSPLANTATION: A FIVE-YEAR FOLLOW-UP

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Background: Treatment of post-transplant osteopathy is a major focus of long-term care after solid organ transplantation.

Treatment with bisphosphonates in combination with calcium and vitamin D3 has been established. In our analysis, we report about oral ibandronate treatment after liver transplantation (LTX) during long-term follow-up, with special emphasis on bone fracture prevention and bone mineral density measurements after termination of this drug treatment.
Methods: We included 57 out of the 142 patients who underwent LTX from May 2006 to December 2008 into the study. 40 of these were followed-up over 5 years. These patients received oral ibandronate treatment for at least 24 months. 33 patients have been assembled retrospectively as a control group. Laboratory tests and DXA measurements of the lumbar spine and the femur were performed pre-transplantation, 3, 6, 12, 24, 36, 48 und 60 months after LTX.
Results: With ibandronate treatment, the bone mineral density was significantly higher than in the control group at 6 months after LTX and at all measuring points thereafter. The changes in percentage reached statistical significance at 12, 48 and 60 months after LTX. Over the entire treatment duration, the rate of bone fractures was significantly lower in the ibandronate group than in the control group. Pre-operative prednisolone treatment had a significant impact on the lumbar bone mineral density at 3 and 12 months after LTX.
Conclusion: Oral ibandronate treatment after LTX decreases the incidence of bone fractures and increases the bone mineral density over a post-transplant period of five years.

P126 THROMBEMBOLIC COMPLICATION IN A PATIENT WITH ACTIVATED PROTEIN C RESISTANCE AFTER ORTHOTOPIC LIVER TRANSPLANTATION

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Most of coagulation factors are synthesized by the liver and therefore orthotopic liver transplantation (OLT) can possibly cure diseases like haemophilia. On the other side thrombophilia can be acquired by transplantation of livers from affected donors.

We here present a case of a 57 year old male who received OLT for liver cirrhosis due to chronic hepatitis B and who suffered from thrombophlebitis of the great saphenous vein about two years after liver transplantation. Investigation revealed the presence of activated protein C (APC) resistance (ratio 1.0; norm > 1.8).Since APC resistance is highly predictive of factor V Leiden mutation, which was not confirmed in a genetic analysis from the patient's peripheral blood, we suspect a genetic variant within the transplanted liver. A definitive diagnosis could not be made, since DNA from the donor liver was not available.

In conclusion, patients after liver transplantation might suffer from thrombembolic complications due to transplantation-acquired thrombophilia with the need of lifelong anticoagulation therapy. In cases like this, it would be of great clinical benefit and important for the patient's treatment, to get access to donor liver DNA.

P127 EX-SITU-BACK TABLE PERFUSION DOES NOT PREVENT ISCHEMIC TYPE BILIARY LESIONS. A PROSPECTIVE RANDOMIZED CONTROLLED MULTI-CENTER STUDY ON LIVER PRESERVATION BY AORTIC PERFUSION WITH HTK SOLUTION COMPARED TO AORTIC PERFUSION PLUS ARTERIAL EX-SITU PERFUSION.

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Propose: To study the impact of arterial ex-situ back-table perfusion to prevent ischemic type biliary lesions (ITBL) after liver transplantation.
Method: Between October 2007 and March 2010, 299 livers retrieved in the Region Mitte and Nord of the DSO, Germany, were included in a prospective randomized controlled multi-center study to compare conventional aortic perfusion (group A) with aortic perfusion plus arterial ex-situ back-table perfusion (group B). Randomization in group A and B was performed during organ procurement. After perfusion, the grafts were shipped to 14 participating transplant centers. Primary end point of the study was the clinical occurrence of

ITBL 6 months after liver transplantation. Secondary end points were initial liver function and ischemia-reperfusion injury of the graft.
Results: Out of 299 randomized livers, 264 were allocated and transplanted in the participating centers. Data of 150 patients were available for final confirmative evaluation. Age and gender of donors and recipients, cold and warm ischemia time were identical. In each group, ITBL developed in 9 patients after identical intervals following transplantation ($P = 0.949$). Likewise, an impact of ex-situ back table perfusion on the secondary end points, liver function or ischemia-reperfusion injury, could not be demonstrated. According to the explorative analysis of the study, donor age, gender, vasopressor use, stay on intensive care in the donor, cold and warm ischemia time, mode of graft recirculation, underlying disease and labMELD in the recipient were not associated with the generation of ITBL. The reason for death in the donor may have an influence on the generation of ITBL ($P = 0.015$).
Conclusion: Ex- situ back table perfusion does neither prevent ischemic type biliary lesions nor has an effect on initial liver function and ischemia-reperfusion injury after liver transplantation.

P128 PNPLA3 IN END-STAGE LIVER DISEASE: ALCOHOL CONSUMPTION, HCC DEVELOPMENT AND LIVER TRANSPLANTATION

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Background & Aims: The rs738409 variant (I148M) of the *PNPLA3* gene is associated with fatty liver disease but has not been addressed in an end-stage liver disease.
Methods: The I148M polymorphism was genotyped in 421 patients with end-stage liver disease, defined as liver transplantation or current enrollment at Eurotransplant.
Results: The G allele of the I148M variant was significantly overrepresented in patients with alcoholic liver disease (ALD, $P < 0.001$) compared to healthy control subjects while expression of the G allele did not differ in the remaining end-stage liver disease entities. In ALD patients, the G allele was further closely associated with hepatocellular carcinoma development (odds-ratio = 2.399; 95% CI: 1.292–4.455; $P = .008$). Transplantation-free survival was significantly decreased when carrying either one or two mutated G allele (CC= 36.8 $\pm$ 10.2 months, 95% CI: 16.7–56.9; GC= 19.6 $\pm$ 4.3 months, 95% CI: 11.0–28.2; GG= 15.2 $\pm$ 8.0 months, 95% CI: 0.0–31.1; $P = .041$) from time of enrolment at Eurotransplant for ALD patients. Analysis of alcohol consumption revealed that wildtype patients consumed significantly more alcohol than heterozygous or homozygous I148M patients (CC = 731.0 $\pm$ 216.5; CG = 601.4 $\pm$ 172.2; GG = 523.3 $\pm$ 190.5 [g EtOH//week]; $P = 0.001$).
Conclusions: In a cohort of end-stage liver disease patients we identified ALD to be predominantly affected by the I148M polymorphism causing a significantly increased risk of HCC development with reduced transplantation-free survival. According to public perception ALD is a stigmatized hepatic disorder and one of the reasons for liver donation aversion. However, we were able to show that the I148M polymorphism highly impairs hepatic malfunction in ALD patients despite reduced alcohol consumption compared to wildtype patients.

P129 PREDICTING SURVIVAL AFTER LIVER TRANSPLANTATION FOR ACUTE LIVER FAILURE BY PREOPERATIVE RECIPIENT FACTORS: MYTH OR FACT?

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Background: Factors predicting survival after liver transplantation (LTx) for irreversible acute liver failure (ALF) are rare. Aim of the present study was to identify prognostic preoperative factors of patients with ALF predicting mortality after LTx to avoid futile transplantation.
Methods: From Chart review we identified 57 patients transplanted for ALF from 12/2000–09/2010. Recipient and donor data were analyzed and correlated with in-hospital mortality and patient survival by univariable/multivariable logistic regression and cox proportional hazards.
Results: 30-days and 12-months survival was 77.2% and 64.9%, respectively. In-hospital mortality rate was 29.8%. Multivariable analysis of preoperatively known factors showed that the lowest pH of the recipient before LTx ($P = 0.0336$) was independently associated with in-hospital mortality and that recipient's BMI ($P = 0.0249$) and the lowest pH before LTx ($P = 0.0198$) were independently associated with the patient survival. pH of 7.29 was the calculated cut-off (ROC) for increased in-hospital mortality. Donor factors did not affect patient survival.
Conclusions: Although ph was an independent risk factor for mortality, this value alone should not be used to deny transplantation in ALF as it cannot replace the clinical assessment of the patient. Instead it should be implemented in the decision making process.

P130 PREDICTION OF EARLY ALLOGRAFT DYSFUNCTION IN LIVER TRANSPLANTATION

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Background: Poor initial graft function is associated with impaired graft and patient survival and has been recently newly defined as early allograft dysfunction (EAD) (Olthoff, KM et al. 2010). Aim of this analysis was to evaluate for clinical relevance and predictive donor information of EAD in a large cohort of OLT recipients.
Methods: 678 consecutive adult patients (mean age 51.6 years; 60.3% males) who received a primary OLT (09/2003–12/2011) were retrospectively analysed. Donor data including laboratory values, parameters of ICU treatment, histology and DRI/ET-DRI were correlated with development of EAD and outcome by univariable/multivariable logistic regression and cox proportional hazards to identify prognostic donor factors. Estimates of relevant factors were used to create a new continuous score of risk to develop EAD.
Results: 40.1% developed EAD. 30-day-survival of grafts with and without EAD was 60.3% and 88.9% ($P < 0.0001$). 30-day-survival of patients with and without EAD was 69.4% and 92.1% ($P < 0.0001$), respectively. Donor BMI, gGT, macrosteatosis and cold ischemia time (CIT) were predictors for EAD. Internal cross validation showed a high predictive value (c-index = 0.626).
Conclusion: EAD correlates with early results of OLT and can be predicted by donor data only. Outcome of high risk organs might be improved by shortening CIT.

P131 THE REGENERATIVE CAPACITY OF THE BILIARY EPITHELIUM INFLUENCES BILIARY COMPLICATIONS FOLLOWING LIVER TRANSPLANTATION

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Background: The aim of this study was to examine the influence of the regenerative activity in damaged biliary epithelium on the development of biliary complications after liver transplantation.
Methods: Common bile duct samples during donor hepatectomy, after cold storage, and after reperfusion were compared to healthy controls by H&E staining and immunohistochemistry for the proliferation marker Ki-67 and further factors necessary for cell regeneration. The bile duct damage score was used to quantify biliary epithelial injury. The results were correlated with the regeneration of biliary epithelial cells.
Results: Control ($N = 16$) and donor hepatectomy bile ducts ($N = 10$) showed regular epithelial morphology and regenerative capacity. After cold storage ($N = 37$) and even more after reperfusion ($N = 62$), epithelial damage, as quantified by the bile duct damage score, was markedly increased, and the biliary regenerative capacity was detected at reduced levels. Within these groups, patients with lower regenerative capacity had an increased risk of biliary complications.
Conclusions: In many cases, the common bile duct epithelium shows considerable damage after cold ischemia with further damage occurring after reperfusion. A part of these damaged bile ducts show a diminished regenerative capacity which leads to an increased risk of biliary complications.

P133 REGULATION OF LIVER LOBE SIZE IN CASE OF CONCURRENT CONTRADICTORY SIGNALS

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Aim: Regulation of liver lobe size is an important issue in hepatic surgery, when employing portal vein ligation (PVL) to induce hepatic proliferation prior to extended liver resection. In this study we investigated size adjustment of the portally deprived-liver lobe in case of a concurrent proliferative stimulus induced by PH.
Methods: Using the model of right PVL plus 70% partial hepatectomy (rPVL+70%PH) in rats, we evaluated liver lobe size recovery on postoperative day (POD) 1, 2, 3 and 7 after operation in terms of liver weight and hepatocyte proliferation. Control groups consisted of right portal vein ligation (rPVL), 70% partial hepatectomy (70%PH) and sham operation (Sham-op). The "right lobe/body weight ratio" (RL/BW) and "caudate lobe/body weight ratio" (CL/BW) were calculated. Hepatocyte proliferation index (PI) was determined on whole slide scans using the HistoCad program (MeVis)
Results: RL/BW increased slightly (1.2-fold) after rPVL+70%PH throughout the observation time, but 3 fold after 70%PH and was reduced to 0.3-fold after rPVL only. In contrast, CL/BW increased remarkably (4.5-fold) after rPVL+70% PH, about 3-fold after 70% PH and remained stable after rPVL only.

Initiation of proliferation (Max PI of 10% on POD2) was delayed in the right lobe compared to the caudate lobe (Max PI of 20% on POD1) and compared to PI in the remnant liver (RL and CL) after 70%PH with a maximal PI on POD 1 (PI = 30%).
Conclusion: The concurrent regeneration and atrophy stimulus acting on the right lobe caused a delayed and reduced initiation of hepatocyte proliferation but did not lead to an increase in the relative weight of the lobe. Using a multigene array approach, the mechanism governing the regulation of proliferation and atrophy will be explored.

P135 PULSE OXIMETRY IS INSUFFICIENT FOR TIMELY DIAGNOSIS OF HEPATOPULMONARY SYNDROME IN CHILDREN WITH LIVER CIRRHOSIS

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Objective: Hepatopulmonary syndrome (HPS) is a severe pulmonary vascular complication from liver cirrhosis or portal hypertension, wherein intrapulmonary vasodilatation (IPVD) causes hypoxemia. Here, we prospectively investigated HPS prevalence and the importance of pulse oximetry for its diagnosis.
Study design: Fifty-six patients with liver cirrhosis between 1–17 years (mean age 4.6 ± 5.0 yrs) were screened for HPS using hyperemic capillary blood gas analysis (CBG) and contrast-enhanced echocardiography. Eleven patients were excluded due to additional conditions that can produce cardiopulmonary dysfunction, e.g. cystic fibrosis ($n = 5$), pulmonary arterial hypertension ($n = 1$) or intracardial shunts ($n = 5$). Patient groups were compared for biochemical and clinical characteristics.
Results: Eighteen (40%) were IPVD+ and had pulse oximetry levels >98%. Two of these (11%) exhibited a moderate HPS with elevated $P\Delta AaO_2$>15 mmHg and PaO_2 < 70 mmHg; they deceased before liver transplantation was performed. CBG sensitivity and specificity in HPS-detection were 94% and 53%, respectively. HPS was associated with late hepatoportoenterostomy ($P < 0.04$) but not with liver disease severity. Liver transplantation led to resolution of HPS.
Conclusions: IPVD is frequent in pediatric patients with liver cirrhosis (40%). Pulse oximetry is insufficient for a timely HPS-diagnosis. Patients with liver cirrhosis should be evaluated for HPS using contrast-enhanced echocardiography and CBG regardless of liver synthesis capacity and clinical chemistry.

P136 ISCHEMIA TIME IS AN IMPORTANT PREDICTOR OF RECURRENCE-FREE SURVIVAL IN LIVER TRANSPLANT PATIENTS WITH HEPATOCELLULAR CARCINOMA

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Background: Ischemia-reperfusion (I/R) injury was demonstrated to promote tumor recurrence after liver resection in patients with hepatocellular carcinoma (HCC). However, the impact of I/R on HCC recurrence in the transplant setting is undefined. The aim of this trial was to assess the impact of ischemia time on recurrence-free outcome in liver transplant patients with HCC.
Patients and methods: Ninety-three liver transplant patients with HCC were included in this prospective trial. The impact of pretransplant evaluated clinical variables and relevant tumor features, including cold and warm ischemia time (CIT, WIT) on recurrence-free survival rates were determined in uni- and multivariate analysis.
Results: Overall 5-year recurrence-free survival rate was 74.1%. Five-year tumor-free survival rates were 88% and 45% in patients with CIT ≤ / > 400 min, and 86% and 20% in patients with WIT ≤ / > 60 min, respectively (log rank < 0.001). In multivariate analysis, none of ischemia times but ^{18}F-FDG-avidity on pretransplant PET, alpha-fetoprotein-levels (AFP) > 400 ng/ml and overall tumor diameter > 10 cm staging were identified as independent predictors of post-LT tumor recurrence ($P < 0.05$). In a multivariate subanalysis of tumors with unfavourable biology (PET + status; increased AFP-level, microvascular tumor invasion), however, WIT > 60 min remained as independent predictor of tumor recurrence. In the subset of patients with PET + tumors, 5-year-recurrence-free survival was 61% and 0% in WIT ≤ / > 60 min, respectively.
Conclusion: Both, CIT and WIT have an important impact on outcome in liver transplant patients with HCC. Increased WIT is an independent promoter of post-LT tumor recurrence in patients with aggressive tumor features, such as increased ^{18}F-FDG-uptake on pretransplant PET, and should, therefore, be significantly reduced in this special set-up.

P137 RESPONSE TO TACE ALLOW IDENTIFICATION OF SUITABLE PATIENTS WITH HEPATOCELLULAR CARCINOMA FOR LIVER TRANSPLANTATION

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Background and Aims: Liver transplantation is a curative treatment option for patients with hepatocellular carcinoma (HCC) and liver cirrhosis. To date, patient selection for transplantation is based on size and number of nodules as assessed by imaging before listing. We hypothesized that changes in tumour features resulting from pre-transplant transarterial chemoembolization (TACE) is a superior criterion to predict tumour recurrence.
Patients and Methods: 136 patients with HCC in cirrhosis with two or more cycles of pre-transplant TACE were included in this study. According to the surgical specimens, 46 patients exceeded the Milan Criteria.
Results: Tumour recurrence occurred in 21 patients (15%). Classification of Milan Criteria according to the imaging at referral was not predictive for recurrence ($P = 0.58$), whereas the Milan Criteria in the imaging immediately before transplantation reflected changes after pre-transplant TACE and were highly predictive ($p < 0.0001$).
Conclusions: Imprecise assessment of size and number of tumour lesions limits prognostic importance of initial imaging. Characteristics of tumour response to TACE are reliably recognized and allow identification of suitable patients for transplantation. Future selection criteria for LT in HCC should consider this aspect.

P138 IMPORTANCE OF PERIBILIARY MICROCIRCULATORY IMPAIRMENT FOR THE GENERATION AND FATE OF EARLY ISCHEMIC TYPE BILIARY LESIONS AFTER LIVER TRANSPLANTATION

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Background: Reason and prevention of ischemic type biliary lesions following liver transplantation remain an unsolved problem. Impaired microcirculation affecting the peribiliary plexus is one of the potential causative factors.
Method: Radiographic features and clinical course in 93 patients were compared with histomorphological alterations apparent in bile duct specimens taken during liver transplantation.
Results: Radiographic alterations occurring in 48 out of 93 patients were classified as affecting solely intrahepatic or intra- and extrahepatic bile ducts (peripheral; $n = 23$) and those restricted to the extrahepatic ducts (central; $n = 25$). Interventional or surgical treatment was deemed necessary in 21 peripheral and 13 central lesions ($P = 0.004$). Nine paeripheral and 2 central ($P = 0.003$) lesions required permanent treatment. Arteriolonecrosis and mural necrosis were the most prominent histomorphological features of peripheral lesions, whereas in central lesions histology was comparable to normal ducts. In normal bile ducts and those with successful treatment, mural inflammatory infiltration and minimal mural hemorrhage after recirculation were the most prominent histomorphological features.
Conclusion: Peripheral biliary lesions and lesions restricted to the extrahepatic biliary ducts are characterized by different histomorphological features. The most important issue is the degree of vascular damage which is significantly higher in peripheral lesions. While the biliary damage of ducts without intramural bleeding but with substantial inflammatory signs indicate good reparative capacity, massive intramural haemorrhage and the absence of inflammatory infiltrates are associated with poor long-term prognosis.

P139 INCREASED PRETRANSPLANT CRP LEVEL IS AN INDEPENDENT PREDICTOR OF MORTALITY IN LIVER TRANSPLANT PATIENTS WITH (LAB)MELD ≥ 30

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Background: The aim of this prospective trial was to evaluate the prognostic value of pretransplant C-reactive protein (CRP)-level for predicting short-term mortality in liver transplant patients with a (lab)MELD score ≥ 30.
Patients and methods: A total of 35 consecutive patients with a (lab)MELD score ≥ 30 at liver transplantation (LT) were included in this trial. The impact of recipient- and donor-specific variables including final pretransplant CRP-levels on posttransplant 3- and 6-months-survival / mortality were analyzed in uni- and multivariate analysis.
Results: Mean (lab)MELD at LT was 36.5 ± 3.6 (range: 30–40). Overall three- and 6-months survival rates were 77.1% and 68.6% respectively. In univariate analysis, ΔMELD > 10, pretransplant waiting time > 3 months, serum lactate-level > 2.4 mmol/L at LTand CRP-level > 5 mmol/L at LT proved to be predictors for early post-LT mortality. In multivariate analysis, only CRP-level (OR 23.2) and pretransplant waiting time (OR 7.2) were identified as independent predictors of early post-LT mortality.
Three and 6-months survival rates post-LT were 93% and 85.7% in patients with CRP-level ≤ 5 mmol/L and 14% and 0% in patients with CRP-level >

5 mmol/L (log rank < 0.001), respectively. Septical complications were the most important reasons for mortality.
Conclusion: Increased pretransplant CRP-level as biological marker of systemic inflammatory response syndrome and waiting time prior LT have a significant impact on outcome in patients with high (lab)MELD scores and should, therefore, be incorporated in individual decision-making.

P140 STATUS QUO AND COMPETITION OF LIVER TRANSPLANT CENTERS IN GERMANY

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Background: Competition among liver transplant centers for organs and recipients may affect recipient selection and outcomes. Here, we describe the status quo of liver transplant centers in Germany and show regional differences in centers competition.
Methods: Data was obtained from Eurotransplant, the DSO and other public sources. Centers competition was calculated by the Herfindahl-Hirschman Index (HHI), which is defined as the sum of the squares of themarket shares of competing firm (transplant centers) within the market (a donor region). The index ranges from 0(highest) to 1(no competition).
Results: There are 24 active liver transplant centers in Germany. This results in 2.9 centers per 10 million (mio.) inhabitants in Germany. This compares to 5.5/10mio. in Belgium, 3.6/10mio. in Austria, 1.8/10mio. in the Netherlands, 1.4/10mio. in USA/Canada and 1.1/10mio. in Great Britain. Within the German donor (DSO) regions the center density is highest in Bavaria with 3.96/10mio., followed by Ost 3.45/10mio., Nord 3.03/10mio., NRW 2.8/10mio., Mitte 2.7/10mio., Nord-Ost 2.6/10mio. and Baden-Württemberg 1.85/10mio. The highest center competition as determined by the HHI is in Nord 0.276, Bayern 0.285 and NRW 0.347, medium competition is found in Mitte 0.385 and Ost 0.443, low competition in Baden- Württemberg 0.593 and no competition in Nord-Ost 1.0.
Conclusion: The concentration of liver transplant centers in Germany is within the range of other Eurotransplant member states, but is significantly higher than in North America or Great Britain. Within Germany there are significant regional differences in concentration and competition of liver transplant centers. Within the current allocation system regional oversupply and over-competition may provoke unfavorable patients selection and may contribute to the observed poor outcomes after liver transplantation in Germany.

P141 PROJECTED CASELOAD FOR TRANSPLANT CENTERS TO OFFER TRAINING IN TRANSPLANT SURGERY ACCORDING TO THE REQUIREMENTS OF THE EUROPEAN BOARD OF SURGERY

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Up to now, there is no standardized training program for transplant surgery in Germany. The EBS logbook for transplant surgery and the launched German specialty "Zusatzbezeichnung Transplantationsmedizin" provide the framework for such programs. The aim of this analysis was to evaluate the caseload needed for a given transplant procedure to realistically train a potential fellow.

Calculations were based on a training period of 2 years and a 75% availability of the trainee.

Based on these assumptions a training center has to provide an annual caseload for one fellow in the specialty: 27 liver transplantations including 2 split-liver transplantations and 14 liver procurements; 27 kidney transplantations including 4 living-donor kidney transplantations, 4 living-donor nephrectomies and 27 kidney procurements; 7 pancreas transplantations and 8 pancreas procurements. Given the 48 hr working directive as well as absences for holidays, conferences, education and/or sickness, the caseload must be calculated with surplus of at least 25% in order to capture the miss of procedures due to absence.

Based on these projected case loads most transplant centers will currently have more surgeons in training as they could have, if they would provide EBS conform training within a reasonable time frame. Dedicated training programs will be necessary to provide adequate training to young transplant surgeons in Germany.

BASIC SCIENCE

P142 20-HYDROXYEICOSATETRAENOIC ACID (20-HETE) OVERPRODUCTION AGGRAVATES ISCHEMIC ACUTE KIDNEY INJURY IN MICE DEFICIENT FOR SOLUBLE EPOXYDE HYDROLASE (SEH) GENE

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Acute kidney injury (AKI) occurring upon ischemia-reperfusion (I/R) is characterized by a imbalance of vasoconstricting and vasodilatory factors, e.g. vasoactive CYP-eicosanoids. Enhancing actions of epoxyeicosatrienoic acid (EET) or blocking 20-hydoxyeicosatetraenoic acid (20-HETE) related mechanisms ameliorated I/R injury in our recent studies. We hypothesized that increased baseline EET levels in mice deficient for the EET degrading enzyme sEH (sEH-KO-mice) might act protective in experimental ischemic AKI.

To test this hypothesis, ischemia was induced through 22 min of left renal pedicle clamping after right nephrectomy in male sEH-KO-mice compared to wildtype (WT). Organs were harvested 2 days after reperfusion. We analyzed changes in renal function, tubular morphology and apoptosis, gene expression of 20-HETE- and EET-producing CYP-isoforms, and the renal CYP-eicosanoid metabolome by liquid chromatography tandem mass spectrometry (LC-MS/MS). Ischemia reduced the creatinine clearance by 80% compared to sham-operated controls. Surprisingly, sEH-KO-mice presented significantly stronger functional decline compared to WT accompanied by higher tubular lesion scores and stronger tubular apoptosis. Significantly higher expression of the 20-HETE producing CYP4a12a gene and protein in sEH-KO-mice was indicative of compensatory up-regulation which may had off-set awaited protective effects of lower EET degradation. LC-MS/MS analysis of renal metabolome from sEH-KO-mice confirmed a significantly stronger production of 20-HETE as a possible explanation for amplified functional decline after I/R injury.

Our results confirm the strong impact of imbalances in CYP-dependent eicosanoid production for acute ischemic kidney injury offering novel promising tools for prevention and treatment of AKI.

P144 RADIOTHERAPY INCREASES STEM-CELLNESS OF HEPATOCELLULAR CARCINOMA CELLS

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Background: Metastasis, resistance to chemotherapy, and eventual relapse have been attributed to a distinct tumor subpopulation known as cancer stem cells (CSCs). Here, we examined the effect of radiation that is increasingly used in bridging therapies such as conformal external beam radiation or selective internal radiotherapy on the development of a putative CSC phenotype in HUH-7 hepatoma cells.
Methods: HUH-7 was cultivated either in monolayer or spheroid culture. Cell cultures were irradiated up to doses of 12 Gy. Expression of the stem-cell markers CD133 and CD44 was determined by FACS analysis. Apoptosis was determined by 7AAD, proliferation by BrdU incorporation.
Results: Spheroid culture conditions significantly increased the content of $CD44^+$ cells (16.05% [day 8] vs. 6.72 [day 0]) but not of $CD133^+$ cells. Radiation dose-dependently increased the fraction of $CD44^+$ cells (36.75% [12 Gray] vs. 19.94% [control]). In comparison to $CD44^-$ cells, proliferation of $CD44^+$ cells was significantly increased, while radiation-induced apoptosis was decreased (7.24% vs. 15.04% [12 Gray]).
Conclusion: Our results suggest, that $CD44^+$ cells contribute to radioresistance of HUH-7 cells. Cotageting of the CSC niche may improve posttransplant tumor related outcomes.

P145 COMBINED THERAPY WITH CLOPIDOGREL AND EVEROLIMUS RESULTS IN SIGNIFICANT REDUCTION OF SKIN ALLOGRAFT REJECTION IN A MURINE TRANSPLANT MODEL

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Background: Our group has previously shown that the combination of Clopidogrel and Everolimus reduced chronic rejection in mouse cardiovascular and lung transplantion models. The aim of this study was to investigate whether this observation also holds true for a skin transplant model which is highly depended on an intact microvasculature. Using a mouse model of skin transplantation we explored the impact of Clopidogrel and Everolimus on microvasculature in transplanted grafts
Methods: Fully allogeneic C57BL/6 ($H2^b$) tail skin flaps were transplanted onto CBA ($H2^k$) recipients treated with Clopidogrel and Everolimus alone or in combination. We analysed the expression of surface molecules and cytokines using qRT-PCR, cell infiltration in the skin grafts by immunohistochemistry on day 30 after transplantation, postoperative morphological changes in skin grafts ($n = 10$/group), as well as mean survival times.
Results: Comparing mean survival times with allograft controls (12.8 + /-2.4 days), skin grafts remained viable significantly longer in the platelet inhibition groups (17.1 + /-3.2 days (Clopidogrel 1 mg/kg/day) and 16.6 + /-2.7 days (Clopidogrel 20 mg/kg/day). Daily application of Everolimus alone (0.05 mg/kg/day) led to prolonged graft survival (18.2 + /-2.3 days) as well as combined anti-platelet and immunosuppressive therapy (19.2 + /-4.1 days). Isograft controls did not reveal allograft rejection.
Conclusions: These results demonstrate that single treatment with Clopidogrel and Everolimus and a combination of both drugs results in strong reduction of skin allograft rejection. Therfore, the role of microvasculature in allograft rejection deserves further investigation.

P146 STEM CELL TRANSPLANTATION IN REGENERATIVE MEDICINE: AGE DEPENDENT DIFFERENCES IN STEM CELL BEHAVIOUR

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Aims: Mesenchymal stromal cells (MSCs) are utilized in cell-based therapies. In this study we compared phenotype, proliferation rate, migration, immunogenicity, and immunomodulatory capabilities of bone marrow derived MSCs from a healthy 6 month old infant (iMSC), and multimorbid donors above 70 years (sMSC).
Methods: Cells were characterized by FACS and mesenchymal lineage differentiation. Their proliferative and migratory potential was compared and the immunogenicity of the MSCs was assessed using FACS, ELISPOT, and donor specific antibodies.
Results: Both groups of MSCs showed the same potential to differentiate into cells of the mesenchymal lineage and the expression of typical MSC surface markers. However, iMSCs showed higher proliferation ($P < 0.001$) and migration ($P < 0.001$) rates. No significant difference was observed in fold change between iMSCs and sMSCs for HLA class I- (24.5 vs. 21.7), β2 microglobulin- (20.6 vs. 14), HLA class II- (1 vs. 2.4), and co-stimulatory molecule expression. Both, iMSCs as well as sMSCs, provoked similar T_H1 and T_H2 responses in unidirectional ELISPOT (spotfrequencies IFNγ iMSC 106 ± 49 vs. sMSC 80 ± 73 and IL-4 108 ± 70 vs. 105 ± 107) assays.
Conclusions: Our results suggest that donor age does not seem to influence the immunogenicity and immunomodulatory properties of bone marrow derived MSCs, but their proliferation and migration capacity.

P147 VISUALIZATION OF HEPATIC VASCULAR ANATOMY IN RODENTS

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Aim/Fragestellung: The aim of this study was to explore which imaging technique gives a sufficient resolution for 3D-visualization of hepatic vascular anatomy and allows hepatic volumetry in rodents.
Methods/Methoden: We evaluated 4 imaging modalities:
In-vivo MRI (3Tesla, Siemens) of rats contrasted with Primovist®,
in-vivo CT (Inveon microPET/CT, Siemens) of rats contrasted with Ultravist®,
in-vivo μCT (TomoScope®Synergy Twin, CT-imaging) of mice contrasted with eXIA160XL &
ex-vivo μCT of explanted rat livers contrasted with Microfil® .
3D-reconstruction was performed using automated volume rendering and semiautomatic segmentation. Quality of reconstruction was assessed in terms of resolution of hepatic branching patterns and vascular diameters.
Results/Ergebnisse: In-vivo MRI and in-vivo CT of rats resulted in resolutions (branching hierarchy 3rdorder, vascular diameter of 1 mm) suitable for calculation of total liver volume.

In-vivo and ex-vivo μCT quality and resolution (branching hierarchy ≥3rd order & vascular diameter of 100 μm) were sufficient for liver lobe dependent volumetry and allowed visualization of vascular remodelling after e.g. portal vein ligation.
Conclusion/Schlussfolgerungen: If optimal resolution is required to investigate liver lobe volume or vascular remodelling processes the use of ex-vivo μCT is recommended. If repeated visualizations are needed to visualize regeneration, in-vivo MRI for rats and in-vivo μCT for mice is suitable.

P148 CONTRAST ENHANCED T-CELL TARGETED ULTRASOUND FOR DETECTION OF ACUTE REJECTION IN RAT RENAL TRANSPLANTATION

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Introduction and aim: Episodes of acute rejection (AR) are a major risk factor for loss of renal graft function. Here we describe an ultrasound-based method using T-cells and microbubbles to detect AR in a rat renal transplantation model.
Methods: $30x10^6$ T-lymphocytes were injected into uni-nephrectomized, allogeneically kidney transplanted rats (Lewis-Brown Norway (LBN) to Lewis) followed by administration of microbubbles conjugated with an anti-CD3 antibody. The renal allograft as well as the native kidney were then analyzed by ultrasonography. Syngeneically transplanted rats (LBN to LBN), rats with ischemia/reperfusion injury (IRI, 45 min warm ischemia), and rats subjected to acute cyclosporine A toxicity (CSA, 50 mg/kg for 2 days i.p.) served as controls. In vivo results were verified by post mortem immunohistochemical CD3 staining.
Results: An increased ultrasound signal was found in allografts undergoing AR (5.41 ± 1.32 A.U.) when compared to native control kidneys (1.09 ± 0.18 A.U.). No differences occurred in syngeneically transplanted kidneys without AR (0.99 ± 0.30 A.U.), kidneys with CSA toxicity (0.12 ± 0.04 A.U.) and kidneys with IRI (0.46 ± 0.29 A.U.).
Conclusion: Contrast enhanced T-cell targeted sonography is a non-invasive method to detect renal AR and differentiate it from IRI and CSA toxicity.

P149 IL-13 SIGNALING VIA IL-13Rα$_2$ TRIGGERS TGF-β$_1$ DEPENDENT ALLOGRAFT FIBROSIS

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Background: We investigated if IL-13/TGF-β$_1$-interaction is responsible for allograft fibrosis.
Methods: FVB or DBA/1 hearts were transplanted into DBA/1 mice. Cardiac tissue was examined by masson trichrome, CD4, CD8 and CD11b staining. Graft-infiltrating cells were analyzed by flow cytometry. IL-13 and TGF-β$_1$ levels were determined by ELISA and collagen was quantified by sircol assay; IL-13Rα$_2$ expression was detected by Western blotting. In some experiments IL-13/TGF-β$_1$ signaling was blocked with IL-13Rα$_2$ siRNA. Expression of profibrotic genes was analyzed by PCR-array.
Results: Allografts were infiltrated by increased numbers of $CD4^+$ ($P < 0.0001$), $CD8^+$ ($P < 0.0001$) and $CD11b^+$ cells ($P = 0.0065$). Elevated IL-13 levels ($P = 0.0003$) and numbers of infiltrating IL-13$^+$ cells ($P = 0.0037$), together with expression of IL-13Rα$_2$, were detected only within allografts. This resulted in increased TGF-β$_1$ levels ($P < 0.0001$), higher numbers of $CD11b^{high}Gr1^{intermediate}$TGF-β$_1^+$ cells and elevated cardiac collagen deposition ($P = 0.0094$). Allograft fibrosis was accompanied by upregulation of multiple profibrotic genes. Blockage of the IL-13/TGF-β$_1$-interaction led to lower numbers of $CD11b^{high}Gr1^{intermediate}$TGF-β$_1^+$, $CD4^+$, $CD8^+$ and $CD11b^+$ cells and prevented collagen deposition ($P = 0.0018$) within these allografts.
Conclusions: IL-13 signaling via IL-13Rα$_2$ induces TGF-β$_1$ and causes allograft fibrosis. Blockage of IL-13/TGF-β$_1$-interaction by IL-13Rα$_2$ siRNA prevents allograft fibrosis. Thus, IL-13Rα$_2$ may be exploitable as a future target to reduce allograft fibrosis.

P150 LEUKOCYTIC ACETYLCHOLINE INHIBITS ATP-MEDIATED IL-1β RELEASE IN RAT RENAL ALLOGRAFTS

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The secretion of interleukin-1β (IL-1β) is tightly controlled. Priming of mononuclear phagocytes with lipopolysaccharide (LPS) induces pro-IL-1β synthesis. A second signal such as extracellular ATP leads to activation of caspase-1 and release of cleaved IL-1β. Previously, we demonstrated that acetylcholine is produced by monocytes activated by acute allograft rejection. We hypothesize that acetylcholine inhibits ATP-mediated IL-1β release.

LPS-primed monocytic U937 cells, naïve human peripheral blood mononuclear leukocytes (PBMC) and PBMC isolated from rat renal allografts during acute rejection were stimulated with BzATP (P2X7 agonist) or nigericine (bacterial pore-forming toxin) in the presence and absence of cholinergic agonists and antagonists.

Acetylcholine, choline and nicotine dose-dependently inhibited BzATP- but not nigericine-induced release of IL-1β from primed U937 cells and naïve PBMC. Inhibition was antagonized by mecamylamine, α-bungarotoxin and strychnine. BzATP-induced ion currents measured by patch clamp technology were abolished by nicotine. Allograft PBMC did not release IL-1β in response to BzATP unless acetylcholine esterase was added.

We suggest a novel anti-inflammatory cholinergic mechanism in monocytes, which is mediated by nicotinic acetylcholine receptor α9. Receptor activation inhibits signalling via P2X7 receptors upstream of caspase-1 activation. This mechanism seems to be effective in vivo in allograft PBMC, where endogenous acetylcholine suppresses secretion of IL-1β.

P151 INHIBITION OF 12/15-LIPOXYGENASE PREVENTS CELL DEATH AFTER HEPATIC ISCHEMIA AND REPERFUSION

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Introduction: Hepatic ischemia-reperfusion-injury (IRI) is an inevitable complication in liver transplant surgery. 12/15-Lipoxygenase (LOX), a protein of the glutathione-peroxidase-4 (GPx-4) signaling cascade, may be overexpressed in IRI models of other organ systems, leading to apoptosis. Aim of this study was to investigate the role of 12/15-LOX inhibition on hepatic IRI and thus gain insights into GPx-4 dependent signaling in the liver.
Methods: Livers of C57BL/6 mice were exposed to 60 minutes of warm ischemia by clamping the common pedicle of the median and left lateral liver lobe and subsequent reperfusion for 90 minutes. Baicalein, an inhibitor of 12/15-LOX, was administered intraperitoneally 30 minutes before operation (group 1). Controls were treated with vehicle dimethylsulfoxide(DMSO) (group 2) or untreated (group 3).Tissue samples were analyzed by TUNEL assay and Western Blot for pro-apoptotic proteins p44/42 MAP kinase (ERK1/2), Jun-amino-terminal kinase (JNK), Poly-ADP-ribose polymerase (PARP) and Caspase-3.
Results: Analysis of hepatic cell death by fluorescence TUNEL labeling showed a significant reduction of apoptotic cells in liver samples pretreated with baicalein(group 1: −77.1%) and withDMSO (group 2: −20.5%) compared to untreated samples (group 1) ($P < 0.0001$). Western Blot analysis revealed a slight downregulation of ERK1/2, JNK, PARP and Caspase-3 after baicalein administration.
Conclusion: Inhibition of 12/15-LOX leads to a significant decrease of hepatic IRI. Hence it could be demonstrated that the GPx-4 dependent apoptosis cascade plays a considerable role in hepatic ischemia models, however preliminary analysis of presumed mediator mechanisms showed only slight signaling differences. This characterization of the mechanisms is under current investigation.

P152 OVEREXPRESSION OF CUZNSOD IMPROVES ENGRAFTMENT OF TRANSPLANTED HEPATOCYTES IN ATP7B KNOCKOUT MICE

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Introduction: Recent successes in hepatocyte transplantation offer new ways to approach cell and gene therapy for metabolic disorders, including Wilson disease with copper induced liver damage. This study addressed the hypothesis that cells with transgene expression of CuZnSOD will be cytoprotected against copper toxicity.

Material and methods: First, human CuZnSOD was cloned into lentivirus vectors (LV). HEPA-1 cells were transduced with CuZnSOD-LV for 16–18 hours. The capacity of cells to withstand oxidant stress and copper toxicity was tested using H_2O_2 and $CuCl_2$ via MTT assays. Afterwards, freshly isolated hepatocytes from GFP positive C57Bl/6 mice were transduced ex vivo with CuZnSOD-LV for 2 hours. Subsequently 10^6 transduced as well as sham-treated cells were transplanted intrasplenically into atp7b knockout mice. For repopulation studies atp7b knockout mice pretreated with monocrotaline and rifampicin were used. Engraftment and repopulation was assessed after 3 days and 3 months, respectively.
Results: HEPA-1 cells were efficiently transduced with CuZnSOD-LV. H_2O_2 and $CuCl_2$ treatment resulted in cell death in untransduced cells, viability assays demonstrated improved oxidative stress and copper resistance of CuZnSOD overexpressing HEPA-1 cells ($P < 0.05$). Ex vivo gene transfer of freshly isolated hepatocytes was successful. Transduced cells showed improved cell engraftment in atp7b knockout mice >2-fold compared to controls ($P < 0.001$). DNA PCR for atp7b and western blot analysis for human CuZnSOD demonstrated cell survival for at least 3 months after transplantation.
Conclusion: Our findings suggest that CuZnSOD overexpression provides an important selection advantage to transplanted hepatocytes in high copper microenvironments and could potentially be one way for future considerations of ex vivo gene therapy in Wilson's disease.

P153 THE FUNCTIONAL INFLUENCE OF ACTIVATING NATURAL KILLER CELL RECEPTORS IN SOLID ALLOGRAFT REJECTION

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Little is known about NK cells and their receptors in solid organ transplantation. To elucidate their functional importance during acute rejection, we used BALB/c mice as donors and $NKp46^{-/-}$, $NKG2D^{-/-}$ and $Ly49^{-/-}$mice (C57BL/6 background) as recipients in a heterotopic HTX model. Wildtype C57BL/6 mice served as controls. Animals were either sacrificed at day 5 (d5) or at day of graft rejection (dRx) for FACS analysis ($n = 5$/group/time point). Although graft survival revealed no significant differences between wildtype and kockout mice (day 7.5 ± 1.5 day), differences of lymphocyte subsets could be observed. Whereas a strong infiltration of NK cells into the allograft could be observed for all groups at d5, especially $Ncr1^{-/-}$ and $NKG2D^{-/-}$ mice showed significant more frequencies of intragraft NK cells compared to controls ($P < 0.001$). Splenic NK cells of all groups were induced and appeared to be less activated than NK cells derived from wildtype or $Ly49^{-/-}$ mice. Induced frequencies of intragraft CD3 + CD4 + T helper cells were only observed in knockout mice ($P < 0.01$) at dRx. In spleen, especially $NKG2D^{-/-}$ mice demonstrated elevated levels of CD3 + CD4 + T cells already at d5. In summary, our results highlight the impact of NK cell receptor deficiency on various lymphocytes subsets during acute cellular rejection.

P155 DOUBLE-DEFICIENCY FOR RORγT AND T-BET DRIVES TH2-MEDIATED ALLOGRAFT REJECTION IN MICE

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Introduction: Th1, Th2 and Th17 cells are thought to be major effector cells in adaptive alloimmune responses. However, their distinct participation in the context of solid organ transplantation remains unclear.
Methods: To investigate this we adoptively transferred T cells from B6.RORγt knockout (KO) mice (prone to Th1), B6.T-bet KO mice (prone to Th2/Th17), and B6.RORyt-T-bet double-KO mice (prone to Th2) in B6.Rag-γchain-KO recipients of fully mismatched Balb/c heart allografts.
Results: T cells deficient for T-bet (Th2/Th17 prone) rejected heart allografts at a more accelerated rate (19.8 ± 6.47d) than cells from RORγt KO mice (>80 d in 63% of mice), indicating a predominance of Th17- over Th1-driven alloimmunity. Unexpectedly, double-deficiency for T-bet and RORγt resulted in early rejection (22.8 ± 3.65 d) featuring high levels of IL-4 (by flow cytometry), a significantly upregulated intragraft mRNA expression of Th2 related cytokines and eosinophilic infiltration. Importantly, IL-4 neutralization in recipients given RORγt-T-bet-DKO T cells significantly prolonged allograft survival (>60 d in 57% of mice).
Conclusion: While Th17 cells predictably promote allograft rejection in the absence of T-bet, our data indicate that Th2 cells, which have generally been thought to protect allografts, may be potent effector cells in allograft rejection in the absence of both T-bet and RORγt.

P156 SPECIFIC TOLERANCE-INDUCING EFFECTS OF EXTRACORPORAL PHOTOPHERESIS

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Objective: Extracorporal photopheresis (ECP) has been used as a therapeutic option for acute and chronic rejection after transplantation (Tx). However, for the first time we assessed tolerance-inducing effects of ECP on subsets of Tregs and DCs after heart transplantation (HTx) for a better monitoring of ECP therapy.
Methods: HTx recipients were treated with ECP for the following ($n = 21$ ECP treatments each group): (1) prophylaxis of acute cellular rejection (ACR) between month 3 to 6 post-HTx ($n = 8$), or (2) histological proven ACR of grade ≥1B (ISHLT 1990, $n = 8$). Each ECP treatment was performed at 2 subsequent days. Peripheral blood analysis by FACS of HTx recipients were compared to of healthy human controls (HC; $n = 9$) as follows: $CD4^+CD25^{high}CD127^{low}$ Tregs activating (CD147) and suppressing subsets (CD120b, CD62L, CD39) as well as myeloid (mDCs) and plasmacytoid (pDCs) subsets.
Results: Incidence of $CD4^+CD25^{high}CD127^{low}$ Tregs increased overall after ECP with a pronounced effect in recipients with prophylactic ECP therapy (6.9 ± 0.7%) compared to the ECP-ACR group (6.0 ± 0.3%) and HCs (5.1 ± 0.7%). Treg activation marker CD147 was significantly up-regulated after ECP prophylaxis (99.7%±0.1%; $P = 0.02$) compared to HCs (97.7 ± 0.8%). Whereas Treg suppression CD120b and CD62L were significantly decreased in ECP-treated recipients compared to HCs but did not differ between the ECP groups. Numbers of $CD39^+$ Tregs, which are known to suppress pathogenic T helper17 cells, did not change after ECP therapy. In comparison to HCs, percentage of pDCs were reduced (14.5 ± 3.6% vs 26.0 ± 2.8%, $P = 0.01$) and mDCs were increased (70.1 ± 4.0% vs 55.6 ± 3.7%, $P = 0.01$) after ECP-prophylaxis but without significant change in ECP-ACR group.
Conclusions: Our results showed that assessment of specific ECP effects on subsets of Tregs and DCs could be valuable to identify responders and non-responders of ECP therapy after Tx.

P157 PRECONDITIONING USING TETRAHYDROBIOPTERIN SAVES MURINE PANCREATIC ISOGRAFTS FROM BRAIN DEATH EXACERBATED ISCHEMIA REPERFUSION INJURY

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Brain death (BD) is thought to aggravate ischemia reperfusion injury (IRI). Recently we were able to show that the nitric-oxide-synthase co-factor tetrahydrobiopterin (BH4) prevents IRI following pancreas transplantation.

Herein we assessed the impact of BD on IRI and tested the therapeutic potential of BH4.

Pancreas transplantation was performed between male C57BL/6 mice using a no-touch technique. Animals were followed for 3 h after BD induction, continuously ventilated trough a tracheostomy.

Experimental groups included ($n = 5$ per group): non-treated BD donors, pre-treatment of BD donors with 50 mg/kg BH4 before organ retrieval, ventilated non-treated donors (no BD, sham group), non brain death non-treated donors. Following 2 hours of reperfusion, microcirculation (functional capillary density, FCD; capillary diameter, CD) and cell viability was assessed by intravital fluorescence-microscopy. Parenchymal damage was assessed by histology and mRNA expression of inflammatory candidate markers was measured by real-time RT-PCR.

BD had dramatic impact on pancreatic microcirculation as highlighted by significantly reduced FCD and CD values when compared to controls ($P < 0.05$). Moreover BD induced mRNA expression levels of IL-1ß, TNFa, IL-6 and ICAM-1. In contrast BH4 treatment resulted in significantly higher FCD and CD values ($P < 0.001$, respectively). BD significantly impacted cell-viability, whereas BH4 treated grafts displayed similar percentages of viable cells as controls ($P < 0.001$). Parenchymal damage in grafts was significantly more pronounced in organs from BD donors ($P < 0.05$). BH4 treatment however ameliorated parenchymal damage in organs from BD donors ($P < 0.05$).

This study provides in vivo evidence that brain death aggravates IRI after pancreas transplantation. Pre-treatment with BH4 offers a novel therapeutic option in preventing BD exacerbated IRI.

P158 N-OCTANOYL DOPAMINE INHIBITS SMOOTH MUSCLE CELL PROLIFERATION: POSSIBLE IMPLICATIONS FOR PREVENTION OF NEO-INTIMA FORMATION IN TRANSPLANTED GRAFTS

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N-octanoyl dopamine (NOD) mitigates acute kidney injury, protects vasculature from cold preservation injury and inhibits T-cell activation. In the present study we addressed how restoration of vascular barrier function after cold preservation is accomplished and if NOD influences the proliferation of endothelial (EC) and smooth muscle cells (SMC).

To this end, EC and SMC were damaged on ice in the presence or absence of NOD. Damage and repair mechanisms were assessed by microscopy and western blot. Proliferation was measured by WST-1 and cell cycle arrest confirmed by PCR.

While both NOD treated EC and SMC were protected against cold preservation injury, severe damage was observed in untreated cells. Upon rewarming only treated EC displayed restoration of barrier function as evidenced by intercellular gap closure. During rewarming p42/p44 was transiently activated, phosphorylation of paxilin in focal adhesion contacts was noted and F-actin stress fibres were formed, which were blocked by Rock inhibitors. Gap closure was more prevalent in the presence of these inhibitors. NOD inhibited EC or SMC proliferation dose dependently. This was associated with down-regulation of cell cycle molecules.

Stress fibre formation may result in potential increased forces at vascular junctions. Our data indicate that stress fibre formation negatively affects gap closure. Since NOD affects proliferation of EC, NOD treatment of organ recipients might not be desirable in situations of vascular damage. However if vascular damage can be prevented either by donor NOD-preconditioning or by limiting cold ischemia time, NOD treatment might be favourable to prevent neo-intima formation through the inhibition of SMC.

P159 AUGMENTER OF LIVER REGENERATION ATTENUATES POSTISCHEMIC LIVER INJURY *IN VIVO*

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ALR, a protein synthesized in the liver is suggested to be protective against oxidative stress-induced cell death. Hepatic ischemia-reperfusion (I/R) injury is triggered by reactive oxygen species. Here, we tested the hypothesis that ALR attenuates hepatic I/R injury *in vivo*.

In mice, a warm hepatic ischemia was induced for 90 min. Either recombinant ALR (100 μg/kg) or vehicle were administered to mice i.a. 5 min prior ischemia ($n = 6$ each group). Sham-operated animals served as controls. Leukocyte migration and sinusoidal perfusion were analyzed using intravital microscopy. ALT/AST (plasma) and caspase-3 (tissue) activities were determined as markers of hepatocellular injury. All parameters were analysed after 60 and 240 min of reperfusion in two separate sets of experiments.

Hepatic I/R (90/60 min) led to a dramatic enhancement of leukocyte recruitment in postinusoidal venules, failure of sinusoidal perfusion as well as a strong elevation of AST/ALT activities. During early reperfusion (60 min), the pre-treatment with ALR improved postischemic perfusion failure ($P < 0.05$) and attenuated liver enzyme activities, whereas leukocyte migration was not affected. After 240 min of reperfusion, the protective effect of ALR was stronger, since the liver enzyme activity, perfusion failure, and leukocyte influx were significantly attenuated. As shown by measurement of caspase-3 activity, postischemic apoptosis (R: 240 min) was reduced in the ALR-treated group ($P < 0.05$).

Our *in vivo* data show that ALR has a therapeutic potential against postischemic liver injury. As a mechanism we suggest a direct protective effect of ALR on apoptotic and necrotic death of hepatocytes followed by attenuation of leukocyte influx into the postischemic tissue.

P160 THE PUTATIVE TUMOR SUPPRESSOR MICRORNA-105 NEGATIVELY REGULATES THE FRIZZLED-7/BETA-CATENIN PATHWAY IN HUMAN HEPATOCELLULAR CARCINOMA

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Aims: Aberrant microRNA (miR) expressions have been observed in different types of cancer. Among the frizzled (Fzd) receptor family, Fzd7 is the Wnt receptor which is most commonly upregulated in a variety of cancers including hepatocellular carcinoma (HCC). *FZH7* was predicted to be a potential target of miR-105 by the use of miR target prediction algorithms in HCC. Therefore, we sought to investigate the functional role of both miR-105 and *FZH7* in hepatocarcinogenesis.
Methods: The expressions of *FZH7* and miR-105 were analyzed in tumor and adjacent non-tumor tissues from 12 HCC patients by gene array and real-time quantitative RT-PCR (qRT-PCR). Transfection studies were performed in human hepatoma cell lines (HepG2, SUN-182) to elucidate the regulatory interrelationsship between miR-105 and *FZH7*.
Results: A significant up-regulation of miR-105 was found in all (12/12) HCC tissues, whereas *FZH7* expression was decreased in 25% (3/12) and similar in 33.3% (4/12) of tumor tissues as compared to non-tumor tissue. MiR-105 expression was negatively correlated with *FZH7* expression. Transfection of miR-105 precursor dramatically inhibited whereas transfection of miR-105 inhibitor enhanced the expression of *FZH7*.
Conclusions: MiR-105 negatively regulates the *FZH7* oncogene in HCC. These findings provide significant insights into molecular mechanisms of hepatocarcinogenesis.

P161 NK-CELLS′ POTENTIAL TO MODULATE ALLOANTIGEN INDUCED T-CELL RESPONSES IN RAT CAN BE INFLUENCED BY GENETIC POLYMORPHISMS WITHIN THE NATURAL KILLER GENE COMPLEX

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Natural Killer cells have been shown to exhibit the capability to negatively regulate immune responses of adaptive immunity. In case of NK-T-cell interactions involved NK-cell receptor proteins encoded by the Natural Killer Gene Complex (NKC) and respective ligand proteins expressed by T-cells following activation have been identified. Whether genetic polymorphisms of NKC-encoded receptor proteins affect NK-cells′ capability in regulating/modulating alloantigen induced T-cell responses is unknown.

NK-cell populations were isolated from rat strains LEW (MHC-haplotype RT1 ^{l}, NKC-haplotype lew) and LEW.TO-NKC (MHC-haplotype RT1 ^{l}, NKC-haplotype to) differing in multiple genetic polymorphisms of NKC-genes and cultured in the presence of IL-2. Mixed lymphocyte reactions composed of constant numbers of lymph node cells of strains LEW or LEW.TO-NKC and irradiated MHC-disparate LEW.1U stimulators (MHC-haplotype RT1^{u}) were supplemented with varying amounts of autologous NK-cells.

LEW.TO-NKC NK-cells inhibited autologous alloimmune T-cell responses stronger than LEW NK-cells respective T-cells even at low amounts. The inhibitory potential was rather mediated by the NK-cell subset lacking expression of the inhibitory NKRP1B receptor than by NKRP1B positive NK-cells.

Genetic polymorphisms of NKC-encoded surface proteins were shown to influence the immunoregulatory potential of NK-cells. It is expected *in vivo* that survival of MHC-disparate tissues might/will differ depending on the recipient′s NKC-haplotype.