POSTERS

INFECTIOLOGY

P001 RBV-FREE 12 WEEK TREATMENT OF HCV-RECURRENCE AFTER LIVER TRANSPLANTATION WITH SOFOSBUVIR/ LEDIPASVIR IN GENOTYPE-1 PATIENTS

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Introduction and Background: HCV-recurrence after liver transplantation used to be a hard issue in the interferon-era. Since the introduction of modern direct acting antivirals, treatment became easier and shorter. Antiviral treatment duration with sofosbuvir (SOF) und ledipasvir (LDV) may be shortened to 12 weeks using ribavirin (RBV) additionally. However, the question, if RBV is really necessary in a 12-week SOF/LDV-treatment in transplant setting, is still unanswered.
Methods: 101 liver transplant patients with HCV-recurrence underwent interferon-free SOF-based treatment at our institution. 51 patients were included in the analysis of antiviral efficacy of SOF/LDV with or without RBV. Group A with the shortest treatment (SOF/LDV for 12 weeks) comprised 29 patients with low stage fibrosis (F0-2) and was compared with 22 individuals in the group B (SOF/LDV with RBV or 24 weeks treatment), which comprised 15 patients treated with SOF/LDV with RBV for 12 weeks, 5 patients treated with SOF/LDV and RBV for 24 weeks and 2 patients treated with SOF/LDV for 24 weeks in case of advanced fibrosis stages.
Results and Conclusions: All 51 patients achieved ETR and SVR 12 disregarding the treatment mode, previous treatment history and fibrosis stage. No patient in any treatment group had virological breakthrough or relapse. The highest prevalence of adverse events was observed in the group B with RBV or prolonged treatment (27.6% vs. 86.4%; $P < 0.001$). In 55% ($n = 11$) of 20 patients with RBV-comedication RBV-dose had to be reduced and in 40% ($n = 8$) of 20 patients RBV-therapy had to be stopped due to predominantly hematological adverse events.

SOF/LDV-combination is a reliable therapy of recurrent genotype-1 HCV-infection after liver transplantation. It is easy to administer and to achieve SVR in immunocompromised patients without interactions with the immunosuppressants. Regarding the high rate of adverse events, there is no need for RBV in the 12 week SOF/LDV-regimen.

P002 MONITORING CYTOMEGALOVIRUS-SPECIFIC CELL-MEDIATED IMMUNITY IN LUNG TRANSPLANT RECIPIENTS: A COMPARATIVE ANALYSIS OF TWO ASSAY SYSTEMS

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Introduction and Background: Monitoring cell-mediated immunity (CMI) to Cytomegalovirus (CMV) in lung transplant recipients is a promising strategy to manage prevention and therapy of post-transplant CMV-infection or reactivation. We compared T-Track® CMV (Lophius Biosciences GmbH, Regensburg) and QuantiFERON®-CMV (Qiagen GmbH, Hilden), two commercially available *in vitro* assays for CMV-specific CMI monitoring that differ in the type of stimulant, the addressed T cell subpopulations and in their read-out formats. T-Track® CMV and QuantiFERON®-CMV were evaluated in terms of routine practicability and clinical significance.
Methods: Blood samples of 30 lung transplant recipients (LuTRs) were examined before and at month six post-transplantation with T-Track® CMV and QuantiFERON®-CMV. T-Track® CMV is an ELISpot-based assay utilizing T-activated® CMV proteins (*a*pp65, *a*IE-1) as stimulants, allowing the quantification of interferon-gamma (IFN-γ)-secreting CD4+ and CD8+ T cells. The peptide-based QuantiFERON®-CMV assay is restricted to the detection of epitope-specific IFN-γ-producing CD8+ T cells by ELISA. The data were compared with viral load, as determined by qPCR.
Results and Conclusions: QuantiFERON®-CMV requires low blood volume and offers an ELISA read-out easy to integrate into diagnostics routine. However, it often generated indeterminate results after induction of immunesuppressive therapy. By contrast, T-Track® CMV revealed a higher sensitivity, albeit needing larger blood volumes. Individual patient data suggest that CMV-specific cellular immunity monitoring, together with surveillance of viral load, might help identifying lung transplantation patients at risk of developing CMV disease and thus might support the management of antiviral therapy decision, especially in intermediate-risk (R+) patients.

P004 CLINICAL OUTCOME IN HEART TRANSPLANT RECIPIENTS (HTX) RECEIVING EVEROLIMUS IN COMBINATION WITH THE CALCINEURIN INHIBITOR TACROLIMUS OR CYCLOSPORIN A IN COMPARISON WITH A CALCINEURIN INHIBITOR FREE IMMUNOSUPPRESSIVE THERAPY

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Introduction and Background: It is currently under discussion whether the combination of mTOR- with calcineurin inhibitors (under dosage reduction) is superior to a calcineurin inhibitor free therapy (mTOR inhibitors ± MMF ± prednisolone).
Methods: We compared 2-year clinical outcomes in 105 patients receiving CNI free immunosuppressive therapy with everolimus or sirolimus ± MMF / ± prednisolone from 26.05.2002–09.09.13 (CNIF-group) to 114 patients receiving everolimus or sirolimus combined with cyclosporine or tacrolimus from 03.02.2002–22.07.2013 (CNI-group). The primary endpoint was recovery of adequate renal function (measured by GFR) between the two groups. Secondary endpoints were two year survival, and laboratory parameters.
Results and Conclusions: Groups were comparable regarding baseline characteristics such as age, primary diagnosis, body mass index (BMI), creatinine values and GFR. Compared with the CNI group, kidney function improved in the CNIF group over time ($P < 0.05$). Glomerular filtration rate improved from 34.8 ml/min at baseline to 42.0 ml/min after 24 months in the CNIF group versus 38.1 ml/min to 39.2 ml/min in the CNI – group ($P < 0.05$). Creatinine value decreased from 2.3 mg/dl at baseline to 1.9 mg/dl after 24 months in the CNIF – group and increased from 2.2 mg/dl to 2.3 mg/dl in the CNI – group ($P < 0.05$). Two year survival did not differ significantly between the groups ($P > 0.05$). Laboratory parameters did not differ significantly between the groups during two year follow up ($P > 0.05$). CNI – free therapy had beneficial effects on kidney function in HTX patients with chronic renal failure compared with patient with reduced CNI – dosage. Secondary endpoints such as survival and laboratory parameters did not differ significantly between the groups. We conclude that CNI free therapy could be an option in patients with progressive renal failure due to CNI – nephrotoxicity.

P005 KIDNEY TRANSPLANT RECIPIENTS SHOW HUMORAL RESPONSE TO 13-VALENT CONJUGATE PNEUMOCOCCAL VACCINE

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Introduction and Background: Kidney transplant recipients are at increased risk of pneumococcal infection, especially of invasive and often lethal courses of the disease. Vaccination is the most effective preventive action. However, due to immunosuppression and decreased kidney function the efficacy of vaccination might be reduced. This study assesses the efficacy of the 13-valent pneumococcal conjugate vaccine (PCV, Prevnar13©) in kidney transplant recipients.
Methods: Serum samples of 26 patients were drawn immediately before, 4 weeks after and 1 year after vaccination and were tested for IgG, IgG2 and IgA-antibodies against 23 serotypes of pneumococcal capsular polysaccharides (PCP).
Results and Conclusions: **IgG**-PCP-antibody concentrations 4 weeks after vaccination showed a mean 2.4-fold increase (CI 95%: 1.4–3.3, $P = 0.001$). A 2-4-fold increase in PCP-antibody concentration after vaccination is considered as positive response to vaccination. One year after vaccination the mean concentration was 1.8-fold (CI 95% 0.8–2.4, $P = 0.06$) above the level measured before vaccination. 42% showed a response that could be considered as positive.

IgG2-PCP-antibody concentrations 4 weeks after vaccination showed a mean 2.3-fold increase (CI 95%: 1.30–3.38, $P = 0.0004$). One year after vaccination the mean concentration was 1.8-fold (CI 95% 1.2–2.4, $P = 0.03$) above the level measured before vaccination.

IgA-PCP-antibody concentrations 4 weeks after vaccination showed a mean 3.6-fold increase (CI 95%: 2.0–5.2, $P = 0.0001$). One year after vaccination the mean concentration was 2.1-fold (CI 95% 1.5–2.7, $P = 0.005$) above the level measured before vaccination.

Kidney transplant recipients respond to vaccination with the 13-valent PCV with a significant increase ($P < 0.002$) in PCP-antibody concentrations of IgG,

IgG2 and IgA subclass and display significantly increased concentrations ($P < 0.04$) of IgG2 and IgA PCP-antibodies 1 year after vaccination.

P006 ANALYSIS OF BLOOD AND URINARY CULTURES IN LONG-TERM KIDNEY TRANSPLANT PATIENTS WITH SEVERE URINARY TRACT INFECTION OR UROSEPSIS

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Introduction and Background: Urinary tract infections are the most common infectious complications after kidney transplantation. Multidrug-resistance, especially in gram-negative germs is a growing problem. Therefore, antibiotic stewardship and the analysis of the local spectrum of isolated germs are recommended.
Methods: We systematically reviewed all kidney transplant patients hospitalized in our clinic with the diagnosis of urinary tract infection from 01.01.2011 to 31.12.2012. We analyzed blood and urine cultures including antibiotic resistogram of isolated germs and compared patients with urosepsis with patients with severe urinary tract infection not fulfilling the criteria for sepsis. In most patients a de-escalation strategy with initial beta lactam antibiotic treatment was chosen.
Results and Conclusions: Urinary cultures were positive in about 88% of cases in both groups, whereas a positive blood culture result was only obtained in 34% of urosepsis patients. In urosepsis patients, the most frequent pathogens identified in urinary culture were Escherichia coli (47%), followed by Enterococcus faecalis (18%). With E. faecalis (33%) being the most frequent pathogen isolated in patients with urinary tract infections the spectrum of isolated germs differed significantly in both groups. Notably, almost a quarter of infections were caused in both groups by Klebsiella pneumoniae and Pseudomonas aeruginosa including multidrug-resistant strains (3 and 4 MRGN). No patient of our cohort died as a consequence of UTI. Therefore initial treatment with broad-spectrum antibiotics followed by de-escalation according to antibiotic resistogram is recommended in this patient group.

P007 CD4 CELL COUNT AS A POSSIBLE BIOMARKER FOR SEVERE URINARY TRACT INFECTION AND UROSEPSIS IN LONG-TERM KIDNEY TRANSPLANT RECIPIENTS

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Introduction and Background: Urinary tract infections are the most common infectious complications after kidney transplantation. Some patients may develop acute pyelonephritis or the full blown picture of urosepsis. As a consequence of immunosuppression features of SIRS may go unrecognized. CD4 cells are pivotal for transplant rejection but also for host defense against infection. In a retrospective analysis we investigated whether CD4 cell count might be a biomarker to estimate the severity of urinary tract infections.
Methods: We performed a retrospective analysis of kidney transplant recipients with urinary tract infection treated at our center in a 2-year period (n−103). We categorized the patients in 4 groups according to the lowest CD4 count (600/µl) and analyzed clinical data and the course of the disease.
Results and Conclusions: Lower CD4 cell count was associated with longer hospital stay, higher CRP-levels and lower thrombocyte count. While breathing frequency was not associated with CD4 cell count, lower pCO2 levels were association with lower CD4 cells. Interestingly, with lower CD4 cell count significantly more blood cultures obtained a positive result. Over the whole study population lower CD4 cell count was associated with fulfilling more SIRS criteria and the diagnosis of sepsis. An association with mortality was not possible as no one of our patients died as a consequence of a urinary tract infection/urosepsis. CD4 cell count is associated with severity of urinary tract infection in kidney transplant patients and should be further evaluated not only as a risk factor developing infectious complications after kidney transplantation but also as a possible biomarker for disease severity to guide immunosuppression.

P008 LOW-DOSE CIDOFOVIR AND CONVERSION TO MTOR IN POLYOMA VIRUS-ASSOCIATED NEPHROPATHY (PVAN) – A CASE SERIES

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Introduction and Background: Polyoma virus-associated nephropathy (PVAN) is an emerging disease in renal allograft recipients with a high rate of allograft loss. Overall reduction in immunosuppression is a cornerstone of PVAN therapy, whereas optimal drug combination, as well as specific antiviral therapy remain a question. We report safety, efficacy and outcome data of a protocol using low-dose cidofovir in a case series of 16 patients with PVAN and progressive renal functional deterioration.
Methods: Patients with biopsy-proven PVAN and creeping creatinine received single low-dose cidofovir according to the Tübingen Cidofovir Protocol, developed to effectively deliver therapeutic drug concentrations at limited nephrotoxicity and were converted to mTOR-based maintenance immunosuppression. Polyoma virus replication and renal function were prospectively monitored over time.
Results and Conclusions: Results from an ongoing case series (since 2007) of currently 16 patients with a median follow-up of 3.9 [0.3–9.1] yrs. are reported. Median time to PVAN diagnosis was 268 [60–2389] days after transplantation. Median eGFR prior to therapy was 28 [10–48] ml/min/1.73 m^2. The protocol allowed antiviral therapy without adverse nephrotoxicity, irrespective of allograft function. 14/16 patients were converted to mTOR-based immunosuppression. 14 patients stabilized or improved allograft function, two patients progressed to ESRD due to PVAN, one of which was successfully retransplanted without recurrence. In patients without allograft loss, polyoma virus clearance from plasma was achieved in 79% of patients after a median of 90 [27–298] days.

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 progressive allograft dysfunction and may prolong allograft survival in these patients.

P009 CLASSIFICATION OF ACUTE REJECTION IN LUNG TRANSPLANTATION: EXPERIENCE OF SECOND OPINION EVALUATION

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Introduction and Background: Acute rejection in lung transplantation has to be classified according to the ISHLT guidelines. Consulting different institutions sometimes leads to different opinions. Results have to be compared.
Methods: Transbronchial biopsies were taken in lung transplant recipients according to the running surveillance program. ISHLT classification was used as recommended. Diagnostic results of 2 institutes of pathology were compared using the same slides. Two pathologists in each institute were involved.
Results and Conclusions: A patients' group of 20 lung transplant recipients was evaluated. The comparison of ISHLT classification of acute rejection reveals an accordance between the two institutions of 75% (15 out of 20 patients).

Differences concerning ISHLT classifications between two institutes exist, but are within a tolerable variation.

P010 INFECTIONS AFTER SOLID ORGAN TRANSPLANTATION: IS THERE A BENEFIT FOR MTOR-I OR CNI? A SYSTEMATIC REVIEW AND METAANALYSIS

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Introduction and Background: Side effects of the immunosuppressive therapy after solid organ transplantation are well known. Naturally, immunosuppressed patients are more susceptible to infections. Recently, significant benefits were shown for mTOR-Is with respect to CMV infections in comparison with CNIs. With other infections, i.e. pneumonitis the situation may look different. We aimed to investigate the differences of mTOR-Is and CNIs with respect to the overall incidence of infections after solid organ transplantation.

Methods: The current literature was searched for prospective randomized controlled trials in solid organ transplantation. There were 1075 trials screened of which 20 could be included (patients−9523). The 1-year and longterm incidence of infections and biopsy proven acute rejection was assessed in metaanalyses.
Results and Conclusions: Metaanalysis on 1-year incidence of infections showed no benefit of an mTOR-I based therapy versus CNI's (RR 0.99, CI 0.94–1.04, $P = 0.68$). There was no difference when mTOR-Is were given either with or without CNIs (mTOR-I w/o CNIs vs. CNIs: RR 1.02, CI 0.94–1.10, $P = 0.66$; mTOR-I with CNIs vs. CNIs: RR 0.97, CI 0.92–1.04, $P = 0.43$). Similar results were seen longterm (mean 40.5 months, RR 1.08, CI 0.97–1.19, $P = 0.15$).

Combination of mTOR-Is and CNIs had the lowest incidence of BPARs (1 year: RR 0.70 vs. CNI, CI 0.59–0.82, $P < 0.001$), and mTOR-I treatment without CNIs the highest (1 year: RR 1.83 vs. CNI, CI 1.45–2.31, $P < 0.001$).
Conclusion: The numerical incidence of post-transplant infections seems to be unaltered by the basic immunosuppressant. However, certain changes do exist (CMV). A more detailed description of infections in future randomized trials should be pursued.

The combination of mTOR-Is and CNIs has the highest immunological potential with the best protection against BPAR

P011 POSTOPERATIVE SERUM CHOLESTEROL-LEVELS PREDICT LONG-TERM OUTCOME AFTER LIVER TRANSPLANTATION

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Introduction and Background: Low serum-cholesterol levels are associated with poor survival in nontransplanted cirrhotic patients independently of the MELD-score. Here we have analysed the effect of serum cholesterol on postoperative outcome after liver transplantation
Methods: From 2007 to 2016 a total of 340 consecutive liver transplant performed at our department were analysed regarding their pre- and postoperative (day 5) serum Cholesterol levels and correlated to postoperative outcome. A cut off of 100 mg/dl was used.
Results and Conclusions: Pre-operative serum cholesterol levels had no effect of patient's survival. However, low serum cholesterol levels were associated with poor long-term outcome. The 5-year survival with a serum-cholesterol of < 100 mg/dl was 50% with a value above the threshold of 72% ($P = 0.002$). Interestingly differences were evident primarily in long-term outcomes, but not in perioperative outcome.

Serum cholesterol may be a valuable marker of long-term-outcome after liver transplantation. In depth analysis have to clarify whether low serum cholesterol serum levels represent poor liver function or whether they may hallmark a unfortunate course of disease independent of liver function.

P012 INFLUENCE OF POSITIVE DUODENAL SWABS ON THE OUTCOME AND PROGRESS AFTER PANCREAS TRANSPLANTATION – ACTUAL GERM SPECTRUM

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Introduction and Background: Pancreas transplantation (PT) shows a higher rate of complications compared with other organ transplantations. Graft thrombosis and intraabdominal infections are the most common causes for relaparatomy. We analyzed intraoperative swabs taken during transplantation. By now we give an overview of the actual microbial results.
Methods: Between 01/2010 and 12/2015 we transplanted 145 pancreas grafts at the Knappschaftskrankenhaus Bochum with 132 simultaneous pancreas-kidney transplantations, 5 isolated pancreas transplantations and 8 pancreas after kidney transplantation. 16 of this were retransplantations. Routine swabs where taken from the organ perfusion solutions, the donor and recipients duodenum, the bladder and from the recipients abdomen.
Results and Conclusions: In total 132 duodenal swabs (DS) were evaluated, 93 separated between donor and recipient, 39 combined. In 96 cases (72.73%) positive microbial results were found. 56 of the donor and 43 of the recipient DS were positive. 72.92% of the DS were positive for Candida (different subtypes), with C. albicans and C. glabrata being most frequently. Likewise Enterococcus, Serratia, Streptococcus, Klebsiella, Stenotrophomonas, Lactobacillus and other germs were detected. 26.52% of the other swabs were positive, primarily with Streptococcus or Staphylococcus. There was no difference in microbial results in the group of retransplantation compared with first PT.

73% of the pancreas were fully functional after transplantation. 13 had been explanted shortly after PT. In 35, 17% cases a relaparatomy was performed. Every third patient showed pancreatitis, wound healing disorders, sepsis or combinations of it.

Woeste et. al already defined positive DS to be a risk factor for intra-abdominal infection. This needs to be verified by further analyzation of our data, in particular to give a recommendation concerning the actual pre-/perioperative antibiotic therapy given during transplantation.

P013 CONTRAST ENHANCED ULTRASOUND OF THE PANCREAS GRAFT

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Introduction and Background: Pancreas transplantation is performed mostly in patients with impaired kidney function or simultaneously with kidney transplantation. Common complications after this kind of major surgery require an imaging method that is not harmful to kidney function.
Methods: A total of 70 B-mode, duplex and CEUS investigations performed using 1 ml of SonoVue (Bracco) on a Siemens Acuson S2000 or GE Logiq S7 ultrasound machine were evaluated in 32 pancreas transplant recipients with normal pancreas transplants, grafts with nonfunction, grafts with proven rejection before and after successful treatment and during a severe pancreatitis and were compared with other diagnostic methods (MR, CT, biopsy). The results were evaluated with the Vuebox (Bracco) software package.
Results and Conclusions: CEUS displays the capillary perfusion of the tissue. Edema of the pancreas graft occurring due to rejection or pancreatitis can impair capillary perfusion, will be reflected in the amount of contrast detected and the dynamics of the influx of the contrast agent.

It is possible to visualize the graft using CEUS. The examination can be easily performed at the patient bedside and can be used several times in a row independent of the kidney function. The method can lead to the earlier diagnosis of the rejection and help to indicate the need for an eventual biopsy. Thus perfusion of the graft can be visualized without detrimental influence on kidney function.

P016 IMMUNOMODULATORY EFFECTS OF EXTRACORPOREAL PHOTOPHORESIS AFTER HEART TRANSPLANTATION

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Introduction and Background: No clear consensus consist on how to use ECP after heart transplantation (HTx). Clinical use of extracorporeal photopheresis (ECP) is based on its ability to induce cell-mediated immune tolerance toward foreign and self-antigens. In this pilot study, we evaluated the stimulatory effects of ECP on immune cells in HTx patients.
Methods: HTx patients received ECP therapy as prophylaxis of rejection (PRX; $n = 7$) or to treat acute cellular rejection (ACR, $n = 5$) or chronic allograft vasculopathy (CAV; $n = 3$). ECP was performed according to a specific treatment protocol for each group. Blood samples were taken before, after the third ECP cycle and two months after the last ECP cycle. Blood samples were analyzed for the tolerance-inducing cell subsets regulatory T cells (T_{regs}), myeloid and plasmacytoid dendritic cells (m and pDCs). The stimulatory effect was calculated from the baseline value without ECP treatment compared with the values after the third ECP treatment and 2 months thereafter.
Results and Conclusions: Our pilot study gave first hints that the response profile between ECP-treated patients with PRX, ACR and CAV differed regarding the cellular parameters mDCs, pDCs and Tregs. A high stimulatory effect for pDCs and mDCs was detected for patients of the PRX (pDCs: 11.1x increase; mDCs: 1.7x increase) and the ACR group (pDCs: 3.7x increase; mDCs: 1.4x increase) two months after the last ECP cycle. ECP-treated patients with CAV showed a lower stimulatory effect two months after ECP treatment for pDCs (1.6x increase) and no effect for mDCs. T_{reg} profile analysis revealed a high stimulatory effect in the CAV and the PRX group (both 1.2x increase) and a moderate reduction in the ACR group (0.9x) two months after ECP treatment. In our pilot study, we showed different stimulatory effects of ECP on DCs and T_{regs} between prophylactic and preemptive ECP therapy after HTx. Immunological monitoring could be valuable to develop an individual ECP therapy strategy in patients without, acute or chronic rejection.

P017 A CASE OF OSTEOMYELITIS IN PATIENT WITH REMAINING ASSIST DEVICE DRIVELINE AFTER HEART TRANSPLANTATION – A CASE REPORT

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Introduction and Background: Implantable ventricular assist devices (VADs) might be a key tool to counter organ scarcity. Despite technological improvements VADs are still related to complications e.g. bleeding, driveline infection, thrombosis or stroke causing an increasing number of patients receiving HTX from device. Due to numerous tissue adhesions HTX is getting technically more challenging. The time-consuming approach often leads to an incomplete removal of driveline and outflow graft material.
Methods: We report about a 49 years old male pat. with ischemic cardiomyopathy who received a VAD in 2013 and HTX in 2014. 1 year later the pat. was admitted to hospital with left sided chest pain. Apart from swelling local findings didn't reveal further signs of inflammation. Inflammatory markers were slightly increased, blood culture sets remained negative. Thoracic CT revealed signs of osteomyelitis in the ventral parts of the left 4th rib. After operative removal osteoid material was sent for microbiol. testing which revealed colonization with Candida and Staph. epidermidis. An anti-infective therapy was initiated. Due to persistent pain despite opioids we reevaluated the thoracic images and a 15 cm long piece of remaining driveline located in the 4th to 5th intercostal space was identified. Indication for driveline removal was set. Afterward a sudden pain relief and decrease of WBC count and CRP was seen and the pat. was discharged.
Results and Conclusions: In long-term VAD support driveline infections are still a key problem. Whether this also affects remaining driveline after HTX is still not known. Due to obligatory immunosuppression after HTX the general risk for infection is increased and the complete VAD excision including the removal of all foreign material seems to be the most appropriate approach. In the described case remaining driveline caused persistent pain and several readmissions to hospital accompanied by social isolation, reduced quality of life, disability to work and a great financial burden for public health system.

KIDNEY

P018 MALIGNANCIES UNDER MTOR-INHIBITOR BASED IMMUNOSUPPRESSION AFTER SOLID ORGAN TRANSPLANTATION – A SYSTEMATIC REVIEW AND METAANALYSIS

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Introduction and Background: Malignancies are one of the major reasons for death with functioning graft in transplantation. In recent years, mTOR-inhibitors were shown to positively influence the occurrence and course of certain tumors. The influence of mTOR-Is on the overall incidence of tumors irrespective of their origin is not entirely clear. This we aimed to investigate using meta-analyses on the most relevant recent transplant trials.
Methods: The current literature was searched for prospective randomized controlled trials in solid organ transplantation. There were 1075 trials screened of which 34 could be included (patients = 12495). The 1-year and longterm incidence of malignancies and biopsy proven acute rejection was assessed in metaanalyses.
Results and Conclusions: A significant reduction of malignancy under mTOR-Is was seen only longterm (1 year: RR 0.82, CI 0.61–1.11, $P = 0.20$; longterm: RR 0.70, CI 0.57–0.85, $P = 0.0003$). This effect remained stable when mTOR-Is were given either without CNIs or in combination with CNIs (mTOR-I w/o CNIs vs. CNIs: RR 0.66, CI 0.48–0.90, $P = 0.0099$; mTOR-I with CNIs vs. CNIs: RR 0.73, CI 0.55–0.95, $P = 0.010$).

Combination of mTOR-Is and CNIs had the lowest incidence of BPARs (1 year: RR 0.68 vs. CNI, CI 0.58–0.80, $P < 0.001$), and mTOR-I treatment without CNIs the highest (1 year: RR 1.72 vs. CNI, CI 1.52–1.95, $P < 0.001$).

After solid organ transplantation patients benefit from an mTOR-I-based treatment regarding malignancy. The combination of mTOR-Is and CNIs provides the best protection against BPARs.

P019 CHARACTERISTICS OF PRE-TRANSPLANT DONOR-SPECIFIC ANTI-HLA ANTIBODIES AND OUTCOME IN KIDNEY TRANSPLANT PATIENTS TREATED WITH A STANDARDIZED INDUCTION REGIMEN

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Introduction and Background: The presence of donor-specific anti-HLA-antibodies (DSA) prior to kidney transplantation (NTX) has been associated with antibody-mediated rejection (AMR) and early graft loss. Uncertainties remain regarding the general applicability of these findings and the optimal choice of induction therapy in DSA-positive patients.
Methods: Day of transplant sera were retrospectively analyzed for the presence of DSA in a cohort of 174 cross-match-negative NTX patients treated with basiliximab induction and tacrolimus-based maintenance immunosuppression. DSA were monitored during the first year post-NTX. Results were correlated with the incidence of rejection and graft loss.
Results and Conclusions: 61 patients (35%) had DSA prior to NTX. We found a higher incidence of AMR in DSA-positive compared with DSA-negative patients (19.7 vs. 8.8%, $P = 0.04$). 5-year graft survival was worse in patients with DSA against both HLA class I and II compared with patients with only HLA class I or II or no DSA (67%, 90%, 90% and 88.1% respectively). Presence of both class I and class II HLA-DSA, individual DSA with mean fluorescence intensity (MFI) >6000 or cumulative MFI >10.000 predicted an increased risk for AMR and graft loss. Multivariate analysis revealed AMR to be the only independent predictor of allograft loss. Loss of DSA 14 days post-NTX predicted excellent allograft survival.
Conclusions: Our study suggests that the presence of DSA against both class I and II HLA as well as high DSA strength prior to NTX predict poor outcome by increasing the risk for AMR. Given the favorable outcome in the majority of DSA-positive patients, our findings call for a differentiated approach toward induction therapy in this patient population.

P020 C5AR1 AND C5AR2 DEFICIENCY IN RENAL ISCHEMIA REPERFUSION INJURY (IRI) AND KIDNEY TRANSPLANTATION IN MICE

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Introduction and Background: In kidney transplantation the early post-transplant ischemia reperfusion injury (IRI) causes rapid complement activation. The complement receptors C5aR1 and C5aR2 serve distinct roles in immune regulation and mediate C5a downstream signals. So far, little is known about the differences between C5aR1 and C5aR2. In this study C5aR1 and C5aR2 deficient mice were tested in renal ischemia reperfusion injury (IRI) and in kidney transplantation (ktx).
Methods: IRI was induced by unilateral clipping of the right renal pedicle for 45 min in C5aR1, C5aR2 deficient and wild type mice (WT; C57Bl/6). Functional magnetic resonance imaging (MRI) to analyze renal perfusion was performed at different time points (d1, d7, week 3) and glomerular filtration rate (GFR) were assessed by inulin clearance after contralateral nephrectomy of the healthy kidney. Renal morphology, inflammation and renal fibrosis were investigated by immunohistochemistry. In a second model isogenic ktx with prolonged cold ischemia time of 90 min was performed. C5aR1, C5aR2 deficient mice served as donors for WT recipients. In addition, WT donor kidneys were transplanted on C5aR1, C5aR2 deficient mice. WT isogenic ktx served as control.
Results and Conclusions: Both C5aR1 and C5aR2 deficiency was beneficial in the IRI model with reduced inflammation. C5aR2 showed strong attenuation of renal fibrosis 3 weeks after IRI. C5aR2 deficient mice showed significantly improved renal perfusion measured by arterial spin labeling (ASL) in functional MRI. In the ktx model C5R2 deficiency of the recipient showed the best renal morphology with attenuated renal injury.

C5aR2 deficiency attenuates renal damage in IRI and ktx via improved renal perfusion and regeneration.

P022 5-YEAR FOLLOW-UP RESULTS OF THE HERAKLES STUDY: SUPERIOR RENAL FUNCTION AFTER EARLY CONVERSION TO AN EVEROLIMUS-BASED CALCINEURIN INHIBITOR FREE REGIMEN

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Introduction and Background: To follow up on renal function (GFR) 5 years after kidney transplantation (KTx) in patients (pts) on immunosuppressive regimens with different calcineurin inhibitor (CNI) exposures.
Methods: 1 year, prospective, open-label, randomized, controlled multicenter study with observational follow-up (FU) to Mo 60 post-Tx. After induction therapy all pts received cyclosporine A (CsA), enteric-coated mycophenolate sodium (EC-MPS) and steroids. 3 Mo post-Tx, 499 pts were randomized 1:1:1 to either a) continue standard CsA (100–180 ng/ml) + EC-MPS ($n = 166$) (STD) or convert b) to a calcineurin inhibitor (CNI)-free regimen with everolimus (EVR) (5–10 ng/ml) + ECMPS ($n = 171$) or c) to a CNI-reduced regimen with EVR (3–8 ng/ml) + reduced CsA (50–75 ng/ml; $n = 162$). All pts continued on steroids according to centers practice. In total 77% of pts completed the FU period.
Results and Conclusions: GFR (Nankivell, ITT) was similar at randomization 3 Mo post-Tx and had significantly improved at Mo12 by +5.6 ml/min (95% CI:[+2.9;+8.3]; $P < 0.001$) and remained significantly improved by +6.7 ml/min in favor of the CNI-free regimen after 5 years (ANCOVA, LOCF, $P < 0.001$; Tab1). There was no significant difference between the CNI reduced and STD groups ($P = 0.2490$). Benefit on renal function was highest for nonswitcher pts: CNI-free Mo60 GFR Nankivell was 78.33 ml/min vs. 64.33 ml/min for CNI-reduced and 61.68 ml/min for STD pts (unadjusted mean eGFR, LOCF; $P < 0.0001$; Tab1). Mean CsA C0 levels at Mo60 were 80 ng/ml in CNI-reduced group and 109 ng/ml in STD group (ITT).
Conclusions: CNI-free as well as reduced CNI in combination with EVR represent both efficacious regimen. CNI-free regimen was associated with significant higher eGFR maintained for 5 years post-Tx. The results of this large trial confirm previous reports of improved GFR after CsA withdrawal with EVR in combination with EC-MPS.

P023 IMMUNOSUPPRESSANT SERUM LEVELS AND VARIABILITY, NON-ADHERENCE, AND LATE REJECTION IN RENAL TRANSPLANT RECIPIENTS

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Introduction and Background: Serum variability and lower average levels of immunosuppressant medication as well as nonadherence to IS medication are found to be associated with rejection episodes and organ loss after successful transplantation. High serum variability can be due to nonadherence, but also to pharmacokinetic factors. The main aim of the study was to investigate whether IS serum variability and % of IS serum levels < target level are good biological markers of IS medication nonadherence and graft rejection. We hypothesize, that rejections, serum variability, % of IS serum levels < target level and self-reported nonadherence will be positively associated with each other.
Methods: IS serum variability, % of low levels, self-reported adherence and rejection episodes were assessed in 267 adult renal recipients from the transplantation centers Erlangen, Hannover and Köln.
Results and Conclusions: The rate of late allograft rejection was 13.5%. As expected, IS serum level variability and % of IS serum levels < target level as well as self-reported nonadherence were significantly positively associated with rejection. Contrary to our expectations, IS serum level variables were not associated with self-reported nonadherence.

High IS serum level variability and high % of levels < target value are not equivalent to self-reported nonadherence (they are not even related), but they all contribute to rejections. Serum values do not only display adherence behavior, but increased variability of IS levels can also be caused by nonbehavioral pharmacokinetic issues. Different measures cover different aspects of nonadherence. Monitoring kidney transplant recipients for all of these aspects is of high value to identify patient at risk. These patients should be screened for pharmacokinetic and adherence issues and receive further psychosomatic evaluation and treatment if necessary to reduce late graft rejection rates.

P024 ASSOCIATION BETWEEN PULSE PRESSURE AND PATIENTS AND GRAFT SURVIVAL IN RENAL TRANSPLANTATION

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Introduction and Background: Systolic blood pressure (SBP) and diastolic blood pressure (DBP) predict graft and patient survival in renal transplant recipients. Pulse pressure (PP) has been associated with cardiovascular and renal endpoints in epidemiological studies and clinical trials.
Methods: In this large retrospective study from CTS, adult recipients of first deceased donor kidney grafts transplanted between 1995 and 2014 were included into the analysis for graft and patient survival if the patient had both a functioning graft and a known blood pressure reading at year 1.
Results and Conclusions: In 38 433 renal transplant recipients a higher PP at year 1 was significantly associated with inferior death-censored graft survival. Similarly, higher PP was significantly associated with lower patient survival. The extent of this association was overall similar to the association of SBP with patient survival, but stronger for PP than for DBP, especially in the age group of 60 years and older, where DBP was no longer predictive and SBP was less predictive for patient survival. In a further analysis in the recipient age group ≥ 60 years we found, that if the SBP is <140 mmHg a higher PP of ≥60 mmHg goes along with inferior patient survival, whereas if the SBP is ≥140 mmHg, a normal PP is associated with normal patient survival, highlighting the superior impact of PP on patient survival in elderly patients. Higher PP predicts higher mortality due to cardiovascular causes in elderly renal transplant recipients.

In our analysis we found evidence that PP 1-year post-transplant is a superior predictor of patient survival, especially in elderly renal transplant recipients and a good predictor of death-censored graft survival in a first renal transplant recipient from a deceased donor. Furthermore, combined analysis of SBP and PP has shown, that high PP adds information to SBP with regard to prediction of patient survival in elderly renal transplant recipients.

P028 MR-ANGIOGRAPHY FOR PRE-OPERATIVE ASSESSMENT OF LIVING KIDNEY DONORS COMPARED WITH INTRAOPERATIVE FINDINGS DURING LAPAROSCOPIC LIVING DONOR NEPHRECTOMY

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Introduction and Background: Preoperative evaluation of the vascular anatomy of living kidney donors (LKD) is crucial. This retrospective study was designed to evaluate the sensitivity of contrast enhanced MR-angiography (CE-MRA) for the evaluation of LKD in the detection of renal vascular variants.
Methods: Preoperative CE-MRA findings of patients who underwent laparoscopic living kidney donation in the years 1997–2005 in our center were evaluated and compared with intraoperative findings. The data was used to calculate sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of CE-MRA in detecting multiple renal arteries and veins in LKD.
Results and Conclusions: CE-MRA findings and surgery reports of 68 patients were evaluated in the study ($n = 68$).

Multiple renal arteries were found in 15 patients (22.06%). Nine of those were detected during preoperative CE-MRA (sensitivity 60%, specificity 100%, PPV 100%, NPV 89.83%). CE-MRA seems to be less sensitive in detecting multiple veins. There were 4 patients with two renal veins (5.88%). None of those additional veins were detected in CE-MRA (sensitivity 0%, specificity 100%, PPV 0%, NPV 94, 12%).

CE-MRA is suitable for the noninvasive investigation of living kidney donors as it is a useful alternative to CTA avoiding radiation or nephrotoxic contrast agents. However, the sensitivity in detecting multiple renal arteries is lower compared with CTA. Vascular variants especially in veins may be missed. New MRA protocols promise to improve the sensitivity.

P030 INDIVIDUALIZED LATE STEROID-WITHDRAWAL FOLLOWING ABO-INCOMPATIBLE RENAL TRANSPLANTATION

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Introduction and Background: Currently, there is no sufficient evidence to justify steroid withdrawal following ABO-incompatible (ABOi) renal transplantation. We compare a group of patients with late steroid withdrawal (group A) with a group of patients, who remained on triple immunosuppression including low-dose steroids (group B).
Methods: To date, we performed 43 ABOi kidney transplantations at our centre. An individualized steroid withdrawal was carried out in a selected group of 11 patients with stable graft function (serum creatinine <1.5 mg/dl, urinary albumin/creatinine ratio <200 mg/g), no previous rejection episode, and absence of donor specific HLA antibodies (DSA). We compared them with patients on triple immunosuppression ($n = 31$). The observational period of group A started at the beginning of steroid withdrawal and after the first year post-transplant for group B adapted to timing of steroid withdrawal. The minimum follow-up period was 6 months.
Results and Conclusions: Patient characteristics were not different between groups. Steroid withdrawal was initiated at a median of 14.5 (range 10–34) months and took a median of 4.5 months (range 1–22). The observation time was 44 (median, range 23–66) vs. 20 (12–81) months in group A and B, respectively ($P = 0.06$). Patient survival was 100% in group A and 94% in group B ($P = 0.537$). Death-censored graft survival was 100% in group A compared with 90% in group B ($P = 0.28$). Incidence of biopsy-proven rejection episodes was 17% compared with 0% in group A and B, respectively. At the end of follow-up, serum creatinine was 1.53 ± 0.59 mg/dl in group A and 1.5 ± 0.69 mg/dL in group B, respectively ($P = 0.934$). In group A, one patient developed *de novo* DSA, whereas none of the patients of group B developed *de novo* DSA.

In conclusion, individualized late steroid-withdrawal is feasible at an acceptable rate of rejection episodes. Close monitoring of renal function and DSA during and after steroid-withdrawal is recommendable. Further prospective trials are required to better identify patients at low risk.

P033 THERAPEUTIC EQUIVALENCE OF GENERIC TACROLIMUS FORMULATIONS IN ADULT RENAL RECIPIENTS

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Introduction and Background: Generic formulations (GEN) of immunosuppressive drugs are approved on the basis of bioequivalence in healthy volunteers. It has been suggested that bioequivalence should also be shown in transplant patients, especially for critical dose drugs like tacrolimus. A review of published literature was undertaken to identify articles comparing GEN with innovator tacrolimus (PRG) in adult *de novo* renal recipients for evidence of comparable efficacy and safety.
Methods: PubMed, Google Scholar and congress proceedings were systematically searched to identify all English articles from 2005 to Dec 2015. Acute rejection (AR), graft survival (GS), and safety for each GEN were compared with PRG using statistics provided in the articles and by Fisher's exact test.
Results and Conclusions: >4000 articles were captured resulting in 24 articles reporting *de novo* renal cohorts treated with 6 different GEN. Only 11 cohorts included a comparative PRG group: 8 GE*N* Hexal (287 patients treated/163 patient years exposure/274 patients with clinical outcome), 2 GEN Teva (54/27/54), 1 GEN Chong Kun Dang (45/10/45). Mean/median follow-up was 42 days to 1 year. All except one GEN v PRG comparisons were not significant.

Most studies were retrospective with historical controls. Only 3 studies were prospective, and randomised with a parallel PRG control group. 5/11 articles were congress abstracts. The single study reporting a significant difference in AR used a historical control group and the GEN group size was much smaller than PRG (39 v 159).

Although there is a shortage of well-controlled randomised studies, the currently available patient data support therapeutic equivalence of generic tacrolimus formulations to the innovator product in the adult *de novo* renal transplant setting.

P034 RESULTS FROM SPARTACUS – A MULTICENTRE, PROSPECTIVE RANDOMIZED STUDY: EVALUATION OF PK PROFILE AND CLINICAL OUTCOMES WITH TACROLIMUS HEXAL® VERSUS PROGRAF® IN *DE NOVO* RENAL TRANSPLANT RECIPIENTS

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Introduction and Background: As only few data exists for PK profile, safety and efficacy of generic Tacrolimus (TAC) vs reference drug in renal transplant recipients (RTxR), SparTacus study was designed to compare PK profile of TAC Hexal® with Prograf® in RTxR and to evaluate respective renal function.
Methods: 76 *de novo* RTxR were randomized to this prospective two-phase open-label study, to receive either TAC Hexal® ($n = 35$) or Prograf® ($n = 41$), both with in combination with enteric-coated mycophenolate sodium, steroids, and basiliximab induction. Starting dose of TAC was 0.15 mg/kg/day, adjusted to target trough levels (C0) as follows: 8–12 ng/ml from Tx to month (M) 1; 5–10 ng/ml up to M3; and 5–8 ng/ml up to M6. Primary objective was to demonstrate comparable PK at M1 post-Tx and noninferior renal function (GFR, Nankivell) at M6 in TAC Hexal® vs Prograf®. Efficacy and safety outcomes at M6 were also assessed.
Results and Conclusions: 44 patients were available for PK analysis. At M1, PK parameters [dose-normalized TAC 12-h-AUC (h/10^3XL), Cmax (1/10^3XL) and mean 12 h TAC C0 (μg/L)] were comparable between both groups. At M6 renal function showed better results for TAC Hexal® (n = 24) vs Prograf® ($n = 27$) with an unadjusted mean of 72.1 vs 63.4 ml/min and adjusted mean of 47.7 ml/min TAC Hexal® vs Prograf® 38.6 ml/min. This between treatment difference of 9.05 ml/min (95% CI 0.25–17.85) was noninferior ($P = 0.0003$) and superior ($P = 0.0442$) in TAC Hexal® vs Prograf®. The Incidence of composite efficacy events and the individual components were comparable in both groups. Incidence of AEs was comparable between TAC Hexal® vs Prograf® (AEs: 97.1% vs 97.4%; SAEs: 54.3% and 43.6%). In conclusion TAC Hexal® vs Prograf® had a similar PK profile along with better renal function and comparable efficacy and safety in *de novo* RTxRs.

P035 FIRST TREATMENT OF RELAPSING RAPIDLY PROGRESSIVE IGA NEPHROPATHY WITH ECULIZUMAB AFTER LIVING KIDNEY DONATION – A CASE REPORT

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Introduction and Background: IgA Nephropathy (IGAN) is the most common type of glomerulonephritis worldwide. Treatment can be challenging, its crescent and progressive form is rare but can rapidly lead to end stage renal disease. Patients receiving kidney transplantation due to IGAN experience a recurrence in up to 60%, leading to chronic graft failure. The pathology is complex and not completely understood, but complement components as C3, C4d and C5 seem to be involved. We present a case of a young living donation recipient who suffered from ESRD due to rapid progressive IgA nephropathy and who incurred rapid recurrence in the graft.
Methods: In September 2014 a 28 year old male patient was hospitalized due to IgA-Nephropathy with crescents. Cyclophosphamide, steroids and 3 cycles of plasmapheresis could not stop end stage renal disease.

After 8 months of peritoneal dialysis the patient received blood group compatible living donation by his 57 year old mother. Immunosuppression consisted of tacrolimus, mycophenolic acid and steroids without induction therapy. 2 months later acute graft failure occurred, kidney biopsy was performed and showed recurrence of progressive IGAN.

Cyclophosphamide was given in a cumulative dose of 6 g in addition to tacrolimus and steroids (1 mg per kg bodyweight), but graft function could not be restored. As a rescue therapy Eculizumab was started with a single dose of 900 mg once weekly for 4 times, according to singular case reports in native kidneys when hemodialysis was already initiated. After a cumulative dose of 1800 mg Eculizumab hemodialysis was stopped, but kidney function did not recover.
Results and Conclusions: In this case Eculizumab was not effective in progressive IGAN recurrence after transplantation. Due to multiple infectious complications and lymphocele after transplantation, therapy was started when hemodialysis already was required. Maybe earlier start of therapy is more effective, further investigation is required.

P036 DYNAMICS AND DIAGNOSTIC RELEVANCE OF SERUM UROMODULIN LEVELS IN KIDNEY GRAFT RECIPIENTS

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Introduction and Background: The glycoprotein Uromodulin is exclusively produced in renal tubular cells of the ascending limb of Henle's loop. A recently developed ELISA for the quantification of UMOD in serum (sUMOD) was used to assess the tubular function of kidney grafts. In this study we compared tubular and glomerular graft function in uncomplicated post-transplant (Tx) courses and in rejection (R) crises.
Methods: 90 recipients of kidneys from deceased donors were included in this study. Quantification of sUMOD was done by ELISA (EUROIMMUN). Albumin- and IgG-uria were measured by nephelometry to characterize glomerular graft function. Basic immunosuppression included cyclosporin A, steroids and azathioprine. R was divided into **s**teroid-**s**ensitive (**ssR**) and **s**teroid-**r**esistant (**srR**).
Results and Conclusions: Recipients' pre-Tx sUMOD levels were close to the detection limit (2.3 ng/ml; normal values: 222 ± 95 ng/ml). Thereafter a comparable sUMOD increase was observed in immediate graft function (IGF, $n = 60$, median (m) 46 ng/ml) and in delayed graft function (DGF, $n = 30$, m 41 ng/ml) until day 5 post-Tx. Between days 7 and 25 post-Tx significantly different sUMOD levels were measured due to a further sUMOD increase in IGF (m 58 ng/ml) and a decrease in DGF (m 34 ng/ml). After the end of dialysis treatment of DGF patients (m day 13 post-Tx) sUMOD levels did not recover until day 25 post-Tx (end of observation). Glomerular proteinuria disappeared with improved graft function.

In R glomerular damage (proteinuria) was stronger than tubular damage (assessed by sUMOD levels). The pre-R period was characterized by increasing amounts of urinary albumin and IgG but reduced sUMOD levels (srR: m 47 ng/ml, ssR: m 43 ng/ml). During a successful therapy glomerular proteinuria disappeared but pre-R reduced sUMOD levels remained lower in srR (m 48 ng/ml) compared with increasing sUMOD levels in ssR (m 60 ng/ml) indicating a long-lasting tubular impairment in severe R. We suppose that sUMOD is a biomarker for the tubular function of kidney grafts.

P037 ECULIZUMAB – HIGH PRICE TREATMENT FOR PRICELESS KIDNEY GRAFT FUNCTION IN A PATIENT WITH ATYPICAL HEMOLYTIC UREMIC SYNDROME SHORTLY AFTER ALLOGENIC KIDNEY RE-TRANSPLANTATION

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Introduction and Background: Atypical hemolytic uremic syndrome (aHUS) is a rare disease and even less common in patients after kidney transplantation. It is characterized by thrombotic microangiopathy (TMA), which leads to low platelet counts, anemia and acute renal failure. Especially patients developing aHUS in the post-transplantation period are on high risk for transplant failure. The therapy of aHUS contains plasmapheresis and the recently launched treatment with high priced Eculizumab, a C5 compliment antibody. However, there is still a lack of experience in the Eculizumab-treatment in patients after kidney transplantation.
Methods: We present a case report of a 74-year old woman with end stage renal disease (ESRD) caused by membranoproliferative glomerulonephritis (MPGN), who received her second kidney transplantation in our center and developed the symptoms of an hemolytic uremic syndrome shortly after the transplantation. A kidney biopsy showed clearly thrombotic microangiopathy, but the treatment with plasmapheresis showed no improvement in the renal function. After starting therapy with Eculizumab weekly her symptoms as well as the graft function immediately improved and continued until we were able to discharge the patient with acceptable renal function.
Results and Conclusions: Eculizumab appears to be an effective treatment of aHUS also in patients recently after kidney transplantation, but still there is no clear consensus of how long the treatment should be given. Long time follow-up of these patients will help to assess the accurate therapy.

P038 TREATMENT WITH LITHIUM REDUCE ISCHEMIA-REPERFUSION INJURY IN AGED AND STEATOTIC LIVER IN RATS

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Introduction and Background: Lithium has been widely used in the treatment of mental illness. It acts on many stress and survival pathways especially on autophagy pathways. Recent studies showed that treatment with lithium can reduce ischemia-reperfusion (I/R) injury in liver via a modulation of MAPK and GSK3b pathways. These pathways are also affected in steatotic and aged, so-called marginal livers, albeit to a different extent. In this study, we aimed to compare the effects of lithium in selective warm I/R model of normal, aged and steatotic liver in rats.
Methods: Normal, steatotic (induced by feeding a high fat and methionine-choline reduced diet for 14 days) and aged (1.5–2 years) rats received lithium (2 mmol/kg/day, 3 days before and after ischemia). Selective warm ischemia/reperfusion was induced by clamping the hepatoduodenal ligament of the left lateral and median lobe for 60 min. Animals were observed for 30 min, 6 h and 24 h ($n = 4$–6/group). Read-out parameters consisted of serum liver enzyme levels, HMGB1 translocation and release, liver neutrophil infiltration, MAPK, GSK3b, Caspase 3, mTOR, LC3 and p62 expression levels.
Results and Conclusions: Treatment with lithium protected against I/R injury in normal, steatotic and aged liver. The effect was most pronounced in aged livers followed by the steatotic liver and less pronounced in normal liver. Lithium treatment reduced inflammation and apoptosis via a modulation of MAPK pathway, as well as induced autophagy and reduced necrosis via a modulation of GSK3b pathway.

On the basis of these data, we conclude that treatment with lithium may be a simple way for protecting against I/R injury in steatotic and aged liver. Further work is needed to elucidate potential common dysregulatory events for a more precise targeting of IRI in marginal livers.

LIVER

P039 AT1R ANTIBODIES AT 1-YEAR NEGATIVELY IMPACT 5-YEAR NATIVE RENAL FUNCTION IN LIVER TRANSPLANT RECIPIENTS

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Introduction and Background: Angiotensin II Type-1 Receptor (AT1R) antibodies have been associated with pulmonary hypertension, renal allograft loss, and fibrosis progression in liver allograft recipients especially if combined with HLA donor-specific alloantibodies (DSA). However, long-term outcome in liver allograft recipients is not only impacted by allograft fibrosis but also renal function. We therefore sought to determine if native renal function was impacted in liver allograft recipients by the presence of AT1R antibodies.
Methods: Primary liver allograft recipients at Baylor University Medical Center from 1/00 to 4/09 had their prospectively collected pretransplant (1269 patients) and year-1 post-transplant (795 patients) serum tested retrospectively for AT1R (>10) antibodies. AT1R-antibody testing was accomplished with standardized solid phase assay. Since AT1R antibodies have been associated with hypertension this factor was not controlled for in multivariable modeling.
Results and Conclusions: Pretransplant AT1R did not change the median delta creatinine from pretransplant to 3-months post-transplant. In patients with vs. without AT1R at 1-year post-transplant a median unadjusted change in MDRD6 of −5.4. vs. −1.1 ml/min ($P = 0.01$) was found. In multivariable analysis when controlling for diabetes (DM) and calcineurin inhibitor (CNI) use at 1-year AT1R-Ab at 1-year remained statistically significantly associated with a decline in GFR (calculated by MDRD6) from year 1 to 5 post-transplant ($P = 0.018$, Table 1). This decline may have been more pronounced ($P = 0.06$) in patients on a CNI; however, the decline was most pronounced in diabetic patients with AT1R at year-1 ($P = 0.004$). AT1R antibodies post-liver transplant are associated in multivariable analysis with an increased risk of native renal function decline especially in diabetic patients. AT1R positive patients may benefit from CNI free immunosuppression.

P040 PROGRESSION OF FAMILIAL AMYLOIDOSIS AFTER DOMINO LIVER TRANSPLANTATION IN DONOR AND RECIPIENT

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Introduction and Background: Liver transplantation (LT) is the first-line-therapy in patients with familial amyloidosis (AP), although the disease may worsen after LT. Furthermore, there are reports about transmission of disease in domino recipients (DR). Aim of this work was to evaluate a single center cohort of AP and DR after domino-LT.
Methods: Data were collected from patients records. Electroneurography, transthoracic echocardiography (TE), cardiac MRI and organ biopsy results were evaluated.
Results and Conclusions: The cohort includes 24 AP (11 Val30Met, 13 non-Val30Met) and 23 DR. Only patients with available 5-year follow up data after LT were included $n = 14$ AP (8 male), age 36-61 years, survival 4.7-12.9 years, signs of PNP in 14/14, cardiac involvement in 9/14 (4 proven by biopsy, 5 suspected by MRI, scintigraphy or TE); $n = 13$ DR (11 male), age 46-69 years, survival 4.7-15.2 years.

In AP electroneurography showed a progress in 64.2% (9/14 patients, 5 with Val30Met) after 3.7 (1.1-7.9) years post-LT, only one showed an improvement. 7 patients reported subjective worsening of symptoms.

Cardiac aggravation was seen in 12 patients in TE. In 2 patients (both Val30Met) there was a suspected diagnosis of cardiac amyloidosis, one patient received a pacemaker. Increase of deposits was shown in 2 patients (both non-Val30Met) by cardiac MRI. 1 of 3 patients (non-Val30Met) showed first signs of new deposits after heart transplantation in MRI.

In the DR cohort rectal biopsy samples showed amyloid deposits in 2 patients after 7.9 and 9.9 years. Gastrointestinal symptoms occurred after 4 and 11 years, symptoms of PNP after 3 and 7 years. One patient died after 12 years because of de-novo-amyloidosis.

Most AP showed an aggravation after LT. Considering the availability of new therapeutic drugs, the optimal timing of LT needs discussion. In DR, de-novo-amyloidosis occurs earlier than expected. Therefore, recipients for DLT need to be carefully selected.

P042 HUMAN HEPATIC *ATP7B* KNOCKOUT CELLS EVADE TOXIC COPPER BY DOWNREGULATION OF *CTR1*

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Introduction and Background: Wilson Disease (WD) is an inherited autosomal recessive disorder caused by mutations in the *ATP7B* gene encoding for a copper (Cu) efflux pump. Loss of function impedes hepatic Cu excretion via the bile and ceruloplasmin. WD patients show high Cu accumulation in the liver and brain and present heterogeneous symptoms. Therapy with chelating agents can attenuate the course of disease. Orthotropic liver transplantation remains the only curative therapy. The molecular mechanisms following long-term Cu exposure have not been explored using a human hepatic cell line that lacks functional *ATP7B* expression.
Methods: HepG2 *ATP7B* KO cells were grown in media containing various Cu concentrations. Cell growth was determined by trypan blue stainings. mRNA expression was measured by RT-qPCR analysis. Cell viability was assessed by MTT assay. Intracellular Cu concentrations were determined by atomic absorption spectrometry (AAS). Ctr1 protein expression was analyzed by flow cytometry and Western blot (WB) analysis.
Results and Conclusions: KO cells could be propagated in cell culture media containing elevated Cu for more than 100 days, however at a reduced proliferation rate. A high cell survival of up to 12-fold was observed in the cells at highest Cu concentration (1 mM) as compared to control (36 $\pm$ 4% and 3 $\pm$ 2%, respectively). RT-qPCR analysis of various genes involved in Cu homeostasis indicated that *CTR1* mRNA expression was consistently down-regulated by 66.1 $\pm$ 3% following day 10 of Cu exposure. Concomitantly, a significant decrease of total CTR1 protein was observed that was reversed when cells were regrown in standard media. Our results suggest that human hepatocytes which lack *ATP7B* can evade long term toxic Cu exposure by a decreased expression of *CTR1*, a transporter known to be essential for basolateral Cu uptake. This makes *CTR1* an interesting new target for therapy of WD.

P043 HEPATOCYTE TRANSPLANTATION TO THE LIVER VIA THE SPLENIC ARTERY IN A JUVENILE LARGE ANIMAL MODEL

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Introduction and Background: Hepatocyte transplantation (HcTx) has shown promising results for treatment of metabolic liver disease in newborns and children. The most common route for application is the portal vein, which however is difficult to access in newborns. Easier accessible routes are needed to establish HcTx for clinical routine. The spleen has already been studied as alternative implantation and application site for hepatocytes. We here investigate the feasibility of HcTx via an interventionally placed catheter in the splenic artery in a juvenile pig model.
Methods: Göttingen minipigs (6–13 kg) were repetitively infused with human hepatocytes into the splenic artery via catheterization of the femoral artery. The animals were sacrificed either directly after cell infusion ($n = 2$), two days after infusion ($n = 1$) or 14 days after infusion ($n = 1$). The splenic and portal venous blood flow was controlled via color-coded Doppler sonography. Computed tomography was performed after the second cell infusion and at the end of follow up in the animal scarified 14 days after HcTx. Blood samples for clinical chemistry were taken before and after transplantation. Tissue samples from the liver, spleen, and lung were stained for human CK18.
Results and Conclusions: Catheter placement was feasible in all cases. Repetitive transplantation of 1.00E+08 cells per kg BW per session was possible without adverse effects on blood flow in portal vein or splenic artery. In one animal, partial thrombosis was observed in the distal splenic artery at day two after infusion, completely resolving during the follow-up period. Immunohistochemistry demonstrated cell translocation through the portal-venous system into the liver, beginning directly after infusion. Smaller numbers of cells relocated into the lung.

In conclusion, our results demonstrate that HcTx via interventional access to the splenic artery is feasible in juvenile minipigs. The splenic route should therefore be further evaluated as interventional approach for HcTx.

P044 IMPACT OF LIVING DONOR BILE DUCT ANATOMY ON DONOR BILIARY COMPLICATIONS

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Introduction and Background: In the US and Western Europe, living donor liver transplantation is an option to extend the limited donor organ pool. Whereas in Asian countries cadaver donations are not performed for religious reasons, living donation is being controversially discussed in the North America and Western Europe because of donor morbidity and increased biliary complications in the recipient. In this study, we investigated the impact of donor biliary anatomy on biliary complications in living donors.
Methods: We performed a retrospective investigation of the biliary anatomy of all adult living liver donors from 2004 to 2015 at the liver transplantation center of the Department of General, Visceral and Vascular Surgery of the University Hospital Jena. Preoperatively performed MRCP examinations have been re-evaluated and classified according to the classification by Huang et al. We included a total number of 92 patients aged between 20 and 63 years with a median age of 40.6 years. Only right split (segments V-VIII) livers of 40 men and 52 women have been used. MRCP is a mandatory part of the step-wise concept for donor evaluation in preparation for any planned living donation.
Results and Conclusions: 65.2%, 15.2%, 17.4% and 2.2% of the 92 patients were classified as type A1, A2, A3 and A4, respectively, according to the classification of Huang et al. The donor mortality was 0%. There were no grade IV and V donor complications according to the Clavien classification.

Complex biliary anatomy is not per se a contraindication against living donation. Very good living donor results can be achieved in Germany by careful donor evaluation and selection, excellent surgical technique and interdisciplinary team work.

P045 ONE LIVER FOR THREE RECIPIENTS – THE FIRST CASE OF DOMINO-SPLIT-LIVER TRANSPLANTATION IN MAPLE SYRUP URINE DISEASE (MSUD)

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Introduction and Background: The enzymatic defect in MSUD results in accumulation of neurotoxic metabolites of branched-chain amino acids (BCAA). Liver transplantation (LTX) has shown to be a curative strategy in patients nonresponsive to diet. Because of sufficient enzyme activity in extrahepatic tissues in healthy people, the MSUD liver graft is a suitable domino organ. Here, we present the first case of a technical challenging ex-situ split of a MSUD domino-organ transplanted into 2 pediatric recipients.
Methods: The domino-graft donor was a 21-year female (58 kg) suffering from MSUD with recurrent metabolic derailments despite strict diet. Preoperative evaluation revealed an absent infrahepatic V. cava with a complete venous drainage by the azygos/hemiazygos system. Hepatectomy was performed at the intersection between suprahepatic V. cava and hepatic veins, centric transection of portal vein and bile duct and division of the A. hepatica propria. The organ was allocated to a 14-year-old girl (55 kg) with primary sclerosing cholangitis. Due to excellent organ quality and feasible anatomy a backward split for a girl of 3 months (5 kg) with biliary atresia in bad condition was performed. Splitting of the domino-graft resulted in a left-lateral (200 g) and a right-extended graft with partial segment IV resection because of an aberrant bile duct from left side (740 g). Left-lateral LTX was done in standard technique. Right-extended LTX was performed in piggy back technique after reconstruction of the right, middle and segment I vein with an iliac vein graft.
Results and Conclusions: The postoperative course was without relevant complications and the 3 recipients were discharged on postoperative day 28, 29, and 45, respectively, with good organ function. BCAA in plasma were normal in the 2 domino-graft recipients, the MSUD patient showed mildly elevated but stable BCAA concentrations despite an unrestricted diet. Split-Domino-LTX enabled successful transplantation of 3 patients of the waiting list with only one deceased donor graft.

P048 MUNICH RESECTION CRITERIA (MUCRES) AS A SELECTION CRITERION FOR RESECTION OR TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA CONFINED TO THE LIVER

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Introduction and Background: Liver resection and liver transplantation are potentially curative treatment options for hepatocellular carcinoma. Available criteria, such as the MILAN criteria, largely rely on number and sizes of lesions but have a low selectivity in terms of outcome and are not helpful to decide, who should be resected and who should primarily receive a transplant.

We have developed simple criteria based on inflammatory markers and liver function tests which differentiate HCC patients with good and poor oncological outcome after liver resection.
Methods: Patients with HCC confined to the liver undergoing liver resection and/or transplantation were included into the analysis. Patients were grouped in inside and outside the Munich Resection Criteria (MucRes).
Results and Conclusions: Survival of patients undergoing liver resection ($n = 150$) within the MucRes showed a 5-year-survival of 73.5% as compared to patients outside the MucRes 36.8%, $P < 0.001$. Liver transplant patients ($n = 109$) within the MucRes showed a 5-year-survival of 67.5% similar to patients outside the MucRes 75.7% (n.s.). The MucRes was independent of the MILAN criteria.

The Munich Resection Criteria differentiates well between patients with good oncological outcome after resection and those with poor oncological outcomes, who should primarily receive a transplant.

P050 ASSOCIATION BETWEEN HELICOBACTER PYLORI AND END-STAGE LIVER DISEASE IN PATIENTS UNDERGOING LIVER TRANSPLANTATION

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Introduction and Background: Various intestinal and extra-intestinal human diseases are known to be associated with Helicobacter pylori. Recently, Helicobacter pylori genomic DNA was detected in liver tissue of patients suffering from chronic liver diseases suggesting an effect of Helicobacter pylori on the progression of these diseases. Of note, the majority of these data come from Asia, northern Africa and southern Europe where the prevalence of Helicobacter pylori is known to be high. In this study, we examine the role of Helicobacter pylori in a northern European patients undergoing liver transplantation for end-stage liver diseases.
Methods: We conducted a retrospective study where we analyzed explant liver tissue of patients who underwent liver transplantation at the University Hospital of Muenster. DNA was extracted from formalin-fixed explant livers. Samples were consecutively analyzed for Helicobacter pylori status using PCR.
Results and Conclusions: A total of 50 patients (mean age 50.8 $\pm$ 11.1; 19 females) were included in this study. DNA was extracted out of each liver sample. Interestingly, no Helicobacter pylori-DNA was detected in any of liver tissues in our patient cohort.

In conclusion, our study suggests that Helicobacter pylori might not play a crucial role in the pathogenesis and progression of chronic liver disease in northern European population. Further studies are warranted to clarify the role of Helicobacter pylori in liver disease progression.

P051 ISOLATED SOLITARY SPLENIC METASTASIS FROM HEPATOCELLULAR CARCINOMA AFTER LIVER TRANSPLANT: A CASE REPORT

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Introduction and Background: Isolated splenic metastasis of hepatocellular carcinoma (HCC) after liver transplant is exceedingly rare. This is the second report of post-liver-transplant (LTx) spleen metastasis all over the world. Treatment of solitary extrahepatic metastasis from HCC after LTx is not standardized and will be discussed.
Methods: A 76-year-old women with a history of hepatitis-C-related cirrhosis with HCC in segment VII of the left lobe of the liver received an orthotopic liver transplant. 32 months after LTx isolated spleen metastasis was diagnosed by abdominal wall computed tomography, and the patient received total splenectomy. The histopathologic examination confirmed the lesion as a metastasis from the HCC. Immunosuppressive regimen was not changed, since LTX the patient received mTOR-inhibitors.
Results and Conclusions: Immunosuppressive regimen has not been changed postoperatively, since LTx the patient received mTOR-inhibitors and mycophenolate. The following postoperative course was uneventful and the oncologic follow-up examination showed no pathologic results so far. Surgical treatment in isolated metastasis like splenic metastasis from HCC cancer patients after LTx is an individual but successful treatment option.

P053 PULSE WAVE VELOCITY (PWV): A RISK FACTOR FOR CARDIOVASCULAR DISEASE AFTER PEDIATRIC LIVER TRANSPLANTATION (PLTX)?

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Introduction and Background: Today pediatric liver transplantation is the standard therapy for end stage liver disease in children. One challenge that lies ahead is to reduce the side effects of immunosuppression, that among others lead to an increased risk for cardiovascular disease. In adults the pulse wave velocity (PWV) is an independent risk factor for cardiovascular events. Data for the pediatric cohort are not existing, therefore the aim of this study was to measure the PWV in patients after pediatric liver transplantation (pLTx) for the first time and to determine, whether there is evidence for an increased cardiovascular risk.

Methods: Blood pressure and PWV (single and 24 h measurement) were measured in all patients after pLTx routinely by an oscillometric device (Mobil-O-Graph, I.E.M., Stolberg, Germany) during all visits. For each PWV measurement the age specific z-score was calculated by means of the corresponding reference values (Elmenhorst J et al. Atherosclerosis. 2015; 238 (1): 9-16)
Results and Conclusions: We performed 97 measurements (76 single and 21 24 h measurements) at 65 patients (male $n = 35$). The mean and the median Z-score were both 0.1 (min -5.5, max 6). Thus our data do not indicate that the PWV is generally increased after pLTX. Further prospective studies are needed to eventually identify patients or patient groups with an increased risk to develop cardiovascular problems after pLTx.

P054 THE SAME MELD-SCORE VALUES ARE ASSOCIATED WITH DIFFERENT 90-DAY MORTALITY IF MEASURED BEFORE COMPARED WITH AFTER INSERTION OF A TRANSJUGULAR PORTOSYSTEMIC STENT SHUNT

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Introduction and Background: Originally developed for prediction of 90-day-mortality (m90) of cirrhotic patients after placement of a transjugular portosystemic stent shunt (TIPSS), the model of end-stage liver disease (MELD) score is now used as an indicator of the severity of chronic liver disease and guides the allocation of donor-livers for transplantation according to the sickest first principle. Parameters included in the MELD score may change following insertion of a TIPS-stent. We examined the association with mortality of MELD-scores before TIPSS-insertion compared with MELD-scores after TIPSS-insertion.
Methods: Consecutive cirrhotic patients who received a TIPSS-procedure in our institution between 2004 and 2015 were retrospectively analyzed and follow-up was completed for 365 + 90 (455) days after TIPSS insertion. Patients on the wait-list for liver transplantation were excluded. MELD scores were calculated before TIPSS and 30, 90 and 365 days after TIPSS. Age, Gender, Indication for TIPSS (hemorrhage vs ascites), emergency procedure (yes/no), MELD-score and timing of MELD-score (before/after TIPSS) were included in binary logistic regression with m90 as dependent variable.
Results and Conclusions: 175 consecutive patients were included (31.4% female; mean age 60.4 ± 10.7 years; MELD before TIPSS 15.8 ± 6.2, alcoholic liver disease 81.1%, refractory ascites 75.5%). After backward exclusion of factors only MELD-score (OR 1.14, 95% confidence interval (95% CI) 1.09–1.20; $P < 0.001$) and timing of MELD score after as compared to before TIPSS-insertion (OR 0.46; 95% CI 0.31–0.68; $P = 0.001$) were independently associated with 90-mortality.

The same numeric MELD score was associated with a significantly lower mortality if measured after as compared to before TIPSS-insertion.

P055 PROTEIN QUALITY CONTROL SYSTEM IN HEPATOCYTE-LIKE CELLS DERIVED FROM INDUCED PLURIPOTENT STEM CELLS OBTAINED FROM FAP PATIENTS

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Introduction and Background: The correct folding of the human transthyretin (TTR) protein is essential for the formation of stable TTR tetramers which play a crucial role in the pathogenesis of familial amyloid polyneuropathy (ATTR-FAP). Recently, the idea emerged that the protein quality control (PQC) system is an important parameter of the disease. Several genes of the PQC were identified and mostly relate to ER-associated degradation (ERAD), chaperoning, unfolded protein response (UPR) or protein folding. However, the availability of primary hepatocytes from FAP patients is limited.
Methods: Urine-derived cells from FAP patients carrying different *TTR* variants were transfected with episomal vectors to generate induced pluripotent stem cells (iPSCs) which were differentiated into hepatocyte-like cells (HLCs). The hepatic character of HLCs was assessed by gene expression, immunostainings and functional analysis. HLCs were analyzed for gene expression related to PQC by RT-qPCR analysis. TTR expression was determined by Western Blot. The effect of Tafamidis, the only approved drug in the EU for stabilization of the TTR tetramer, was also analyzed.
Results and Conclusions: A high expression of hepatic markers, like albumin and *HNF4a*, was observed in the HLCs derived from FAP patients ($n = 5$). *TTR* mRNA expression in the HLCs was almost identical to human hepatocytes. Various forms of TTR (monomer, dimer and tetramer) could be detected in the cell culture supernatant of HLCs. From a set of 42 genes related to PQC, six genes were significantly affected ($\Delta ct > 2$ as compared to controls). All 6 genes are associated to the extracellular co-chaperoning. Tafamidis was found not to alter the PQC-related genes when applied to the HLCs. The data suggest that iPSC-based hepatic cells derived from FAP patients are an excellent model to study patient-specific disease mechanisms, including the role of the protein quality control system.

P056 IS THERE A STANDARD INDICATION FOR LIVER TRANSPLANTATION BECAUSE OF HEPATOCELLULAR CARCINOMA IN CIRRHOSIS? A COMPARISON OF EIGHT INTERNATIONAL GUIDELINES

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Introduction and Background: Liver transplantation is the only curative treatment for tumor disease and the underlying cirrhosis. Aim of this work was to compare guidelines of different countries and associations regarding the indication for liver transplantation because of hepatocellular carcinoma (HCC) in presence of cirrhosis.
Methods: To compare the indication for liver transplantation for HCC in cirrhotic liver we performed a systematic literature search and analyzed the following guidelines published after January 1st 2010: North America (AASLD), Spain (SEOM), Europe (EASL-EORTC and ESMO-ESDO), Asia (APASL), Japan (JSH), Italy (AIOM) and Germany (S3 guidelines).
Results and Conclusions: Guidelines based on the BCLC staging system (AASLD, SEOM, EASL-EORTC, ESMO-ESDO) recommend transplantation for patients within Milan criteria and Child-Pugh A and B cirrhosis with the exception of the case of single HCC <2 cm and Child-Pugh A cirrhosis, whose first-line therapy is resection. Patients with HCC and Child-Pugh C cirrhosis are not candidate for transplantation. German and Italian guidelines recommend transplantation for all patients within Milan criteria independently from Child-Pugh stage. JSH guidelines do not recommend transplantation for Child-Pugh A and B patients with HCC. Asian guidelines exclude Child-Pugh A patients from transplantation. In case of Child-Pugh B patients, transplantation is the second-line therapy if a resection is not possible for patients within Milan criteria. A standard regarding the indication for liver transplantation for HCC in cirrhotic liver does not exist, even when they claim to be evidence based. Despite European guidelines, Germany and Italy use their own national guidelines which partially differ from the European guidelines. Unless the baseline risks, the interventions, and the outcomes will be described, it will be difficult to compare and interpret the benefit of these guidelines.

P057 INFLAMMATORIC PARAMETERS ARE USEFUL FOR THE PROGNOSIS OF PATIENTS WITH HEPATOCELLULAR CARCINOMA AFTER LIVER TRANSPLANTATION

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Introduction and Background: Liver transplantation (LT) is an attractive curative treatment modality for early hepatocellular carcinoma (HCC) especially in patients with underlying liver dysfunction. Different characteristics of the tumor will be included to predict the outcome and recurrence probability after LT: histopathological features, serum tumor markers and response to pretransplant treatments. In the last times, inflammatory markers like C-reactive protein or neutrophil-to-lymphocyte ratio (NLR) have become the focus of attention.
Methods: We collected the data of 95 patients with HCC who undergo a liver transplantation in our center in a period of 9 years (2009–2014). Associations between NLR and survival (overall survival (OS), disease-free survival (DFS)) related to recognized predictors like serum tumor markers and histopathological features of the explanted liver were analyzed.
Results and Conclusions: The patients were divided into a low-NLR subgroup (NLR<5; $n = 86$) and the high-NLR subgroup (NLR>5; $n = 9$). Preoperative high-NLR showed predictive value for the OS and DFS; the 1-3-5-years DFS were 34%, 28%, 23% in the high-NLR group vs. 90%, 83%, 71% in the low-NLR ($P < 0.05$). The OS was in 29% in the high-NLR group vs. 66% ($P = 0.03$). Univariate and multivariate analysis identified preoperative high-NLR as prognostic factor for recurrence ($P = 0.04$; hazard ratio (HR) = 3.7), besides an AFP>40kU/l ($P = 0.0001$; HR = 2.1) and the finding of vascular invasion in the specimen ($P = 0.002$; HR = 4.2).

In conclusion, our results indicate that preoperative NLR is a simple prognostic marker for the outcome and recurrence probability in HCC patients after LT.

LIVER / PANCREAS

P058 FULMINANT ATYPICAL HEMOLYTIC-UREMIC SYNDROME (AHUS) EARLY AFTER LIVER TRANSPLANTATION

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Introduction and Background: Orthotopic liver transplantation (OLT) is frequently accompanied by dialysis-dependent kidney injury. Most often, hepatorenal syndrome is the underlying pathophysiology and resolves early after transplantation. If renal function does not recover, further diagnostics are required. Here we present a case of atypical hemolytic uremic syndrome (aHUS) as underlying cause.
Methods: A 61 year. old patient was liver transplanted for acute liver failure of unknown cause, accompanied by dialysis-dependent acute kidney injury. Despite excellent primary allograft function and good clinical condition, renal function had not recovered three weeks after transplantation. Kidney biopsy revealed thrombotic microangiopathy (TMA).
Outcome: Plasmapheresis was initiated. Several days later, the patient developed fever and, subsequently, sudden cardiac arrest. After cardiopulmonal resuscitation he continuously required maximum doses of catecholamines under continuous renal replacement therapy and plasmapheresis. Differential diagnosis of TMA revealed aHUS as underlying disease. The patient was put on the complement C5 inhibitor eculizumab and only then slowly improved. 12 months later, he is in excellent condition, renal function has recovered and stabilized with an eGFR of 44 ml/min/1.73 m^2 under continuous eculizumab therapy. Genetic screening revealed a risk polymorphism for aHUS.
Conclusion: aHUS is a rare differential diagnosis of kidney injury after OLT. Transplantation, the use of calcineurin inhibitors as well as infections present complement activating conditions that may result in aHUS in patients with inherent predisposition. The clinical course of the disease is variable, however may accelerate dramatically. Eculizumab provides an effective therapeutic option. Awareness of the disease and early treatment initiation may save patients in these situations.

P059 SWITCH OF IMMUNOSUPPRESSION TO DIFFERENT MTOR INHIBITORS AND ITS IMPACT ON RENAL FUNCTION IN LIVER TRANSPLANT RECIPIENTS

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Introduction and Background: Renal impairment in long-term liver transplant recipients is mostly a consequence of calcineurin inhibitor (CNI)-based immunosuppressive regimens and often results in an increased morbidity and mortality. Conversion to mTOR inhibitor-based immunosuppression may result in renal recovery. One of the most observed adverse events of mTOR inhibitors is hyperlipidemia. Until now, there are sparse data comparing Everolimus vs. Sirolimus, in respect to renal recovery and hyperlipidemia.
Methods: We retrospectively analyzed data of patients who underwent liver transplantation (LT) between 1996 and 2010 at our center and who were converted from CNIs to mTOR inhibitors. Renal function was evaluated by calculating the estimated glomerular filtration rate (eGFR) using the MDRD4 formula.
Results and Conclusions: During the study period, 42 patients were converted to Sirolimus (32 males; mean age 52.7 years) and 36 to Everolimus (22 males; mean age 59.4 years). Six weeks after conversion, the eGFR showed a significant covariable adjusted increase of 3.03 ml/min (from 60.46 ml/min to 63.50 ml/min; $P < 0.001$) in the Sirolimus group and of 8.68 ml/min (from 49.15 ml/min to 57.83 ml/min) in the Everolimus group. A higher increase of eGFR was observed in the Everolimus group within the first six weeks. However, there was no significant difference between both the groups ($P = 0.0695$). No further statistically noticeable changes in the course of eGFR were observed beyond week six. Both cholesterol and triglycerides revealed significant increases during the 12 months after changing medication. However, the difference between both groups was not significant. After conversion, four cases of graft rejection were observed in both groups.

In conclusion, no significant difference in renal recovery and hyperlipidemia was seen after conversion from CNI′s to either an Everolimus-based or a Sirolimus-based immunosuppression. In our study, both regimens represent a real option to CNI′s in case of intolerable adverse effects.

P060 VASCULAR COMPLICATIONS AFTER LIVER TRANSPLANTATION – PREDICTABLE IN CASE OF VASCULAR ABNORMITIES?

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Introduction and Background: Vascular complications are rare but appear in about 7 % of deceased donor liver transplantations. They have a major impact on the graft function and survival and directly impair patient survival. Vascular complications encompass the hepatic artery, portal vein and venous outflow system. However, most complications affect the arterial and portal venous perfusion. This study evaluates abnormal vascular variations of the hepatic artery as a risk for vascular complications following liver transplantation. According to the literature vascular variation of the hepatic artery appear in around 30% of the population.
Methods: From January 2010 until June 2015, we performed 469 liver transplantations at our institution. Within this cohort 31 vascular complications were identified. We evaluated several parameters including age, MELD, comorbidity, gender, indication for transplantation, re-transplantation, split liver transplantation, donor parameters as well as vascular variations of the recipient according to the preoperative computer tomography.
Results and Conclusions: We detected 31 vascular complications with an incidence of 8.4 %. These 31 complications appeared in 26 patients, 4 of these patients underwent re-transplantation and one graft developed two complications simultaneously. According to the literature arterial complications were more frequent compared with portal vein thrombosis. 42.3 % of our patients with arterial complications showed vascular variations in preoperative computer tomography.

This incidence of vascular variations was elevated in patients with vascular complications after liver transplantation compared with the general population. Vascular complications are rare but can cause severe complications leading to organ failure with increased patient morbidity and mortality.

P062 STENTING OF THE PANCREATIC DUCT AS A THERAPEUTIC OPTION IN THE TREATMENT OF PANCREATIC FISTULA AFTER PANCREAS TRANSPLANTATION

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Introduction and Background: Pancreatic fistula is a severe and relative common condition after pancreas transplantation. In most cases therapy comes down to drainage and watchful waiting until the fistula closes on its own. Placement of the pancreas graft in a retroperitoneal position with enteric drainage via a duodenoduodenostomy allows for endoscopic investigations and interventions.
Methods: We report the case of a 29 years old woman with a combined pancreas-kidney transplantation who developed a pancreatic leakage. At first, the fistula had been treated conservatively with drainage. However, the secretions did not subside after 3 months. On MRI and ultrasound an enlarged pancreatic duct was described and a diagnostic ERP had been initiated. This showed a papillary stenosis and a narrowing of the pancreatic duct right in its middle. So a papillotomy with stenting had been done. From this moment on, the output of the fistula was decreasing and the drainage could be removed 3 weeks after the intervention. The stent was in place for another 3 weeks. The visualization of the pancreatic duct on stent removal showed no further fistula.
Results and Conclusions: Most pancreas grafts are still placed intra-abdominally and enteric drainage is achieved by an anastomosis to the jejunum. That means that this anastomosis cannot be reached by upper g.-i. endoscopy routinely and that options to intervene at this place are limited. Not surprisingly there are only few reports on stenting of the pancreatic duct in a transplant setting in the literature. Taking the lessons learned in nontransplant pancreatic medicine, the retroperitoneal position of the pancreas graft in a retroperitoneal position with duodenoduodenostomy widens the range of diagnostic and therapeutic options considerably. This is not only true for the treatment of pancreatic fistulas but also for bleeding episodes at this side.

P063 UNEXPECTED REASON FOR PANCREAS-GRAFT DYSFUNCTION: GIANT ARTERIOVENOUS FISTULA

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Introduction and Background: The development of arteriovenous fistula in the pancreas graft after simultaneous pancreas-kidney transplantation is a rare but severe complication in long-term follow up.
Methods: In this case report, we present a 66-year old female with type 1 diabetes mellitus and associated end-stage renal failure who underwent successful simultaneous pancreas-kidney transplantation. In a 12-year-follow-up she presented with elevated fasting glucose levels. CT angiography showed a giant arteriovenous fistula of the graft between splenic artery and splenic vein. There was no biopsy of the pancreas-graft in the patient's history. We performed endovascular coil embolization of the fistula and observed normalized blood glucose levels.
Results and Conclusions: Arteriovenous fistulas of pancreas grafts are rare complications causing pancreatic dysfunction. Endovascular treatment can be considered as therapeutic option for fistula repair without loss of pancreatic function.

THORACIC ORGANS

P064 THE INFLUENCE OF EXTRACORPOREAL PHOTOPHERESIS ON NFκB SIGNALING AND CYTOKINE EXPRESSION IN LUNG TRANSPLANT PATIENTS

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Introduction and Background: Lung transplant patients suffering from chronic lung allograft dysfunction often receive extracorporeal photopheresis (ECP) in addition to calcineurin inhibitor (CNI) based immunosuppression. CNI partly inhibit the NFκB pathway, which induces the transcription of pro-inflammatory cytokines. The mechanisms of the observed ECP-mediated immunosuppression remain unclear. In this study we analyzed, if ECP contributes to immunosuppression by inhibiting NFκB signaling.
Methods: As NFκB activation is tightly related to its nuclear location, the nuclear translocation rate and intracellular expression levels of IFN-γ were analyzed after PMA/ionomycin stimulation in T cells of 13 lung transplant patients procured before and after ECP ($n = 33$) by Multispectral Imaging Flow Cytometry, which combines flow cytometry and fluorescence microscopy.
Results and Conclusions: After ECP the nuclear NFκB translocation rate in stimulated T cells was significantly reduced (mean ± SD [%]) from 51.5 ± 13.8 to 44.7 ± 14.5 ($P = 0.01$). The capability of ECP to impair nuclear NFκB translocation was additionally proven by an in vitro model, in which blood cells of healthy controls ($n = 4$) were treated with methoxypsoralen and UVA. Compared with nontreated cells, nuclear NFκB translocation rate was substantially decreased in ECP-treated T cells from 74.2 ± 11.5 to 48.1 ± 18. Similarly, the intracellular IFNγ expression (mean ± SD mean fluorescence intensity [MFI]) was diminished from 6310 ± 1693 to 3619 ± 1430.

In conclusion, these results provide first evidence that ECP impairs NFκB signaling, and consequently decreases NFκB-dependent expression of IFNγ, which may partly explain the well-known immunosuppressive effect of ECP.

P065 TWO STEP TRACHEA TISSUE TRANSPLANTATION – A LAST RESORT OPTION FOR REFRACTORY BONCHUS INSUFFICIENCY

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Introduction and Background: The transfer of a human trachea represents the last therapeutic chance in patients with refractory bronchus insufficiency. Only few cases are reported in literature. As a direct trachea transfer has been associated with poor results, a two-step concept with in vivo or in vitro conditioning of the tissue has been suggested. These procedures, although successful, are often very complex. We here report a new and easy two-step approach.
Methods: Case Report: A 53-year-old patient with abscess pneumonia and consecutive empyema underwent several operations in 2014 finally resulting in a right pneumonectomy and thoracic fenestration. Following this course, the patient also developed bleeding of the pulmonary artery and bronchus insufficiency. The pulmonary bleeding was controlled through an intra-pericardial approach but the attempt to cover the bronchus insufficiency was unsuccessfully twice. Despite the fact that a tracheal stent could not cover the defect completely, the patient was at least able to breeze spontaneously with gauze packing of the pleural space. After long rehabilitation he could be discharged home. Due to the contaminated pleural space, a tracheal transfer appeared to be the only therapeutic option. In spring of 2016, a trachea from a brain death donor became available and was transferred into the rectus sheath of the abdominal wall as the first step of our approach. After tolerance of the graft was verified, the graft was explanted again after 6 weeks and used for replacing the native and diseased trachea. Immunosuppression was achieved with low dose tacrolimus. The patient could be discharged home 5 days after the final trachea transfer.
Results and Conclusions: A two-step approach for trachea tissue transplantation consisting of initial implantation into the abdominal wall followed by re-explantation for trachea exchange after graft acceptance had been verified to be a valuable and technically easy approach to this often deadly clinical condition.

P066 HU FAILURE: WHAT IS THE COURSE OF A HU CANDIDATE IN THE CURRENT ERA?

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Introduction and Background: Decision making for HU listing or MCS implantation is crucial for prognosis with increasing HTx waiting time and superimposable indications for end stage heart failure patients. The aim of this study was to investigate and characterize rate and time point of therapy failure of HU listed patients defined as: death while on the waiting list, the need of permanent MCS implantation or delisting due to good or bad condition.
Methods: 447 HU listed patients at our institution between September 2007 and December 2014 were investigated. Of those, 97 (21.7%) patients suffered therapy failure. 15 patients (15.5 %) died while on the HU waiting list, 75 (77.3%) underwent durable MCS implantation and 7 (7.2%) were disqualified for HU due to good or bad clinical condition between September 2007 and December 2014.
Results and Conclusions: The median time until therapy failure was 34 days after HU listing. The median waiting time until HTx was 73.4 days (1–971), for patients with therapy failure was 110.1 days (2–496). The estimated 1-year mortality for patients with HU failure was 42.5%.

Our results suggest that half of the HU listed patents cannot tolerate 5 weeks on the waiting list. In these patients, early MSC implantation may possibly lead to improved results in the presence of the current HU allocation system. An optimized selection algorithm using score systems and early decision making may improve results. Further prospective studies are needed to identify a patient cohort that would benefit from early MCS implantation.

P067 CLASSIFICATION AND CARE OF WOUNDS AFTER VAD IMPLANTATION

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Introduction and Background: Results after left ventricular assist device (LVAD) implantation are impaired by driveline infections. The aim of this study was to analyze our institutional rate of infections and present a classification and treatment plan.
Methods: Between 2010 and 2016 we performed 130 LVAD implantations. 60 LVAD patients were seen as outpatients regularly. Driveline exit were classified 1) free of irritation; 2) redness; 3) secreting; 4) redness and secreting; 5) redness, secreting and purulent; 6) wound healing deficit; 7) secreting with wound healing deficit. Sternal wounds were classified: 1) free of irritation, 2) instable, 3) granuloma, 4) wound healing deficit, 5) purulent wound healing deficit. Follow up consisted of regular visual controls, therapy was applied according to classification and microbial testing.
Results and Conclusions: In 60 patients we categorized driveline exits class 1: 17 cases (28%), class 2: 11 cases (18%), class 3: 6 cases (10%), class 4: 6 cases (10%), class 5: 12 cases (20%), class 6: 1 case (2%), class 7: 7 cases (12%). Therapy consisted in dressing change with Metalline: 36 %, with polyhexanide ointment + Metalline: 20%, dry gauzes only: 31%. Sternal repositioning was necessary: 0.4 %. Two patients with local + systemic infection were transplanted. Out of 60 patients we found sternal wounds to

class 1: 47 cases (78%), class 2 and 3: 0 case, class 4: 4 cases (7%), class 5: 3 cases (5%), class 6: 6 cases (10%). Therapy consisted in wound dressing change with sterile gauzes in 3%, wound dressing change with polyhexanide ointment and gauzes in 2% and without any therapy in 89%. Surgical intervention was necessary in 4 % and consisted in wound debridement and negative pressure therapy.

Modern left ventricular assist device technology can be used successfully for heart failure. Survival rates in end stage patients are good, technical failure and death due to driveline infections are rare. Patient comfort however is impaired by driveline problems. Thus, improved wound care strategies are necessary.

P068 EFFECTS OF SILDENAFIL ON PULMONARY HYPERTENSION AND RIGHT VENTRICULAR FUNCTION AFTER HEART TRANSPLANTATION: REPORT ON THREE PATIENTS

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Introduction and Background: The use of the PDE5-Inhibitors sildenafil (SIL) in idiopathic pulmonary arterial hypertension is well established, whereas their efficiency in pulmonary hypertension due to left heart disease (PH-LHD) and after heart transplantation (HTx) is still a matter of debate. In the outpatient department of our center, SIL is regularly administered as an off-label therapy to treat PH-LHD, also after heart transplantation (HTx).
Methods: We retrospectively investigated three patients with echocardiographic findings of PH and right ventricular (RV) distress 4.6, 10.1 and 24.9 years post-HTx in which no other cause of PH could be identified but chronic LHD with pulmonary congestion before HTx. Before and at least 30 days after administration of sildenafil (60 mg/d), routine echocardiographic assessments were analyzed.
Results and Conclusions: Under SIL treatment there were no changes in left ventricular ejection fraction [57, 48, 39 vs. 56, 47, 40 (%)] and mitral insufficiency.

In contrast, under SIL treatment, estimated pulmonary arterial systolic pressures [52, 46, 35 vs. 35, 44.34 (mmHg)] and RV functional parameters were improved in all patients: RV global strain [16, 11, 11 vs. 20, 13, 14 (%)] fractional area chance [31, 37, 29 vs. 36, 38, 33 (%)], max. diameter of inferior vena cava [20, 38, 34 vs. 18, 34, 31 (mm)]. RV dimensions (RV end-diastolic and end-systolic area), tricuspid insufficiency were reduced in two of three patients. Concomitantly the reported overall physical agility and dyspnoea were markedly improved in all three patients.

The results warrant further investigation but give rise to the hypothesis that sildenafil is beneficial on pulmonary hemodynamics and RV function in PH-LHD, even when initiated only many years after HTx.

P069 REPORT OF INTESTINAL TAC NON-ABSORPTION AFTER HEART TRANSPLANTATION

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Introduction and Background: Rejection of donor heart is a consequence of under-immunosuppression and a common complication within the first months after transplantation. Tacrolimus (TAC) is well established immunosuppressant used for the prevention and treatment of allograft rejection in heart transplantation (HT).
Methods: An Afro American male veteran with dilated cardiomyopathy underwent HT. From the patient's medical history different abdominal surgeries were known, no intestinal interruption seen in subsequent CT scan. After HT, C0-monitoring of TAC was performed daily. Despite ever increasing oral TAC dosage, serum levels remained below acceptable trough levels. We attempted switch to other galenic preparations, without any effect. We changed immunosuppressive protocol to Cyclosporin, to Everolimus, but to no avail. Medication levels remained highly below therapeutic levels. We added ursodeoxycholic acid to oral TAC medication but did not achieve stable trough levels of TAC thereafter. Only intermittent i.v. TAC applications served to keep the patient in an acceptable range again and again. However, three months after HT the patient required resuscitation for asystole as acute rejection of donor heart. ECMO was implanted as temporary mechanical circulatory support. As a result of i.v. application the serum TAC level was higher than the range desired. Sepsis as effect of high dosing immunosuppressive agents led to the patient's demise.
Results and Conclusions: We present a large variability in TAC blood concentration and various futile attempts to stabilize these levels. One reason for such varying drug levels might be the effect of cytochrome P450 (CYP), particularly CYP3A subfamilies in the intestine, as a consequence of previous abdominal surgeries. This is the rare report of intestinal TAC nonabsorption after HT. It seems previous abdominal surgeries led to impaired absorption capability of orally administered TAC which led to under-immunosuppression and therefore acute heart rejection.

P070 LATE-ONSET OF AMIODARONE-INDUCED HYPERTHYROIDISM UNDER IMMUNOSUPPRESSION AFTER HEART TRANSPLANTATION

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Introduction and Background: Hyperthyroidism after amiodarone treatment is an often described and dreaded consequence, which usually appears in the next hours till weeks after treatment. Immunosuppressive drugs like tacrolimus and prednisolone are known to inhibit the pathogenesis of autoimmune disorders or are used to treat hyperthyroidism, respectively. In this study, we report about five patients with hyperthyroidism under immunosuppression after heart transplantation (HTx).
Methods: All patients were diagnosed as amiodarone-induced hyperthyroidism although the last treatment with amiodarone was before HTx.

After HTx all patients were treated with an immunosuppressive drug regimen consisting out of tacrolimus ($n = 4$) or cyclosporine ($n = 1$) plus mycophenolate mofetil (2–3 g/day) and at least 5 mg prednisolone. The detection of the strong hyperthyroidism occurred between 1 and 19 months after the last amiodarone treatment, which was also between 1 and 15 months post-transplantation. Four of the patients presented with clinically symptoms with hyperthyroidism or even almost a thyrotoxic crisis and, therefore, had finally to be treated with an operative (hemi-) thyroidectomy. Additionally, three of these patients were treated with thyreostatic drugs. Only one patient could treated effectively with an injection of dexamethasone into the thyroid combined with thyreostatic drug therapy.
Results and Conclusions: These cases emphasize the need for a regular monitoring and consequent immediate therapy of signs of hyperthyroidism in the laboratory for all patients post-HTx who were once treated with amiodarone before HTx. Although tacrolimus and prednisolone are known to reduce the risk for a thyroid autoimmune disease, the immunosuppression seems to affect the thyroid switching into hyperfunction still months after the last amiodarone treatment. Further studies are needed to investigate the pathogenetic mechanism of the immunosuppression-induced hyperthyroidism.

IMMUNOLOGY

P071 *EX VIVO* LUNG PERFUSION REDUCES EARLY INFLAMMATION IN THE RECIPIENT DUE TO PROTECTION FROM INFLAMMASOME-MEDIATED ISCHEMIA/ REPERFUSION INJURY

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Background: Portable ex vivo lung perfusion (EVLP) may improve organ quality due to normothermic oxygenated conditions compared with cold storage in perfusion solution. The INSPIRE trial is currently worldwide the only randomized, multicenter, international trial directly comparing standard of care (SOC) cold preservation with the Organ Care System (OCS). Little is known regarding potential immunological mechanisms participating in EVLP. Thus, we aimed to determine inflammatory profiles of recipients with SOC vs. OCS preserved lungs.
Methods: Blood plasma and perfusion solutions of 33 patients with OCS- vs. 26 patients with SOC-preserved lungs were available with diagnoses of idiopathic fibrosis, cystic fibrosis, idiopathic pulmonary hypertension, emphysema. Samples were analyzed for cytokines and chemokines by multiplex protein arrays. Donor, recipient demographics, cold ischemia time (CIT), PGD scores were assessed.
Results and Conclusions: Clinical evaluation revealed significantly shorter CIT of OCS- vs. SOC-preserved lungs ($P < 0.0001$). PaO2/FiO2 ratios were not different between groups but freedom from PGD3 was significantly higher in the OCS group ($P = 0.035$). OCS recipients showed significantly lower IL-6, CXCL8-10, CCL2 plasma levels ($P < 0.001$) at T0. IL-6 levels correlated with CIT and PGD score. Inflammasome targets IL-1b, IL18 were reduced, In perfusates, higher cytokine, chemokine levels were detected. IL-1RA was significantly higher in OCS perfusates arguing for its contribution to reduced inflammation.

Reduced inflammation in plasma of OCS recipients can be achieved during EVLP by production of antagonists like IL-1RA that counterbalance inflammasome activation and inflammation. In SOC recipients, direct correlation of clinical parameters with IL-6 plasma levels confirms a pathophysiological link between inflammation and IRI. We provide evidence that EVLP creates an anti-inflammatory milieu by promoting antagonists of inflammation with impact o*n* improved clinical outcome.

P072 IMMUNOLOGICAL ASPECTS OF IRON OVERLOAD IN HEART AND KIDNEY TRANSPLANTATION

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Introduction and Background: Clinical data suggest that iron (Fe) overload deleteriously affects graft survival after heart (HTX) and kidney transplantation (KTX) but possible immunological mechanisms underlying this phenomenon have not been elucidated.
Methods: To identify the mechanistic influence of Fe in a murine model of HTX or KTX, fully allogeneic Balb/C donor organs were transplanted into Fe overloaded C57Bl/6 recipients.
Results and Conclusions: Following HTX, Fe overload accelerated acute and chronic rejection as observed by a shortened graft survival (acute: HTX vs. HTX+Fe; $P < 0.05$; chronic: HTX vs. HTX+Fe; $P < 0.01$) and elevated ISHLT-rejection score ($P < 0.01$). FACS analysis revealed that in contrast to a pronounced graft infiltration of $CD4^+$ T ($P < 0.01$) and $CD3^-NKp46^+$ NK cells ($P < 0.05$), reduced frequencies of regulatory T cells (T_{Reg}) were detected in the graft and spleen ($P < 0.01$, respectively) derived from Fe overloaded recipients. This was accompanied by lower intragraft and splenic mRNA expression levels of anti-inflammatory cytokines (IL-10, TGF-beta) and Foxp3. Following KTX, analogous observations were retrieved analyzing NK cells, $CD4^+$ and T_{Reg} cells and expression profiles. Whereas transplantation per se activated splenic NK cells, this was further accentuated following Fe overload ($P < 0.01$). Interestingly, intragraft induction of hepcidin and diminished CD71 expression ($P < 0.05$, respectively) suggest that the allograft itself – initially derived from a healthy donor – is affected by the Fe overload of the recipient. Based on our data we provide novel insights into the understanding of disturbances in Fe homeostasis and their consequences following transplantation suggesting novel perspectives for personalized immunosuppression in the future. This might lead to further improvements of personalized immunosuppression.

P073 ASSOCIATION OF THE SINGLE NUCLEOTIDE POLYMORPHISM RS2488457 OF THE *PTPN22* GENE WITH REJECTION IN KIDNEY TRANSPLANTATION

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Introduction and Background: To prevent graft rejection after kidney transplantation the patient have to take immunosuppressants for a lifetime. Because immunosuppressants exhibit strong side effects, it might be a strategy to individualize immunosuppressive therapy to improve transplantation success for some patients. Suitable for this are genetic biomarkers in terms of polymorphisms. They can predict the risk of an immunologically related graft rejection preoperatively. The rejection of a kidney transplant is mostly based on T cell reactivity. Therefore we have considered a suppressor of the signal cascade of the T cell receptor (TCR) which is encoded by the gene *PTPN22*. This gene is expressed in lymphocytes and encodes a lymphoid protein tyrosine phosphatase (LYP).
Methods: Data were analyzed from 232 renal transplant patients of which 166 have not rejected the kidney allograft and 66 have a rejection within the first year after transplantation. All patients with ABO incompatible and combined organ transplantation as well as patients with panel reactive antibodies (PRA) $\geq$ 5% were excluded. We investigated the influence of the following *PTPN22* SNPs on the susceptibility to kidney allograft rejection: rs1217388, rs1310182, rs2476601 and rs2488457. The analysis was performed using the endpoint genotyping method. For the evaluation we have differentiated between the modes of inheritance.
Results and Conclusions: For three of the four investigated SNPs in *PTPN22* no significant differences in the genotype distribution were observed between patients with and without rejection. However, the SNP rs2488457 occurred significantly more in patients with rejection compared with patients without rejection by assuming a recessive mode of inheritance. By assuming a codominant inheritance this difference has also been observed but not significantly.

We conclude that LYP is a relevant protein for immune regulation in kidney transplantation and further studies on genotype dependent functional differences are needed.

P074 DEVELOPING A DONOR SPECIFIC B-CELL ELISPOT ASSAY FOR IMMUNOMONITORING AFTER TRANSPLANTATION BY MEANS OF HEPATITIS-B VACCINATION RESPONSE

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Introduction and Background: Short term survival rate after solid organ transplantation is acceptable, but long term outcome is still insufficient. Donor specific memory-B cells seem to play an important role in acute and chronic allograft rejection. However to this date no assay is available to accurately identify and quantify these cells in the recipient. The aim of our research is to establish a donor specific total IgG B-cell ELISpot to meet this requirement. To proof the concept of detecting multiple antigen-specific memory B-cells by total IgG-ELISpot we chose the model of Hepatitis-B (Hep-B) immunity in vaccinated and unvaccinated blood donors.
Methods: PBMCs of vaccinated and unvaccinated healthy individuals were isolated and incubated with Hepatitis-B-vaccine containing HBs-antigen for three days. Cells were washed and put on goat-anti-human-IgG coated ELISpot plates overnight. After rinsing, biotinylated anti-IgG antibody was added, left for 2 h on the plate, washed away and streptavidin-ALP was added. Spots appeared after a short incubation with BCIP/NBT.
Results and Conclusions: There was a statistically significant difference in Δ-spot-number between vaccinated and unvaccinated individuals with p-values <0.05. We could successfully distinguish vaccinated from unvaccinated individuals. Due to this we assume, that it is possible to detect and quantify antigen-specific memory-B-cell reactivity in vaccinated and unvaccinated individuals using a total IgG-ELISpot.

The total IgG ELISpot can reliably quantify the immune response of Hep-B vaccinated individuals in vitro as expected. We are currently validating this concept in transplant-recipients by measuring the donor specific memory-B-cell response after incubating recipient-PBMCs with irradiated donor-cells.

P075 PROSPECTIVE ANALYSES OF CIRCULATING B-CELL SUBSETS IN ABO-COMPATIBLE AND ABO-INCOMPATIBLE KIDNEY TRANSPLANT RECIPIENTS

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Introduction and Background: Immunosuppressive strategies applied in renal transplantation traditionally focus on T-cell inhibition. B cells were mainly examined in the context of antibody-mediated rejection, whereas the impact of antibody-independent B-cell functions has only recently entered the field of transplantation. Similar to T cells distinct B-cell subsets can enhance or inhibit immune responses. In this study, we prospectively analyzed the evolution of B-cell subsets in peripheral blood of ABO-compatible ($n = 27$) and ABO-incompatible ($n = 10$) renal transplant recipients.
Methods: Patients donated blood samples prior to and on day 21, day 100 and day 365 post-transplantation. Peripheral blood mononuclear cells were isolated using density-gradient centrifugation and subsequently analyzed by 10-color flow cytometry. Interleukin-10, granzyme-B and transforming growth factor beta as major B-cell associated immunosuppressive cytokines were analyzed by intracellular cytokine staining.
Results and Conclusions: Activated B cells were transiently and plasmablasts were permanently decreased in patients without signs of rejection throughout the first year. In patients with histologically confirmed renal allograft rejection, activated B cells and plasmablasts were significantly elevated on day 365. Rituximab treatment in ABO-incompatible patients resulted in long-lasting B-cell depletion and in a naïve phenotype of repopulating B cells one year following transplantation. Acute allograft rejection was correlated with an increase of activated B cells and plasmablasts and with a significant reduction of regulatory B-cell subsets. Taken together, our study demonstrates remarkable effects of standard immunosuppression on circulating B-cell subsets. Furthermore the B-cell compartment was significantly altered in rejecting patients. A specific targeting of deleterious B-cell subsets could be of clinical benefit in renal transplantation.

BASIC SCIENCE

P076 BRYOSTATIN-1 LIMITS NEUTROPHIL TRANSENDOTHELIAL MIGRATION FOLLOWING ISCHEMIA-REPERFUSION INJURY: IMPACT FOR THERAPY

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Introduction and Background: Ischemia-reperfusion injury (IRI) is an inherent component of solid organ transplantation and axiomatically linked to graft damage. In the kidney, vascular endothelial cells (EC) are highly vulnerable to IRI. These cells are the first site of graft injury, while neutrophils are the first line of host defense after reperfusion. The degree of renal EC damage predicts the severity of neutrophil transendothelial migration (TEM), with neutrophils in turn orchestrating the influx of subsequent leukocytes waves into the graft. Therefore, EC integrity and neutrophil TEM represent promising targets to attenuate IRI. One drug known to stabilize EC integrity and to limit neutrophil TEM is Bryostatin-1, an activator of the EC second messenger protein kinase C delta. Therefore, we examined the role of Bryostatin-1 on neutrophil TEM in a*n in vitro* IRI model.
Methods: We used an *in vitro* IRI model with human umbilical vein ECs (HUVECs) and human neutrophils (approved by the ethic committee (STUDY00000261) to study the role of Bryostatin-1 in IRI-induced neutrophil TEM. HUVECs were exposed to either normoxic (21% O_2) or hypoxic (1.5% O_2) conditions for 20 hours (h) with and without Bryostatin-1 (1-100 nM) followed by 2 h exposure to Calcein-AM dye labeled neutrophils. TEM to saline or the chemoattractant leukotriene B_4 (LTB_4) was determined by measuring fluorescence intensity and myeloperoxidase (MPO) production.
Results and Conclusions: Bryostatin-1 dose-dependently inhibited human neutrophil TEM under normoxic and hypoxic conditions. Bryostatin-1 (100 nM) blocked 75% ($P < 0.05$) of TEM toward LTB_4 in normoxic conditions; this was intensified when HUVECs were placed in hypoxic conditions (83%, $P < 0.001$). These data were further supported by a mirrored effect when MPO production (a marker of neutrophil activation) was measured. In summary, these promising *in vitro* results demonstrate that our model recapitulates IRI-induced EC damage, and most importantly that Bryostatin-1 alters neutrophil TEM in an *in vitro* IRI model.

P077 EPOR$_2$/ßCR$_2$-INDEPENDENT EFFECTS OF LOW-DOSE EPOETIN-ALPHA IN PORCINE LIVER TRANSPLANTATION

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Introduction and Background: Ischemia-reperfusion injury (IRI) remains the key component of graft damage during transplantation. Mechanistically, cold-induced apoptosis, microcirculatory disturbances and radical oxygen species formation contribute to severe endothelial injury in IRI. High-dose Epoetin-alpha (EPO) induces anti-inflammatory and anti-apoptotic effects via the EPOR2/ßcR2-receptor complex, with the potential risk of pro-thrombotic effects. However, our previous work indicates that low–dose EPO has EPOR2/ßcR2-independent protective effects, possibly via direct effects on the endothelium. Therefore, we aimed to examine possible cytoprotective effects of low-dose EPO in a porcine liver transplantation model.
Methods: Seventeen landrace pigs (weighing 40–45 kg) underwent allogenic liver transplantation (follow-up 6 h) with a portojugular shunt. Criteria for successful transplant were survival until study end point, hemoglobin at sacrification >7 mg/dl. Animals were divided into two groups: donor and recipient treatment with low-dose EPO (65 IU/kg) or vehicle, each 6 h before cold perfusion and 30 min after warm reperfusion. Blood and liver samples were taken 30 min, 2, 4 and 6 h after reperfusion.
Results and Conclusions: Fourteen our of 17 animals (82.4%) fulfilled the inclusion criteria. Concerning the initial values there were no differences between the groups (vehicle vs. EPO): hemoglobin 9 ± 0.49 vs. 9.18 ± 0.88 mg/dl, cold ischemic time 13.49 ± 0.18 vs. 13.84 ± 0.35 h, warm ischemic time 46.43 ± 1.99 vs. 44 ± 2.71 min. EPO-treated animals showed a significantly lower score in the blinded, histopathologic examination while no changes in serological markers (GOT, GPT, AP, bilirubin) were noted. In conclusion, donor and recipient treatment with low-dose EPO reduces the acute inflammatory response in IRI possibly via EPOR2/ßcR2-independent mechanisms and represents a clinically applicable way to reduce IRI associated graft injury.

P078 CUSTODIOL-N ATTENUATES THE COLD STORAGE-INDUCED DEVELOPMENT OF GRAFT VASCULOPATHY IN A RAT AORTIC TRANSPLANTATION MODEL

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Introduction and Background: The aim of this study was to evaluate the effect of the new preservation solution Custodiol-N on the development of chronic vasculopathy after cold storage in comparison with traditional HTK solution.
Methods: Aortae of LEW/Crl rats were stored in Custodiol-N or traditional histidine-tryptophan-ketoglutarate (HTK) solution at 4 °C for 24 h, 48 h, or 1 week and then transplanted orthotopically into other LEW/Crl rats. Aortae stored in saline and aortae without cold ischemia were used as control groups. Animals were sacrificed 16 weeks after transplantation. The transplanted aortae were evaluated histologically for vasculopathy (intimal proliferation); investigators were blinded. ANOVA was used for statistical analysis.
Results and Conclusions: In the 24 h cold storage series, aortae stored in saline showed marked intimal proliferation ($14.1 \pm 5.2\%$ of the luminal area (as delineated by the internal elastic lamina; $n = 7$), the intima of aortae in the other groups was almost normal. After 48 h cold storage, almost no intimal proliferation was observed in the Custodiol-N group, slight to moderate intimal proliferation in the HTK group ($0.6 \pm 0.3\%$ vs. $4.2 \pm 1.9\%$; $P = 0.08$; $n = 7$). After 1 week, severe intimal proliferation occurred in the HTK group ($21.3 \pm 3.9\%$) while intimal proliferation in the Custodiol-N group was significantly lower ($3.6 \pm 1.3\%$; $P < 0.05$; $n = 7$).

The new Custodiol-N solution markedly attenuates the development of chronic vasculopathy compared with HTK solution, especially in the situation of prolonged cold ischemia.

P079 TACROLIMUS PREVENTS CELL DEATH AFTER HEPATIC ISCHEMIA-REPERFUSION-INJURY

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Introduction and Background: Tacrolimus currently represents one of the most relevant immunosuppressive drugs to avoid rejection after liver transplantation. Apart from rejection, the hepatic ischemia-reperfusion-injury (IRI) is a well-known, yet inevitable complication of major liver surgery and liver transplantation. The aim of this study was to scrutinize the endogenous role of tacrolimus in relation to cell death mechanisms of hepatic IRI.
Methods: Livers of C57Bl/6 mice were exposed, each by a 65% fraction, to 60 minutes of warm ischemia and subsequent 90 minutes of reperfusion. Tacrolimus was applied 24 h prior to laparotomy. Non-pretreated mice and mice pretreated with baicalein, a potent hepatoprotective drug, were used as control groups. The gained tissue samples of the respective liver lobes were analyzed using TUNEL assays to detect apoptotic cells, as well as Western Blots for pro-apoptotic proteins ERK1/2, JNK, PARP and Caspase-3.
Results and Conclusions: The analysis of hepatic cell death by means of TUNEL staining showed a significant reduction of apoptotic hepatocytes by 75% after tacrolimus pretreatment ($P < 0.001$), compared with the untreated control group. The additional pretreatment with baicalein could further raise the level of cell death reduction up to 79%. By the use of Western Blot analysis, a significantly lowered expression of JNK (−84%; $P < 0.05$) and PARP (−60%; $P < 0.05$), as well as a negative regulation trend related to ERK1/2 and Caspase-3 could be substantiated after tacrolimus pretreatment. Regarding these results it could be demonstrated that the pretreatment with tacrolimus leads to a significant decrease of cell death after hepatic IRI. Hence it can be stated that tacrolimus does not only play a major role in immunosuppression, but additionally possesses an endogenous protective effect on IRI. Further obtained results suggest that this tacrolimus induced hepatocyte protection is mediated by regulation of several pro-apoptotic enzymes, significantly by JNK and PARP.

P080 ISCHEMIA REPERFUSION INJURY (IRI) CAUSES LOCAL RELEASE OF FREE HEME WHICH AGGRAVATES ACUTE KIDNEY INJURY (AKI)

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Introduction and Background: Acute kidney injury (AKI) is a frequent complication after solid organ transplantation. Especially, lung- and heart transplantation are associated with blood loss and the need of packed red blood cell (pRBC) transfusions. Although pRBC are beneficial blood products also have adverse effects. Release of toxic extracellular hemoglobin (hb) and free heme has been shown to contribute to acute organ injury. In this study, generation of free heme in renal ischemia reperfusion injury (IRI) was investigated in a mouse model.
Methods: IRI was induced by 15, 35 and 45 min renal pedicle clamping in mice. Sham surgery served as control. Mice were sacrificed at 2 and 4 h after IRI. Free heme was measured in the renal tissue as well as in the circulating blood. qPCR for pro-inflammatory cytokine expression, histology and immunohistochemistry for acute kidney injury and inflammation were done.
Results and Conclusions: In correlation with duration of ischemia time the free heme generation in the tissue increased. The contralateral kidney which was not clipped served as a control in these experiments. By increasing ischemia time the local renal tissue damage aggravated and more pro-inflammatory cytokines (TNF-alpha, MCP-1, IL-6) were produced.

Free heme which is generated in aging pRBC is pro-inflammatory and aggravates AKI in an experimental renal IRI mouse model. Strategies to bind free heme in IRI would be promising in future studies.

P082 EVIDENCE THAT REWARMING INJURY AFTER EXTENDED COLD INCUBATION IS ELICITED BY ENERGY DEFICIENCY

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Introduction and Background: We have previously shown that cold-induced injury to diverse cell types is mediated by redox-active iron ions and have developed protective solutions for cell and tissue storage. Here, we study the limits of extended cold incubation in a model cell type, the relatively robust murine fibroblast cell line L929, in such an optimized preservation solution.
Methods: Adherent cultures of L929 cells were incubated at 4°C in a slight modification of the tissue preservation solution TiProtec®, i.e. in TiProtec supplemented with deferoxamine to a final concentration of 0.5 mM and with 50 g/l Dextran 40. Rewarming was performed in cell culture medium or TiProtec. Cell viability was assessed by the release of lactate dehydrogenase (LDH), cellular ATP content was determined enzymatically. High-resolution respirometry was performed using an Oroboros Oxygraph-2k.
Results and Conclusions: A two-week incubation of L929 cells at 4°C in modified TiProtec showed good protection at the end of cold incubation (LDH release 2 ± 2 %). However, during subsequent rewarming at 37°C in cell culture medium LDH release increased drastically to 81 ± 1 %. This rewarming injury was partially inhibited by rewarming in TiProtec (42 ± 6 %). Experiments with modified solutions showed that this protective effect of TiProtec was due to its components alanine and glycine and its slightly acidotic pH. As these components/features are known to inhibit energy deficiency injury, we next measured ATP. Cellular ATP content after 2 weeks of cold incubation amounted to 11 ± 6 % of initial values and did not recover during rewarming. First results of oxygen consumption analyses indicated a hampered oxidative phosphorylation after prolonged cold incubation.

In summary, these results show that long-term cold incubation even in – to current knowledge – optimized preservation solutions can be followed by a pronounced rewarming injury that is elicited by energy deficiency. The underlying cellular/mitochondrial alterations are subject to further study.

P083 TEMPERATURE DEPENDENCE OF INTERCELLULAR GAP FORMATION AND CYTOSKELETAL ALTERATIONS IN MONOLAYERS OF PORCINE AORTIC ENDOTHELIAL CELLS

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Introduction and Background: The endothelial lining of vessels acts as a barrier between tissue and blood. Hypothermia leads to damage of this barrier, caused by intercellular gap formation and endothelial cell death. Here, we studied the intercellular gap formation in monolayers of endothelial cells and the underlying cytoskeletal alterations at different temperatures.
Methods: Primary porcine aortic endothelial (PAE) cells were incubated for 48 h in Krebs-Henseleit (KH) buffer (supplemented with 5 mM glucose and 1 mM deferoxamine) at 4°C, 10°C, 15°C and 21°C, and afterwards rewarmed in cell culture medium at 37°C for 1 h. Cells incubated at 4°C were additionally rewarmed to 21°C for 1 or 2 h. Gap formation was studied by phase contrast microscopy, actin filaments and microtubules by fluorescence microscopy.
Results and Conclusions: Cold incubation of PAE cells at 4°C in KH buffer containing glucose and deferoxamine, the latter effectively inhibiting cell death after cold incubation, resulted in strong cell retraction and gap formation in the endothelial monolayer. This gap formation was fully reversible after rewarming to 37°C. During 4°C incubation degradation of actin filaments (stress fibres and peripheral band) and disintegration of microtubules was observed; this was reversible with rewarming to 37°C. Rewarming of PAE cells to 21°C showed partial reversibility of gap formation and incomplete reconstitution of the cytoskeleton. Cold incubation at 10°C or 15°C both resulted in gap formation, degradation of actin filaments and disintegration of microtubules, although less marked than at 4°C. At 21°C actin filaments and microtubules of PAE cells were only slightly degraded and disintegrated, and gap formation was prevented. Cold-induced gap formation and cytoskeletal damage at all temperatures were reversible during rewarming to 37°C.

The present study shows that gap formation occurs over a wide range of temperatures and that for complete reconstitution of barrier function temperatures above 21°C are required.

ORGAN PRESERVATION

P084 CONTINUOUS NORMOTHERMIC *EX VIVO* KIDNEY PERFUSION IS SAFE IN HEART BEATING DONOR KIDNEY TRANSPLANTATION AND IMPROVES RENAL GRAFT FUNCTION IN DONATION AFTER CIRCULATORY DEATH

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Introduction and Background: Hypothermic kidney storage causes preservation injury and is poorly tolerated by renal grafts, especially in donation after circulatory (DCD) kidney transplantation. We investigated whether static cold storage (SCS) can be safely replaced with a novel technique of pressure-controlled normothermic *ex vivo* kidney perfusion (NEVKP).
Methods: Right kidneys were removed from 30 kg Yorkshire pigs in a model of HBD and either preserved in cold histidine-tryptophan-ketoglutarate (HTK) solution for 8 h ($n = 5$), or subjected to 8 h of pressure-controlled NEVKP ($n = 5$) followed by renal heterotopic autotransplantation. In a second set of experiments, renal grafts were subjected to 30 minutes of warm ischemia followed by storage in cold HTK ($n = 5$) or NEVKP ($n = 5$) for 8 h. All pigs were followed for 10 days.
Results and Conclusions: During NEVKP physiologic perfusion conditions were maintained with low intrarenal resistance (IRR) and normal electrolyte and pH parameters. Injury markers aspartate aminotransferase (AST) and lactate dehydrogenase (LDH) were below the detectable analyzer range (HBD grafts) or did not increase significantly during NEVKP (DCD grafts). Perfusate lactate concentration decreased from baseline until the end of perfusion in HBD grafts ($P < 0.001$) and DCD grafts ($P < 0.001$). Post-transplantation, HBD grafts preserved with NEVKP vs. SCS demonstrated similar serum creatinine peak levels (2.0 ± 0.5 vs. 2.7 ± 0.7 mg/dL; $P = 0.11$). In DCD kidney transplantation, renal grafts preserved with NEVKP vs. SCS demonstrated lower serum creatinine on day 1–7 ($P < 0.05$) and lower peak values (5.5 ± 1.7 vs. 11.1 ± 2.1 mg/dL, $P < 0.01$). The creatinine clearance on day 4 was increased in NEVKP preserved grafts (39 ± 6.4 vs. 18 ± 10.6 ml/min,

$P = 0.01$). Serum NGAL at day 3 was lower in the NEVKP group (1267 ± 372 vs. 2697 ± 1145 ng/ml, $P = 0.03$).
Conclusion: Continuous pressure-controlled NEVKP is feasible and safe in HBD kidney grafts and improves renal function in DCD kidney transplantation.

P085 NORMOTHERMIC DONOR LUNG PRESERVATION USING OCS MAINTAINS IL-33-DRIVEN EPITHELIAL INTEGRITY AND SUPPRESSES INFLAMMATION IN THE RECIPIENT

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Introduction and Background: INSPIRE trial revealed significant reduction of PGD grade 3 using the Organ Care System (OCS) compared with standard of care (SOC) for lung preservation. To investigate immunological mechanisms initiated by OCS vs SOC preservation, samples of INSPIRE patients were assessed for proteins involved in epithelial integrity, endothelial activation and immune response.
Methods: Blood plasma and perfusion solutions from 33 patients with OCS- and 26 patients with SOC-preserved lungs were analysed using multiplex protein assays. Donor and recipient demographics, cold ischemic times and PGD scores at 0 (T0) and 24 h (T24) were assessed and correlated with plasma proteins.
Results and Conclusions: Clinical evaluation (OCS vs. SOC) revealed mean recipient age: 50 vs. 49 years, diagnosis: idiopathic fibrosis ($n = 17$ vs. 10), cystic fibrosis ($n = 7$ vs. 8), idiopathic pulmonary hypertension ($n = 3$ vs. 3) and emphysema ($n = 6$ vs. 5), mean total cold ischemic times: 257 vs. 531 minutes. In OCS group, no PGD score >2 was observed in contrast to 19% cumulative PGD 3 in SOC group. IL-33, IL-10, IL-6, IFN-g concentrations were significantly higher in OCS vs. SOC perfusion solutions. High IL-10 and IL-31 levels caused a shift towards an anti-inflammatory milieu resulting in significantly lower IL-6 and IL-8 levels in OCS-recipient plasma at T0. Only in SOC patients, IL-6 and TNF-a levels at T0 correlated with cold ischemic time and IL-6 with PGD score >2. In both groups, plasma IL-6, IL-10, IL-8 and IL-33 concentrations peaked at T0 creating a favourable IL-10/IFN-g ratio only in OCS patients. During OCS preservation, IL-33 expression promotes an anti-inflammatory milieu guided by high IL-10 and IL-31 levels counterbalancing inflammatory reactions in the recipient. Strong correlations of plasma IL-6 and IL-8 levels with cold ischemic times and PGD scores in SOC patients underline clinical relationship between inflammation and graft function. OCS preservation initiates an anti-inflammatory cascade counteracting graft dysfunction.

P086 PORCINE ISLET ISOLATION: INFLUENCED BY ORGAN PRESERVATION SOLUTION AND ANIMAL AGE

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Introduction and Background: The transplantation of porcine islets into man might soon become reality for patients with type 1 diabetes mellitus. Therefore, porcine islets of high quality and quantity, and a scalable isolation process with strict quality control are necessary to provide the best possible off the shelf product. In this study, we provide a comparative study evaluating islet isolation outcome and in vitro survival based upon organ preservation solution (OPS), donor age and cold ischemia time (CIT).
Methods: Göttinger minipig pancreata were harvested according to the standards of human organ retrieval including in situ cold perfusion with either HTK or Belzer® UW solution. Pancreas tissue was characterized histologically and by quantification of apoptotic cells using TUNEL staining prior to islet isolation. The isolation process was performed according to a modified Ricordi method and isolation outcome was assessed by determining islet particle numbers (IP), islet equivalents (IEQ) and isolation factor (IF). Isolated islets were cultured for 24 and 48 hrs for assessment of in vitro survival.
Results and Conclusions: Our results showed a positive impact of HTK over Belzer® UW solution on endocrine tissue viability independent of CIT. Islet isolation resulted in a significantly higher islet yield in the HTK groups compared with the Belzer® UW groups. Remarkably, the usage of HTK solution resulted in stable islet yields even after prolonged CIT and showed superior survival rates of islet in vitro compared with Belzer® UW. Younger porcine donor organs resulted generally in lower islet yield and survival rates.

In summary, HTK solution should be preferred over Belzer® UW solution for the preservation of organs from porcine origin. HTK allows for maintaining endocrine tissue viability and promotes reproducible islet isolation outcome and survival even after longer CIT. The usage of retired breeder animals over young animals for islet isolation is highly advisable in order to yield high quality and quantity.

P087 NORMOTHERMIC *EX VIVO* KIDNEY PERFUSION FOR GRAFT QUALITY ASSESSMENT PRIOR TO KIDNEY TRANSPLANTATION

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Introduction and Background: Normothermic *ex vivo* kidney perfusion (NEVKP) represents a novel approach for renal graft preservation and functional improvement in kidney transplantation. We investigated the possibility to utilize NEVKP as a tool for graft quality assessment prior to transplantation.
Methods: Kidneys from 30 kg pigs were recovered in heart-beating donation (HBD) (group A), following 30 minutes of warm ischemia (WI) (group B), or 60 minutes of WI (group C) with 5 animals in each group. Following 8 h of NEVKP, kidney autotransplantation was performed with resection of the contralateral kidney. Pigs were followed for 3 days. Perfusion characteristics and biomarkers during NEVKP were investigated and correlated with post-transplant renal function.
Results and Conclusions: During NEVKP, intrarenal resistance (IRR) was significantly different from initiation of perfusion until hour 5 with lowest values in healthy grafts (group A), moderately increased values in moderately injured grafts (group B), and highest values in severely injured grafts (group C) ($P < 0.05$). Healthier grafts without warm ischemia time (group A) vs. DCD kidneys (group B and C) demonstrated significantly improved acid base homeostasis with higher pH values for hours 1–6 ($P < 0.05$), higher HCO_{3-} for hours 1–5 ($P < 0.05$), and higher base excess (BE) for hours 1–5 ($P < 0.05$). Lactate clearance was significantly improved in noninjured grafts (group A) vs. DCD kidneys at hours 1–5 ($P < 0.05$). Post-transplantation, renal function was significantly decreased in grafts exposed to prolonged warm ischemia times with significant differences for serum creatinine and serum BUN on day 1–3 ($P < 0.05$, respectively). Pearson correlation demonstrated a correlation of 0.831 between IRR at NEVKP BL ($P < 0.001$), and of -0.878 between pH at NEVKP hour 1 ($P < 0.001$) with post-transplant renal function, respectively. In addition to the improvement of renal function in kidney transplantation, NEVKP allows graft quality assessment prior to transplantation.

P089 COLD STORAGE AND CRYOPRESERVATION OF HUMAN HEPATOCYTES IN MODIFICATIONS OF THE VASCULAR PRESERVATION SOLUTION TIPROTEC

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Introduction and Background: Primary human hepatocytes are important for pharmacological and toxicological research as well as for cell transplantation and bioartificial liver support. Effective medium- and long-term storage options are necessary to ensure availability of these cells. However, hepatocytes are very susceptible to cold-induced injury as well as to cryopreservation injury. We here assessed solutions based on the vascular preservation solution TiProtec for hepatocyte cold storage and cryopreservation.
Methods: Human hepatocytes (10^6 cells/ml) were stored at 4°C or cryopreserved in serum-containing supplemented cell culture medium (Williams' E) or (serum-free) modifications of TiProtec. For cryopreservation, all solutions were supplemented with 10% DMSO and a standard protocol (-1°C/min in a controlled-rate freezer) was applied. After cold storage or rapid thawing, respectively, cells were seeded onto collagen-coated 6-well-plates without further purification steps. Cell attachment and metabolic activity were assessed.
Results and Conclusions: Cell attachment was significantly better after 24 h cold storage in modified TiProtec (with increased iron chelator concentrations) than in cell culture medium (92 ± 15% of control cultures vs. 51 ± 14%; $P < 0.01$). Cell attachment decreased with increasing storage time. After 48 h

storage in modified TiProtec, attachment amounted to 63 ± 9% (cell culture medium: 22 ± 12%). After cryopreservation, cell attachment (25 ± 29% vs. 14 ± 11%) and metabolic activity (resazurin reduction: 41 ± 35% vs. 23 ± 11%) were markedly improved in a low-chloride modification of TiProtec compared with cryopreservation in cell culture medium.

In summary, improvement of cell attachment and function of human hepatocytes was achieved after cold storage in modified TiProtec solution. For cryopreservation, modified TiProtec constitutes a serum-free alternative to classical serum-containing cryopreservation media.

P090 UNIVERSITY OF WISCONSIN VS. BRETSCHNEIDER CARDIOPLEGIA IN HEART TRANSPLANTATION – NEW FACTS FOR AN OLD TOPIC

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Introduction and Background: Countless preservation solutions (PS) have been used for myocardial protection in heart transplantation (HTx). The most widely used are the University of Wisconsin solution (UW) and Bretschneider's solution (HTK), but there are only few studies comparing these two which also presented controversial results. Aim of this study was to review outcome in patients undergoing HTx at the University Jena, where both, UW and HTK, were used in a period of 15 years.
Methods: A retrospective analysis of cardiac allograft recipients between 1999 and 2015 was performed. Primary isolated HTx were included, combined HTx and re-HTx excluded. The study group (n = 131) was divided into 2 groups: Group 1 (n = 77, 1999–2007) was preserved with UW, group 2 (n = 54, 2007–2015) with HTK. Pre-, peri-, and postoperative parameters of donors and recipients were analyzed and taken into account as influencing factors. Outcome variables were cardiac Troponin I (cTNI), hemodynamic parameters measured by Swan-Ganz catheter and 30-day survival. Multivariate regression analysis was performed to compare the two groups.
Results and Conclusions: cTNI was significantly lower in UW than in HTK during the first postoperative week and PS had significant impact during the first 3 postoperative days. Hemodynamic situation was significantly better in UW than in HTK during the first 3 postoperative days and PS had significant impact on cardiac index and central venous pressure during this period. 30-day survival was 84.4% in UW and 79.6% in HTK, but PS had no significant influence on short-term mortality.

UW appears to provide significant better myocardial protection as evident by better graft function after HTx compared with HTK. These functional findings are supported by a not significant trend toward better 30-day survival in UW compared with HTK.

LIVING DONATION

P093 LIVING RENAL DONATION – GENDER EFFECTS ON QUALITY OF LIFE

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Introduction and Background: A careful donor selection is very important as well as a consistent donor follow-up. Gender specific effects might be detected concerning quality of life.
Methods: Living renal donors at the Transplant Center Heidelberg, University Hospital were evaluated using the standardized 36-item short form health survey [SF-36] questionnaire).
Results and Conclusions: Altogether 211 living renal donors were evaluated (131 female, 62.1%). The SF-36 physical component summary score was comparable in female and male donors (51.8 ± 10.1 vs. 53.9 ± 7.9; ns). The SF-36 mental component summary score was significantly lower in female donors compared with male donors (47.6 ± 13.0 vs. 51.7 ± 11.0, P = 0.012). In all subscale male donors presented higher scores compared with female donors. Male donors had the highest scores in social functioning, female donors in physical functioning. In most of the SF-36 scales, female donors showed comparable or even better results compared with a German general population. However, in the scales social functioning, emotional role functioning and mental health female donors had lower scores compared with an age- and gender-matched general population. Male donors presented higher scores in all SF-36 sub-scales compared with an age- and gender-matched general population (significant scales: vitality, physical component summary score).

Quality of life assessed by the SF-36 questionnaires shows several gender specific differences in living renal donors. Especially, female donors are on increased risk concerning mental and emotional health after donation. Careful evaluation of these female donors is mandatory.

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P094 LIVING RENAL DONATION – ASSOCIATION BETWEEN GENDER AND MENTAL STRESS AFTER LIVING DONATION

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Introduction and Background: In living renal donation, careful donor selection is as important as consequent donor follow-up. This includes both, physical and mental health. There might be some gender specific differences. The question to be answered by this evaluation was: Are there any associations between gender and signs of mental stress or impairment?
Methods: Living renal donors at the Renal Transplant Center Heidelberg were evaluated using standardized questionnaires (Hamilton Anxiety Depression Scale, HADS-D; Perceived Stress Scale (PSS)).
Results and Conclusions: Altogether, 211 of 261 (80.8%) questionnaires could be analyzed. Mean age at time of donation was 51.7 ± 9.9 years (131 female), and mean time after donation was 9.7 ± 5.2 years. Results on the HADS-D depression scale (4.0 ± 3.71 vs. 3.68 ± 3.58) and as the anxiety scale (5.09 ± 3.54 vs. 4.4 ± 3.56) were comparable in female and male donors. Female and male living donors aged >60 years had better results compared with a German general population. Female and male living donors aged 40 to 59 years showed comparable results to a German general population. Mental stress was evaluated using the PSS. Female donors presented significantly increased mental stress compared with male donors (P = 0.003). Generally, there is no increased mental stress after living donation compared with a general population. However, there are distinct gender- and age-specific differences. Female donors should be evaluated carefully concerning mental health.

P096 FATIGUE, DEPRESSION, ANXIETY, AND QUALITY OF LIFE IN LIVING KIDNEY DONORS

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Introduction and Background: In recent years, fatigue has been discussed as a potential problem after living kidney donation (LKD). Increased fatigue might affect donors' quality of life (QOL), but prospective studies assessing fatigue with a standardized instrument are still rare. Research is especially needed on possible influencing factors, e.g. sex, age, depression, kidney function, recipient outcome, and social interaction with the recipient.
Methods: Donors were prospectively assessed before and 1 year after LKD. QOL was evaluated with the Short-Form 36-Item Health Survey (SF-36), anxiety and depression with the Hospital Anxiety and Depression Scale (HADS), and fatigue with the Multidimensional Fatigue Inventory (MFI-20).
Results and Conclusions: Of 68 German-speaking donors (LKD February 2012–May 2015), pre- and postoperative data were available from 47 donors (69%). Mean age at LKD was 54.9 years (SD=10.3), 64% were female. The majority of recipients were adults (89%); 47% were the donor's child, 38% spouse/partner, 9% sibling, and 6% other.

Significant QOL decreases were observed in the SF-36 in 'vitality' (P = 0.001), 'social functioning' (P = 0.03), and the 'mental component summary' (P = 0.04), while the 'physical component summary' was not different from the preoperative level. In the affected domains, the preoperative score was superior to the general population, whereas the postoperative score was similar to the general population. Neither the MFI-20 nor the HADS showed significant pre- to postchanges.

There were strong correlations (r = 0.6–0.9) between fatigue, vitality, mental QOL, anxiety, and depression, but only 4 of 47 donors showed clinically relevant depression scores 1 year after LKD. No significant associations were found with sex, age, or serum creatinine/GFR. Moderate correlations (r = 0.3–0.5) were observed between donor-rated physical well-being of the recipient and changes in donors' mental well-being. These and other variables affecting donors' vitality and mental well-being should be explored more thoroughly.

P098 LIVING RENAL DONATION – ADHERENCE OF DONORS TO FOLLOW-UP ASSESSMENTS

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Introduction and Background: Careful follow-up assessments of living donors are necessary for early detection of risk factors concerning donor's renal function and general health. Adherence of living kidney donors to regular check-ups at the transplant center was evaluated.
Methods: Living kidney donors at the Transplant Center Heidelberg were assessed regarding adherence to regular follow-up visits.
Results and Conclusions: Regular follow-up visits were performed by 46.9% of the living kidney donors (44.3% female). 28.5% donors regularly visited an outpatient nephrologist or a general practitioner. No donor check-ups were done by 32.8% of the female and 23.8% of the male donors. The following reasons for missing follow-up visits at the transplant center were "no need" (40.5%), satisfactory care by the outpatient physician (29.7%), too long distance (13.1%). Reorganization was performed 2012 to improve adherence to donor follow-up. A significant increase of follow-up visits at the transplant center was noticed (36.4% vs. 77.7%, $P < 0.001$).
Conclusion: Adherence to follow-up visits is comparable with literature data. Reorganization improved the donor adherence significantly. The aim to perform follow-up examination at the transplant center at least once yearly to ensure a consistent and effectual long-term living renal donor care.

ETHICS / PSYCHOSOMATICS

P100 FORCIBLY DISPLACED PATIENTS PRESSURIZE LIVER TRANSPLANT LIST IN GERMANY

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Introduction and Background: In 2015 more than one million people arrived in Germany seeking refugee status. The continued influx of migrants is a major challenge for Germany's health care system, which is tasked with providing essential medical services for the new arrivals — and may have to deal with novel and unexpected challenges such as the urgent need for transplantation of asylum-seekers and refugees.
Methods: Currently, there are no guidelines at either the national or supranational level regarding the provision of liver transplant services to non-residents.
Results and Conclusions: Most centers accept non-residents only in case of acute but not for chronic liver failure. With the massive influx of forcible displaced people also people with chronic liver disease arrive that require urgent liver transplantation. Some of those specifically request refugee or asylum-seeker status to be transplanted, which heats up a debate whether these people should be listed to be transplanted with a organ from the national donor pool. With this question many ethical and practical issues are implied. Here, we tell the story of 5 foreign nationals who came to Germany in 2015 to be transplanted. Each individual scenario is different, but highlights the problems that arise with these cases.

P101 A PSYCHOTHERAPY MANUAL FOR THE OPTIMIZATION OF IMMUNOSUPPRESSANT ADHERENCE AFTER KIDNEY TRANSPLANTATION: RESULTS OF THE FEASIBILITY STUDY

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Introduction and Background: Up to 67% of renal transplant (RT) recipients are classified as nonadherent to immunosuppressant (IS) medication. Nonadherence is significantly correlated with transplant rejection and loss. Therefore, effective interventions to improve medication adherence among RT recipients are needed. But only a limited number of interventional psychotherapy studies on the transplant population is available. The objective of this manual is to optimize adherence to immunosuppressant medication and to stabilize mental well health. Outcome variables for the feasibility study are the acceptance by the patients and their study participation rate. Furthermore acceptance of an electronic medication event monitoring system (MEMS) was examined.
Methods: Inclusion criteria: 18 months after renal transplantation, admission by nephrologist, German speaking, no further cognitive or psychiatric disability. The manual is based on the health believes model and cognitive behavioral therapy and includes following techniques: Psychoeducation, the Life-Routines Model, and behavioral contracting. It consists of one individual and seven group sessions in four months. Contents are illness history and acceptance, as well as prevention of depressive symptoms. Psycho-education focuses on effects and side-effects of IS, marital and family relationships. Immunosuppressant adherence was monitored and supported using a novel electronic pillbox (MEMS) VAICA Simple med ©, which is coupled to a password-protected website. Optimization of adherence was focused on in every session according to the electronic feedback reports.
Results and Conclusions: Seven patients (age: 63.1 (54–78) female/male: 2/7) took part after informed consent. They showed high acceptance and high participation rates (91%). The technological properties of the VAICA Simple med© were assessed as consumer-friendly. A multicenter clinical trial has been planned to scrutinize the treatment outcome.

P102 AVOIDANCE OF LIVER TRANSPLANTATION IN SEVERE ALCOHOLIC LIVER DISEASE PATIENTS ABSTINENT FOR 6 MONTH

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Introduction and Background: Most transplant centers demand a 6 months period of alcohol abstinence prior to listing for liver transplantation (LT) in alcoholic liver disease (ALD). However, the 6-months rule was frequently challenged since the 6-months period is arbitrary and there are probably multiple other psychosocial factors that predict alcohol relapses. Nevertheless, clinical experience shows that many patients with ALD who stop drinking recompensate during their waiting period to a stage where they do not need a liver transplantation anymore. So far, no data are available on the rate of ALD patients, improving during their waiting period, so that a LT can be prevented.
Methods: From 2007 to 2014 546 patients were listed for LT at Transplant Center Munich. ALD transplant recipients (ALDTX) and ALD patients removed from wait-list (ALDR) were retrospectively compared regarding demographic data, psychiatric diagnoses and addiction parameters.
Results and Conclusions: ALD was the second most indication for listing to LT. 29% ($n = 157$) of patients were removed from wait-list. Improvement of liver function was the main indication (57%) for removal, whereas mostly ALD patients improved. Length of sobriety was significantly shorter in ALDR compared with ALDTX. No difference could be detected regarding number of daily drinks or prior alcoholism treatment between both groups. However, ALDR patients, which improved during their waiting time, had the longest abstinence period and lowest daily alcohol amount prior listing. In contrast to psychosocial or addiction parameters only length of sobriety was significantly associated with the probability of delisting due to improvement of liver function.

Further prospective studies are necessary to identify protective factors which secure persistence alcohol abstinence and contribute to the avoidance of LT in ALD patients.

P104 PSYCHOSOCIAL AND SEXUAL FUNCTIONING IN PATIENTS ON VENTRICULAR ASSIST DEVICE SUPPORT – A CROSS-SECTIONAL PILOT STUDY

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Introduction and Background: Implantation of ventricular assist devices (VAD) may have psychological and physiological effects on the individual in the long-term. There is paucity in the literature describing VAD patients' concerns and questions about psychosocial and sexual outcomes. This study aimed to (a) assess psychosocial and (b) sexual functioning, and (c) needs for information regarding sexuality while being on VAD support.
Methods: A cross-sectional design was used and a sample of $n = 59$ VAD patients completed a battery of standardized questionnaires. Median age was 60 (±SD 14) years, 83.1% of patients were male, and 74.9% were married or lived with a partner. Median time on device was 743 days (range 362–2.657), dilative (52.6%), ischemic (45.6%) cardiomyopathy, and others (1.8%) being the diagnoses for VAD implant.
Results and Conclusions: Self-reported quality of life (QoL [SF-36, range 0–100]) was impaired being 31.4 for the physical, and 43.1 for the mental component score; anxiety (HADS, range 0–21) was 6.1, and depression (6.5) symptoms were within normal ranges, and overall life satisfaction (VAS, range 0–100) was 54.5. Patients expressed impairments regarding sexual functioning (PAIS, range 6–24) median being 15 due to their disease. Overall, 59.3% admitted the VAD impacted their sexual life. The driveline was perceived to 'disturb' (56.9%), and to 'hamper' (54.5%) sexuality, to be less 'attractive to a

partner' (46.5%), 37.9% felt 'mentally frozen', and 62.0% felt impaired by the battery pockets. Younger patients (≤60 years) reported on a better physical component of their QoL ($P < 0.005$), and higher depression symptoms ($P < 0.03$). Younger men perceived a higher disturbance of their sexual life ($P < 0.04$), whereas device types did not impact psychosocial and sexual functioning.

Psychosocial communication training for sexual counseling and written information might be supportive to patients to better cope with their condition.

P105 STANDARDIZED EVALUATION OF CANDIDATES PRIOR TO LIVER TRANSPLANTATION WITH THE TRANSPLANT EVALUATION RATING SCALE (TERS): PSYCHOMETRIC PROPERTIES OF THE INSTRUMENT

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Introduction and Background: The Transplant Evaluation Rating Scale (TERS) was developed to provide a standardized evaluation of the psychosocial functioning of patients, prior to transplantation. Yet, the first two items of TERS are based on psychiatric diagnoses referring to DSM, which leads to a duplication of disorder-specific and symptom-specific contents, that makes it complex and ambiguous to rate. Furthermore, it would be necessary to update the instrument every time new DSM guidelines are published. The objective of this study was therefore to investigate if a revised version of TERS (diagnoses-corrected by omission of the first three items) can be suggested.
Methods: In 85 patients awaiting liver transplantation, the discrimination capacities, predictive value, convergent validity, and interrater reliability of the original version (TERS10) and the diagnoses-corrected version (TERS8) were analyzed.
Results and Conclusions: In both versions, patients with psychiatric diagnoses (69.4%) exhibited significantly higher TERS mean values than patients without psychiatric disorders. This also held for patients that were excluded from the transplantation waiting list in the psychosomatic evaluation (25.9%) compared with patients who were eligible. Furthermore, both versions were significant predictors of patient group membership (eligible versus excluded). Moreover, the items social support and previous coping were significantly correlated with the respective self-ratings. Interrater reliability was $0.786 \leq r \leq 0.842$ ($P < 0.001$) for TERS10 and $0.842 \leq r \leq 0.709$ ($P < 0.001$) for TERS8.

Our results substantiate good psychometric properties of the revised (diagnoses-corrected) TERS, which is of great benefit for standardized psychosocial evaluation prior to liver transplantation. We therefore suggest further validation in other samples of transplantation patients.

P107 IS THERE A RELATIONSHIP BETWEEN OBESITY AND ADHERENCE TO IMMUNOSUPPRESSANTS IN PATIENTS AFTER RENAL TRANSPLANTATION?

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Introduction and Background: It is known from the literature that physicians frequently have a negative bias toward obesity which has been shown to also influence their perception of medication adherence.
Methods: We examined the relationship of post-transplant obesity with different measures of adherence to immunosuppressants (IS) and depression. In a cross-sectional study 241 kidney transplant recipients who were at least 1 year post-transplant (mean 7.2 years) participated of whom 23.7% ($n = 57$) were obese (BMI ≥ 30 kg/m^2).
Results and Conclusions: No associations between obesity, depression, self-rated adherence and physicians' estimation of adherence to IS were found. Also the occurrence of acute biopsy-proven rejection episodes within the previous 12 months did not differ between groups. However, obese patients exhibited a significantly higher IS serum level variability. Since IS serum level variability cannot be seen as a pure measure of adherence, the study does not provide convincing evidence that obesity is associated with nonadherence to IS in patients after kidney transplantation.

In conclusion, a negative perception of adherence in obese patients is not justified. Nevertheless, the higher serum level variability in obese patients might not exclude a potentially higher incidence of chronic rejections and graft failure at later time points.

SIGNIFICANCE OF MARGINAL DONORS AND RECIPIENTS

P108 EXTENDED PANCREAS DONOR PROGRAM – THE EXPAND STUDY: A PROSPECTIVE MULTICENTER TRIAL TESTING THE USE OF PANCREAS DONORS OVER AGE 50

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Introduction and Background: Pancreas transplantation is the only curative treatment option for patients with type 1 diabetes. Organ shortage and restrictive allocation criteria are the main reasons for increasing waitlists leading to severe morbidity and mortality. We designed a study to increase the donor pool with organs exceeding the currently allowed donor criteria.
Methods: The aim was to extend the organ pool by using organs with extended donor criteria (EDC) either from donors age 50 to 60 or with a BMI 30 to 34 kg/m^2. Therefore a new allocation system was implemented. The study was a prospective, multicenter, nonrandomized, two-armed trial. The primary endpoint was pancreas graft survival and function after 3 months. Rejection episodes, kidney function and waitlist time were secondary endpoints. Patients who agreed to participate and received an EDC allograft were included as study group patients, recipients of a standard criteria organ as control-group patients. Patients received standard immunosuppressive treatment. Follow-up was 1 year.
Results and Conclusions: 79 patients were included in 12 German centers. 18 received an EDC organ, 61 a standard criteria organ. Recipient demographics were similar. Mean donor age was 51.4 ± 5 years in the EDC group vs. 31.7 ± 12 in the control group. Insulin-free graft survival was 83.3% for EDC organs vs. 67.2% for standard organs ($P = 0.245$) after 3 months. Pancreas graft survival was 83.3% in the EDC group after 1 year and 83.5% in the standard group. Kidney graft survival was 94.4% in both groups after 1 year. Rejection episodes or morbidity did not differ between groups.

The EXPAND study shows for the first time in a prospective trial that EDC organs of donors older than 50 years can be used with similar outcome. Therefore, organ shortage and waiting times can be reduced by transplanting carefully selected EDC organs without additional risk. This study substantiates the full implementation of EDC organs in the pancreas allocation system.

www.clinicaltrials.gov: NCT01384006

P109 LIVING KIDNEY DONATION IS SAFE FOR ELDERLY DONORS

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Introduction and Background: Living donation in kidney transplantation has proven to provide superior results for the recipients compared with DBD graft or dialysis. Nevertheless the safety of the donor is a major concern.
Methods: We analyzed 94 living kidney donors above the age of 65 years (mean 69 years, range 65 to 79 years). 37 donors were above the age of 70 years. Donation was performed between 1999 and 2015 in two German transplant centers. 43 donors were male. 11 donors had a BMI above 30 and 46 took antihypertensive medication at time of donation. Before donation donors had a normal kidney function with a mean s-creatinine of 0.8 mg/dl (range 0.4–1.2 mg/dl) and a clearance of 90 ml/min (MDRD).
Results and Conclusions: Donors were discharged from hospital after a mean of 6.2 days with a s-creatinine of 1.3 mg/dl (range 0.8–2.1 mg/dl).

For 79 donors at least 1 year follow up (FU) is available. None of the donors died, none required dialysis or kidney transplantation. After a mean FU time of 4.4 years the mean s-creatinine of the donors was 1.2 (range 0.7–1.8 mg/dl), with a calculated clearance of 58 ml/min (MDRD).

The mean age of the recipients was 51 years (range 26 to 77 years). Recipient data with at least 1 year FU is available for 89 patients. 7 (8%) recipients died. 18 grafts were lost, resulting in a graft survival of 78%.
Conclusion: Living donation from elderly donors is safe for the donor with regards to stable kidney function in all donors analyzed. For the (younger) recipients living donation from elderly donors might have an inferior graft outcome compared with younger donors, but it has to be kept in mind, that the alternative for living donation from an elderly donor might be staying on dialysis for more than 5 years with an inferior patient survival.

P111 APPLICATION OF THE LIVER MAXIMUM FUNCTION CAPACITY TEST (LIMAX) IN ACUTE LIVER FAILURE – A HELPFUL TOOL FOR DECISION-MAKING IN LIVER TRANSPLANTATION?

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Introduction and Background: Acute liver failure (ALF) may require high-urgency liver transplantation (LTx) despite an aggressive intensive medical management. Current prognostic scores do not apply for all patients, thus a reliable tool to enable identification of individuals in need of LTx are highly required. The liver maximum function capacity test (LiMAx), already applied in liver surgery, might represent such an appropriate option. Below a case of ALF after *Amanita phalloides*-intoxication is presented to discuss the potential of the LiMAx-test in this setting.
Methods: LiMAx and rotational thromboelastometry (ROTEM) were performed in a 27-year old male patient prior to and after high-urgency LTx. Retrospective analysis of these data was performed with respect to clinical and laboratory parameters.
Results and Conclusions: In accordance with clinical appearance of hepatic encephalopathy, coagulopathy (confirmed by ROTEM) and acute kidney failure, the LiMAx-test constituted a fulminant course of ALF with hardly any detectable metabolic activity (11 μg/h/kg; at norm >315 μg/h/kg) 6 days after toxin ingestion. Following subsequent LTx with a marginal donor-organ (95% hepatosteatosis), uptake of liver function was demonstrated by increase of the liver capacity on postoperative days 3 and 10 (114 and 304 μg/h/kg, respectively). The patient eventually was discharged from hospital on day 26 after LTx without major complications. In conclusion, ALF often is associated with a critical state of the patient that requires almost immediate decision-making regarding further therapy. Application of a noninvasive liver function test might help to determine the prognosis of ALF and support decision-making for or against LTx as well as acceptance of a critical donor organ in case of a critically ill patient.