ELEVATOR PITCH PRESENTATIONS

Clinical Liver Other

EP001

A MULTICENTER, RANDOMIZED, PLACEBO-CONTROLLED TRIAL OF EXTRACT OF JAPANESE HERBAL MEDICINE DAIKENCHUTO TO PREVENT BOWEL DYSFUNCTION AFTER ADULT LIVER TRANSPLANTATION (DKB 14 STUDY)

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Background: Postoperative early oral or enteral intake is a crucial element of the Enhanced Recovery After Surgery (ERAS) protocol. However, normal food intake or enteral feeding cannot be started when a patient has bowel dysfunction, especially after liver transplantation (LT). Therefore, we conducted a multicenter, randomized, double-blind, placebo-controlled trial to determine the enhancement effects of Daikenchuto (DKT) upon oral/enteral caloric intake in patients undergoing LT (UMIN000014326).
Methods: One hundred and twelve patients undergoing LT at 14 leading Japanese centers were enrolled. Patients were randomly assigned to receive either DKT (15.0 g/day) or matching placebo from postoperative day (POD) 1 to 14. Primary endpoints were total oral/enteral caloric intake, abdominal distension and pain on POD 7. Secondary endpoints included sequential changes of total oral/enteral caloric intake after LT, numeric rating scales for abdominal distention and pain, portal venous flow and speed to the graft and so on.
Results: A total of 104 patients (DKT, $n = 55$; placebo, $n = 49$) were included and evaluated in the statistical analysis. There were no significant differences between the two groups in terms of primary endpoints. However, postoperative total oral/enteral calorie intake was significantly accelerated in the DKT group than in the placebo group ($p = 0.023$). Moreover, portal venous flow (POD 10, 14) and speed (POD 14) were significantly higher in the DKT group compared with the placebo group ($p = 0.047$, $p = 0.025$, $p = 0.014$, respectively).
Conclusion: Postoperative administration of DKT effectively enhances total oral/enteral calorie intake after LT and would contribute to performance of ERAS.

Clinical Kidney Metabolic complications

EP002

OUTCOME OF BARIATRIC SURGERY IN OBESE RENAL TRANSPLANT RECIPIENTS: SINGLE CENTER EXPERIENCE

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

We aimed to assess the outcomes of metabolic surgical procedures among renal transplants compared to conventional group of patients.
Patients and methods: In this retrospective study, we analyzed the collected data of obese patients (BMI > 38) after kidney transplantation who underwent metabolic surgical procedures during the last 5 years ($n = 25$ cases) in comparison to control obese group without this type of surgery ($n = 41$ cases). Roux-en-Y gastric bypass was the most common procedure.
Results: The two groups of patients were matched regarding their demographic data, type of donor, cases with IHD, type of induction and maintenance immunosuppression. Most of patients in bariatric group were females (60% vs. 84% males in other group, $p = 0.03$). The basal and last follow up mean BMI values were (38.3 ± 8.9 and 33.3 ± 7.3) vs. (44.2 ± 5.6 and 44.2 ± 6.7) with mean weight loss percentage $15.4 \pm 5.1\%$ vs. $0.4 \pm 0.2\%$ in the control group ($p = 0.05$). The 2 groups were matched regarding pre-transplant diabetics but the total number of diabetics in the control group was significantly higher (73.3% vs. 40%, $p = 0.042$).the 2 groups were matched regarding cases with gall bladder stones, sleep apnea and hyperuricemia management. We observed no significant difference between the 2 groups regarding rejection episodes, graft and patient outcomes ($p > 0.05$). There were no postoperative complications except strangulated hernia in one case; and postoperative DVT and pulmonary embolism in another.
Conclusion: Metabolic surgical techniques may be used safely and effectively-with some precautions- to control obesity among renal transplant recipients. Longer term and larger studies are needed to evaluate metabolic parameters and long term patient and graft outcome.

Clinical Kidney Cardiovascular complications

EP003

LEFT VENTRICULAR HYPERTROPHY AS PROGNOSTIC FACTOR AFTER KIDNEY TRANSPLANTATION: DOES PATTERN TYPE MATTER?

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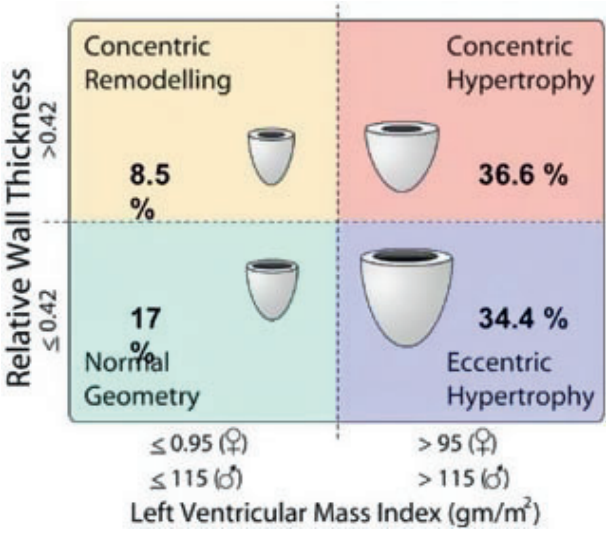
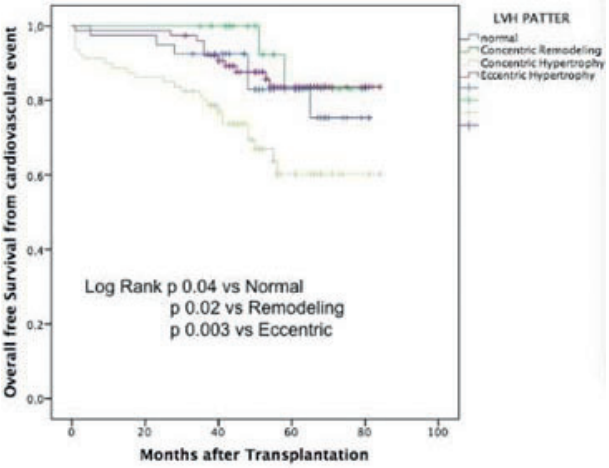
Introduction: Left ventricular hypertrophy is one of the most important prognostic factors of cardiovascular survival in CKD and/or dialysis patients. Few studies have evaluated the prognostic impact of LVH measured by echocardiography in kidney transplant patients. LVH could be classified in concentric remodelling, concentric or eccentric LVH. Our main objective was to evaluate the prognostic impact of LVH after renal transplant as well as to assess whether there is difference among the different types of LVH.
Methods: The echocardiograms performed as screening for admission on transplant waiting list from 2010 to 2013 were evaluated retrospectively. All echocardiograms were carried out no earlier that 6 months before transplant by three expert cardiologists. A cardiovascular combined endpoint was used, including: atrial fibrillation, heart failure, stemi with or without need of myocardial revascularization, sudden cardiac death, ictus, aortic dissection.
Results: Out of 465 renal transplant patients from 2010 to 2013, 236 were included in the analysis, the remaining patients were excluded because an echocardiogram before transplant was not available or it was done earlier than 6 months before transplant. From the results obtained it has been possible to classify patients into 4 categories: regular, concentric remodelling, concentric LVH, eccentric LVH. (Figure 1).



Patients with HVI had more cardiovascular events compared to other patients, although the data was not significant (22% vs 13% χ^2 $p < 0.15$). When we analysed according to LVH type, only patients with concentric hypertrophy had worse prognostic compared to others groups (including eccentric) (Figure 2).



Finally, cox regression logistic analysis to predict cardiovascular events showed that only Concentric LVH was predictive of cardiovascular events in our cohort (Table 1).

	HR	95 % IC	p
Sex (F vs M)	0.97	0.48–1.80	0.82
Diabetes before Transplant (Y vs N)	2.14	1.1–4.57	0.048
Age Recipient (each Year)	1.058	1.021–1.096	0.002
GFR (CK-EPI) at 1 years	0.99	0.98–1.09	0.46
Previous Cardiovascular Event	1.17	0.50–2.73	0.70
LVH (Y vs N)	1.19	0.39–3.64	0.75
LVH (Concentric vs others)	2.83	1.31–6.12	0.008
ACEi or ARBs after transplant (Y vs N)	1.10	0.44–2.74	0.82

Conclusion: Among geometric patterns only concentric LVH was related to an increase in cardiovascular events.

Clinical Kidney Infection

EP004

SAFETY AND EFFICACY OF SOFOSBUVIR-BASED DIRECT-ACTING ANTIVIRAL AGENTS IN KIDNEY TRANSPLANT RECIPIENTS WITH HCV: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Outcome data on sofosbuvir (SOF)-based therapy in patients with kidney transplantation (KTx) with hepatitis C virus infection are limited with individual studies having a small sample size and limited SVR12 (sustained virological response) data. In this work, we aimed to perform a systematic review and meta-analysis to evaluate the efficacy and tolerability of SOF-based DAAs in KTx recipients.
Methods/materials: We conducted a systematic literature search in MEDLINE, EMBASE, The Cochrane Library, Web of Science, and ClinicalTrials.gov as well as major transplantation meetings. We included studies with SVR data in HCV infected KTx recipients treated with SOF-based DAAs. All statistical analyses were conducted by R 3.3.1 (The R Foundation for Statistical Computing).
Results: We included eleven studies with a total of 360 KTx recipients. Most KTx recipients (208/236 = 88.1%) had HCV-1 infection. The overall rate of SVR12 reached 94% (95% CI: 88% to 97%). No publication bias was observed ($p = 0.11$). The clearance rate of HCV RNA at the end of treatment (EOT) (12 weeks) was 94% (95% CI: 87% to 97%). SVR4 reached 99% (95% CI: 93% to 100%) in a total of 117 KTx recipients. The rate of rapid virological response (RVR) was 73% (95% CI: 55% to 85%). The SOF-based DAAs did not impact the kidney function, whereas the liver enzyme parameters (such as ALT, ATS) had decreased during and after anti-HCV therapy. The most frequent AEs were headache 6.9% ($n = 25/360$), asthenia 4.4% ($n = 15/360$), fatigue 3.3% ($n = 12/360$) and gastrointestinal symptoms (nausea or diarrhea) 1.7% ($n = 6/360$).
Conclusion: SOF-based treatment is highly effective and well tolerated in KTx recipients with HCV infection.

Clinical Kidney Cancer

EP005

DE-NOVO CANCERS AFTER KIDNEY TRANSPLANT: EVIDENCE FROM A INVESTIGATION IN A HIGH-USE MTOR INHIBITORS TRANSPLANT CENTER

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Background: An excess of cancer risk among kidney transplant (KT) recipients has been well documented in several countries. To better quantify the risk of de novo cancers (DNC) after transplant and to identify major risk factors for cancer occurrence we have carried out a investigation in our center.
Methods: A preliminary study was conducted on a retrospective cohort of 732 patients (2004–2009). Patients with a pretransplant cancer (178), history of cancer (except NMSC, 12), follow-up less than 30 days (6) and pediatric patients (6) were excluded. Person years (PYs) at risk of cancer were computed from 30 days after transplant to date of cancer diagnosis, death, or to study closure, whichever comes first. The risk of developing a DNC (excluding NMSC) was assessed through sex- and age-standardized incidence ratios (SIR and 95% confidence intervals, CI) computed by dividing the observed cases with expected ones from Spanish Cancer registries.
Results: 530 KT recipients (62% men, median age 52.2 years) summed up 3598.4 PY; median time of follow-up: 6.9 years (IQR: 5.2–8.6). Thirty-five transplant patients (6.6%) developed a DNC cancer: solid tumors (29 cases: 7 lung, 6 prostate, 5 kidney, 3 melanoma), PTLD (4:3 non-Hodgkin's lymphoma), KS(2). The overall incidence rate was 9.92 cases/103 PYs and the excess risk, as compared to the general population for all tumor was 1.2-fold higher (95% CI: 0.9–1.7). Excess risk was found for patients with age less than 45 years (SIR = 3.7, 95% CI: 1.0–9.5) and in the 45- to 60-year age group (SIR = 2.0, 95% CI: 1.0–3.4). Elevated SIRs were noted for KS (SIR = 57.2, 95% CI: 6.9–206.6), kidney carcinomas (SIR = 7.5, 95% CI: 2.4–17.4) and melanoma (SIR = 5.8, 95% CI: 1.2–17.0).

Conclusions: Our study provides information about the excess of cancer risk following KT in a high-use mTOR inhibitors center even if a larger cohort of patients and a longer period of follow-up are necessary to better characterize cancer development in KT.

Clinical Kidney Infection

EP006 RISK OF BK VIREMIA WITH EVEROLIMUS VERSUS MYCOPHENOLATE MOFETIL ADDED TO A DE NOVO BELATACEPT REGIMEN

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Introduction: BK viremia is a common infection following kidney transplantation. *In vitro* data suggest that inhibition of the mTOR–SP6-kinase pathway prevents expression of early viral genes necessary for replication. We hypothesized that the utilization of an mTOR inhibitor (mTORi) instead of MMF as the antiproliferative agent in combination with belatacept would reduce the risk of BK viremia.
Methods: Retrospective analysis of 58 kidney transplant recipients receiving *de novo* belatacept with rATG induction +/- maintenance corticosteroids who were either converted from MMF to everolimus at 30 days post-transplant as part of a clinical protocol ("Everolimus group", $n = 43$) or remained on MMF ("MMF group", $n = 15$). All patients were screened with monthly quantitative BKV DNA PCR in plasma for the first 6 months post-transplant. We compared the incidence of BK viremia at 6 months in the two groups using Pearson's chi-squared test.
Results: Demographic and clinical characteristics are listed in the Table.

Characteristic	Everolimus group ($n = 43$)	MMF group ($n = 15$)	p Value
Male gender (%)	58	67	0.56
Race (%)			0.23
White	39	73	
Black	11	13	
Other	44	20	
Ureteral Stent (%)	9	20	0.66
Acute Rejection (%)	11.6	6.7	0.54
6-month eGFR (ml/min/1.73 m^2)	62	58	0.55
BK infection			
6-month incidence of viremia (%)	27	20	0.56
Mean onset of viremia (POD)	117	63	0.16
Peak viral load (copie/ml)	376 372	45 783	0.42

The incidence of BK viremia at 6 months was not significantly different between the 2 groups. Viremia appeared later in the everolimus group than in the MMF group (mean POD 117 vs. 63; p = 0.16) but this difference was not statistically significant. There were no differences in the peak viral load or time to peak viremia between the 2 groups.
Conclusion: No differences were seen in the incidence or severity of BK viremia among kidney transplant recipients on everolimus vs. MMF in combination with belatacept. There was a non-significant trend toward later onset of viremia in the everolimus group. Additional follow up is ongoing to examine outcomes at 1 year post-transplant.

Clinical Kidney Other

EP008 ONE-YEAR OUTCOMES OF A COHORT OF RENAL TRANSPLANT PATIENTS RELATED TO BMI IN A STEROID SPARING REGIMEN

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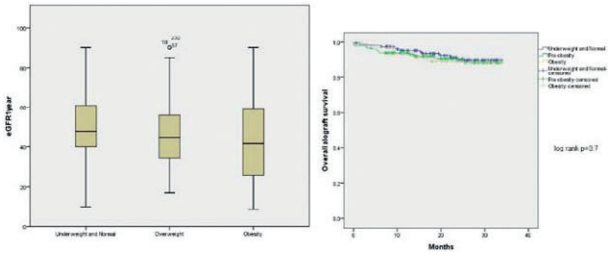
Background: The prevalence of overweight and obese kidney transplant recipients (KTR) has risen in parallel to the obesity epidemic that has affected the general population over the last two decades. At present, there is an ongoing debate regarding the suitability for transplantation of obese patients.
Methods: Data was prospectively collected on consecutive single organ KTR transplanted between January 2014 and March 2016. The patients were stratified according to their body mass index (BMI) using the WHO classification. As a measure of allograft function MDRD eGFR was used at 3, 6 and 12 months post-Transplant.
Results: We included 370 KTR: 126 female, aged 52.7, range 19–77 years, followed up for 19.5+ 8.6 months (0–33 months). In total 155 KTR (41.9%) were underweight or of normal BMI at transplant, while 148 (40%) were overweight, and 67 (18.1%) were classified as obese [47 (12.7%) class 1, 11 (3%) class 2, 9 (2.4%) class 3]. Overweight and obese KTR had a higher incidence of pre-transplant diabetes (p = 0.21), but no difference was found in new onset hyperglycemia post-transplant (p = 0.35). There was also no difference in post-transplant hospital length of stay (p = 0.386). Obese and overweight KTR had a significantly lower eGFR than underweight and normal BMI KTR at 3 and 6 months post-transplant, a finding that did not persist at 1 year follow up. Overall, 23 patients lost their grafts and 20 patients died during follow-up. Kaplan Meier analysis showed no difference in allograft loss between the different BMI groups (log rank p = 0.7).



Conclusion: In this single center study, which utilized short-term data, overweight and obese patients were shown not to have inferior outcomes regarding renal function at 1 year post transplant.

Clinical Pancreas/Islet Ischemia-reperfusion and preservation

EP009 CONTRIBUTING FACTORS AND IMPACT OF MICROBIAL CONTAMINATION IN HUMAN ISLET ISOLATION AND TRANSPLANTATION

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Background: The microbiological safety of islet preparations is of paramount importance. Preservation medium contamination is frequent and its impact on islet yield and function remains unclear.
Methods: All microbiological samples collected during islet isolations from 2006 to 2016 were analyzed and compared to isolation and transplantation outcomes.
Results: Microbiological contamination of the preservation medium was found in 297 of 463 (64.1%) processed donor pancreases. We identified 475 microorganisms including *Staphylococcus* species (261/475, 54.9%), *Streptococcus*species (33/475, 6.9%) and *Candida* species (25/475, 5.3%). Microbial contamination was associated with longer warm ischemia time (from cross-clamp to pancreas explantation), as well as lower number of islet equivalents (IEQ), islet yield, purity and stimulation index. Twelve of 204 (6%) preparations accepted for transplantation showed microbial contamination after isolation; nine were contaminated with Candida species. Six patients were transplanted with a sample with late microbial growth discovered after the infusion. Insulin-independence and function were not affected by early (preservation medium) or late (culture medium) contamination. From 2012, we implemented an additional sampling one day after isolation that allowed to reduce by half the number of patients incidentally transplanted with a contaminated preparation.
Conclusion: Pancreas preservation fluid microbial contamination is associated with lower islet yield and lower *in vitro* function, but not with changes in graft survival and function. Testing of the culture medium one day after isolation allows to reduce the risk of incidental transplantation with contaminated islets.

Clinical Kidney Cardiovascular complications

EP010 MORTALITY PREDICTION IN RECIPIENTS WITH DIABETES MELLITUS AND END-STAGE RENAL FAILURE UNDERGOING SIMULTANEOUS PANCREAS-KIDNEY TRANSPLANT: A FOCUS ON CARDIOVASCULAR RISK FACTORS

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Background: Diabetes mellitus is a potent risk factor for cardiovascular disease. Simultaneous pancreas and kidney transplantation is an innovative treatment option that aims to establish insulin independence and normoglycaemia in patients with end-stage renal failure. However, the selected recipients must undergo extensive risk assessment preoperatively to improve post-operative outcomes.
Aim: To determine which preoperative clinical cardiovascular parameters are associated with an increased risk of mortality one-year postoperative.
Methods: Conducted was a retrospective analysis of all patients undergoing Simultaneous Pancreas & Kidney Transplant (SPK) at a tertiary centre between 2004–2014. Data collection included age, Body Mass Index (BMI), history of ischaemic heart disease (IHD) and hypertension (HTN), cholesterol/high-density lipoprotein ratio (C/HDL), demographics and smoking status. The primary outcome of interest was post-transplant survival.
Results: A total of 151 patients included (62% male, 28% female). Mean age was 41 years. 69% of patients were receiving renal replacement therapy (35% haemodialysis, 34% peritoneal). Total mortality was 21%. Multivariate Cox proportional hazards modelling revealed that age >45 years conferred a four-fold increase in mortality risk within the first post-transplant year (Hazard Ratio = 3.9, confidence interval = 1.19–12.8). All other cardiovascular parameters were not significant.

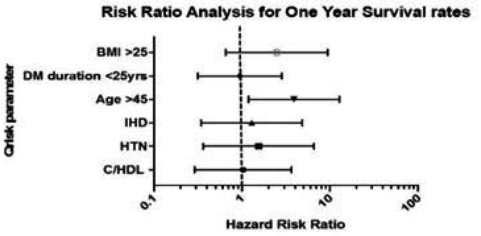

Figure 1. *The Hazard Risk Ratio that several cardiovascular markers bestowed on the overall one-year survival rates in recipients who underwent a SPKT between 2004-2014. Age demonstrated a significant increase in the risk ratio (log rank p=0.025).*

C/HDL: Choiesterol : HDL ratio; IHD :Ischaemic Heart disease ; HTN: Hypertension ; SPK : Simultaneous Pancreas –Kidney Transplant .

Conclusion: Age >45 years was the only parameter associated with a statistically significant increased risk of death following the procedure. With regards to the BMI, C/HDL and presence of IHD, our results suggest that greater flexibility with patient selection can be cautiously exercised.

Clinical Kidney Metabolic complications

EP011 NUTRITIONAL APPROACH FOR KIDNEY TRANSPLANT CANDIDATE; ONE-YEAR OUTCOME

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Background: Perioperative nutritional support for kidney transplant candidates are important to control post-operative protein catabolism which causes muscle loss and immunodeficiency. The aim of this study was to evaluate the change of nutritional status and clinical course during one-year after transplantation as an outcome of ESPEN's nutritional suggestions.
Methods: This is a prospective single center study of 30 adult kidney transplant recipients in 2014–2015 and compared with a historical control group. We provided a meal with 30 kcal/kg body weight energy and 1.4 g/kg body weight protein intakes that were recommended by ESPEN guideline, and a following protein restriction with 1.0 g/kg body weight from 3-months after transplantation (High protein group; $n = 15$). For a historical control, we provided a meal with 30–35 kcal/kg body weight energy and 0.8–1.0 g/kg body weight protein meals just after transplantation (Low protein group; $n = 15$). We evaluated nutritional status by blood samples, and abdominal fat mass/ L3 skeletal muscle mass index (L3SMI) by CT scan, before, 3-months, and 1-year after transplantation.
Results: There were no significant differences about sex, age, dialysis vintage between both groups. L3SMI and serum Alb level were significantly decreased 3-months after transplantation in both groups, but were recovered only in high protein group at 1-year later. Abdominal fat mass was increased in low protein group. Post-transplant impaired glucose tolerance and viral/bacterial infectious diseases within one-year after transplantation were highly occurred in low protein group. There was no significant difference in estimated GFR levels between 2 groups, however, proteinuria appeared in high protein group 1-year after transplantation.
Conclusion: Our nutritional strategy was succeeded to prevent transplant complications especially in the early perioperative period. Further analysis is required to for ideal kidney transplant nutritional support.

Clinical Kidney Other

EP012 CARDIAC REMODELING IN STRUCTURE AND FUNCTION AT 6 MONTHS AFTER KIDNEY TRANSPLANTATION

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Introduction: Cardiovascular disease accounts for 35–50% of the causes of mortality in chronic kidney disease. The majority of patients in substitution therapy of our country are of limited economic resources, therefore they are infradializados. This factor produces more cardiac deterioration than described in the world statistics, and has a direct impact on the prognosis of kidney transplantation.
Aim: Demonstrate and to quantify the improvement in the echocardiographic parameters from the six months of renal transplantation in patients with stable renal function.
Materials and methods: An observational, analytical and prospective study of 23 patients with chronic kidney disease transplanted in 2016, who had a glomerular filtration rate ≥80 ml/min (CKD-EPi) at six months post-transplant were performed. The following pre-transplant and post-transplant results were compared: echocardiographic parameters, Sokolow-Lyon index, cardiothoracic index, serum albumin, mean arterial pressure, use of antihypertensives and uresis in 24 h. The Wilcoxon test was performed to establish ranges of the parameters evaluated in two measurements. A value of $p \leq 0.05$ bimarginal was established as statistically significant.
Results: See Table 1.

	Before transplant	After transplant	p-Value
LVEF	57.17 ± 10.4	64.09 ± 9.8	0.001
RVEF	0.56 ± 0.09	0.6 ± 0.08	0.000
PASP	44.57 ± 13.8	39.7 ± 11.04	0.000
TAPSE	19.7 ± 4.8	23.09 ± 3.6	0.000
Gross septum IV	18.8 ± 3.0	15.2 ± 2.4	0.000
LV MASS	123.3 ± 6.5	118.5 ± 6.6	0.000
Sokolow Index	39.1 ± 5.5	35.8 ± 4.1	0.001
Cardiothoracic Index	1.5 ± 0.5	1.37 ± 0.4	0.001
Medium Blood Pressure	102.9 ± 12.3	90.4 ± 11.9	0.001

Conclusions: There is a significant improvement in cardiovascular function in our population at six months post-transplant, despite the fact that renal transplantation is performed with greater cardiac deterioration than that described in patients from other countries.

Basic Heart Immunology

EP013 BLOCKED OF BAT3 PROMOTES TRANSPLANT TOLERANCE BY INDUCING IL-10 EXPRESSION IN DENDRITIC CELLS

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Objective: To explore the effect of Bat3 on DCs during transplant tolerance induction.
Methods: Allogeneic heart transplants were performed between WT and Bat3flox/floxCD11c-Cre+ mice, to test the effect of Bat3 on graft survival and graft infiltrating lymphocytes. In vitro, we generated WT and Bat3cko bone

marrow derived dendritic cells (BM-DC), and then tested their expression of co-stimulatory molecules, cytokine production and the function on T cells after LPS stimulation. Furthermore, we tested the effect of Bat3 on IL-27/IL-10 expression using a luciferase reporter assay and Chip-PCR.
Results: In murine heart transplant models, Bat3cko mice could prolong the graft survival, and graft infiltrating T cells in Bat3cko mice group expressed more IL-10 and Foxp3, but less IFN-g and IL-17. The RNA-seq of graft infiltrating T cells showed that T cells in Bat3cko mice group expressed a more-tolerant phenotype. In vitro, Bat3cko BM-DC expressed lower amounts of CD80, CD86 and MHC class II and secreted more IL-27 and IL-10 as checked by ELISA after 100 ng/ml LPS stimulation. Moreover, they could induce T cells to express more IL-10 in a co-culture experiment. At last, we found that Bat3 could inhibit IRF1-induced IL-27 and IL-10 expression as determined by a Luciferase Reporter Assay. The bindings of IRF1 to IL-27 and IL-10 promoter were enhanced in Bat3cko BM-DC as we found using Chip-PCR. Co-IP experiments showed that Bat3 could bind to IRF1.
Conclusion: Bat3 could bind to IRF1. Loss of Bat3 on DC could increase IL-27/IL-10 expression, and then inhibit T cell response and induce transplant tolerance.

Clinical Others Histocompatibility

EP014 VIRTUAL CROSSMATCHES IMPACT ON KIDNEY DISCARD RATE

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Background: A virtual crossmatch (VXM) is used to ascertain the presence of HLA antibodies in a transplant recipient's serum and to determine, virtually, the flow cytometric crossmatch (FXM) results with an available donor. VXM testing is routinely used to aid in the selection of import donor kidneys for highly sensitized patients. A VXM can be a valuable tool in helping to reduce cold ischemia time and donor organ discard. This study evaluates the impact of the VXM on the discard rate of kidneys for a single Organ Procurement Organization (OPO).
Methods: A calibration curve was developed for VXM by comparing the mean fluorescent intensity (MFI) values for the donor specific antibodies to the corresponding median channel shift (MCS) values. A linear regression was performed and the slope was calculated. The slope was entered into an algorithm for estimating the MCS for a given MFI value, therefore predicting a FXM result.
A logistic regression model was utilized to compare the number of VXM tests performed between December 2014 and July 2016 to the monthly percent of discarded kidneys.
Results: A statistically significant relationship was observed between the possibility of a kidney being discarded and the number of virtual cross matches performed ($p = 0.0347$) (Table 1).
Table 1 Parameter estimates.

Term	Parameter Estimate	Std Error	Likelihood Ratio $\chi 2$	p-Value	OR	95% CI
Intercept	−1.29	0.39	12.28	0.0005	—	—
# Renal VXM	−0.04	0.02	4.46	0.0347	0.964	(0.931, 0.997)

We see that for each unit increase in the number of virtual cross matches leads to a 0.04 decrease in the log-odds of a kidney being discarded. This relationship is displayed in the following figure:

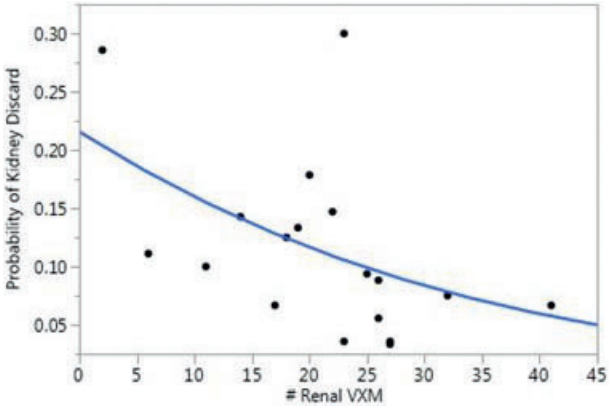

Figure 1 Relationship between VXM and probability of kidney discard.

Conclusion: The increase in the use of VXM is one of the factors responsible for a significant reduction in the discard rate of kidneys observed at our OPO.

Basic Cell Immunology

EP015 TUNING THE MIGRATION CAPACITY OF REGULATORY T CELLS

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Background: Regulatory T cell (Treg)-based therapy is a promising approach to treat allograft rejection. To be effective, Tregs must express homing receptors for migration to inflammatory sites. For example, expression of the chemokine receptor CXCR3 on Tregs is essential to guide Tregs to locations of Th1-inflammation. We hypothesized that migration capacity of thymic Tregs could be fine-tuned during the *in vitro* expansion.
Methods: Naive CD4+CD25+ thymic Tregs were isolated from pediatric thymuses by magnetic bead-separation. Tregs were expanded with artificial antigen-presenting cells, rapamycin and IL-2. The cells were re-stimulated after 7 days without rapamycin. For Th1-polarizing conditions, IL-12 and IFN-gamma were added to cultures.
Results: Thymic Tregs cultured under Th1-polarizing conditions significantly increased CXCR3 and T-bet expression and showed >2-fold higher expansion capacity compared to Tregs cultured in neutral conditions. Expression of CXCR3 persisted even after removal of the polarizing cytokines. Tregs cultured with Th1-inducing cytokines maintained a stable phenotype, including high FOXP3 expression and low TSDR methylation. Levels of other Treg-associated markers remained unchanged between neutrally and Th1-cultured Tregs. Th1-polarized Tregs did not acquire the ability to produce Th1-cell associated cytokines such as IL-2 or IFN-gamma and potently suppressed proliferation of Th1-effector T cells *in vitro*. In contrast to neutral cultures, expansion under Th1-conditions enabled thymic Tregs to migrate toward the CXCR3-specific chemokine CXCL10 *in vitro*.
Conclusion: Expansion conditions of thymic Tregs can be manipulated to specifically and stably tailor the cells' homing capacity. The ability to direct Tregs toward specific tissues or sites of inflammation may enable optimal targeting as a therapeutic *in vivo*. This more targeted action might reduce pan-immunosuppression often associated with polyclonal Treg administration.

Basic Kidney Immunology

EP016 ECTOPIC LYMPHOID STRUCTURES ARE PRESENT PREDOMINANTLY IN GRADE I T-CELL-MEDIATED RENAL TRANSPLANT REJECTION

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Background: Effectively suppressing the alloimmune response directed against a transplanted kidney is a major challenge. Within this process, interaction between BCL6+ T follicular helper (Tfh) cells and B cells via interleukin-21 (IL-21) leads to alloantibody production. Whether or not T-B cell interactions take place in ectopic lymphoid structures (ELSs) in the allograft is under debate. Here, we investigated if ELSs are present in renal allograft biopsies of patients undergoing acute T-cell-mediated rejection (grade I and II) or acute/active antibody mediated rejection.
Material & methods: Fifteen renal transplant biopsies of patients showing a primary diagnosis of either C4d+ acute/active antibody mediated rejection (a/aABMR, n = 5), T-cell-mediated rejection grade I (TCMRI, n = 5), or T-cell-mediated rejection grade II (TCMRII, n = 5) were included. Formalin-fixed, paraffin-embedded (FFPE) tissue sections were stained for T cells (CD3), B cells (CD20), activated B-cells (CD79A) and follicular dendritic cells (FDCs, CD23). In addition, a double immunofluorescent staining for IL-21 and BCL6 was performed. Slides were analyzed for the presence and composition of infiltrate.
Results: Infiltrates of CD3+ T cells were detected in all 15 biopsies. In TCMRI, CD20+ B cells formed aggregates surrounded by T cells in the tubulo-interstitial compartment. CD23+ FDCs were present in these aggregates, suggesting the presence of ELSs. In contrast, allograft biopsies showing a/aABMR and TCMRII showed diffuse spread of T and B cells. While IL-21 was present in all biopsies investigated, co-localization with BCL6 was predominantly observed in biopsies with TCMRI.
Conclusions: Ectopic lymphoid structures with FDC networks and BCL6+IL-21+ cells are predominantly found in TCMRI and suggest a pivotal role for T–B cell interaction in this type of acute renal allograft rejection.

Basic Cell Immunology

EP017 INFLAMMATORY CONDITIONS DICTATE THE IMMUNOMODULATORY EFFECT OF MSC ON B CELL FUNCTION

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Background: The immunomodulatory capacity of mesenchymal stem cells (MSC) makes them a promising therapeutic tool for immune disease and organ transplantation. The effects on MSC on B cells have recently gained interest, since they are able to abrogate memory and plasmablast formation and induce regulatory B cells. It is however unknown how MSC interact with B cells under inflammatory conditions.
Methods: In the present study MSC were isolated from adipose tissue from kidney transplant donors and pre-treated with 50 ng/ml IFNγ for 72 h (MSC-IFNγ) to simulate inflammatory conditions. Mature B cells from spleens were obtained by CD43- selection with magnetic activated cell sorting. CFSE-labeled B cells were co-cultured with MSC at a 10:1 ratio and stimulated with anti-IgM, anti-CD40 and IL-2. B cell proliferation and phenotype were analyzed by flow cytometry, and IL-10 and TNFα production were quantified by milliplex assay.
Results: MSC were not capable of inhibiting the proliferation of stimulated B cells. In contrast, MSC-IFNy significantly reduced B cell proliferation. However, MSC increased the percentage of IL-10 producing regulatory B cells (CD19+CD24hiCD38hi), whereas MSC-IFNy lacked this capacity. Indoleamine 2,3 dioxygenase (IDO) expression is highly induced on MSC pre-treated with IFNy. The addition of tryptophan (TRP) to the B cell - MSC-IFNy co-cultures to abolish the effect of overexpressed IDO, restored B cell proliferation and partially rescued the induction of regulatory B cells.
Conclusions: Immunological conditions dictate the effect of MSC on B cell function. Under immunological quiescent conditions MSC stimulate regulatory B cell induction, whereas under inflammatory conditions MSC inhibit B cell proliferation and are not able to induce regulatory B cells. Knowing how to appropriately pretreat MSC is essential for the design of specific MSC.

Clinical Kidney Immunology

EP018 CLINICAL RELEVANCE OF DE NOVO DONOR-SPECIFIC HLA ANTIBODIES (DSA) IN RENAL TRANSPLANTATION

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Introduction: De novo donor-specific antibodies (DSA) are known to be correlated with poor graft outcome and the development of acute and chronic rejection.
Patients and methods: In our study we prospectively analyzed 218 renal transplant recipients between 2006 and 2015. All patients were tested with Luminex solid-phase assay at different points in time (1, 3, 6, 12 months) after renal transplantation for the occurrence of de novo donor-specific antibodies. The data was correlated with clinical parameters and histopathological results from protocol and indication biopsies.
Results: One year after renal transplantation 37 patient (17%) developed de novo donor-specific antibodies. 67% showed positivity for DSA class 1, 22% for DSA class 2 and 11 % for both, class 1 and class 2.

There was a strong correlation between the incidence of DSA in female recipients and poor organ quality.

Patients with a high immunological risk, either due to high PRA levels or former transplantations, patients with high overall mismatch, and patients whose immunosuppressive drugs had been reduced, had a significantly elevated risk of developing DSA.

Patients with DSA developed a significant reduction of graft function and a six times higher risk of graft failure with need to hemodialysis. Only 70% of the patients who developed DSA had a functioning graft one year after renal transplantation.

The incidence of rejection was significantly elevated one month after transplantation in the group of patients with DSA. One year after transplantation 49% of the patients with DSA showed a histological proven rejection, in comparison to only 14% of the patients without DSA.
Discussion: Monitoring for the development of de novo DSA after renal transplantation identifies patients with a high risk for rejection episodes, decline of renal function and poor graft survival. The knowledge about the individual risk may help to stratify decisions on immunosuppression and may help to reduce the risk of AMR.

Basic Cell Immunology

EP019 STIMULATION OF ANTIGEN-SPECIFIC REGULATORY T CELLS USING ARTIFICIAL ANTIGEN PRESENTING CELLS

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Antigen-specific Regulatory T cell (Treg)-based adoptive immunotherapy is a promising approach to treat graft rejection. The major limitat for the development of such immunotherapy is the need to achieve a clinically relevant number of antigen-specific Tregs through in vitro expansion. For this purpose we have developed an Artificial Antigen Presenting Cell (AAPC) model derived from murine fibroblasts genetically modified to express some human molecules involved in T cell stimulation. We used as a model the $HA_{306-318}$ influenza hemagglutinin peptide to investigate the ability of AAPCs to amplify specific Tregs from circulating Tregs (cTreg, $CD4^+CD25^+$) or naïve cells ($CD4^+CD25^-$). cTregs and naïve T cells were purified from peripheral blood mononuclear cells of healthy donors by magnetic sorting. $CD4^+$ cells were stimulated in primary culture by HA peptide-loaded autologous APCs in the presence of rapamycin and interleukin 2 for 7 days. Cells were then restimulated with the peptide either by autologous APCs or AAPCs in the same conditions for 9–12 more days.

Less than 1% of HA-specific Tregs ($CD4^+CD25^+FoxP3^+$) were generated after the first stimulation of either cTregs or naïve CD4+ cells by autologous APCs.

Restimulation with either autologous APCs or AAPCs led to a variable number of specific CD4+ cells according to donor (7–20% of total cells). Among them, the frequency of HA specific Tregs was 30–50% for both cTregs and induced Tregs. iTregs were able to significantly inhibit the proliferation of CFSE-labelled effector cells.

AAPCs were as efficient as autologous APCs to amplify specific Tregs with a fold expansion rate about 7. By extrapolating to a 460 ml bag of blood, it would be possible to obtain up to 300.10^6 specific iTregs, compatible with clinical needs.

In a transplantation context, our expansion protocol should be adapted for donor alloantigen specific Tregs.

Translational Pancreas/Islet Immunology

EP020 VASCULAR SEQUESTRATION OF DONOR-SPECIFIC ANTIBODIES AND ENDOTHELIAL CHIMERISM PROTECT PANCREATIC ISLET GRAFTS FROM HUMORAL REJECTION

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[1]Inserm U1111, France; [2]Edouard Herriot University Hospital, France; [3]Inserm U1039, France; [4]Inserm U1148, France; [5]Paris Translational Research Centre For Organ Transplantation, France; [6]University Hospital, Strasbourg, France; [7]Necker Hospital, Assistance Publique-Hôpitaux De Paris, France; [8]Geneva University Hospital, Switzerland; [9]National Taiwan University Hospital, Taiwan; [10]Lyon-Sud University Hospital, France; [11]French National Blood Service, France

Introduction: Antibody-mediated rejection (AMR) is widely recognized as the first cause of transplant failure. Patients grafted with allogeneic islets for type-1 diabetes can develop donor specific antibodies (DSA). However, we recently reported that DSA did not accelerate the rate of graft attrition in a large cohort of islet recipients.

We undertook this translational study to identify the molecular mechanisms underlying the resistance of allogeneic islets to AMR.
Methods and results: *In vitro*, DSA, either polyclonal immune sera or murine anti $H\text{-}2^k$ mAb, were able to bind to CBA ($H\text{-}2^k$) islets and induce complement-dependent destruction of islet cells.

In contrast, repeated IV injections of DSA to C57BL/6 RAG2 KO ($H\text{-}2^b$) diabetic mice, did not impact CBA islet grafts function *in vivo*, reproducing what observed in patients.

Live imaging studies demonstrated that DSA were sequestrated in recipients' vascular bed and were unable to reach islet parenchyma. Interestingly, islet graft vasculature did not develop AMR lesions upon DSA transfer, in

contrast with what observed in heart transplants. This difference was explained by the fact that donor endothelial cells were progressively replaced by endothelial cells from recipient origin (i.e. endothelial chimerism) in islet grafts but not heart transplants.
Conclusion: Our experimental study demonstrates that vascular sequestration of DSA and endothelial chimerism combine to protect allogeneic islets from humoral rejection. This study could have important clinical implications for islet grafted patients.

Clinical Kidney Rejection

EP021 DIAGNOSTIC VALUE OF SPOT URINE PROTEIN EXCRETION TO UNCOVER SILENT DE-NOVO DONOR SPECIFIC ANTIBODIES AND ANTIBODY-MEDIATED REJECTION 1 YEAR AFTER KIDNEY TRANSPLANTATION

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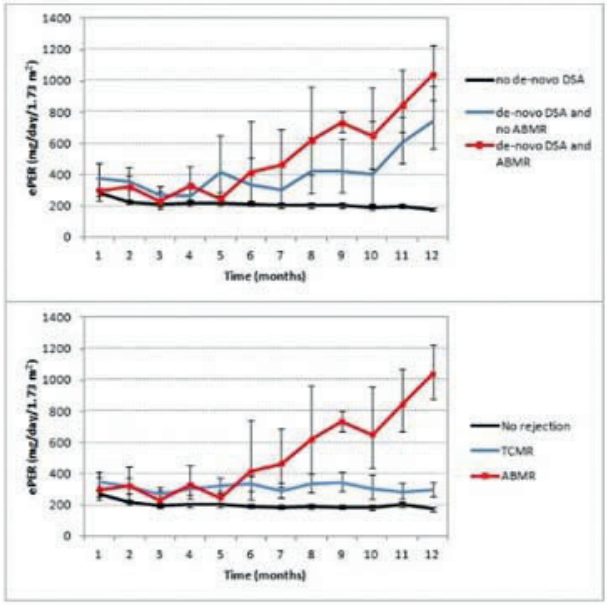
Background: De-novo donor-specific antibodies (DSA) may indicate endothelial cell injury and ongoing antibody-mediated rejection (ABMR). We aimed to assess whether an increase in spot urine protein excretion during the first year after kidney transplantation predicts silent de-novo DSA and ABMR at 1 year.
Methods: This prospective study included 79 non-sensitized patients who received a kidney transplant between Dec 2013 and Jan 2016. Estimated protein excretion rate (ePER) was calculated monthly from spot urine protein-to-creatinine ratios. At 1 year, all recipients underwent surveillance graft biopsy and were screened for de-novo DSA. Positive sera were subjected to single antigen bead (SAB) testing (LABScreen SAB assays; One Lambda). The presence of silent de-novo DSA was determined based on SAB reactivity using a mean fluorescence intensity threshold >1000 and stable graft function within the first year (variability in serum creatinine <20% from baseline). Silent ABMR was defined by additional histologic evidence of capillaritis and/or glomerulitis.
Results: Among the 79 study patients, 10 (12.7%) developed de-novo DSA at 1 year. According to the surveillance biopsy, 5 patients (6.3%) fulfilled histologic criteria for ABMR, 16 patients (20.3%) had T cell-mediated rejection (TCMR), while 58 patients (73.4%) had no evidence of rejection. Linear mixed model analyses demonstrated a significant difference in slope of ePER over time between patients with silent ABMR, de-novo DSA and no ABMR, and no DSA ($p < 0.001$), and between patients with silent ABMR, TCMR and no rejection ($p < 0.001$).



Receiver operator characteristic analyses showed that ePER at 1 year discriminated between patients with DSA and no DSA (AUC 0.97; 95% CI 0.95–1.0), and between patients with ABMR and TMCR or no rejection (AUC 0.98; 95% CI 0.96–1.0).
Conclusions: An increase in ePER during the first year after kidney transplantation appears to predict silent de-novo DSA and ABMR phenotype at 1 year.

Translational Liver Immunology

EP022 ASSESSMENT OF THE IMMUNOGENICITY OF CULTURED EXTRAHEPATIC CHOLANGIOCYTES IN VITRO AND IN VIVO

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Background: Treatments for biliary conditions are limited due to the lack of tissue for cellular therapy. Our group recently developed a 3D culture system to expand primary human extrahepatic cholangiocyte organoids (ECOs) *in vitro*, as well as a system to derive cholangiocytes from human induced pluripotent stem cells (hIPSCs). As both these systems can derive organoids from autologous tissue, we aim to investigate the immunogenicity of these therapies in allogeneic and autologous settings. It is also important to determine the relative roles of HLA class I and II in cholangiocyte immunogenicity, as this has implications for the use of allogeneic therapies.
Methods: We assessed the *in vitro* HLA class I and II expression in ECOs with or without exposure to IFN-γ through qPCR, immunofluorescence and FACS analysis, using a primary cholangiocyte control. We interrogated the *in vivo* immunogenicity of ECOs in an allogeneic humanised mouse model. Immunodeficient NOD.Cg-*Prkdc*^{scid} *Il2rg*^{tm1Wjl}/SzJ (NSG) mice were engrafted with ECOs under the kidney capsule and reconstituted with human splenocytes ten weeks later.
Results: Exposure to IFN-γ caused a significant upregulation of HLA I and HLA II mRNA and protein in ECOs after short-term culture, to levels equal to or greater than primary cholangiocytes. Engraftment into NSG mice led to formation of duct-like structures expressing human cytokeratin 7 and cytokeratin 19. These structures were lost after splenocyte reconstitution and infiltration of human CD45+ cells was observed in the graft. Data on the *in vitro* and *in vivo* immunogenicity of hIPSC-derived cholangiocytes are pending.
Discussion: These data show that ECOs express HLA II after exposure to pro-inflammatory cytokines, potentially increasing their immunogenicity. Additionally, preliminary *in vivo* experiments suggest that ECOs are rejected in an allogeneic setting. Experiments are ongoing to investigate the immune response to autologous ECOs and hiPSC-derived cholangiocytes.

Translational Kidney Rejection

EP023 TCR NGS BASED EVIDENCE FOR DIFFERENTIAL DIAGNOSIS AND PERSONALIZED THERAPY IN BKV NEPHROPATHY

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BKV nephropathy (BKVAN) is a serious complication after renal transplantation (RTx) leading to a graft loss in up to 50 % of affected patients. The diagnosis is based on assessment of BKV viral load in serum and typical histological findings in transplant biopsy. In some cases, the clinical and histological presentation of BKV nephropathy can mimic acute rejection or both complications occur simultaneously. The correct diagnosis of graft function deterioration und subsequent therapeutic interventions are, however, essential due to completely contrary therapeutic approaches in rejection and BKV nephropathy. Thus, specific tools for precise differential diagnosis are required for kidney transplant patients with BKV reactivation and prolonged/unclear graft function deterioration. Here, we present a case of personalized therapy for renal graft function deterioration based on analysis of transplant infiltrated T-cells in a living-related RTx patients with sustained severe BKV-reactivation (VL >400 000 copies/mL) and histological findings of acute rejection BANFF IIa. In details, the initial histological diagnosis of BKVAN led to IS decrease and mTOR-switch. Due to the clinical response lack the patient underwent a second transplant biopsy, which demonstrated severe T-cell infiltrations providing histological diagnosis of acute rejection BANFF IIa. Due to the known difficulties with differential

diagnosis and clinically suspected BKVAN, we applied our new technology identifying specificity of tissue infiltrating T-cells. In details, T-cell receptor (TCR) sequences of the graft infiltrated T-cells were analyzed by means of next generation sequences in T-cells obtained from the graft biopsy. In parallel, BKV-specific and allograft-specific TCR repertoires were obtained by NGS from.

Clinical Kidney Rejection

EP024 MICROVASCULAR INFLAMMATION AT 4 MONTHS POSTTRANSPLANT IS ASSOCIATED WITH TRANSPLANT GLOMERULOPATHY AT ONE AND TWO YEARS INDEPENDENT OF REJECTION AND DONOR SPECIFIC ANTIBODIES

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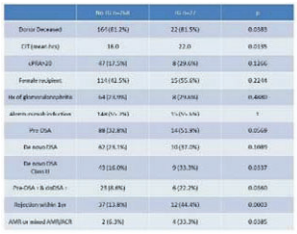
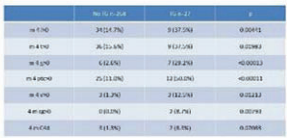
Aim: Study factors that are associated with transplant glomerulopathy (TG) in flowcytometric crossmatch negative kidney transplant recipients with no desensitization.
Methods: Single center retrospective analysis of characteristics and outcomes of kidney transplants with available HLA data 9/2011-4/2015. Single antigen bead studies were done pre transplant and at 4 months, 1 and 2 years. Flowcytometric crossmatch was done at time of transplant. For cause and surveillance biopsies were obtained at 4 months, 1 and 2 years and scored by Banff criteria. TG was considered if present at 1 or 2 surveillance biopsy. Antibodies were considered DSAs if MFIs >500. Follow up was through 8/2016. Antibodies posttransplant were considered de novo (dnDSA) if they were not present pretransplant.
Results: Biopsy data at 1 and/or 2 years was available on 296 patients, 27 (9.1%) developed TG. TG group had longer cold ischemia and inflammation at 4 month (ptc > 0, g > 0, v > 0, i > 0, t > 0). Rejection in first yr and AMR were also more common. There was no significant difference in cPRA > 20%, glomerulonephritis, retransplants, female gender or immunosuppression induction and steroid avoidance. Antibodies pretransplant or de novo were not significantly different but the presence of both pre-DSA and dnDSA as well dnDSA class II were significantly higher in TG group. Stepwise logistic regression was done and only glomerulitis and peritubular capillaritis were independently associated with TG at 1 or 2 years, g > 0 OR 6.1 (1.57–23.7) and ptc > 0 OR 4.85 (1.74–13.6).ROC AUC 0.72.





Conclusion: Microvascular inflammation at 4 months posttransplant independently predicted TG at 1 and 2 years.

Basic Kidney Histology

EP025 WHOLE SLIDE IMAGES MORPHOMETRY OF THE GLOMERULI, INCLUDING CHRONIC CHANGES IN SUBSEQUENT BIOPSIES FROM TRANSPLANTED KIDNEY RECIPIENTS

Robert Swider[1], Agnieszka Perkowska-Ptasinska[1], Anna Stachurska[2], Jadwiga Fabijanska-Mitek[2], Radoslaw Zagozdzon[3], Marcin Poterski[1], Jakub Golab[3], Slawomir Gruca[3], Magdalena Durlik[1]
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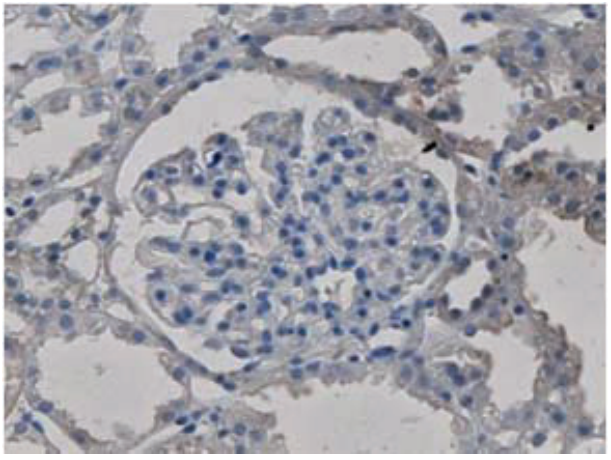
Aims: The most common complication of renal transplantation is Chronic Renal Allograft Dysfunction (CRAD). CRAD is characterized by a gradual decline in kidney function. The histopathological chronic changes are characterized by interstitial fibrosis and tubular atrophy, intimal thickening of renal arteries and transplant glomerulopathy. Glomerulopathy is a significant process influencing transplanted kidney damage. The aim of the research was to perform a morphometric analysis of the glomeruli in subsequent biopsies without chronic changes.



Transplanted kidneys came from brain-death (DBD) donors. Implantation biopsies were used as control. Histopathological changes were evaluated by using Banff scores. 67 recipients underwent subsequent renal biopsies in 0, 12 and 24 m (homogenic group). 4 μm-thick sections were prepared from representative renal cortex. To perform IHC anti-cytokeratin, anti-E-cadherin, anti-vimentin, anti-S100A4 were used. For morphometric analysis of glomeruli all above were chosen for staining (epithelial and mesenchymal marker). IHC was performed using DAB/Hematoxiline (HDAB). Proprietary algorithms have been designed to process .czi files in original resolution on a server with Intel Core i7 CPU and 4xNVIDIA GPU. All morphometric calculations were automated and verified by nephropathologist in expert system.

The analysis excluded the glomeruli with the characteristics of glomerulonephritis.

Results: Glomeruli were analyzed from subsequent kidney transplant recipients. It was found that glomerular morphometric parameters were in gradual decline (Feret diameter 192.98, 185.59, 180.40 μm). The ratio of the nuclei/presence of glomerular vascular surface in subsequent biopsies, was decreasing (15.07%, 14.76%, 13.96%), which indicates chronic changes of mesangium (increasing extracellular matrix (ECM) and decreasing count of cell podocites/mesangial cells). Morphometry and computational medicine are accurate tools for research large amounts.

Clinical Kidney Other

EP026 RENAL TRANSPLANTATION IN A PATIENT WITH ATYPICAL HEMOLYTIC UREMIC SYNDROME CAUSED BY A RARE SYNONYMOUS VARIATION R381R OF COMPLEMENT FACTOR B

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Little is known about outcomes after renal transplantation in patients with atypical hemolytic uremic syndrome (aHUS) especially regarding the specific mutations which caused the disease.

A 49-year-old female was diagnosed with thrombotic microangiopathy and treated with more than 140 therapeutic plasma exchanges. Genetic analysis revealed a rare synonymous variation R381R of complement factor B. She was found to be heterozygous for the CFH H3 haplotype (involving the rare alleles of c.-331C T, Q672Q and E936D polymorphisms as well as for the CD46 rs2796268 and rs1962149), and was diagnosed with atypical hemolytic uremic syndrome.

In April 2016, she underwent renal transplantation from the deceased donor with eculizumab induction, followed by tacrolimus, mycophenolate mofetil and steroids. Eculizumab 900 mg was applied in additional 3 doses of 900 mg followed one week later with the dose of 1200 mg with a plan to prolong intervals between applications and than to completely cease the treatment. Protocol graft biopsy performed one week after the transplant revealed a mild vascular rejection in one of four sampled small interlobular arteries. After the first attempt of the eculizumab application interval prolongation one month after the transplantation serum creatinine increased, without laboratory signs of hemolysis. Biopsy revealed acute allograft

rejection II A (g0, i2, t2, v1). Patient received eculizumab immediately and 3 boluses of steroids and was continued with eculizumab 900 mg on a weekly basis, with slow tapering. Graft function is currently stable without any signs of HUS activity, and eculizumab 900 mg every two weeks.

Complement factor B mutation accompanied with other mutations may have significant clinical consequences with the risk of renal allograft rejection. Eculizumab treatment should be individualized, and requires close follow-up of the patients.

Translational Kidney Other

EP027 LIVE TISSUE STAINING AS A NEW PREDICTING CLINICAL TOOL IN ORGAN TRANSPLANTATION

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Background: The quest for objective graft assessment prior to transplantation is the Holy Grail of transplantation as it could predict graft outcomes and enhance patient experience. It would have been highly desirable for selection of suitable organs and optimization of clinical outcomes. The use of expanded-criteria donor kidneys demands careful pre-implantation assessment. However, histopathological analysis of the pre-transplant biopsy is time consuming. Our aim is to establish a rapid assessment tool of donor kidney quality and investigate its predictive value for clinical use.
Methods: Based on the Biopsychronology study using rodent kidneys (Hermann/Ashraf et al.) we started a prospective clinical trial at Innsbruck Medical University in October 2015 to implement live confocal real time analysis as a clinical tool for deceased donor kidney transplantation. A semiquantitative score for quantification purposes of the imaging results has been created and is compared to the biopsy-histology result. The score displays the sum of viable cells divided by the number of non-viable cells per examined area (glomerulus, proximal and distal tubules; with an overall score of −3 (nonviable) up to +3 (100% viable).
Results: So far, 38 kidney transplant recipients (8 female, 21%; 9 re-transplants, 24%) have been recruited and successfully transplanted. The median recipient age was 59.2 years; the median donor age was 61.4 years. Mean ± SD cold ischemia time was 14 ± 4.9 h. Overall, 14 patients developed DGF (36.8%). In the group with positive scores 1–3, DGF rate was 8/24, 33.3%. The DGF rate in the group with negative scores −3 to 0 was 6/14, 42.9%; $p = 0.73$. The mean ± SD serum creatinine and serum urea at discharge were 2.2 ± 1.1 mg/dl and 80.2 ± 36.8 mg/dl. No organ has been discarded so far on basis of the imaging result.
Conclusion: Our preliminary data has confirmed that this approach is feasible and safe. The real time imaging provided us detailed information about the organ quality.

Clinical Kidney Histology

EP029 TREATING BORDERLINE INFILTRATES WITH CORTICOIDS BOLUS: DOES IT MAKE SENSE?

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Fundació Puigvert, Spain

Background: Borderline infiltrates are present in 15% of protocol biopsies. Since subclinical rejection is related to a worse kidney graft survival, we are concerned about these infiltrates being the initial histological manifestation of insufficient immunosuppression. If this is so, in these cases increasing immunosuppression may improve graft survival. Furthermore, and even though not having any clinical evidence, in 2015 we started treating with corticoids bolus some of these patients and performed a follow-up biopsy 3 months after treatment.
Methods/Materials: Since 2008 we have performed 570 protocol biopsies. We registered the incidence of borderline infiltrates and the histological evolution in a second biopsy. In all cases of borderline infiltrates, we increased patient's tacrolimus target levels and we administered corticoids bolus to 14 patients with borderline infiltrates.
Results: In our series we identified 62 grafts with borderline infiltrates. We increased tacrolimus levels to all 62 and administered corticoids bolus to 14 of them. Demographic and baseline characteristics of both groups showed no statistical significance differences. We have performed 10 follow-up biopsies in the treated group and 30 in the other one. The 10 follow-up biopsies in the treated group remain with borderline infiltrate in 30 % and 10% shows subclinical humoral rejection. In the untreated group 27 % present borderline infiltrated and 10% show subclinical humoral rejection.
Conclusions: Corticoids bolus do not reduce the inflammation in the short follow-up biopsies. A longer follow up is necessary to determine the prognosis of this inflammation category in protocol biopsies.

Clinical Kidney Immunosuppressive agents

EP030 EVEROLIMUS (EVE) ASSOCIATED TO TACROLIMUS (TAC) IN RENAL TRANSPLANT RECIPIENTS AS IMMUNOSUPPRESSION TREATMENT

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Hospital General Universitario Gregorio Marañón, Spain

Introduction: The combination of Everolimus a proliferative signal inhibitor is utilized as immunosuppressant in combination with CNI in renal transplantation. This approach resulted in excellent efficacy in renal function outcomes due to a less CNI exposure. When Everolimus is combined with reduced exposure to CNI have yielded good renal function while maintaining efficacy. The present paper reports our experience with renal grafted patients treated with TAC and Mycophenolate (MP) who were switched to EVE.
Patients and methods: From october 2012, 50 deceased kidney grafted patients (30 men and 20 women), were switched from TAC+MP to TAC+EVE. The age of patients was 54 ± 10 years, with 8 ± 5 years followup period. The immunosuppression treatment was based on Prednisone, MP and TAC. MP was stopped according to an abrupt conversion protocol. EVE was started at 1.0 mg day divided in two doses and blood concentration was maintained between 3–5 ng/ml and TAC between 4–5 ng/ml blood concentration.
Results: After EVE renal function improved in 85% of patients, with serum creatinine of 1.7 mg/dl, 15% remained without changes. No proteinuria was developed. No significant changes were observed in lipid metabolism or the necessity of statins, erythropoietin and ACE inhibitors doses. CMV infection was lesser.
Conclusion: Immunosuppressive therapy as maintenance TAC+EVE, replacing TAC+MP based immunosuppressive regimen in renal transplantation is safe and have no impact on lipid metabolism. Graft renal function was preserved.

Clinical Kidney Other

EP031 TRANSPLANT RENAL ARTERY STENOSIS: CAN WE ACCURATELY IDENTIFY PATIENTS AT RISK?

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Background: Transplant Renal Artery Stenosis (TRAS) commonly causes hypertension and graft dysfunction. Magnetic Resonance Angiography (MRA) is a sensitive, non-invasive diagnostic tool compared to Digital Subtraction Angiography (DSA), but has low specificity, resulting in over-treatment with little cost benefit. This study aims to identify patients at high risk of TRAS, minimising over-investigation.
Methods: Data was collected retrospectively from all renal transplant patients undergoing MRA and/or DSA over 5 years. This included aetiological factors for TRAS, blood pressure (BP) and serum creatinine (CR) trends prior to MRA, correlation of MRA and DSA findings, and angioplasty outcomes.
Results: 150 patients underwent MRA at a median time of 108 (range 30–1591) days post transplantation. MRA was positive in 44/150 (29%). In the month prior to MRA, a significant change in BP and CR was seen in patients with a positive (6.5 mmHg, 18.6 mmol/l), vs negative MRA (0.5 mmHg, −11.4 mmol/l, $p = 0.04$ & $p = 0.0026$ respectively). 32 patients underwent DSA, of which 21/32 (66%) were consistent with MRA. Angioplasty was performed in 19/21 (90%) of these, with good outcome and no significant complication. Post-angioplasty there was a significant fall in CR (−34 mmol/l, $p = 0.0003$). Comparison of patients in whom TRAS was identified vs excluded on DSA revealed a higher rate of diabetes (9/21 vs 1/10, $p = 0.106$) and DCD transplantation (12/21 vs 3/8, $p = 0.1475$). No correlation was found between TRAS and recipient ethnicity, use of arterial patch, back-table reconstruction, nor number of renal arteries.
Conclusions: The incidence of TRAS in our unit is consistent with published literature. In our cohort, a rise in CR and BP are the most reliable predictive factors of TRAS. CR increment of >25 mmol/l over 4 weeks is associated with high likelihood of TRAS and improved graft function after angioplasty. Though not statistically significant, DCD transplantation and recipient diabetes contribute to the incidence of TRAS.

Clinical Kidney Surgical technique

EP032 NOVEL 3D PRINTED SIMULATION TRAINING TOOL FOR ROBOTIC ASSISTED KIDNEY TRANSPLANTATION

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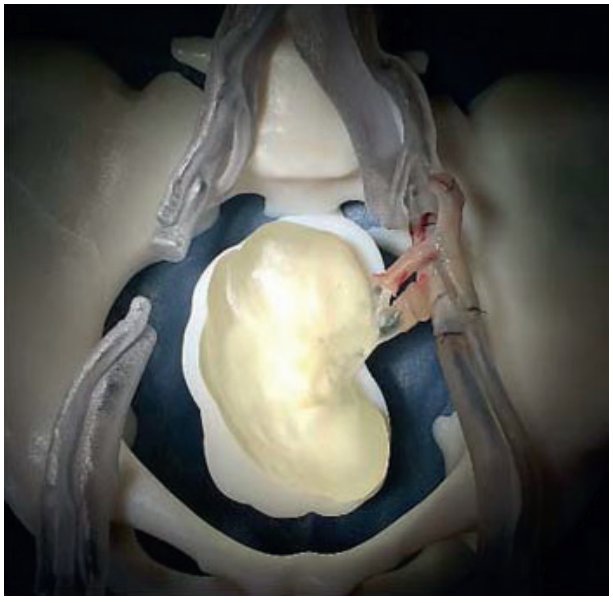
Background: Robotic-assisted surgery is a new technique for kidney transplantation. It requires the acquisition of new skills by transplant surgeons for a complex task. Kidney transplant surgeons have limited experience with robotic surgery and there is a learning curve at the start of this procedure. Skill acquisition can be cumbersome and expensive. The key part of the operation is the vascular anastomoses prior to reperfusion. We aim to develop a low cost, high fidelity simulation model that transplant surgeons can use to quickly develop their robotic surgery skills.
Method: A hybrid model of the vascular structures for anastomosis during the kidney transplant operation was developed. The model consisted of:

1. 3D printed pelvis with a 3 cm gap where the external iliac vessels are present.
2. 3D model of a kidney with renal vessels.
3. Deceased donor human vessels.

A tissue bank has been established in order to collect cadaveric blood vessels not utilised after deceased donor retrieval in the United Kingdom. Vessels included carotid arteries and iliac arteries and veins. The donors are screened for infection during the retrieval process.
Results: Vessels are cut to size and attached in an end to end fashion where the 3D printed iliac vessel gap exist. Further vessels are attached to the 3D printed renal vessels and placed on the operating table. The transplant surgeon is then able to use the Da Vinci robot to perform the anastomosis between the renal and iliac vessels just like in a real robotic kidney transplant. Two transplant surgeons tested the model so far.



Discussion: This is a novel hybrid model for robotic assisted kidney transplant vascular anastomosis simulation that is easily reproducible. The use of human tissue in an operating theatre environment allows a high fidelity model to be developed. It may be of great benefit for training transplant surgeons in a new technique to improve safety. The model is currently undergoing validation studies

Clinical Kidney Immunosuppressive agents

EP033 NON-ANTIGEN-SPECIFIC IMMUNOADSORPTION DOES NOT REDUCE COST OF ABO-INCOMPATIBLE LIVING DONOR KIDNEY TRANSPLANTATION

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Background: In 2001 we introduced a protocol for ABOi transplantation based on antigen-specific immunoadsorption (IA). This protocol has been shown to be safe and effective. One issue however has been the high price of the single-use antigen-specific Glycosorb®ABO columns. In order to reduce cost associated with ABOi kidney transplantation a protocol based on non-antigen specific IA was implemented in 2013 using the reusable Therasorb Ig flex® columns. In this study a cost-analysis comparing the protocols was undertaken.
Methods/Materials: All adult HLA-compatible patients with an anti-A/B IgG titre of ≥1:8 undergoing ABOi LD kidney transplantation between 2009–2016 were included ($n = 38$). The cost-analysis included purchase of immunoadsorption columns and other expenses for the IAs.
Result: There was no difference between groups in anti-A/B IgG titre at baseline or on the day of transplantation. At 90 days after transplantation patient and graft survival was 100% in both groups and mean s-creatinine 125 μmol/l. Patients undergoing non-specific IA required 6 preoperative treatments on average and those receiving antigen-specific IA needed 4 ($p < 0.001$). Non-specific IA was more time-consuming than antigen-specific IA resulting in higher surrounding costs ($p = 0.000$). Consequently there was no significant difference in total cost for the IAs.(median €19590 for non-specific IA and €18182 for antigen-specific IA).
Conclusion: Non-antigen specific IA allows for successful ABOi kidney transplantation. However with higher surrounding expenses compared with antigen-specific IA the potential benefit of a lower column price disappears. In conclusion, considering the overall cost, the potential risks of an increased number of IAs and the transient hypogammaglobulinemia induced by the therapy, we cannot recommend non-antigen specific immunoadsorption over antigen-specific immunoadsorption for HLA-compatible patients undergoing ABOi kidney transplantation until further evidence is provided.

Clinical Kidney Surgical technique

EP034 200 UNILATERAL DUAL KIDNEY TRANSPLANTATION (UDKT) FROM EXPANDED CRITERIA DONORS (ECD): TECHNICAL ASPECTS AND LONG TERM FOLLOW-UP

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Background: One option for using kidneys from ECD, is dual kidney transplantation (DKT). DKT can be carried out by several techniques but the unilateral placement of both kidneys (UDKT) offers the advantages of single surgical access and shorter operating time. Data concerning 200 UDKT performed in a single centre in Italy were retrospectively analyzed.
Methods: From june 2003 to march 2017 200 UDKT were performed using kidneys from ECD donors with a mean age of 73 ± 6.04 years. The technique consists of transplanting both kidneys extraperitoneally in the same iliac fossa; 95% of UDKTs were positioned in the right iliac fossa, lengthening the right renal vein with an inferior vena cava patch. In all cases pretransplant biopsy was performed with a mean Karpinski score of 4.68 ± 0.88. Mean cold ischemia time was 16.5 ± 3.75 h, and recipient age was 64.8 ± 5.4 years.
Results: After a median follow up of 60 (24.4–86.4) months, patient and graft survival at five years were 90.4% and 85.8%, respectively. 1, 3 and 5 years serum creatinine were respectively 127.5 ± 54.1, 135.8 ± 52.4, 140.3 ± 48.6 μmol/l, creatinine clearance were 56.8 ± 22.1, 53.3 ± 21, 52.4 ± 18.2 ml/min. Delayed Graft Function incidence was 31.5% and acute rejection occurred in 27 patients (13.5%). The most frequent complications were lymphocele requiring laparoscopic treatment (8 patients), followed by wound dehiscence (8 patients). Graft removal was necessary in 3 cases of renal vein thrombosis (involving 1 kidney in 2 patients, both in 1), in 2 cases of non-reperfusion of 1 kidney. Surgical correction was needed for hematoma (2 patients), incisional hernia (1 patient), stenosis of ureteroneocysto-anastomoses (2 patients), which necessitated re-anastomosis of the ureter and urinary leaks (2 cases), treated by re-anastomosing the ureter.

Conclusions: Extraperitoneal unilateral positioning of two kidneys from ECD donors through a single Gibson incision is feasible and is not associated with an increased risk to the recipient.

Clinical Kidney Immunosuppressive agents

EP035 HLA-SENSITIZED KIDNEY TRANSPLANT RECIPIENTS RECEIVING RITUXIMAB AND INTRAVENOUS IMMUNOGLOBULIN AS PART OF INDUCTION THERAPY: A SINGLE CENTER EIGHT-YEAR EXPERIENCE

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Background: Intravenous immunoglobulin (IVIG) and rituximab (RTX) can improve kidney transplantation (KT) in HLA sensitized KT recipients.
Methods: We analyzed 6 months outcomes of RTX and IVIG as induction therapy, together with thimoglobulin, tacrolimus, mycophenolate mofetil, and steroids in patients (pts) with anti-panel antibodies (PRA) >60%, positive fluxocitometry crossmatch, or donor specific antibodies (DSAs) – group 1. We also analyzed a second group with the same induction therapy except for RTX and IVIG – group 2. The primary end points were acute rejection (AR), graft loss or death; secondary endpoints were GFR, proteinuria, incidence of infections and of RTX-related adverse events during the first 6 months after KT.
Results: Group 1 included 46 and group 2 34 pts (57.5% males, 71.3% Caucasian, 50 ± 8 years at TR). Average follow-up was 60 ± 29 months. The mean of HLA mismatches (MM) was 4.1; PRA were present in 56 pts (70%) and HLA antibodies in 60% ($n = 64$) at KT, 14 of whom had DSAs and 6 had a positive crossmatch.

Pts in group 1 were younger ($p = 0.04$), had been more frequently submitted to a previous KT (37.2 vs 14.7%, $p = 0.03$) and HLA class I (82.6 vs 55.9%, $p = 0.009$) and class II (76.1 vs 45.2%, $p = 0.002$) antibodies. No differences were found in the development of leucopenia, infections or neoplasias. The AR rate in the first 6 months was higher in group 1 (23.9% vs 5.9%, $p = 0.031$). Pts with early AR had more HLA MM (4.38 vs 4.04, $p = 0.036$) and lower GFR at 6th month after KT (47.4 vs 66.6 ml/min/1.73 m^2, $p = 0.011$). Death-censored allograft survival was 100%.

In multivariate analysis, induction with RTX and IVIg was associated with early AR, in a model adjusted for MM and previous DSAs (HR: 7.1; $p = 0.028$). AR was not associated with early graft loss or death during the follow up period.
Conclusion: Higher immunologic risk pts, whose induction therapy included RXT/IVIG, despite a higher rate of AR, had similar short-term results when compared to lower immunologic risk KT pts.

EP036 LONG TERM 5 YEARS BENEFITS OF BELATACEPT IN KIDNEY TRANSPLANTATION: A SYSTEMIC META-ANALYSIS

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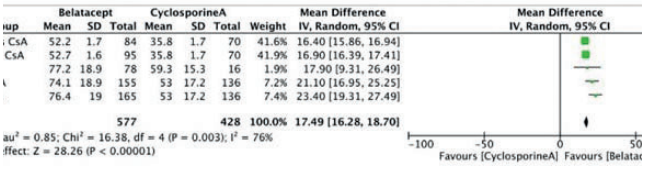
Aim: The most feared outcome of kidney transplant recipient is the chronic kidney scarring leading to declining in the function of their transplanted kidney. Furthermore, immunosuppressive drugs have side effects that increase risks of cardiovascular disease, cancer and chronic kidney transplant scarring. Belatacept may give much-needed immunosuppression and provide long-term functioning whilst, avoiding unwanted side effects of other immunosuppressant drugs. Here, we conduct a meta-analysis to assess long-term outcomes of belatacept from the time of transplantation.
Methods: We analysed the current literature between 2000–2016 following PROSPERO approval describing the 5 years long-term benefits of an immunosuppressive agent, Belatacept as an alternative to CNI in renal transplant by searching the PubMed, EMBASE, Cochrane, Crossref, and Scopus using MeSH terms.
Results: In this analysis, five study groups comprising data from 1005 renal transplant recipients were sought. Renal function [Calculated glomerular filtration rate (cGFR)] was better with belatacept at 60 months with mean difference of 17.49 ml/min/1.73 m^2 whilst, no difference in acute rejection was observed. Along with, that NODM, Hypertension, triglyceridemia were significantly lower in Belatacept group.



Conclusion: Present 'analysis outlines the 5 years benefit of Belatacept in terms of better functioning but no increased risk acute rejections. The factor of concern as post-transplant lymphoproliferative disorder as post-transplant lymphoproliferative disorder in Epstein-barr virus-seronegative recipients has not dealt well thus further studies are required to confirm this benefit.

Clinical Liver Cancer

EP037 RESULTS OF LIVING DONOR LIVER TRANSPLANTATION AND LIVER RESECTION FOR TREATMENT HEPATOBLASTOMA IN CHILDREN

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Background: Achievement of complete surgical resection is the mainstay of multimodal treatment for hepatoblastomas. Radical resection of hepatoblastoma can be obtained either conventionally by partial hepatectomy or by total hepatectomy with orthotopic liver transplantation thereafter, but time and place of the surgery differs considerably across the world.

The aim of this study was to study results of surgical treatment patients with hepatoblastoma in our center in period 2005 to 2016 years by liver resection and liver transplantation and compare outcome between liver resection group and liver transplantation group.
Methods/Materials: 65 children with a hepatoblastoma have entered the study. The age range at surgery was 8 months to 5.6 years (median 28 months), with a male to female ratio of 3:1. 3 patients (4.6%) were PRETEXT group I, 21 (32.3%) group II, 33 (50.8%) group III and 8 (12.3%) group IV. 12 patients PRETEXT I-II underwent primary surgery. 53 patients were treated with preoperative chemotherapy. 51 patients received postoperative chemotherapy. The standard perioperative treatment is 4 cycles of preoperative chemotherapy followed by surgical treatment and 2 postoperative cycles of chemotherapy («PLADO» or «superPLADO»). Patients with PRETEXT IV tumors, multifocal tumors and tumors invading major vessels of the liver underwent liver transplantation.
Results: The overall 1-,3- and 5-year survival rate for 57 patients after liver resection and for 8 patients after LDLT in the study was 91.2%, 84.2%, 73.7% and 100%, 87.5%, 75%, respectively. Recurrence-free 1-,3- and 5-year survival rate for 57 patients after liver resection and for 8 patients after LDLT in the study was 87.7%, 78.9%, 71.9% and 100%, 87.5%, 75%, respectively.
Conclusion: Resection and transplantation technology in combination with chemotherapy allows to obtain a good long-term outcome. We did not find any difference in the long-term results between resection and transplantation groups.

EP038 PROPOSAL OF PROGNOSTIC SURVIVAL MODELS BEFORE AND AFTER LIVER RESECTION FOR HEPATOCELLULAR CARCINOMA IN POTENTIALLY TRANSPLANTABLE PATIENTS

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Background: The aim of this study was to develop a novel tool for predicting survival before and after liver resection for hepatocellular carcinoma, with possible implications for primary and salvage liver transplantation.
Materials and methods: Patients who underwent liver resection for HCC between January 2000 and December 2012 at two Centers, and who were considered transplantable due to <70 years old and absence of preoperative macrovascular invasion, were identified from a prospectively collected database. Two regression models were constructed, the first to classify patients into two groups – *pre-low* and *pre-high* risk - based on preoperative variables, and the second to reclassify low-risk patients according to postoperative variables. Nomograms were built up on the basis of the two optimal models to yield a tool easily classifying patients into the two risk groups, i.e. low and high risk.

Results: Five-hundred-twenty-four out of 927 consecutive patients who had undergone LR for HCC were selected. Cirrhosis, aspartate transaminase, alpha-fetoprotein, MELD score, nodule number, and diameter of the largest nodule at tumor diagnosis were pre-operatively found to be significantly related to overall survival post-LR. Microvascular invasion and satellites were selected to reclassify prognosis in the resulting preoperative low risk group. The converted low risk group demonstrates the same 5-year survival as the high risk preoperative one (48% vs 43%, p-value = 0.45).
Conclusion: The new models were strongly predictive of patients' probability of survival after LR for HCC on liver cirrhosis. Patients with a high mortality risk assessed before LR should be consider for LT because of its significantly higher benefit of long-term patient survival. Patients who remain at low mortality risk after LR may be considered cured and their survival will probably be similar to that after LT. Patients who convert from low to high risk after LR s.

Clinical Liver Other

EP039 LIVER RETRANSPLANTATION IN ADULTS: A CROATIAN SINGLE-CENTRE EXPERIENCE

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Background: Liver retransplantation (re-LT) is the only treatment option for patients with irreversible graft failure. However, it is associated with poorer outcome compared with the primary LT. The aim of this study was to analyze a single centre's experience with re-LT for patients with poor graft function after primary LT.
Methods: This is a retrospective analysis of indications, timing, surgical techniques and outcomes of patients who underwent re-LTs after primary LT between 2000 and 2017 in our centre.
Results: Of the 1012 primary LTs, 73 (7.2%) patients required a first and 11 (1.1%) a second re-LT. Alcoholic liver disease (45.8%) was the most common diagnosis, followed by chronic hepatitis C (25%) for the primary LT. Majority of re-LTs were performed within 6 months, early (16.4%, day 0–7; 19.2%, day 8–30) and intermediately (24.7%, 1–6 months), of primary LT. Major indications for the first re-LT were: biliary complications (28.8%), hepatic artery thrombosis (23.3%), recurrent diseases (viral/autoimmune, 21.9%) and primary graft non-function (16.4%). All re-LT patients underwent modified piggyback LT with cadaveric allografts, in 45.2% of cases with hepatico-jejunal anastomosis. The 1-, 3-, 5- and 10-patient survival rates after first re-LTs were 61.6%, 60.0%, 51.8% and 46%, respectively. Survival of patients with re-LT within 6 months, was significantly poorer than of those re-transplanted later (p = 0.007). The 1- and 3-patient survival after second re-LT was 53%. Sepsis related multiple-organ failure was the most common cause of death in 72.3% of cases after re-LTs.
Conclusion: Liver retransplantation offers acceptable patient survival. Early re-LTs show worse outcomes than later ones. It is up to individual transplant program to decide whether to perform multiple LTs based on organ availability, center's volume and patients' outcomes.

Clinical Liver Immunology

EP040 PROGNOSTIC SIGNIFICANCE OF PREOPERATIVE NEUTROPHIL-LYMPHOCYTE RATIO IN PATIENTS UNDERGOING LIVER TRANSPLANTATION WITH HCC WITHIN MILAN CRITERIA

Su-Kyung Kwon[1], Deok Gie Kim[1], Jee Youn Lee[1], Hyung Soon Lee[2], Jung Jun Lee[3], Soo Jin Kim[1], Jae Geun Lee[1], Dai Hoon Han[1], Dong Jin Joo[1], Gi Hong Choi[1], Myoung Soo Kim[1], Jin Sub Choi[1], Soon Il Kim[1]
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Background: Systemic inflammatory responses have been shown to reflect the promotion of angiogenesis, and DNA damage and tumor invasion through up-regulations of cytokines. The neutrophil-lymphocyte ratio (NLR) is a simple index of systemic inflammation and reported as a predictor of poor survival in patients with various cancers. The purpose of this study is to evaluate the prognostic value of the preoperative blood NLR in patients undergoing liver transplantation (LT) with hepatocellular carcinoma (HCC) within Milan criteria.
Methods: Retrospective analysis was performed on a database of recipients who underwent LT for HCC within Milan criteria between September 2005 and December 2015. Among 266 patients, any patients with any infection sign, history of recent blood transfusion, antibiotics and operation before transplantation, and early death after LT were excluded. The cutoff value of NLR was decided by receiver operating characteristic (ROC) curve analysis. Kaplan-Meier analyses were performed to identify the predictive value of the above factors for disease-free survival (DFS).
Results: A total of 247 patients were included finally. 26 (10.66%) patients were experienced tumor recurrence. The mean value of NLR of the HCC recurrence group is higher than no recurrence group. In the elevated NLR group above cutoff value (2.20), the recurrence rate of HCC was higher than the normal group (14.2% vs 4.5%) (HR: 3.43, 95% CI, 1.15–10.32; p = 0.02). The preoperative NLR ≥2.20 was independent predictor of poor disease-free survival (p = 0.010).

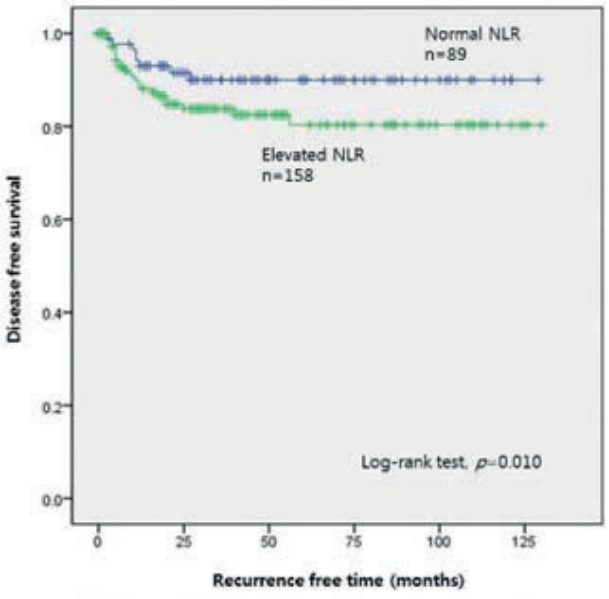

Fig1. Kaplan-Meier survival analysis recurrence free survival

Conclusion: Preoperative NLR can be easily obtained. The elevation of preoperative NLR could be an effective predictors of tumor recurrence and prognosis for patients after LT with HCC.

Variables	Elevated NLR (n = 158)	Normal NLR (n = 89)	p-Value
Sex male:female	137:21	70:19	0.099
Age (years)	53.59 ± 7.10	55.19 ± 6.40	0.080
NLR	5.43 ± 4.76	1.54 ± 0.42	<0.001
Platelet counts (×103/mm^3)	80.24 ± 49.93	90.67 ± 40.5	0.94
HCC recurrence no.	22 (14.2%)	4 (4.5%)	0.020

Clinical Liver Surgical technique

EP041 LIVER TRANSPLANTATION FOR PATIENTS WITH UNRESECTABLE ECHINOCOCCUS ALVEOLARIS

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Aim: To study the immediate and long-term results of the liver transplantation for patients with unresectable hepatic Echinococcus Alveolaris.
Material and methods: 22 liver transplantations were performed at our center between January 2011 and March 2017 for patients with unresectable liver disease. 21 living donor liver transplantations have been performed. 1 cadaveric liver transplantation has been performed. 16 patents (72.7%) had parasitic invasion of the inferior vena cava (IVC). 7 patients (31.8%) had parasitic invasion of the right atrium. Reconstruction of the main vessels has been performed by synthetic PTFE-conduits. Nonradical surgical treatment in anamnesis was performed in 18 patients (81.8%). Parasitic invasion into neighboring organs was identified in 14 patients (63.6%). All patients were treated by Albendazole for 6 months after surgery.

Results: The duration of surgery has been 430 (390–480) min. The intraoperative blood loss has been 1500 (1300–2200) ml. Duration of cold ischemia has been 30 (25–45) min. The morbidity has been 45.4%. The biliary complications (Grade A, B (ISGLS, 2011) were prevailed – 4 patients (18.2%). Crisis of transplant rejection, demanded of the pulse therapy by glucocorticoids has been evolved in 1 patient (4.5%). Hospital mortality rate was 4.5%. The postoperative hospital stay was 20 (15–23.5) days. The long-term survival rate is 100%. The disease-free survival rate was 86.4%.
Conclusion: Realization of the liver transplantation with resection and reconstruction of the main vessels, including resection of the IVC, and even the right atrium may be the only radical method of treatment of unresectable hepatic Echinococcus Alveolaris. Liver transplantation promotes for satisfactory immediate and long-terms results of the surgical treatment. These interventions should be performs only in highly specialized centers with a developed programs of surgical hepatology and liver transplantation.

Clinical Liver Immunosuppressive agents

EP042 CONVERSION FROM CALCINEURIN INHIBITOR-BASED TO EVEROLIMUS-BASED IMMUNOSUPPRESSION IN LIVER TRANSPLANT RECIPIENTS: LONG-TERM OUTCOME

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Background: Renal impairment has been recognized as an increasingly prevalent complication of liver transplantation (LT). Exclusion or minimization of calcineurin inhibitors (CNI) has been the cornerstone of management strategies. The aim of this study is to review the clinical outcomes of CNI-to-everolimus switch in liver transplant patients in our institution.
Material/methods: Outcomes in 92 LT recipients who were switched from CNI-based to everolimus-based immunosuppression between May 2013 and September 2016 were retrospectively analyzed.
Results: The most frequent indication for everolimus conversion was post-transplant renal impairment (n = 74, 80.4%). Median time to conversion was 11 (3–34) months post-transplant. There were 37 (40.2%) early conversions (<6 months post-transplant) and in 16 patients, everolimus was started in de novo setting (at 4 weeks post-transplant). Median follow-up time after conversion was 43 (26–63) months.

None of the patients experienced acute rejection. The baseline glomerular filtration rate (GFR), evaluated with the 6-variable MDRD-6 formula was 93.542.2 ml/min. Mean GFR at conversion was 63.5 ± 17.2, which showed a significant improvement at 3 months (73.5 ± 17.2 ml/min) from the time of conversion with an average increase of 9.9 ± 13.8 ml/min. In both patient groups with (n = 74) or without (n = 18) renal impairment at conversion, a further improvement in renal function was found at 1 year.

In a total of 27 (29.3%) patients, everolimus was discontinued due to adverse events, which had a suspected relation to everolimus. The most frequent reason was incisional hernia repair (n = 9). There was a significantly increased risk of incisional hernia in patients with early everolimus conversion (34.2% vs. 13.0%, p = 0.02, OR = 3.4).
Conclusion: Conversion from CNI-based to everolimus-based immunosuppression after LT is associated with a significant and long-term improvement in renal function, especially in patients with renal impairment.

Clinical Liver Other

EP043 COMPETING RISK ANALYSIS FOR INCISIONAL HERNIA OCCURRENCE AFTER LIVER TRANSPLANTATION

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Background: Incisional hernia (IH) is a frequent complication after liver transplantation (LT), with a reported incidence of 4–32%. IH is frequently a late complication, occurring months or years after transplantation, and, for this reason, its occurrence is often undetected because a considerable proportion of patients die within the first year of LT. The aim of our retrospective analysis was to characterize the factors contributing to IH after LT in the patient population of our institute, and to define the association between IH occurrence and patient death.
Methods/materials: We analyzed 519 consecutive LTs from June, 2003 to December, 2011. Detection of IH was by computed tomography scan, records of objective examinations and of IH repair. Analyses of the two competing outcomes by means of a competing risk regression model were done with a variety of pre-, intra-, and post-operative factors.
Results: The following independent risk factors were detected on multivariate analysis in 74 (15%) patients who developed IH after LT: severe porto-systemic encephalopathy associated with portal hypertension with esophageal varices (p = 0.001, SHR = 4.011), pre-LT creatinine serum level (p = 0.002, SHR = 1.239), UNOS status IIb and III (p < 0.001 for both, with SHR equal to 5.988 and 6.226, respectively), pre-LT body mass index greater than 29 (p = 0.011, SHR = 3.031), the presence of portal vein complications (p = 0.001, SHR = 4.332), and length of graft survival following LT (p = 0.002, SHR = 0.173).
Conclusions: Prospective, randomized, clinical trials should be encouraged to determine the potential beneficial role, if any, of the addition of a surgical device on the overlay position to decrease the incidence of IH, without additional morbidity after LT.

Clinical Liver Other

EP044 COMPREHENSIVE COMPLICATION INDEX AND POST-LIVER TRANSPLANT DEATH PREDICTION: A CLOSE LOOK TO SEE FAR AWAY

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Allocation philosophy for liver transplantation (LT) is worldwide based on MELD score. However, if on one side this score represents the cornerstone of priority process, on the other side no definitive evidence exists on its ability in predicting post-LT death. As a consequence, new scores able to predict post-LT survival are required. The comprehensive complication index (CCI) calculated during the post-operative hospital stay has been never evaluated in a LT setting, potentially representing an interesting predictor of long-term mortality. The aim of the present score is to investigate potential predictors of CCI, and then to compare CCI with other predictors of post-LT death.

A retrospective analysis based on 99 consecutive LT patients undergoing transplant at Sapienza University of Rome during the period 2011–2016 were evaluated. Median time after LT was 22 (IQR: 12–32) months.

At ROC analysis, the best predictor of CCI >50 was the labMELD value at the moment of LT (AUC = 0.794; p < 0.0001), followed by D-MELD value (AUC = 0.771; p = 0.001). UNOS status 1A, donor and recipient age or HCV-related cirrhosis were not predictors of high post-LT CCI values.

When CCI was tested as a predictor of post-LT death, it was the unique statistically significant variable able to predict death, with an excellent 0.921 of AUC (p < 0.0001). Nor labMELD neither D-MELD were similarly efficacious at predicting death after LT.

The CCI cut-off value of 50 had a sensitivity of 61.1% and a specificity of 93.8%, with an excellent diagnostic odds ratio of 23.8.

MELD is strongly connected with initial poor post-LT course: as already known, MELD-based allocation system is connected with an inevitable higher number of potential complications. Initial clinical course identified by CCI value very well predicts the entire post-LT story of the patient, resulting as the unique predictor of death when compared with MELD or D-MELD.

Groups	Pre-transplant Baseline Creatinine	GFR	Before everolimus conversion Conversion Creatinine	GFR	After everolimus conversion Month 3 Creatinine	GFR	Month 12 Creatinine	GFR
Renal (n = 74)	1.0 ± 0.4	90.2 ± 42.8	1.3 ± 0.1	57.6 ± 11.0	1.1 ± 0.2	69.0 ± 15.2	1.1 ± 0.2	71.5 ± 15.7
Non-renal (n = 18)	0.8 ± 0.3	106.9 ± 37.9	0.9 ± 0.1	85.5 ± 18.9	0.9 ± 0.1	87.8 ± 17.2	0.9 ± 0.2	92.1 ± 24.0

Clinical Liver Cancer

EP045 PREOPERATIVE PROGNOSTIC VALUES OF AFP AND PIVKA-II IN PATIENTS WITH HEPATOCELLULAR CARCINOMA FOR LIVING DONOR LIVER TRANSPLANTATION

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Background: Adult living donor liver transplantation (LDLT) is one of the best treatments for hepatocellular carcinoma (HCC). However, when recurrence of HCC after LDLT occurs, the prognosis is poor because of rapid progression. Preoperative level of α-fetoprotein (AFP) and protein induced by vitamin K antagonist-II (PIVKA-II) reportedly correlate with recurrence of hepatocellular carcinoma (HCC) after LDLT.
Methods: We examined serum AFP and PIVKA-II preoperatively as predictors of HCC recurrence in 461 patients who underwent LDLT using right liver graft for HCC from May 2007 to December 2013. Among these, 77 patients (16.7%) who experienced recurrence were retrospectively reviewed.
Results: Multivariate analysis revealed tumor size >5 cm, AFP >150 nag/mol and PIVKA-II >100 maul/mol as significant independent risk factors for recurrence. The median time to recurrence was 10 months. The median survival time after recurrence was 26 months, and the 1-, 3- and 5-year survival rates after recurrence were 80.5%, 58%, and 28.3% respectively. Preoperatively, not only morphology of the tumor but also AFP and PIVKA-II levels can offers important information for the recurrence after LDLT for HCC.
Conclusion: Thus, combination of tumor markers might be used for expansion of pre-existing strict selection criteria of liver transplantation for HCC.

Clinical Liver Other

EP046 FAILURE OF ENDOSCOPY FOR NONANASTOMOTIC BILIARY STRICTURES AFTER LIVER TRANSPLANTATION

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Background: Predictors of failure of endoscopic retrograde cholangiopancreatography (ERCP) for management of non-anastomotic biliary strictures (NABS) in liver transplant (LT) recipients are largely unknown.
Materials and methods: This was a retrospective analysis of LT recipients between January 1996 and August 2016 at a single center. Patients were included if: adult (≥18 years); recipients of a primary liver graft from deceased donor; affected with NABS in the presence of graft vascular patency, and undergoing ERCP. The study endpoint was identification of predictors of graft loss among all the clinical donor and recipient variables retrieved from medical charts.
Results: 93 LT patients (male 87.1%; mean (SD) age 51 (6.1) years; Caucasian 100%) with NABS were introduced into current analysis. Treatment was initiated at a mean (SD) of 23.2 (16.1) months after LT (median (IQR) 20 (9–33)). The overall number of procedures was 382 with a mean (SD) of 4.3 (4.4) per patient (median (IQR) 2.5 (2–5)). Three procedures (0.7%) failed due to technical reasons. A total of 19 patients (20.4%) were referred to further surgery or radiology after non-successful endoscopy: 11 patients (11.8%) were re-transplanted; 5 (5.4%) underwent hepatico-jejunostomies (coupled with liver resection in 2 cases), and 3 (3.2%) were treated with radiology-guided percutaneous drainage. The overall 5-year graft survival rate was 71%. Graft loss was associated with shorter time from transplantation to treatment ($t = -2.33$; $p = 0.023$); higher serum bilirubin ($t = 4.45$; $p < 0.0001$) and higher GGT ($t = 3.56$; $p < 0.0001$) at treatment; sepsis (chi-square = 4.35; $p = 0.039$), and bilobar involvement (chi-square = 7.99; $p = 0.004$).
Conclusions: Our experience suggests that failure of ERCP for management of NABS after LT is associated with a more severe grade of disease, as per shorter time from transplantation to treatment, higher bilirubin and GGT at treatment, bilobar involvement and sepsis.

Clinical Liver Cancer

EP047 MICROWAVE ABLATION AND SALVAGE TRANSPLANTATION FOR PATIENTS WITH HEPATOCELLULAR CARCINOMA

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Background: There are no studies evaluating a strategy based on microwave laparoscopic ablation (MLA) followed by salvage liver transplantation for HCC patients.
Methods: Between 2009 and 2016, 166 patients were treated with primary MLA, followed by transplantation in the event of a transplantable recurrence or liver failure. A similar cohort of 170 patients enrolled for primary transplantation during the same period served as a control group. All patients enrolled were diagnosed as HCC within the Milan criteria, with Child A-B cirrhosis, and were judged unsuitable for liver resection or percutaneous ablation. A propensity score analysis was performed to match the two groups.
Results: Ablation was complete for 91% of nodules. No mortality occurred. Over a median follow-up of 31 months in the study group, 91 patients (55%) had HCC recurrences, and 58 (35%) were listed for transplantation.

The propensity score analysis generated two matched groups of 85 patients treated using one or other of the two strategies. While the laparoscopic ablation strategy saved one in two organs by comparison with the control group (35 vs. 70 liver transplants were performed), the intention-to-treat survival rates at 1, 3, and 5 years were similar, with 87%, 79%, and 68%, respectively, in the study group, and 88%, 79%, and 68% in the control group ($p = 0.82$). After transplantation, 10 HCC recurrences occurred, 8 in the control and 2 in the study group.
Conclusion: First-line MLA followed by salvage liver transplantation achieves survival figures that are at least as good as first-line transplantation, while limiting the number of grafts required.

Clinical Liver Other

EP048 ISCHAEMIC-TYPE BILIARY LESIONS AFTER DCD LIVER TRANSPLANTATION: FROM RADIOLOGICAL FEATURES TO CLINICAL PROGNOSIS

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Ischaemic-type biliary lesions (ITBL) can be one the major causes of morbidity and graft loss after liver transplantation (LT) from donation after circulatory death (DCD). The diagnosis is based on magnetic resonance cholangiopancreatography (MRCP) features; previous radiological classifications are based on intra-hepatic anatomical zones and disease progression, both of difficult application to our DCD population. Aim of this study is to detect the main MRCP features which are universally applicable, to stage ITBL disease in DCD liver recipients and predict the clinical outcomes.

All the ITBL cases of a prospectively collected DCD -LT database were studied: two expert liver radiologists reviewed all MRCP images independently. Different radiological patterns were identified and their associated clinical outcomes were analysed.

Of 371 DCD -LT, 40 (11%) ITBL cases have been diagnosed. Median time from grafting to development of IC was 4 months and 88% of the cases were early (asymptomatic) ITBL. At univariate analysis the ALP value at one month was the only predictor of ITBL. Seven of 40 ITBL cases died, 10 were re-listed for re-LT and 5 had been re-grafted. Eight patients were managed with biliary drainage and 24 were treated conservatively. MRCP showed three main features: biliary strictures, saccular ducts and filling defects. The majority (85%) had biliary strictures; 4 of these were associated with saccular ducts and other 4 with filling defects. The presence of only one of these features was significantly associated with a better outcome (conservative management or biliary drainage) compared with those had more then one characteristics ($p = 0.01$). The presence of all three radiological characteristics was significantly associated with a worse outcome (re-listing or graft loss) ($p = 0.02$).

Biliary strictures are a common finding, but if combined with filling defects and saccular ducts, are associated with the worst prognosis so that early re-LT is indicated.

EP050 1998-2012 POLISH RESULTS OF KIDNEY TRANSPLANTATION FROM ANTI-HCV POSITIVE DONORS

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Background: Kidney transplant (kTx) is the best method of renal insufficiency treatment. In dialyzed, mortality rises along the time on dialysis. There is a continuing shortage of organs for transplantation, hence a propensity to expand the donor pool with extended criteria donors, anti-HCV(+) included. In the above case a transmission of HCV genotype to recipient is present. It has been proven that contamination with more than one HCV genotype did not worsen kTx outcomes. There are 2.6% anti-HCV(+) donors in Poland. Utilization is only possible in case of anti-HCV(+) and anti-HCV RNA(+) recipients.
Methods: Retrospective analysis covered 8675 deceased donors (1998–2012 Polish data from "Poltransplant"). The early (after 12 months) and late (after 60) graft and patient survival was assessed in kTx recipients, with documented (11410/12867) recipient and donor data spanning at least 1 year after kTx. 7016 kTx recipients with known anti-HCV status were included in comprehensive analysis, according to anti-HCV profile of recipient and donor. The results are in absolute and % values, p (<0.05) assessed with chi-square test.
Results: 12m survival: (R)recipient (95%), (G)graft (89%), total; R (95% vs 89%, p = 0.0004), G (88 vs 79, p = 0.0005) in HCV(−) to HCV(+/−) vs HCV(+) to HCV(+); R (95 vs 94, p = 0.2), G (88 vs 83, p = 0.0003), HCV(−) to HCV(−) vs HCV(−) to HCV(+); R (93 vs 95, p = 0.004), G (82 vs 89, p < 0.0001) in HCV (+/−) to HCV(+) vs HCV(−) to HCV(−); R (95 vs 89, p < 0.0003), G (88 vs 79, p = 0.0002) in HCV(−) to HCV(−) vs HCV(+) vs HCV (+) 60m survival: R (86%), G (75%), total; R (84 vs 88, p = 0.01), G (63 vs 71, p = 0.001) in HCV (+/−) to HCV(+) vs HCV(−) to HCV(−); R (88 vs 80, p = 0.003) in HCV(−) to HCV(−) vs HCV(+) to HCV(+).
Conclusions: Worst anti-HCV serological profile was HCV(+) to HCV(+), although transplanting HCV(+) to HCV(+) did not worsen outcomes in that group. Worse kTx outcomes of HCV(+) over HCV(−) donors can be attributed to HCV(+) status of the recipient.

LEP001 INTERNATIONAL TRANSPLANT NETWORK (ITN) PROJECT FOR DEVELOPING COUNTRIES: ANALYSIS AND DISCUSSION OF THE 1ST PHASE'S FINDINGS

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Aim: The aim of the 1st phase of the ITN Project is determining the current state of organ donation and transplantation services in participant countries including legal and organizational aspects, donation activities and transplant practices; analyzing the needs of the countries and mapping the issues to be prioritized in different contexts; contributing to their developing a roadmap for building an effective donation and transplantation system of their own. The 2nd Phase of the ITN Project is dedicated to the implementation of these roadmaps.
Methods: In the 1st Phase of the ITN Project, which is the phase of data conducting and needs assessment, representatives of 77 participant countries from three continents attended 7 workshop events organized in Istanbul between 2015–2017. A survey consisting of 39 questions on the existing state of legal and organizational infrastructure in their countries as well as qualifications of key persons in the field of transplantation was conducted. A questionnaire was prepared by the project team in English and shared with the country representatives before the workshops to be filled in and presented at the workshops. The data were then coded and analyzed in SPSS.
Results: One-fourth of the participant countries have serious deficiencies about their legal infrastructure in the sense that no legislation on organ donation and transplantation exists. Thirty-one countries have no national authority for donation and transplantation. More than half of the countries have problems about regional coordination, organ retrieval-allocation processes and data collection systems. Coordinators are usually nurses, physicians, nephrologists, intensive care specialists, anesthesiologists and social workers. According to the findings, brain death cases have not been diagnosed in 38 countries. When these countries are categorized in terms of the type of the transplantation activities; there are countries where 1- kidney, liver, hearth, and other types of transplantation.

LEP002 PRE-ISCHEMIC HOPE PRECONDITIONING PROTECTS LIVER GRAFTS FROM APOPTOSIS AND INFLAMMATION

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Background: For many years static cold storage (SCS) has been the gold standard to preserve and protect the liver from the ischemia-reperfusion injury (IRI) during transplantation. Nowadays researchers are evaluating the feasibility of using a machine perfusion to transcend the limits of SCS to improve the quality of grafts. It's been proved that Hypothermic Oxygenated PErfusion (HOPE) achieves better preservation. Our main goal is to compare for the first time the benefits of HOPE prior to or after the SCS.
Methods: Rat livers (n = 9) were preserved for 10 h in SCS (IGL-1) and then reperfused 2 h in our "*ex vivo*" system at 37°C to evaluate its function (control group). A second and third group were preserved by 2 h of HOPE prior (Pre-ischemic, n = 9) and after (End-ischemic, n = 9) SCS respectively. Perfusate samples were collected at 0, 30, 60 and 120 min for transaminases and lactate. Tissue samples were analysed.
Results: Transaminases and lactate were significantly lower in the Pre-ischemic HOPE group ($p < 0.05$) compared to the control and End-ischemic HOPE groups. This is correlated to a lower expression of apoptosis (Caspase-3, AIF $p < 0.05$) and pro-inflammatory factor (HMGB1 $p < 0.05$) and to a higher expression of Beclin-1 ($p < 0.05$). Bile production was not significantly different between groups.
Conclusion: Dynamic preservation prior to SCS seems to initialize long lasting protection mechanisms for the liver that can be proved during "*ex vivo*" reperfusion; we demonstrated the benefit of Pre-ischemic HOPE compared to SCS and End-ischemic to prevent IRI. The balance between inflammation/apoptosis and autophagy seems to play a key role in the protection of the liver during Pre-ischemic HOPE.

LEP003 INTERACTION OF INNATE IMMUNE CELLS AND REGULATED CELL DEATH IN EARLY HEPATIC ISCHEMIA REPERFUSION INJURY

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Background: Ischemia reperfusion injury (IRI) remains an important problem in clinical organ transplantation. There is growing evidence that innate unconventional effector T cells play a key role in mediating early hepatic IRI. Regulated cell death (RCD) events like ferroptosis and necroptosis are involved, but the mechanisms underlying the T cell-RCD crosstalk are poorly understood.
Methods: In this study we investigate early immunological events in a well-established model of hepatic IRI in genetically targeted mice to study the role of RCD events. We used ferroptosis resistant *knockout* (ko) mice which underwent a 90 min partial warm ischemia, followed by 24 h of reperfusion. Furthermore, we used a clinically more relevant model where we blocked the pathway of RCD (inhibition of ferroptosis) by drugs. Hepatocellular injury was evaluated by HE-histology and serum-transaminase measurement. Hepatic leukocyte subsets, e.g. innate effector cell populations and cytokine secretion were characterized by immunohistochemistry, ELISA, RT-PCR and polychromatic FACS.
Results: Mice resistant to ferroptosis induction (or mice deficient for a key ferroptosis regulator) were protected from hepatic IRI (serum transaminase levels 920 U/l vs. 2540 U/l in wt controls; p = 0.02). We found that unconventional CD27-gdTCR+ and CD4-CD8- double-negative (DN) T cells, which are the major effector cells in hepatic IRI, are significantly reduced in the livers of those mice, where the RCD pathway is blocked (either genetically or by drugs). We further show that the proinflammatory cytokine TNFα, which can induce further necroptosis events, is reduced in these KO animals.
Conclusion: Ferroptosis events appear to be the initial activator for hepatic IRI and lead to further progression by activating innate unconventional CD27-gdTCR+ and CD4-CD8- double-negative (DN) T cells. This opens new therapeutic options to improve LTx outcomes.

LEP004 A NOVEL INTERACTION BETWEEN TYPE-1 INTERFERONS AND INTERLEUKIN 10 IMPACTS THE THERAPEUTIC EFFICACY OF CO-STIMULATION BLOCKADE IN TRANSPLANTATION

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Background: Prolongation of graft survival via co-stimulation blockade (CoB) is disrupted by inflammatory responses, limiting its clinical translation. This effect is mediated in part by type-1 interferons (TI-IFNs); however, the mechanisms remain unknown. Surprisingly, the immunomodulatory role of interleukin 10 (IL-10) in CoB regimens is largely unexplored. We investigated the importance of IL-10 in graft protection and tested the hypothesis that TI-IFNs alter the function of IL-10 on alloreactive T cells.
Materials/methods: Skin transplants were performed from Balb/c to C57BL/6 mice treated with donor-specific transfusion, anti-CD154 ± anti-IL-10R blocking antibody. The impact of TI-IFNs on IL-10 signaling in mouse T cells was assessed via Phospho-flow measure of phospho-STAT3 induction in response to IL-10 or IL-6 (as control) following exposure to IFN-b. Gene and protein expression in T cells exposed to TI-IFNs was determined via microarray, quantitative PCR, and Western Blotting.
Results: DST+MR1 provided an MST of 105 days while concomitant blockade of IL-10 reduced it to 47 days. Following incubation with IFN-b, phospho-STAT3 production in response to IL-10, but not to IL-6, was reduced in memory and regulatory T cells. This selectively reduced signaling translated into inhibition of genes induced by IL-10 in T cells. Altered IL-10 signaling was not associated with lower IL-10R expression or increase in Suppressor of Cytokine Signaling (SOCS) 1 and 3. Instead, our analysis suggests a novel "cross-regulatory" role for IFN-b-induced STAT1 that prevents STAT3 phosphorylation.
Conclusion: Our results highlight the importance of IL-10 for CoB's therapeutic effect. They also show that TI-IFNs selectively inhibit T cell ability to respond to IL-10 through a novel mechanism. Defining the causal relationship between TI-IFNs' inhibition of IL-10 signaling and TI-IFNs' disruption of CoB's effect may reveal novel strategies to optimize the use of CoB for transplanted patients.

LEP005 EARLY ADMINISTRATION OF PREGNANE-X-RECEPTOR (PXR) AGONISTS IMPROVES RECIPIENT SURVIVAL FOLLOWING ORTHOTOPIC LIVER TRANSPLANTATION

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Introduction: We have previously demonstrated reduced ischaemia-reperfusion injury and improvement in liver functions following activation of the PXR in an animal model. Long-term benefits of PXR activation in clinical transplantation have not been studied to date. Our aim in this study was to investigate the effect of early PXR activation on graft and recipient survival following orthotopic liver transplantation.
Methods: Liver transplants that took place at a single transplant centre between 2010 and 2016 were included in this retrospective study. Predicted PXR activation value (PPAV) was calculated for each patient on day 7 based on potency/total dose of PXR activators administered within the first week post-transplantation. Patients were divided into low and high PXR activation groups based on PPAV values. Graft and patient survival were analysed as primary endpoints. Postoperative vascular, biliary and infective complication rates were also investigated and compared between the groups.
Results: Overall, 205 transplant recipients were included in this study. Of these, 22 had redo transplants and 24 received grafts from DCD donors. The high PXR activation group included 104 patients. No significant difference was noted between the two groups in demographics or perioperative details. Death-censored graft survival was not significantly different between the two groups. On the other hand, patient survival was significantly improved in the high PXR activation group [5 year survival: 99% in high group versus 77.5% low group; Log rank = 0.001]. Cox regression analysis identified PPAV as a significant independent predictor for survival. Infective complication rates were noted to be higher in the low PXR activation group [43.3% versus 25.6% high group; P = 0.02].
Conclusion: PXR activation within the first week of liver transplantation is an independent predictor of patient survival. This may in part be due to lower infection rates associated with PXR activation post-transplantation.

LEP006 IMPROVED LONG-TERM OUTCOMES OF PANCREAS TRANSPLANTATION IN THE MODERN ERA: ANALYSIS OF ALLOGRAFT HALF-LIVES AND PREDICTIVE DEMOGRAPHIC FACTORS

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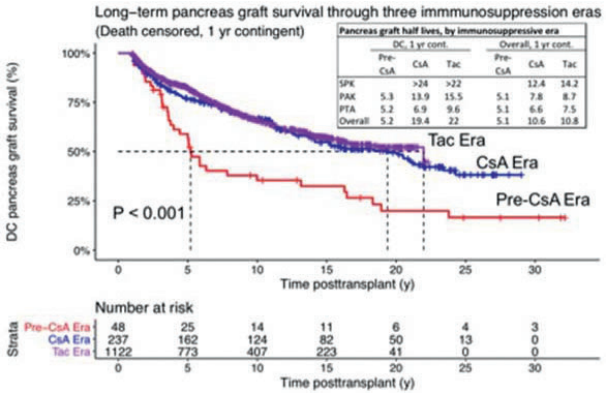
Background: In contrast to other solid organ transplants, the characteristics of long term surviving pancreas transplants have not been well described. Our objective was to measure graft half-lives through three transplant immunosuppression eras and characterize the demographic and other predictive factors in transplants with >10-year graft survival.
Methods/materials: A retrospective review of 2022 pancreas transplants performed in 3 standard immunosuppression eras [pre-CsA (1978–1986), CsA/Aza (1986–1993), and Tac/MMF (1997–2016)] was performed to measure graft half-lives and to compare demographic, surgical, and immunologic features of those with shorter (<10 years) and longer (>10 years) survival.
Results: Graft survival at all time intervals increased markedly from the pre-CsA era to the CsA era and then incrementally in the modern Tac era (Figure). The one-year survival contingent half-lives of each category of transplant and each era are presented (Figure inset). As expected, simultaneous pancreas and kidney (SPK) transplants had the longest graft survival with a death censored (DC) T1/2 of >22 years. Pancreas after kidney (PAK) and Pancreas transplant alone (PTA) had decreased T1/2 (15.5 years and 9.6 years, respectively). In the two latter eras (CsA/Aza and Tac/MMF) 40% pancreas transplants survived >10 years. In bivariate analysis long term survivors (>10 years) tended to have the following characteristics: SPK transplants ($p < 0.001$), older recipients ($p < 0.001$), male recipients ($p < 0.001$), primary transplants ($p < 0.001$), bladder drained ($p < 0.001$), leaner recipient ($p = 0.009$), locally recovered allografts ($p = 0.005$), and lower pDRI ($p = 0.012$).



Conclusions: Pancreas graft survival continues to improve with graft half-lives >20 years in optimal circumstances. Such half-life determinations may help in weighing the risk/benefits in comparison to alternative therapies, especially as islet transplantation and closed-loop insulin pumps evolve.

LEP007 EXTENDED EFFICACY OF LOW-DOSE VALGANCICLOVIR FOR PREVENTION OF CYTOMEGALOVIRUS DISEASE IN INTERMEDIATE-RISK KIDNEY TRANSPLANT RECIPIENTS- TWO YEARS FOLLOW UP

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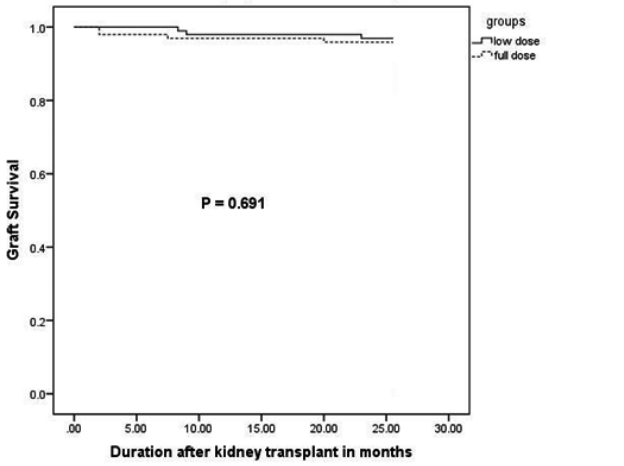
Background: In a previous study, we evaluated one year outcome of using low dose valganciclovir (VGC) prophylaxis for cytomegalovirus (CMV) infection in intermediate risk kidney transplant recipients. Whether this effect persists in the long term is unknown. We aimed to evaluate 2 years follow up of such adopted prophylaxis.
Materials and methods: We randomized 2 matched groups of kidney transplant recipients (1:1) to receive valganciclovir as 450 mg daily (group 1) or 900 mg daily (group 2) for the first 6 months after kidney transplant. Serologically, all patients were at moderate risk for CMV infection. Long-term outcomes including CMV disease, acute rejection, graft loss and patient survival were assessed.



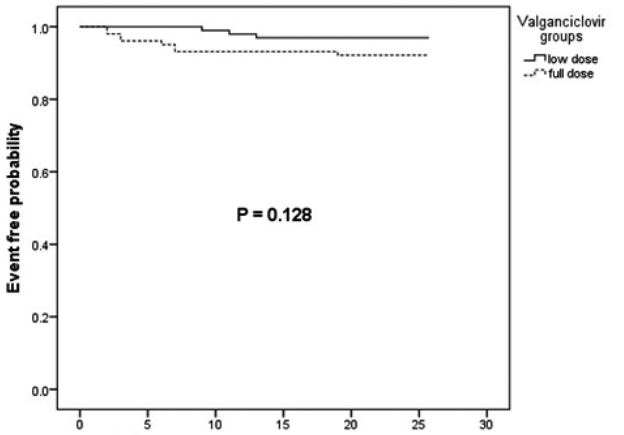


Figure2: Time to cytomegalovirus infection of kidney transplant recipients who recieved 6 months of valganciclovir prophylaxis (group1: low dose versus group2: standard dose

Results: Through the second year of follow up, CMV infection was reported in only one patient in group 1 (in month 13) and one patient in group 2 (in month 19) ($p = 1$). Biopsy proven acute rejection episodes were not statistically different between the groups (2 episodes in group 1 and 6 in group 2) ($p = 0.431$). New onset diabetes after transplant was reported in 8.1% in group 1 and 13.2% in group 2 ($p = 0.535$).Graft failure were equal in both groups (one in each) at 2 years of follow up ($p = 1$) (figure 1).Patient survival was comparable in both groups (100% in group 1 versus 97.9% in group 2, $p = 0.661$).The total number of 2 years CMV infections was numerically less in group 1 ($p = 0.128$) (figure 2).

	Total	Group 1 (low dose VGC)	Group 2 (standard dose VGC)	p-Value
Number of patients	196	98	98	
CMV infection during the second year	2 (1%)	1 (1%)	1 (1%)	1.0
CMV infection since transplant up to 2 years	11 (5.6%)	3 (3%)	8 (8.3%)	0.128
Acute rejection episodes	8 (4%)	2 (2%)	6 (6.1%)	0.431
NODAT	21 (10.7%)	8 (8.1%)	13 (13.2%)	0.535
Graft failure	2 (1%)	1 (1%)	1 (1%)	1.0
Patient survival	194 (98.9%)	98 (100%)	96 (97.9%)	0.661

Conclusion: Low dose valganciclovir prophylaxis for 6 months was associated with sustained reduction of CMV infection up to 2 years post kidney transplant without significant impact on the acute rejection, NODAT or patient and graft outcome.

LEP008 PRE-EMPTIVE LIVE DONOR RENAL TRANSPLANTATION VERSUS LIVE DONOR TRANSPLANTATION AFTER A PERIOD ON DIALYSIS IN ADULTS: A META-ANALYSIS OF OUTCOMES

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Background: The benefits of pre-emptive renal transplantation (PKT) as compared with transplantation after a period of dialysis (non-PKT) are well reported but can be biased by a higher proportion of live donors in the PKT group. We sought to eliminate this bias by comparing outcomes of PKT with non-PKT among adult live donor renal transplants.
Methods: A comprehensive search was performed of 6 databases including Embase, Medline, Web-of-science, Cochrane, Pubmed publisher and Google Scholar. All studies including the terms pre-emptive renal transplantation were screened. The methodology was in accordance with the Cochrane Handbook of Systematic Reviews of Intervention and written based on the PRISMA statement.
Results: The initial search yielded 3528 results; 222 were selected for examination of the full text; after exclusions and removal of duplicates 22 yielded outcomes that were used for the meta-analysis. On comparing PKT with non-PKT using a fixed effects model, there was a significant difference in 5 year patient survival (OR 0.698; 95% CI 0.58–0.83; $p < 0.0001$) and less acute rejection (OR 0.76; 95% CI 0.71–0.82; $p < 0.0001$. Using a random effects model, there was significantly less graft loss at 5 years (OR 0.62; 95% CI 0.51–0.76; $p < 0.0001$) in PKT as compared with non-PKT.
Conclusion: PKT appears superior to non-PKT in terms of renal allograft survival and acute rejection, but not patient survival. Whilst we accept that the review included low level evidence with heterogeneity between studies, steps should be taken to prevent the need for dialysis before transplantation in adults with ESRD. This means earlier referral for transplantation to allow more time for identification and screening of live donors and transplantation earlier in the course of disease.

LEP009 STEROID WITHDRAWAL IN HIGH RISK KIDNEY TRANSPLANTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Objectives: Steroid withdrawal (SW) is proved safe in low risk patients. However, debate remained whether SW is safe to use in high risk kidney transplant (HRKT). The goal of this study was to summarize the available data to elucidate the safety of SW in HRKT.
Methods: We did the electronic search of database CENTRAL, MEDLINE and EMBASE. HRKT is defined as repeat KT, African American recipients and panel reactive antibody (PRA) greater than 20%. All randomized controlled trials or cohort studies involving HRKT in which steroids were avoided or withdrawn at any time point after kidney transplantation were eligible for inclusion.
Results: Seven cohort studies and one RCT involving 22 075 patients were included. Pooled analysis demonstrated comparable graft loss (RR = 0.91, 95% CI 0.76–1.09) and patient survival between SW and steroid maintenance. Sensitivity analysis showed there is no difference in graft loss in those with early steroid withdrawal in one week (RR = 0.90, 95% CI 0.73–1.10). Sub-analysis also suggested SW is not associated with increased graft loss in African Americans (RR = 0.89, 95% CI 0.69–1.14). To the contrary, pooled analysis found SW was associated with reduced risk of death (RR = 0.90, 95% CI 0.84–0.98). Sensitivity analysis showed there is significantly reduced death in SW group in those with early steroid withdrawal in one week (RR = 0.90, 95% CI 0.84–0.98). Sub-analysis also suggested SW is associated with reduced patient death in African Americans (RR = 0.90, 95% CI 0.83–0.98). SW was not associated increased risk of acute rejection or biopsy proved acute

Figure 1. Graft loss between SW and steroid maintenance group.

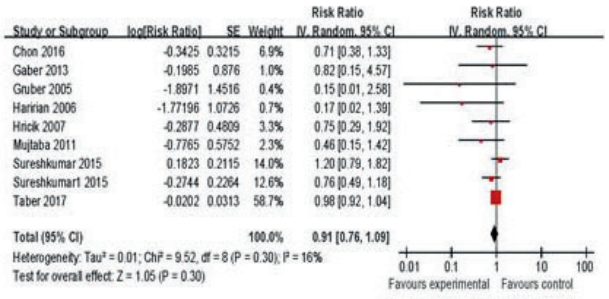


Figure 2. Patient death between SW and steroid maintenance group.

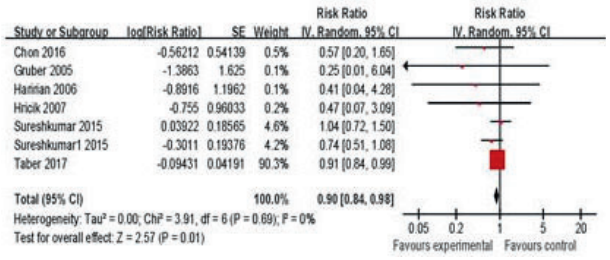


Figure 3. Acute rejection between SW and steroid maintenance group.

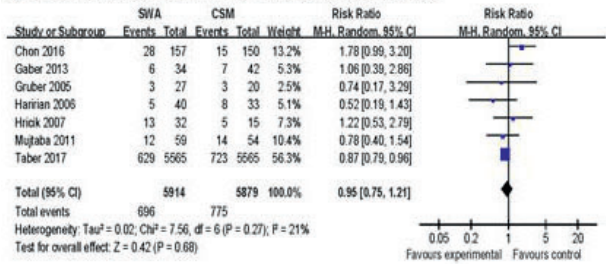


Figure 4. PTDM between SW and steroid maintenance group.

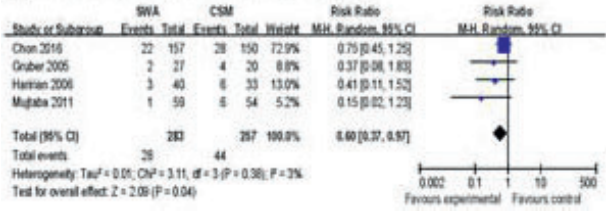
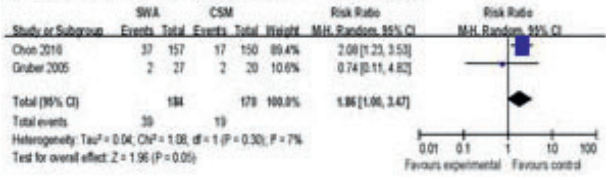


Figure 5. CMV infection between SW and steroid maintenance group.



rejection (RR = 0.95, 95% CI 0.75–1.21), and diabetes mellitus post transplant was significantly reduced after SW (RR = 0.60, 95% CI 0.37–0.97). SW was not associated with increased risk of CMV infection (RR = 1.86, 95% CI 1–3.47).

Conclusion: SW is safe in HRKT in terms of graft survival and rejection. It can significantly reduce the risk of death and diabetes mellitus post transplant.

LEP010 SYSTEMATIC REVIEW OF OUTCOMES FOLLOWING TRANSPLANTATION WITH ORGANS RECOVERED FROM CDCD DONORS USING NORMOTHERMIC REGIONAL PERFUSION

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Background: Normothermic regional perfusion (NRP) is a novel approach to organ recovery from donors after circulatory death (DCD). NRP is increasingly common, but the extent of clinical benefit is not yet fully understood. The aim of this study was to perform a systematic review of current evidence with regards to delayed graft function (DGF) and primary non-function (PNF) in NRP-kidneys and ischaemic cholangiopathy (IC) and PNF in NRP-livers.
Methods: MEDLINE and EMBASE databases were searched up to June 2017 for studies reporting on outcomes after transplantation of organs retrieved from NRP-DCD donors. Two authors independently extracted data and assessed for bias using the Cochrane ROBINS-I tool.
Results: Initial search identified 280 articles; 86 were duplicates. After screening by abstract, 76 articles remained. After further screening, there were 5 articles reporting kidney data (3 with a comparator group) and 2 articles on liver data (1 with comparator group). The average rate of PNF in NRP-livers across both studies was 6.1%, it was 0.0% in the only study with a comparator group (DBD donors). Rate of IC was reported by one study, it was 0% in both NRP and DBD arms. Average rate of DGF in NRP-kidneys was 23.7%, vs. 28.7% in those studies with a comparator group (DBD donors). A meta-analysis for studies reporting on NRP-kidneys showed a significant reduction in DGF following NRP-DCD kidney transplant versus DBD [OR = 0.47 (0.27, 0.81); $p < 0.01$]. This result may be explained by bias in the DBD comparator arm selection, with the possible inclusion of extended donors. We detected a moderate to severe risk of bias across all studies.
Conclusion: This systematic review is limited by the small number of studies published to-date. However, transplantation of NRP recovered organs seems to be associated with a significant improvement in clinical outcomes. Further analysis is warranted upon publication of additional studies.
NRP effect on the development of DGF vs DBD.

LEP011 INSULIN-PRODUCING CELLS FROM ADULT HUMAN BONE MARROW MESENCHYMAL STEM CELLS CONTROL CHEMICALLY-INDUCED DIABETES IN DOGS

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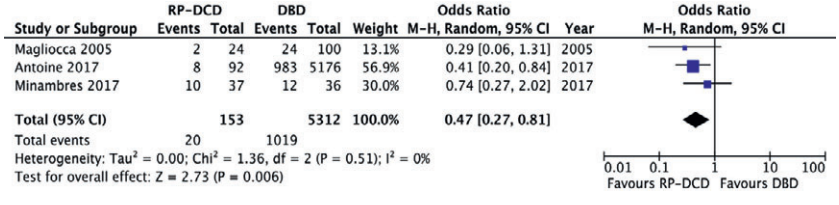
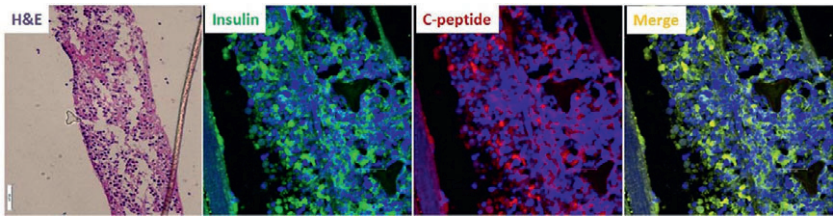
[1]Urology and Nephrology Center, Mansoura, Egypt; [2]Faculty of Veterinary Medicine, Mansoura University, Egypt

Background: Evidence was provided that human bone marrow-derived mesenchymal stem cells (HBM-MSCs) could be differentiated to form insulin-producing cells (IPCs). Transplantation of these cells was able to cure chemically-induced diabetes in nude mice. The efficacy of these cells to control diabetes in large animals was carried out to evaluate the sufficient number of cells needed/kg body weight and to determine the functional longevity in vivo.
Materials/methods: Ten male mongrel dogs weighting 15–20 kg were used in this study. Diabetes was chemically-induced in 7 dogs by a mixture of alloxan and streptozotocin. Three non-diabetic dogs served as normal controls. Differentiated HBM-MSCs (5 million/kg) were encapsulated in Theracyte capsules and transplanted beneath the rectus sheath. Each dog received 2 capsules. One dog died 4 days postoperative from inhalation pneumonia. The remaining 6 dogs were followed up for 6–18 months.
Results: Four dogs became normoglycemic within 6–8 weeks with normal glucose tolerance curves providing evidence that the transplanted cells were glucose-sensitive and insulin-responsive. In the remaining 2 dogs, fasting blood glucose was reduced but did not reach euglycemic levels. The sera of all transplanted dogs contained human insulin and c-peptide but negligible levels





of canine insulin. When the HBM-MSCs- loaded capsules were removed, rapid return of diabetic state was noted. The harvested capsules were examined by immunofluorescence. IPCs were seen and co-expression of with c-peptide was confirmed (Figure 1). Furthermore, all the pancreatic endocrine genes were expressed by the transplanted cells.
Conclusions: This study provided evidences that Theracyte capsules could protect the xenogenic HBM-MSCs from the host immune response. This is an important issue when clinical stem cell therapy is considered for definitive treatment for T1DM.

LEP012 A GENE-EXPRESSION SIGNATURE IN PERIPHERAL BLOOD ENABLES EARLIER DETECTION OF ACUTE REJECTION IN KIDNEY TRANSPLANT RECIPIENTS

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[1]King'S College London, MRC Centre for Transplantation, DTIMB, UK; [2]Guy'S And St Thomas' NHS Foundation Trust, UK; [3]Nihr Comprehensive Biomedical Research Centre At Guy'S And St Thomas' NHS Foundation Trust, UK; [4]King'S College Hospital NHS Foundation Trust, UK; [5]East Kent Hospitals University NHS Foundation Trust, UK; [6]Beth Israel Deaconess Medical Center, Harvard Medical School, US; [7]Institute of Psychiatry Psychology and Neuroscience, King's College London, UK

Background: Acute rejection (AR) is often indicated by an increase in creatinine levels after a considerable graft damage has already occurred. There is, therefore, a need for early identification of AR.
Samples: We examined RT-qPCR expression of 22 literature-based genes in 335 longitudinal whole-blood samples from 27 stable kidney transplant recipients (KTRs) from the KALIBRE study (Kidney Allograft Immune Biomarkers of Rejection Episodes) and 237 samples from 27 KTRs with a biopsy-proven cellular rejection during the first post-transplant year. Creatinine levels in stable KTRs reached no higher than 20% above the reference range and had less than 15% standard deviation.
Methods: To account for post-transplantation changes unrelated to rejection, we generated time-adjusted gene expression as the residuals of linear mixed-effects models with stable patients. To select a parsimonious AR signature, we used penalised logistic regression with a pre-biopsy sample in rejectors and the median gene expression for each stable patient. As a test set we used the longitudinal data.
Results: A 7-gene signature of AR showed area under the curve (AUC) 0.95 (95% confidence interval 0.91–1.00), sensitivity 0.85, specificity 0.93, positive and negative predictive values 0.92 and 0.86 and cross-validated AUC 0.85 (0.75–0.95). The estimated probability of rejection increased as early as six weeks prior to the AR biopsy and decreased after administration of treatment. Notably, gene expression in stable KTRs, as well as in rejectors, showed a pronounced variability, with 22% AR-positive longitudinal samples.
Conclusion: Molecular marker alterations in blood emerge well ahead of the time of clinically overt AR. Monitoring of a gene-expression signature of AR in peripheral blood could unravel AR-related pro-inflammatory activity and provide information on subclinical processes and a further justification for a biopsy in cases of sustained kidney dysfunction.