Poster Sessions

Clinical Cases – Kidney – surgical

P-001 INCARCERATED SMALL BOWEL THROUGH A RENAL PARATRANSPLANT HERNIA AFTER KIDNEY TRANSPLANTATION

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Background: Renal paratransplant hernia occurs when bowel herniates through a defect in the peritoneum over the transplanted kidney and becomes trapped. It is an uncommon and potentially fatal complication of renal transplantation. Less than 10 cases have been described in the literature.
Clinical case: We present the case of a 74 year old female patient, who one month before underwent a deceased donor kidney transplantation because of an interstitial nephropathy and nephroangiosclerosis. The patient comes to the ER department with acute intense right abdominal pain with nauseas and vomiting. Her creatinine levels were normal.
A CT scan is done and a small bowel closed loop obstruction is identified in relation with the incision. The small bowel had radiological signs of ischemia. The patient underwent surgery through the oblique incision in the right iliac fossa with resection of the necrotic small bowel herniated through the defect in the peritoneum and primary anastomosis. The defect was closed with a continuous suture. The postoperative evolution was uneventful with normal renal function at discharge.
Conclusion: Paratransplant hernia associated with ischemic bowel is a surgical emergency and is associated with a high morbidity and mortality. Thus, early diagnosis and surgery are critical. Moreover, meticulous surgical technique during transplantation may help avoid this complication.

P-002 RENAL TRANSPLANTATION WITH ARTERIAL INFLOW FROM AN AXILLO-FEMORAL GRAFT

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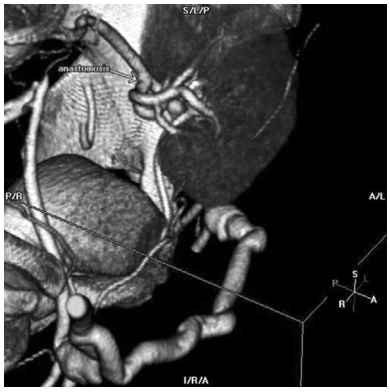
Aims: Haemodialysis is associated with increased cardiovascular morbidity and many patients being presented for transplant assessment are found to have advanced peripheral atherosclerotic arterial disease and for a successful renal transplant, patency and adequate blood flow in the iliac arterial and venous systems is required. Herein, we report a renal transplantation, vascularised by a femero-femoral crossover graft and contralateral axillo-femoral graft.
Methods: A retrospective case-note review was carried out. The patient a 54-year old woman who developed renal failure due to aortic occlusion. This lady had undergone a left sided axillo-superior mesenteric bypass graft to revascularise her gut and was established on haemodialysis through a brachio-cephalic AV fistula. After extensive work up the patient was deemed fit for transplantation, as long as the iliac arterial systems could be revascularised. This was achieved via a right axillo-bifemoral bypass graft. The kidney transplant was performed.
Results: The anastomosis time was 32 minutes and the cold ischaemia time was 10 hours 33 minutes. Post-operatively the patient was managed in the intensive care unit and required inotropic support with noradrenaline for the first 24 hours. The patient was transferred to the ward after 48 hours and became dialysis independent on the fifth post-operative day and at three-month follow-up, the serum creatinine was 104μmol/L. On ultrasound scanning there was a slight suggestion of renal artery stenosis which was ruled out by CT angiogram.
Conclusions: This report clearly demonstrates that renal transplantation can be successfully achieved in patients with extensive aortio-iliac disease requiring axillo-femoral bypass grafting.



P-003 MANAGING EARLY SURGICAL COMPLICATIONS BY KIDNEY GRAFT REPERFUSION WITH A COLD STORAGE SOLUTION

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We report on five patients with early surgical complications posing a threat to future graft function or even the patient's life. Two recipients were treated for renal vein stenosis, another two for renal vein laceration, and a renal vein thrombectomy was undertaken in one patient.These grafts were explanted, reperfused with a cold storage solution (Custodiol, 1000 ml) and reimplanted upon repairing the damaged vessels. The renal vein was reconstructed using a tubulized graft of the donor inferior caval or vein in three patients. A lacerated renal vein was repaired using a donor internal iliac vein graft in one case. Additionally, a renal vein thrombectomy *ex vivo* was performed in one case.The mean age of organ donors was 38.8 years (range, 29-55), with creatitine levels on harvesting being 81 μmol/l (65-108), and glomerular filtration rate 1.46 ml/s (0.82-1.83). The technical success rate of procedures indicated in our center was 100%. After the operation, diuresis increased and mean serum creatinine fell to 127 μmol/l within 1 year and glomerular filtration was 1,4 ml/s. Our tactics allows for quick control of life-threatening bleeding and offers a chance for renal graft salvage.

P-004 ULCUS CRURIS DUE TO PSEUDALLESCHERIA BOYDII INFECTION AFTER RENAL TRANSPLANTATION – A RARE DIFFERENTIAL DIAGNOSIS IN A COMMON LESION

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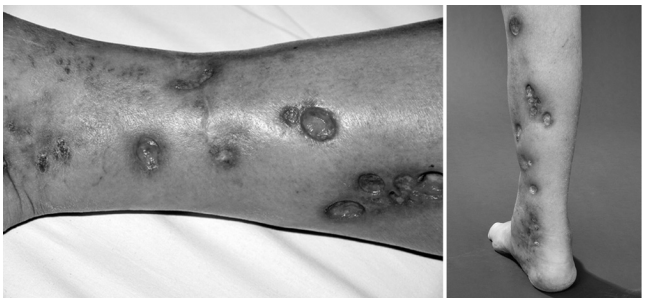
We report the case of a 66 year old male renal transplant recipient who developed painful ulcerous lesions in his right lower leg 10 months after transplantation. Immunosuppressive therapy consisted of tacrolimus, mycophenolat mofetil and steroids.
His general condition was not compromised, the function of the kidney transplant was stable. There was no history of trauma. A vascular genesis was excluded by ultrasound, there were no specific laboratory findings indicating a rheumatic or immunologic disorder. The microbiological swabs revealed pseudallescheria boydii, the histologic skin biopsy proved a fungal infection. We started an antimycotic therapy using voriconazole 400mg/day and reduced the immunosuppression. The lesions healed slowly and the patient did not develop new ulcers.



Opportunistic infections have become more important since the number of immunocompromised patients increases. Therefore, the knowledge of less frequent infectious pathogens and the sampling of microbiological specimen on a routine basis are crucial in the treatment of transplant patients.

P-005 FIBROMUSCULAR DYSPLASIA WITH RENAL ARTERY ANEURYSM: DILEMMA OF AUTOTRANSPLANTATION

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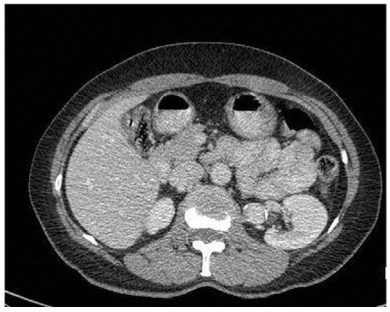
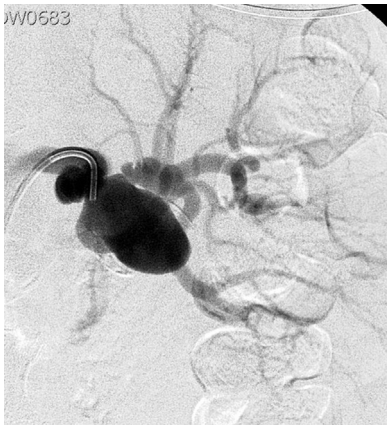
46 years old lady presented with history of left flank pain of several months. There was no history of haematuria or fever. Plain X-Ray of the abdomen showed a curvilinear calcification in the renal hilar region, this was confirmed on a subsequent ultrasound.
For further demonstration of the anatomy she underwent a CT scan which showed a tortuous left renal artery affected by fibromuscular dysplasia with a focal saccular renal artery aneurysm that measured approximately 2.4×1.6 cm.



The aneurysm arises from the main renal artery and has a branch of renal artery arising from it at its base and then the main renal artery continues on beyond the aneurysm to supply the kidney. Renal angiography showed renal artery measured approximately 5 to 6 mm in diameter before the the aneurysm and approximately 5 mm beyond the aneurysm.



A 3-D reconstruction of further MRA images confirmed the complex nature of the aneurym and there were 3 branches arising from the sac.
The right side renal artery was also reported to beady and affected by fibromuscular dysplasia. Her renal functions were normal with a Creatinine of 72mmol/Lit.
This case presented to us with great dilemma and presented to us with the following options:
1. Wait and watch and expect the aneurysm not to grow any bigger and risk rupture.
2. Laparoscopic nephrectomy with bench reconstruction and perform autotransplantation
3. Laparoscopic nephrectomy with bench reconstruction and pool the kidney for altruistic donation for a needy patient.
4. Laparoscopic nephrectomy and discard the kidney.

P-006 POST-BIOPSY RENAL ALLOGRAFT COMPARTMENT SYNDROME

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Introduction: Renal allograft compartment syndrome (RACS) has recently been coined to describe early allograft dysfunction secondary to raised pressure in the retroperitoneal space. This may be caused by direct compression of the renal vessels or by a diffuse renal parenchymal compression. Herein, we report the first case of renal allograft compartment syndrome secondary to a needle core transplant biopsy.
Methods: A retrospective case-note review was carried out where a 45-year-old male had a transplant renal biopsy at 4-weeks after transplant for raising creatinine. Following biopsy patient developed abdominal discomfort and had haematuria.
Results: Doppler ultrasound scanning of graft demonstrated good perfusion but a small haematoma (3x3x3cm) in the upper pole of the kidney at the site of the biopsy. Patient was thereafter assessed conservatively with serial ultrasound monitoring.
After 24 hours, significant deterioration of graft function was observed. The third scan, demonstrated reversed flow in diastole in the upper pole of the kidney with a resistive index of 0.8. With the above findings the kidney transplant was explored immediately and the transplant released from a 300 ml of liquefied haematoma, which was under considerable pressure. In the next 24-hours, the patient showed an immediate return of graft function.
Conclusion: We recommend sequential ultrasound Doppler scanning as an invaluable tool to help identify early RACS and surgical exploration should be sought immediately as indicated. The Doppler ultrasound scanning in this case was performed by a surgical registrar who had been trained in the technique. We feel that it is important for the surgical team to acquire this skill in straightforward Doppler ultrasound techniques.

P-007 SURGICAL AND MEDICAL CHALLENGES WITH KIDNEY TRANSPLANTATION IN VACTERL ASSCOCIATION. CASE REPORT

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Introduction: VACTERL association is a non-random association of (Vertebral, Anal, Cardiac, Tracheo-Esophageal, Renal and Limb) birth defects. Renal anomalies are found in approximately 60-90% of VACTERL patients. These include renal agenesia, unilateral hypoplasia, horseshoe kidney, severe reflux, ureteropelvic junction obstruction, neurogenic bladder. We present our three cases to demonstrate the clinical and surgical challenges these patients represent.
Case reports: One pediatric and two adults were transplanted at a single centre with VACTERL association, follow-up times are 6y, 4y and six months. Only one of them had a suitable native bladder to receive the kidney graft, the two others required a bladder augmentation, but one of them was performed after the loss of the first graft. None of our patients had an uneventful posttransplant course. Two patients had acute rejection and two had reoperation for urologic complications, one patient needed surgical intervention due to a sigmoid prolapse. All three grafts worked at last check up. Those two patients with bladder reconstruction (and having a longer follow-up) suffered from recurrent pulmonary and urinary infections and they were hospitalised several times in every posttransplant year during the follow-up period.
Discussion: Multi-organ involvement in VACTERL patients greatly complicates medical care after transplantation. Careful assessment is required whether the native bladder is suitable for subsequent transplantation. Urinary tract reconstruction seems to be essential prior transplantation. Those works focusing on transplants due to lower urinary tract problems, report comparable outcomes to patients with normal urinary tract.

P-008 REGULAR ULTRASONOGRAPHY IN AUTOTRANSPLANTED KIDNEY – EARLY DIAGNOSIS OF ASYMPTOMATIC OBSTRUCTIVE UROPATHY

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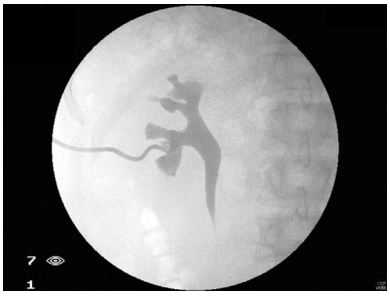
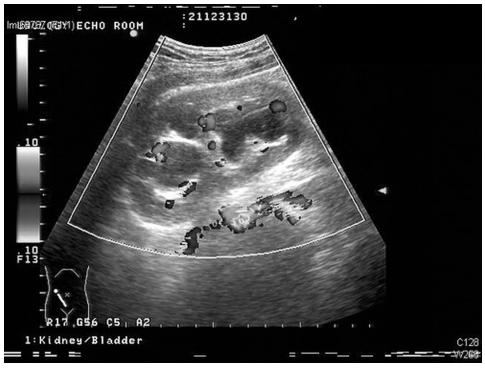
We present a case of kidney transplantation with asymptomatic uropathy early diagnosted by ultrasonography and successfully rescued endoscopically. A



healthy 21-year-old gentleman developed long segment ureteral stenosis, with only proximal 5 cm ureter remained intact, after endoscopic ureter stone manipulation at local hospital.
He was rescued with autotransplantation to contralateral iliac fossa with ureteroureterostomy. The post-operative course was uneventful and he was regularly followed at our outpatient clinic. Seven months later, an asympatomatic graft hydronephrosis with elevated resistive index (RI) was found by routine bedside ultrasonography at clinic.



Computed tomography confirmed graft ureteral stone resulting in obstructive uropathy and DTPA showed good graft function. The ureter stone was successfully disintegrated endoscopically and the patient was free of hydronephrosis with restored RI up to date. We strongly recommand routine bedside ultrasonography for graft kidney for early diagnosis of hydronephrosis.

P-009 IMMUNOSUPPRANT RELATED NEUROTOXICITY AFTER ABO-INCOMPTIBALE KIDNEY TRANSPLANTATION

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Brief History: A 36 y/o male was diagnosed as end-stage renal disease and received regular hemodialysis since 1996. His mother wanted to donate her kidney to him, but their blood types were different (Mother: type B, Son: type A). He was admitted one week before operation for NTUH Kidney Transplantation protocol of ABO incompatible living-related kidney transplantation (ABOi LRKT). The graft was harvested by laparoscopic approach and the transplantation was performed smoothly. There was good urine output after reperfusion and the following days.
Postoperative course was uneventful under immunosuppressant treatment (tacrolimus, mycophenolate mofetil, steroids). But delirium occurred on postoperative day 4, brain CT revealed no specific finding. Tacrolimus related CNS neuropathy or sepsis was suspected. Antibiotics were prescribed and immunosuppressant was changed to Cyclosporin and Rapamune. Brain MRI also revealed no obvious focal lesions of brain. His consciousness improved gradually after ICU care for 12 days. Renal toxicity was found on postoperative day 16. Rapamune was stopped and mycophenolic acid was given again. Progressive dyspnea with elevated BUN/Cr was noted on postoperative day 19. Acute rejection was not favored by initial biopsy report. Anti-A & anti-B titers showed positive results and low-titer Ab-mediated acute rejection was suspected. He was treated with double filtration plasmaphresis (DFPP) for two days. Unfortunately, consciousness disturbance was noted again on postoperative day 20–4 days after re-prescribed mycophenolic acid. Mycophenolate-related neurotoxicity was suspected. He received hemodialysis for two days and stopped mycophenolic acid. He kept his good condition (Cre 2.8) till now.
Neurotoxicity and antibody mediated rejection were not common complications of living related kidney transplantation. We presented this unusual case that received ABOi kidney transplantation and will discuss with the participants about the managements.

Clinical Cases – Kidney – medical

P-010 THE CHALLENGE OF TREATING POLYOMA VIRUS ASSOCIATED NEPHROPATHY

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Background: Polyomavirus associated nephropathy (PVAN) is a feared complication following renal transplantation. Treatment consists of reduction of immunosuppression. This leaves the patients at risk for developing rejection.
Methods/Material: 35 year old standard risk male recipient with IgA nefropathy. Kidney transplanted August 2008 (deceased donor, HLA match 2-1-1). Immunosuppression consisted of Basiliximab, ciclosporin (CyA), enteric-coated mycophenolate sodium (EC-MPS) and steroids. Immediate graft function with stable s-creatinine around 100 μmol/l.
April 2010 he was referred *for a graft biopsy* due to a slight increase in s-creatinine to 120 μmol/l and positive blood BK virus PCR. Immunosuppression consisted of CyA 100 mg × 2 (CyA C0 245 μg/l), EC-MPS 720 mg × 2 (trough 5,2 mg/l) and prednisolone 7.5 mg. *Biopsy confirmed PVAN* with positive SV 40 immunostaining, i2 t 2 v0, C4d negative, IFTA grade 2. Treatment: Stepwise withdrawal of EC-MPS, prednisolon reduction to 5 mg and i.v. cidofovir every second week - 5 infusions. This leads to a clearance of the blood BK virus. A control biopsy in June 2009 was BK negative, i1 t2 v0, C4d negative. s-creatinine stabilized at 130 μmol/l. So fare a success story.
October 2010 increase in s-creatinine to 168 μmol/l and development of proteinuria. Kidney biopsy revealed *antibody mediated rejection*: i3 t1 v0, C4d positive, moderate capillaritis, mild glomerulitis, IFTA grade 2 and development of donor specific HLA antibodies, blood BK PCR negative. Treatment: i.v. methylprednisolon total dosage 1250 mg, i.v. immunoglobulin 500 mg/kg × 4 doses, EC-MPS was reintroduced and CyA dose increased. Control biopsy after treatment: i1 t1 v0, C4d negative, IFTA 2-3, BK negative, IgA nephropathy recurrence, S- creatinine 159 μmol/l.
Conclusion: Withdrawal of immunosuppression in treatment for PVAN is a challenge and must be carefully monitored, with the risk of rejection in mind.

P-011 TREATMENT OF HYPERURICEMIA-GOUT ATTACTS AFTER RENAL TRANSPLANTATION WITH CONVERSION TO EVEROLIMUS MONOTHERAPY

Pedro Errasti, Francisco Javier Lavilla, Asuncion Ferrer. *Renal Unit, University Clinic of Navarra, Pamplona, Navarra, Spain*

A 76 year-old man with a history of hiperuricemia, multiple attacks of inflammatory arthritis and interstitial nephritis was transplanted on decembert 1999 (66 years). Immunossuppression with CyA, MMF steroid. He was discharged from hospital with a creatinine level of 1,6 mg/dl, MDRD 40 ml/min and later stabilitation (creatinina 0,9 - 1,1 mg/dl, MDRD 70-87 ml/min). He was allergic to allopurinol and colchicine (severe cutaneous hypersensibility) detected before renal transplantation. The frecuent flares after renal transplantation of gout were treated with glucocorticoid and NSAD. He had hyperglucemia with a family history of diabetes. Uric acid levels were not controlled with diet, alcohol restrition, good hydratation, losartan etc. Level of uric acid of 8-9,9 mg/dl during 10 year after transplantation. In January 2010 we decided conversion to everolimus (1,5 mg/day) with withdrawal of CyA in 48 hours. Six month later MMF was also withdrawed. The uric acid decreased from a mean of 8,9 mg/dl before conversion to 7,06 mg/day in the last follow-up. Creatinine improved to 0,85 mg/dl and MDRD 93 ml/min. Sligh proteinury of 520 mg/24 h. and microalbuminuria 283 mg/h at last follow-up. Deterioration of hiperglucemia (130-156 mg/d) with glycated hemoglobin fo 6,5-7,3% (everolimus?). Only one episode of not severe gout attack in the last 6 months with normal uric acid of 7 mg/dl. Improvement of tophaceous gout in soft tissues and joints of the hands, was observed (deposition of monosodium urate crystals).
Conclusions: Everolimus is an excellent hipouricemic agent that can be used in patients with hypersensitibity to allopurinol and colchicine. Similar decrease of uric acid has been observed in more than 100 transplant recipient converted to everolimus in the last 5 years in our unit. The case is open to discussion.

P-012 SUCCESSFUL TREATMENT OF REFRACTORY BK VIRUS NEPHROPATHY WITH WEANING ALL IMMUNOSUPPRESSION BUT PREDNISONE – A CASE REPORT

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BKV nephropathy still without approved therapy represents a threat for kidney graft survival.

We report a patient who obtained a kidney graft after desensitization protocol – rituximab, plasmapheresis, IvIg; induction of immunosuppression – basiliximab; maintenance immunosuppression –tacrolimus, MMF and prednisone. An early episode of acute humoral rejection was treated with additional plasmapheresis and IvIg. Three months after Tx, S-creatinine increased (135–185 μmol/l). Renal biopsy was consistent with acute cellular rejection Banff 1A, without signs of BKV and the patient was treated with methylprednisolone. Subsequently, replication of BKV in blood was confirmed (90,000 copies/ml). Next biopsy revealed BK nephropathy stage B, which turned out to be refractory to all possible therapeutical options: stopping MMF, reducing tacrolimus, conversion to dual therapy with rapamycine (blood level 8 ng/ml) and prednisone (7.5 mg), ciprofloxacilin, IvIg (2× 140 g), cidefovir (2 cycles, 0.25 mg/kg á 2 weeks, 7 and 5 doses), rituximab (2× 700 mg) as well as combination of rapamycine and leflunomide finally for 5 months. Repeated renal biopsies, last one 24 months after Tx, oscillated between stage A and B, viraemia between 15,000–30,000 copies/ml, replication in urine remained outside the upper limit of quantification (BKV Q-PCR Alert Kit, Nanogen Advanced Diagnostics, Italy). Thirty months after Tx, S-creatinine reached 358 μmol/l. We decided to stop not only leflunomide but also rapamycine. For altogether 25 days, the patient was treated with 5 mg of prednisone only. We achieved clearance of viraemia as well as viruria for the first time; S-creatinine decreased to 278 μmol/l.
Conclusion: extreme reduction of immunosuppression only, but none of the probative therapies helped to clear BKV. Long term safety of this approach in immunized patient remains to be determined.

P-013 URETERIC STRICTURE IN RENAL ALLOGRAFT – TO REIMPLANT OR NOT?

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SML is a 38 year old female had ESRD due to congenital pelvi-ureteric obstuction. Her mother donated a kidney to her on 5/8/2008. There was immedciate graft function and serum creatinine (Se crea) stabilized at 120-130 umol/L (NR 80-100). Her post-transplant course was complicated by CMV gastritis (resolved with ganciclovir), hypertension and her first urinary tract infection in Dec 2008. Renal sonography then showed mild hydronephrosis only. DTPA scan showed similar findings and a nGFR of 67 ml/min. Graft biopsy (30/1/2009) showed changes c/w acute tubular necrosis but no rejection or ciclosporin A (CyA) nephrotoxicity and IF for C4d was negative. She was maintained on lowdose steroids, CsA and mycophenolate sodium. Over the subsequent months, Se crea showed an increasing trend and sonography increasing hydronephrosis. MR angiography (20/4/10) excluded graft artery stenosis but showed ureteric stricture at the site of implantation into the bladder. This was confirmed by CT urography. An antegrade nephrostomy for a few days in June 2010 resulted in a fall in the Se crea. An antegrade ureteric stent was then inserted for a few weeks but as expected, the problem recurred on stent removal. Our urologists have consulted more experienced Transplant surgeons abroad who are also reluctant to reimplant the ureter citing recurrence of ischaemia or rejection. Repeated DPTA scans have shown a progressive fall in the GFR (from 67, 57.7 and 53.8 ml/min/1.73m2).
Issues: 1) Should the obstruction not be decompressed surgically?
2) If so, what is the best surgical approach?
3) Conversion from CyA to everolimus is also considered except for the distance factor.

P-014 KIDNEY GRAFT VENOUS ANASTOMOTIC STENOSIS: AN UNUSUAL CAUSE OF REVERSIBLE PRIMARY NON GRAFT FUNCTION

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We report herein a case of reversible primary non function of a kidney graft due to severe renal transplant venous stenosis in a 24-year old man. He received his first kidney transplantation for congenital uropathy. The donor was a 28 year-old man with no medical history who committed suicide by hanging. No-flow time was 30 minutes. The right kidney was engrafted in the left iliac fossa. The donor renal vein and artery were anastomosed in an end-to-side fashion to the recipient's external iliac vessels.
Post transplantation, the patient remained anuric and dialysis-dependent. Doppler US at day 2 showed a tight venous stenosis at the anastomotic site. There was neither arterial stenosis nor vascular thrombosis. Angio-MRI confirmed the venous stenosis, presence of vascular flow with neither thrombosis nor kinking. There was no extrinsic compression. Efficient anticoagulant treatment was introduced to prevent venous thrombosis.
After discussion, surgical reintervention was excluded to avoid warm ischemia time. Because of persistent anuria, percutaneous transluminal angioplasty was undertaken for venous revascularization after three weeks time to let the anastomosis heal. The angiography showed a long tight stenosis which was dilated with a 5 French catheter and stented with an endoprothesis (10mm x 40mm). After the procedure, diuresis was immediate and graft function returned to normal within one week (serum creatinemia 90μmol/L). Two months later, doppler US is normal with a permeable vein. This case is interesting because kidney graft venous stenosis is a rare cause of reversible primary non graft function. In spite of late angioplastic treatment, graft function recovered totally. We conclude that anastomotic venous stenosis revascularization should be attempted, even late, providing that graft perfusion is not jeopardized.

P-015 SUCCESSFUL TREATMENT OF PULMONARY MUCORMYCOSIS WITH DESFERASIROX-POSACONAZOLE-AMPHOTERICIN B AFTER KIDNEY TRANSPLANTATION: A CASE REPORT

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Introduction: Mucormycosis is a rare and fatal opportunistic infection following solid organ transplantation. Here, we report the favorable outcome of pulmonary mucormycosis in a renal allograft recipient treated with amphotericin B-posaconazole and adjunctive deferasirox, an iron-chelating agent having a fungicidal effect against Mucorales.
Case report: A 49 year-old Thai male with end stage kidney disease from chronic hypertension underwent a 2/6 HLA match cadaveric kidney transplantation. The patient had a long-term history of snuff abuse. The immunosuppressive protocol consisted of tacrolimus, mycophenolate mofetil (MMF) and prednisolone. He had delayed graft function from acute vascular rejection type IIA and was successfully treated with thymoglobulin. Thirty-nine days post-transplant, he developed fever, cough and right anterior pleuritic chest pain. The chest CT scan showed bilateral multiple pulmonary nodules (largest 4 cm with cavitation in left upper lobe). Transbronchial biopsy revealed non-septate branching broad hyphae consistent with Mucorales which subsequently grew *Mucor* spp. having minimal inhibitory concentration to posaconazole of 0.25 μg/ml. MMF was stopped and 4 mg/kg of liposomal amphotericin B (LAMB) was started. Six-days after treatment, there was no clinical improvement. Surgical resection of the left upper lobe mass was done and 2-weeks of oral desferasirox (20 mg/kg/day) followed by oral posaconazole (800 mg/day) were added. He responded well to the treatments and was discharged without renal or hepatic dysfunction. LAMB and posaconazole had been continued for 4 weeks and 1 year respectively. No evidence of clinical and radiological recurrence of pulmonary mucormycosisis were found 2 month after stopping posaconazole and he remained stable with a serum creatinine of 1.6 mg/dl.
Conclusion: LAMB, desferasirox and posaconazole in conjunction with surgical resection can be safely used as a salvage therapy for invasive mucormycosis after kidney transplantation

P-016 METASTATIC SARCOMATOID CARCINOMA TO LIVER AND BONE MARROW IN RENAL TRANSPLANT RECIPIENT: DUE TO EXACERVATION OF QUIESCENT RENAL CANCER?

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We report an unusual case of *metastatic sarcomatoid carcinoma (MSC)* in a renal transplant recipients. An origin of cancer was possible the *calcifed complicated cyst (CCC)* which had changed from the renal mass over 7 years.
A 60-year-old man diagnosed with unknown origin of ESRD started hemodialysis in October 2002. He visited our hospital 1n September 2006. No matter illness were present at the time of pretransplantation work up in 2006 except thrombocytopenia (95000/mm^3-120000/mm^3) and simple acquired cysts with peripheral rim CCC (Bosniak IIF) in right kidney. Bone marrow examination showed hypocellular marrow with increased Megakaryocyte. A deceased donor transplantation was performed in December 2008. In Febrary 2009, he presented with a 3-day history of fever and severe anemia (Hb: 3.9 g/dL). Bone marrow examination revealed unknown origin of MSC. Abdominal Computed tomography (CT) did not show pathologic lesions except more thickened peripheral calcified rim of CCC (Bosniak IIF) than 2 years ago. Positron emission tomography scan showed multiple bone metastases, and multiple hypermetabolic lesions in the liver and right CCC. Pathologic examination of liver biopsy revealed MSC. Retrospectively, we could find the abdominal CT film which had examed other hospital in 2002. CCC was a 3cm sized solid renal mass sug-

gested renal cell cancer. At 3 months after transplantation, the patient died of DIC and hepatic failure.
We could not performed autopsy. But we suggested that our case was a MSC caused by exacervation of quiescent renal cancer. We should remined that some small renal masses had zero growth or regression over several years, like benign features, in ESRD patients. Careful follow- up and examination is essential for kidney transplant candidates.

P-017 EBV LYNPHOPROLIFIRATIVE SYNDROME A CHILD KIDNEY TRANSPLANTATION

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Aged 08 years, treated by peritoneal dialysis before transplantation, until the age of eight years for an undetermined nephropathy, than transplanted in may 2008 from a living related donor (mother). She has positive serology in CMV, HHV6, and negative for EBV, HIV.
Induction therapy consisted in simulect and prednisolone, maintenance therapy: was association of tacrolimus- MMF and prednisone. The apparition of anemia and anorexia one year behind renal transplantation, and a clinical signs as soon as weight loss, digestive disorders: melena, liver and splenic mass, adenopathy, justified biological and radiological investigations: objectived: Hb: 7g/dl and inflammation/no Cells malignant in his blood. CT scan. with injection: The process of tumor ileo caecal junction adenopathy with small satellites, and secondary hepatic localization. EBV PCR: Strong Positive. The diagnosis of non -Hodgkin lymphoma was confirmed, conducted to stopping tacrolimus and lowering the MMF dose. The therapeutic consisted in Rituximab 375 mg/m2, 4 cures at weekly intevalle related by Zovirax for one year. In the following up, patient has a good early evolution concerning here malign desease, and complete remission, with good renal function: GFR: 92 ml/min. have an morbid obesity BMI 33kg/m2 and have developped HNT.
Conclusion: Early detection of cancer in transplant recipients is of great importance. Regular screening for persistent Epstein–Barr virus (EBV) DNA viral load in patients at risk for developing PTLD is recommended.

P-018 VISCERAL LEISHMANIOUSIS IN A CHILD TRANSPLANTED KIDNEY

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Aged 12 years, treateated by hemodialysis since 2007, for an undetermined nephropathy, transplanted kidney in may 2008 from a living related donor (mother) aged 40 years. The post operative were favorable. 8 months later, we noted an a skin lesion at the right calf. Knowing that patient resides in an endemic area of zoonotic cutaneous leishmaniasis with regular stays in Kabylia, sporadic cutaneous leishmaniasis and visceral leishmaniasis, after confirmation of diagnostic of cutaneous leishmaniasis by a skin biopsy, she was treated as a visceral leishmaniasis because of her immunosuppression for 28 days successfully. Without clinically or biologically signs evident. Before treatment her GFR was at 99ml/mn, 21 day after; her GFR was at 75 ml/mn, with a slight disturbance of liver function hence the decision to stop the ongoing treatment was decided before 28 days indicated. So, a marked improvement in the figures of renal function and normalization of blood counts except for mild anemia at 10.4 g/dl. 13 month after; she was treated for an acute rejection confirmed by kidney biopsy, because she has negliged her treatment, her GFR was at 36 ml/mn
15 months later, she developed visceral leishmaniasis with pancytopenia, and splenomegaly, then confirmed by serology WASTERN BLOT who came back positive with a negative bone marrow aspiration. At the end of treatment with Ambisome, serology check was made which proved negative. But we noted persistent leukopenia, which justified a new marrow aspiration. This is repeated with the cultivation and testing PCR to search for bodies of Leishmania (results not yet arrived) Actuelly our patient is 15 years, GFR 28ml/mn, with pancytopenia and hypertension. On: tacrolimus, MMF, steroids, and treatment oh hypertension.

P-019 ANAESTHESIA FOR KIDNEY TRANPLANTATION IN A PATIENT WITH PRADER WILLI SYNDROME

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We present a case of allogenic kidney transplantation in a patient with Prader Willi Syndrome (PWS). This 42 year old man had renal failure requiring haemodialysis. He was on the transplant waiting list due to increasingly difficult dialysis access. His current fistula was not functioning well. Relevant examination revealed a body mass index of 37, learning disabilities, poor dentition, large tongue, short neck and poor mouth opening. During his previous anaesthetic he had been difficult to intubate and ventilate and venous access had been problematic. Recovery from muscle relaxation had been prolonged and he had suffered post-operative confusion. Magnetic resonance venography (MRV) revealed superior vena cava (SVC) occlusion. The kidney was to be transplanted on the right side leaving only the left femoral vein for central venous access.
There were many challenging aspects in this case suitable for discussion:
Airway Management:
– PWS is associated with difficult intubation and ventilation
– Awake fibreoptic intubation was complicated by the patient's learning difficulties
Venous access:
– MRV had demonstrated SVC occlusion
– Multiple previous failed arteriovenous fistulae limited the options for peripheral venous and arterial access
Fluid management:
– PWS has been associated with pulmonary oedema
– The Oesophagael Doppler monitor intra-operatively compensated for femoral central venous pressure monitoring
Hypotonia and prolonged duration of muscle relaxants:
– PWS predisposes to muscle hypotonia
– Anaesthesia was maintained with total intravenous anaesthesia. Guided by depth of anaesthesia monitoring (bispectral index), propofol and remifentanil infusions avoided the need for muscle relaxant drugs
Postoperative care:
– Hypoventilation and both central and obstructive apnoea are very common in PWS. High dependency care is obligatory.
– Pain management complicated by communication difficulties and opioid sensitivity
– Learning difficulties may affect compliance with anti-rejection medication and follow up.

P-020 HEADACHES ONE YEAR AFTER RENAL TRANSPLANTATION

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We report the case of a 49-year-old female, who underwent living donor kidney transplantation because of bioptically proven IgA nephropathy. Due to donor-specific antibodies with a positive B-cell crossmatch a special pretreatment protocol was necessary prior to transplantation. This regimen consisted of rituximab, intravenous immunoglobulins, plasmapheresis and antithymocytce globulin induction therapy. The immunosuppressive maintenance therapy included tacrolimus, mycophenolate mofetile and steroids. Serum creatinine at discharge was 1.4 mg/dl.
One year after transplantation the patient presented to the emergengy department with arterial hypertension and right sided headaches accompanied by nausea and vomiting. On examination the patient had no fever, the clinical status was unremarkable and laboratory investigations showed no systemic signs of inflammation (WBC 7.1 G/l, CRP $<$ 0.1 mg/dl). The cerebral CT-scan and magnetic resonance imaging were unremarkable.
Lumbar puncture confirmed lymphocytic pleocytosis of 33 cells/μl with an elevated total protein. Two days later the patient developed a temperature of 40 $^{\circ}$ C and a rash of grouped vesicles located to the right dermatome C3 became visible. Cerebrospinal fluid was tested positive for Varizella-zoster virus (VZV), indicating a VZV-meningitis. Therapy was started with intravenous aciclovir and pregabaline orally to prevent herpetic neuralgia. The patient could be discharged without any pain after 16 days. Three months later, she was still free of symptoms and serum creatinine was stable at 1.2 mg/dl.
Primary infection with VZV leads to varicella (chickenpox), whereas herpes zoster results from reactivation of endogenous latent VZV infection. In highly immunocompromised hosts such as our patient, reactivation of VZV may present in an atypical manner and may be difficult to diagnose.
Transplant patients remain at substantial risk for severe VZV-related complications and visceral dissemination in the immunosuppressed patient is a life-threatening emergency. Accurate diagnosis is essential for starting an antiviral therapy immediately.

P-021 PRE- TRANSPLANT HbA1c LEVEL IS AN EARLY PREDICTIVE MARKER FOR NEW-ONSET DIABETES MELLITUS IN RENAL TRASPLANT RECIPIENTS

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Background: Despite the fact that Glycosylated hemoglobin (HbA1c) is recommended in the American Diabetes Association guidelines as a criteria for the diagnosis of type II DM in the general population. However, it's value for the prediction of New-Onset Diabetes Mellitus (NODAT) in renal transplant population has never been investigated. In this study, we aimed to investigate the predictive role of HbA1c level in NODAT.
Methods: Between January 2007 and December 2008, seventy-one renal transplant recipients who were non-diabetic at baseline were enrolled. 25 patients (35.2%) developed posttransplant NODAT within the first year; 7 (9.8%) with sustained NODAT (longer than 3 months). Patients were divided into 3 tertiles according to pre-transplant HbA1c level as $\leq$ 4.8% (I tertile, low), 4.8-5.0% (II tertile) and $>$5.0% (III tertile, high).
Results: Pre-transplant mean age was 35.5$\pm$11.1 years and 56% was male. Mean HbA1c level was 4.9$\pm$0.5%, fasting blood glucose 98.6$\pm$34.0 mg/dl, HOMA-IR 1.56$\pm$1.57, serum procalcitonin 0.22$\pm$0.29 ng/ml, total cholesterol 171$\pm$47 mg/dl, triglyceride level 179$\pm$91 mg/dl and body mass index (BMI) 22.8$\pm$4.2 kg/m2. 5 patients (7%) were hepatitis C positive; of which 80% had NODAT. HbA1c level was positively correlated with male gender (r=0.32; $p<0.01$) and triglyceride levels (r=0.26; $p<0.05$). Pre-transplant dialysis time was shorter and NODAT was higher in the highest HbA1c tertile. In multiple linear regression analysis, pre-transplant dialysis time (t= 2.58, p=0.01), male gender (t= 2.19, p=0.03) and HbA1c level (t= 4.1, $p<0.001$) were independent predictors of NODAT. There was no association between HOMA-IR and NODAT.
Conclusion: HbA1c level is an independent predictive marker for New-Onset Diabetes Mellitus in renal transplant Recipients.

P-022 LATE ACUTE RENAL DYSFUNCTION: A CHALLENGE DIAGNOSIS

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We report the case of a 39 years old man, with acute renal dysfunction 6 years after his second renal transplantation. The first living related transplant failed for primary non function. A second deceased donor kidney transplant shared the DR1 with the first kidney. Donor Specific Antibodies (DSA) and cross-match (XM) were negative. Induction therapy was basiliximab and maintenance therapy TAC and steroids.
Serum creatinine (Scr) was stable around 2 mg/dl for 3 years, when a first episode of acute renal dysfunction occurred (raise in Scr $>$25% of baseline, slight positive XM, no detection of BKV replication).
An increasing in immunosuppression and steroid pulses, without renal biopsy, produced a modest improvement of renal function.
Three years afterwards (Apr 2010) a second episode of acute renal dysfunction occurred with acute raise of Scr to 7.2 mg/dl. Reduced though level of TAC, positive XM, presence of DSA against DR1, hyperecogenicity of the transplanted kidney, complete active reflux with BKV active plasma replication (copies $<$10,000/ml) were detected.
Differential diagnosis between acute rejection (AR), BKVN, chronic renal dysfunction was challenging.

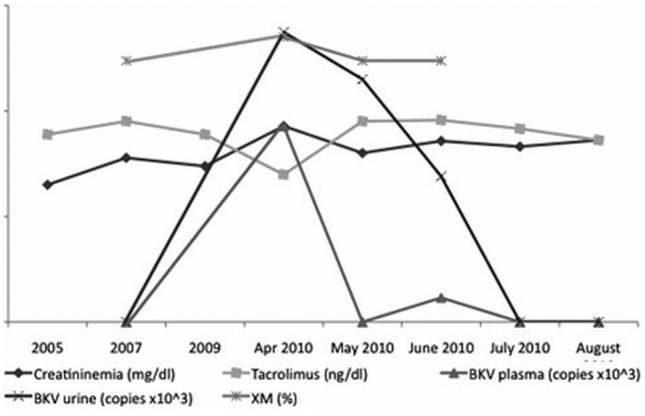

Figure 1

Renal biopsy showed acute humoral rejection type I without signs of BKVN. Therefore he had an increasing in immunosuppressive therapy, steroid pulses, plasma and photo-apheresis. Interesting we observed the disappearance of BKV plasma replication associated with a slight improvement of renal function. (Figure 1)
We hypotize that the alteration of microenviroment in renal allograft, due to the inflammatory state of AR, might have promoted the transfer of BKV in plasma from the site of latency.
The immunosuppressive therapy, reducing the inflammation (evidenced by the reduction of creatininemia) should have reduced this transfer.
Differential diagnosis between AR and BKVN is difficult long-term after transplant and sometimes the diseases can be related. Biopsy is always required in acute allograft dysfunction.

P-023 HOW MANY TIMES CAN PARVOVIRUS B19-RELATED ANEMIA RECURE IN SOLID-ORGAN TRANSPLANT RECIPIENT?

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Parvovirus B19 (PB19) infection is known to cause acute erythroblastopenia mediated anemia in solid-organ transplant recipients. Intravenous immunoglobulins (IVIG) and the decrease of immunosupression level are supposed to induce a long term remission although there is no consensus about the dose and the schedule of IVIG administrations. However, few reports have shown that PB19-related anemia can recur despite this treatment, with a maximum of 3 recurrences reported.
In this report, we describe in detail two kidney recipients with PB19 infection. They experienced respectively nine and seven PB19-related anemia recurrences. Immunosuppression level was decrease and IVIG were administered at each recurrences followed by a transitory normalization of hemoglobin level and a decrease of serum PB19 viral load. Episodes were separated by several months.
Interestingly enough, they show high serum ferritin level with a high transferrin saturation rate whereas they have not received iterative blood transfusions.
To our knowledge, the maximum of recurrences of PB19-related anemia reported is three episodes in immunocompromised patients.
These two patients raise an original therapeutic management question about a frequent viral infection in solid-organ transplant recipients. One patient is currently receiving IVIG every three month as a preventive strategy with no recurrence to date.

Clinical Cases – Pancreas – medical

P-024 RARE CASE OF URETERAL OBSTRUCTION IN A RENAL TRANSPLANT RECIPIENT: Candida albicans FUNGUS BALL

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Acute renal failure resulting from ureteral obstruction by fungus balls is uncommon in kidney transplantation recipients. We report a patient diagnosed with ureteral obstruction caused by a Candida albicans fungus ball. A 60-year-old male with end-stage renal disease due to IgA nephropathy underwent cadaveric kidney transplantation. Immunosuppressive treatment consisted of tacrolimus, mycophenolate mofetil, methylprednisolone and basiliximab. The warm and cold ischemic times were 18 minutes and 23 hours, respectively, and the patient required hemodialysis during the first 3 weeks following transplantation, after which the kidney gradually began to function. The patient was discharged with a creatinine level of 2.6 mg/dl. Two months after transplantation, the patient presented with decreased urine output and increased serum creatinine (5.56 mg/dl). The graft showed hydronephrosis without vascular anomalies on Doppler ultrasound and a percutaneous nephrostomy was performed. A culture from sampled urine grew Candida albicans and the patient was diagnosed with ureteral obstruction caused by a fungus ball, which was detected by MRI. The patient was treated with fluconazole intravenously and through direct irrigation of the nephrostomy catheter. After 15 days urine samples were sterile and the nephrostomy catheter was removed after confirming that the passage of the ureter was restored. Two months after catheter removal, the patient was doing well with a serum creatinine level of 2.4 mg/dl.
Although ureteral obstruction in renal transplant recipients caused by fungus balls is a rare complication, it should be considered in cases with hydronephrosis and acute renal failure. Treatments with topical irrigation and systemic administration of antifungal agents are very effective, however surgical reconstruction should be performed when the treatment with such agents is unsuccessful.

P-025 ACUTE INFLAMMATORY SYNDROME INDUCED BY MYCOPHENOLATE MOFETIL IN A PATIENT FOLLOWING PANCREAS TRANSPLANTATION

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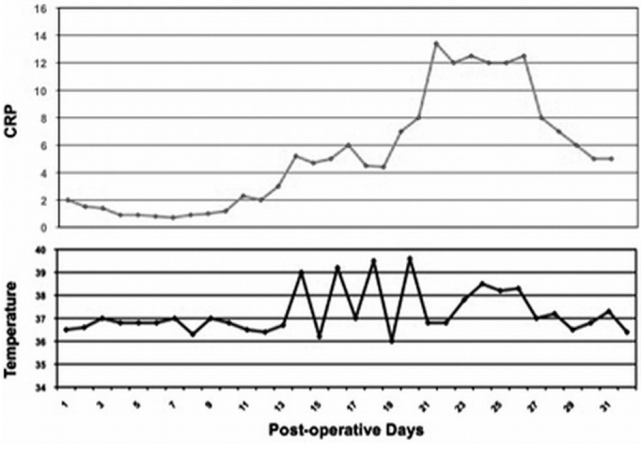
We report on a patient received a pancreas graft after kidney transplantation (PAK), who developed an acute inflammatory syndrome characterized by fever and muscle pain within 14 days after transplantation.
The initial immunosuppression consisted of Basiliximab, Tacrolimus, mycophenolate mofetil (MMF, in form of Cellcept) and steroid. Due to gastrointestinal symptom, Cellcept was switched to Myfortic on POD 8. Prophylaxis for CMV infection was carried out with valgancyclovir. Cultures a variety of samples were sent for microbiological investigations. Due to staphyloccus haemolytics found in the intraabdominal drain, the patient was treated with Vancomycin. However, there was no improvement of the symptom. The C-reactive protein was elevated up to 13.41 mg/dl while procalcitonin was only slightly elevated up to 0.84 ng/ml. Further investigations consisted of Chest X-Ray, abdominal MRT, Echocardiograph, which did not show any evidence of source of the symptom. Upon suspicion of acute inflammatory syndrome induced by MMF which has been reported in 3 cases in the literature, MMF was switched to azathioprine on POD 25. Within 24 hours, a rapid and complete resolution of the symptom was observed.



This report demonstrates that MMF can also induce acute inflammatory syndrome in patients following PAK.

Clinical Cases – Liver – surgical

P-026 RECONTRUCTION OF THE HEPATIC OUTFLOW OF A AMYLOID HEPATIC ALLOGRAFT (AHA) FROM A PATIENT RECEIVING A COMBINED HEART LIVER TRANSPLANTATION – A CASE REPORT

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Introduction: Surgical technique in domino-liver tx has been adapted to the requirements of both the recipient/donor in Familial Amyloidosis (FA)-domino-liver Tx. However the most challenging aspect is the suprahepatic infracardial division of the liver in piggy-back technique: while the FA donor should be left with an optimal condition for the IVC anastomosis the AHA graft should yield sufficient hepatic vein length as well. Here we describe a case of a domino LTx with the FA patient receiving a combined heart-liver graft due to end-stage amyloidosis.
Patients and technique: A 51 yo pt. with FA and a 53 yo pt with Hep. C and HCC consented to the combined transplant and to receive an AHA graft respectively. The AHA graft presented with exceptionally short hepatic veins which had to be dissected within the parenchyma leaving the IVC in situ and rather short vessels in the AHA graft. Therefore a sophisticated reconstruction had to be performed backtable using the deceased donors IVC to create a common ostium for anastomosis in the second recipient.
Results: Although the FA patient presented with an unfavourable anatomy the combined transplantation succeeded and 3 months postoperatively liver and cardiac function are normal. Even though the back table preparation involved an elaborate reconstruction of the hepatic outflow cold ischemia time was limited and the recipient was discharged on day 12 with normal liver function.
Conclusion: Domino transplantation in piggy-back technique is a safe procedure and expands the donor pool even in combined heart and liver tx. However the anatomical premises are challenging as to providing both patients with adequate hepatic venous outflow. Venous reconstruction of the AHA graft using the donor IVC is a feasible and safe option.

P-027 EARLY OCCURRENCE OF KAPOSI'S SARCOMA IN POST TRANSPLANT PATIENT TREATED SUCCESSFULLY WITH EVEROLIMUS

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Kaposi's sarcoma (KS) is an unusual neoplasm that is being seen more frequently in transplant recipients.
We report on a case of early occurrence of Kaposi's sarcoma in post transplant recipient, treated successfully with Everolimus.
The case is interesting in that it demonstrates occurrence of Kaposi's sarcoma at an early stage. The latency period was just 5 month for this case. The short period of latency between transplantation and KS diagnosis suggested that KS development in transplant recipients is associated with rapid reactivation of latent HHV-8 infection.
A 50 year old man with hepatitis B related liver cirrhosis and hepatocellular carcinoma received living donor liver transplantation in February 2009.
Six months following the uneventful transplantation, brownish to violet coloured, maculonodular lesions with irregular shape were noted on the left leg. An incisional skin biopsy revealed the diagnosis of KS. PCR for HHV 8 infection was positive. The involvement of other organs was excluded by clinical, radiologic and endoscopic examination. At that time, maintenance immunosuppression consisted of the usual triple medications: Cyclosporine, Mycophenolate Mofetil and Prednisolone. Hepatitis B immunoglobulin and Lamivudine were used for HBV prophylaxis. When KS was diagnosed, M-tor inhibitor (everolimus) was started and the other immunosuppressants were discontinued until a steady serum level of sirolimus reached. The skin lesion became progressively flattened and gradually disappeared. Total duration of the treatment was 3 months.
Conclusion: Our experience demonstrate that KS can occur on an early stage of postoperative period of liver transplanted patients.

P-028 TRANSJUGULAR INTRAHEPATIC PORTOSYSTEMIC SHUNT (TIPSS) IN A CHILD TRANSPLANTED WITH A LEFT LATERAL SEGMENT FROM A SPLIT LIVER GRAFT

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Introduction: The use of Transjugular intrahepatic portosystemic shunts (TIPSS) has been shown to be a therapy for a liver transplant recipients who develops gastrointestinal bleeding due to portal hypertension. We reported a case of 3,7 years old girl.
Case Report: At age of 8 months she underwent a liver transplantation (OLTx) with left lateral segment procured from an in situ split liver graft for biliary atresia. Two months after OLTx she developed an anastomotic biliary stricture that required several balloon dilatation and stent placement by percutaneous transhepatic cholangiography. Three years after OLTx she developed a vanishing bile duct syndrome and gastrointestinal bleeding due to portal hypertension. An endoscopy showed a grade 1 oesophageal varices. A therapy with beta blockers failed to control the relapse of gastrointestinal bleeding. TIPSS was performed for uncontrollable intestinal bleeding and led to identification of significant stenosis of the portal vein anastomosis (pressure in mesenteric vein: 26 mmHg). Stenosis was successfully dilatated with 6 and 8 mmm catheter. A shunt was created between the sovrahepatic vein and the portal vein with a 8 X 60 mm Wallstent. After TIPSS procedure intraportal pressure was reduced to 12 mmHg, the porto-systemic gradient was 5 mmHg. Nine years after OLTx and 6 years after the placement of TIPSS the patient is doing well, no recurrence of gastrointestinal bleeding have occurred. The picture of the vanishing bile duct syndrome is stable.
Conclusion: Placement of TIPSS is effective to control haemorragic complication of portal hypertension and can be safely placed in recipients of a left lateral segment liver graft.

P-029 TRIPLE LIVER TRANSPLANTATION FOR RECURRENT AUTOIMMUNE HEPATITIS INITIALLY MASQUERADING AS FULMINANT WILSON'S DISEASE

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In 2006, a 15 year-old female patient presented with symptoms of decompensated acute liver failure requiring listing for liver transplantation (LTx). Further lab tests were suggestive of Wilson's disease as serum levels of copper and caeruloplasmin were significantly reduced and copper excretion strongly increased upon penicillamin intake. Genetic analysis confirmed compound heterozygosity for Wilson's disease featuring two heterozygous mutations in exon 14 and 20 of the ATP7B gene, respectively. Further seemingly confirming the Wilson's diagnosis, the post-LTx histology was consistent with a decompensated course of Wilson's disease resulting in liver cirrhosis.
Over the subsequent 28 months she developed numerous acute rejection episodes responsive to high-dose steroids but recurrent despite high-dose CNI- and mTOR-based immunosuppressive regimens, finally resulting in chronic allograft failure requiring listing for re-LTx.
Upon re-LTx her clinical course was again characterized by recurrent rejection episodes resistant to conventional treatment regimens leading yet again to allograft failure with cirrhosis and the requirement for re-re-LTx by living donation from her mother 21 months after the second LTx.
Before the third LTx she was pre-conditioned by plasmapheresis and Rituximab to prevent recurrence of allograft failure from a potentially antibody-mediated damage. However, despite this and maximum immunosuppression including Alemtuzumab, photopheresis and plasmapheresis following re-re-LTx our patient again developed recurrent rejection episodes and signs of early-onset allograft failure and cirrhosis.
Over her total clinical course, histologies of representative liver biopsies repeatedly showed cellular rejection infiltrates combined with signs of interface hepatits, cholangitis, lympho-plasmacytic infiltrates, and progressive fibrosis.
Careful reevaluation of her case revealed that the Wilson's diagnosis was not quite accurate, rather the culprit was recurrent LKM-positive autoimmune hepatitis initially masqueraded by Wilson's disease. Subsequently, our patient was put on steroids and azathioprine with outcomes as yet to be determined.

P-030 A RARE CAUSE OF ACUTE LIVER FAILURE: ADULT ONSET STILL'S DISEASE – CASE REPORT AND SYSTEMATIC REVIEW OF THE LITERATURE

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Introduction: Acute liver failure (ALF) requiring orthotopic liver transplantation (OLT) has a declining incidence over the past years. More than 50% of ALF are still of unknown origin. A rare cause of ALF is Still's disease. Adult onset Still's disease (AOSD) is a systemic rheumatic disorder of unknown etiology. About 75% of patients with this disease present with elevated serum liver enzymes, but hepatic failure is a rare complication of adult Still's disease.
Case Report: We present the case of a 24-year-old woman, who was admitted with acute liver failure. Because of the fulminant course an extracorporeal liver support system (Prometheus®) was necessary. King's college criteria were clearly fulfilled, the MELD score was 40, and therefore high urgency OLT became necessary. One episode of an acute rejection could be managed with high dose application of methylprednisolone for three days. For the immunosuppressive therapy we use MMF and Tacrolimus. Nine month after the transplantation the patient has a good liver function. Actually there is no sign of another manifestation of AOSD.
Discussion: The diagnosis of AOSD was made in accordance with well-established criteria including arthalgia, fever, sore throat, rashes and hepatosplenomegaly. Our search of the literature found only few cases, which reported about patients with adult Still's disease which developed acute liver failure. Only in six cases of these OLT was necessary. The early detection of the diagnosis of an AOSD could avoid the development of liver failure. Treatment comprises non-steroidal anti-inflammatory drugs, corticosteroids, methotrexate, ciclosporin A, azathioprine (among others immunosuppressive drugs) and successful application of biological drugs, for example anti-tumour necrosis factor and anti-Interleukin 1.
Conclusion: In each case of unclear liver failure in young patients Still's disease is an important differential diagnosis.

P-031 LIVER TRANSPLANTATION IN A PATIENT WITH AN INTRAABDOMINALLY LOCATED LEFT VENTRICULAR ASSIST DEVICE

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Liver Transplantation (LTx) is an effective treatment modality in patient with certain congenital metabolic liver disease. Propionic Acidemia (PA) is an autosomal recessive disorder caused by deficiency of propionyl-CoA carboxylase in the liver and other tissues which participates to the formation of substrate of the mitochondrial respiratory chain. Its deficiency leads to accumulation of toxic substances resulting in severe metabolic decompensation. The present original case reports a 16-year-old male with PA who was admitted for metabolic decompensation and dilated cardiomyopathy as frequently described in this disease and immediately treated with the placement of a Left Ventricular Assist Device (LVAD). The use of LTx in organic acidemia, which are Non- Liver-Oriented-Disease (NLOD) is still controversial. Indeed the liver is only partly involved in the disorder. Unsatisfactory outcomes could result from extrahepatic manifestations which affect the postoperative course. At this time, however, early LTx is the sole therapeutic procedure for NLOD patients with severe manifestations which may lead to improvement of quality of life and life-expectancy.
This case raised many questions that were discussed multidisciplinarily: Optimal timing and sequence for LTx and removal of LVAD? The difficulty of LTx given the partly intraabdominal position of the LAVD? The possibility of arrhythmia during LTx? The adaptation of immunosuppression with a foreign device? Given the absence of irreversible damage on myocardial biopsies, the potential amelioration of the cardiac function with a better metabolic control and the recovery of the ejection fraction, a planned LT was then proposed. The piggy-bag technique via a short right sub-costal incision was preferred. The patient had an uneventful peroperative course and the LVAD was removed 3 days after the LT. The patient was discharged at day 24 with a normal liver and cardiac function.

P-032 DIAPHRAGM RUPTURE IN A LIVER TRANSPLANT PATIENT UNDER CHRONIC IMMUNOSUPPRESSIVE THERAPY WITH SIROLIMUS. CLINICAL CASE

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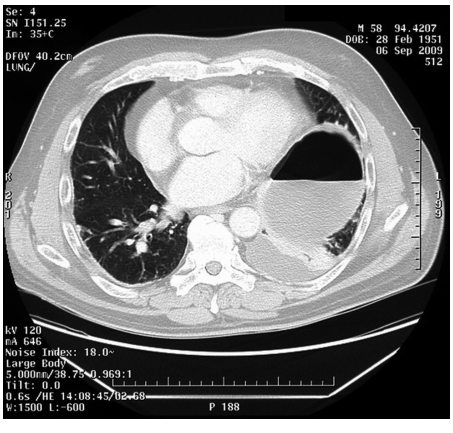
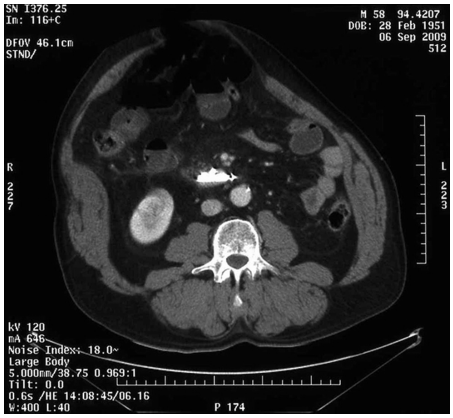
After 16 months since an uneventful liver transplantation for alcoholic cirrhosis with hepatocarcinoma performed at our institution, a 58 year-old Caucasian male patient (BMI 29) arrived at the emergency room of our hospital complaining of diffuse abdominal and left shoulder and hemi thorax pain, fever (38°C), and dyspnoea, retching with alimentary vomiting the day before.
He was a diabetic patient type II and he developed after transplantation large incisional hernia in the median portion of the J-shaped laparotomy for which he was scheduled for surgical correction. The immunosuppressive regimen was switched to sirolimus (through level 4-8 ng/ml) monotherapy 2 months after transplantation for renal toxicity cyclosporine related. After CT scan, an emergency midline laparotomy was performed, revealing the upwards displacement of the gastric fundus through a tear of the central part of the left hemi diaphragm, without involvement of the oesophageal hiatus.
Reduction of the large gastric hernia required a 5 cm widening of the diaphragmatic tear; He was discharged 14 days after surgery after antibiotics treatment for post operative pneumonia.
Vomiting and large incisional hernia could have triggered off a very rare pathol-





ogy, unexpected considering that the patient's history did not report traumas, previous lesions or alterations in the breathing or digestive mechanics.
A probable iatrogenic vascular impairment after hepatectomy could be considered as a contributing factor to a possible diaphragm weakness. Moreover, the chronic immunosuppressed state of this previously liver transplanted patient using a drug (sirolimus) with well-known antiproliferative and anti-neoangiogenetic effects and clearly correlated with a high-risk of incisional hernia and impaired wound healing, in addition to diabetes, could have contributed to the spontaneous diaphragmatic rupture.

P-033 DOES LATE RECURRENCE AFTER HEPATECTOMY FOR HCC IMPACT ON SURVIVAL AFTER LIVER TRANSPLANTATION FOR HCC RECURRENCE? A CASE REPORT

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Liver transplantation (LT) has been described as a treatment for hepatocellular carcinoma recurrence after hepatectomy for HCC with different results in the so called "salvage transplantation". The aim of presenting this clinical case is to discuss this option and to analyze if patients can be optimized to achieve best results.
A 42 year-old man with hepatitis C virus (HCV) and end stage liver disease was diagnosed of a single 4 cm HCC during follow-up. At diagnosis the patient didn't have portal hypertension so a partial liver resection has performed. The pathological exam revealed a single 5.2 cm well differentiated HCC without vascular invasion but presented satellite lesions. After 23 months of follow-up the patient presented HCC recurrence as a single 1 cm HCC. At that time liver cirrhosis had progressed the patient presented with portal hypertension and LT was indicated.
LT was performed after 2 months of recurrence diagnosis (waiting list 15 days), with piggy-back technique and temporal porto-caval shunt. Pathological examination of the liver revealed 2 well differentiated HCC nodules (1.5 x 1 and 1.5 x 0.5 cm) without satellite lesions and without vascular tumor invasion. The patient could be discharged from Hospital at day 6. Patient immunossupresive therapy consisted on tacrolimus and MMF.
Six years after LT and 8.5 after hepatectomy the patient is alive and doing fine. No HCC recurrence has been diagnosed during follow-up.
LT is a good option to treat patient with HCC recurrence after LT in whom a new liver resection is not possible. The time to recurrence after resection probably reveals the tumor's aggressiveness.

P-034 IS SORAFENIB A NEW TESSERA IN THE MOSAIC OF PATIENTS WITH ADVANCED HEPATOCELLULAR CARCINOMA BEFORE LIVER TRANSPLANTATION?

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Hepatocellular carcinoma (HCC) remains a significant disease worldwide and its incidence is expected to increase. In selected patients, liver transplantation offers a 5-year disease free survival $>$ 75%. Sorafenib, a multikinase inhibitor targeting angiogenesis, cell survival, and proliferation in HCC is a standard therapy for advanced stage disease. However, there is little evidence in the use of Sorafenib as a neoadjuvant therapy prior to LT.
Herein we report the case of a patient to whom Sorafenib was administered prior to liver transplantation because of advanced HCC beyond Milan criteria. The patient was not eligible to liver transplantation (LT) because of the presence of an HCC with a concomitant right portal trombosis.
After the patient was started with Sorafenib a complete regression of hepatic lesion and partial regression of portal trombosis were seen. The patient underwent then LT and after 30 months of follow-up he is still disease free. Post-LT immunosuppressive therapy consisted of low dose steroids (methilprednisolone) slowly tapered over three months and Rapamycin, utilizing the interesting antitumoral effect of this class of drugs.
It is our opinion that patients with advanced HCC outside the Milan Criteria need a multimodal approach involving surgical and/or loco-regional radiologic treatment associated with Sorafenib in order to lower tumour burden before LT and to propose proper post-LT immunosuppressant therapy based on mTOR inhibitors to reduce the risk of post LT HCC recurrence. The use of Sorafenib as neoadjuvant therapy before liver transplatation is feasible and deserves investigation in large clinical trial.

P-035 LIVER TRANSPLANTATION AFTER THREE-WEEK HEPATIC COMA

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Introduction: Mushroom poisoning with Hypholoma fasciculare is a medical emergency, because of rapid evolution towards fulminant liver failure (FLF). Despite advances in intensive care management of FLF, its mortality in the absence of emergency ortothopic liver transplantation (OLT) is still high.
Case report: A 52-year old woman developed vomiting and diarrhea 3 hours after the ingestion of honey stump mushrooms. Two days later she was admitted to a regional hospital with jaundice, dyspnoe, severe cytolysis (ALT 9400 U/l; AST16400 U/l), coagulopathy (INR 6) and azotemia. Two days after admission she developed hepatic encephalopathy, was intubated and transferred to our hospital. Mushroom poisoning with Hypholoma fasciculare and fulminant liver failure (FLF) were diagnosed. Extracorporal detoxification with therapeutic total plasma exchange and renal replacement with continuous veno-venous hemodiafiltration were started. Supportive treatment with appropriate measures for 19 days was not effective and coma persisted. Twenty days from stage IV hepatic encephalopathy and 17 days from listing to transplantation a blood group identical OLT was performed. Two days after OLT the patient regained consciousness but liver parameters improved slowly. She was discharged from ICU on 19th postoperative day. At routine check 3 months after OLT the patient was feeling well with no significant deficit of central nervous system.
Discussion: In recent studies from the US the median time from encephalopathy to transplantation was 4, and from listing to transplantation 2 days. Non-transplanted FLF patients died while being on the waiting list after a median of 5 days. Due to limited availability of donor organs in Estonia the patient was transplanted on 21st day of hepatic coma, fortunately encephalopathy was reversible. To ensure earlier availability of donor organs Estonia holds cooperation talks with Eurotransplant.

Clinical Cases – Liver – medical

P-037 TRANSIENT IMPROVEMENT OF ACQUIRED HEPATOCEREBRAL DEGENERATION IN A PATIENT WITH HCV CIRRHOSIS AFTER LIVER TRANSPLANTATION: A CASE REPORT AND REVIEW OF LITERATURE

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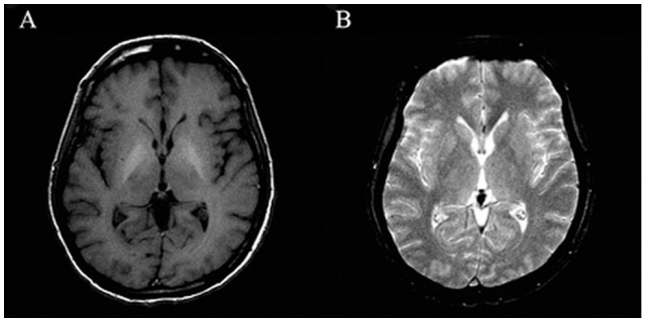
Acquired (non-Wilsonian) hepatocerebral degeneration (AHD) is an infrequent neurological disorder in patients with liver dysfunction and long-standing portal-systemic shunting. The clinical manifestations include dysarthria, ataxia, tremor, and cognitive dysfunction. The pathogenesis is thought to be heavy metal deposition, particularly manganese, in the basal ganglia and other brain tissues. Typically, patients with AHD respond poorly to conventional therapy. The information regarding the effect of orthotopic liver transplantation (OLT) is scarce and conflicting.
Here we present a 56-year-old man with hepatitis C (HCV) cirrhosis who presented with parkinsonism. Magnetic resonance imaging (MRI) brain showed typical features of AHD.
He was diagnosed with AHD and his parkinsonism symptoms remained refractory to medications. He received OLT in December 2009, which led to rapid clinical improvement of AHD. However, the patient developed recurrence of AHD 6-week post OLT, which may or may not related to recurrent HCV in-

Abstract P-037 – Table 1. Patient characteristics of reported cases of patients with AHD who received OLT

ID	Paper Ref.	Age at LT	Sex	Cirrhosis etiology	Clinical status before LT	Clinical status after LT	Follow up
1	Parkes et al., 1970	56	M	N/A	HE	Cognitive impairment and movement disorder improved	50 days
		17	M	N/A	HE	Patient died from infection 6 days post transplant	N/A
2	Powell et al., 1990	44	F	N/A	AHD	Intellectual function and neurological signs resolved completely	12 months
3	Pujol et al., 1993	N/A	N/A	N/A	HE	5 patients had bradykinesia and cognitive deterioration that improved	10-20 months
4	Counsell and Warlow, 1996	52	M	Alcohol	HM	No improvement of hepatic myelopathy	18 months
5	Troisi et al., 1999	60	F	HCV	HM	HM improved	1.5 years
6	Lewis et al., 1999	45	M	Congenital hepatic fibrosis	AH	Pt died from infection 2 weeks post transplant	N/A
7	Spahr et al., 2000	N/A	N/A	N/A	HE	Parkinsonism improved in all 3 patients	4 months
8	Layrargues, 2001	60	F	Primary biliary cirrhosis (PBC)	HE/AHD	Asterixis, buco-linguo-facial dykinesia resolved completely	2 months
9	Stracciari et al., 2001	59	M	Alcohol and HCV	AHD	Movement disorder and cognitive disorder resolved completely	12 months
10	Lazeyras et al., 2002	Mean 55 (44-69)	4 M/4F	N/A	MHE	Parkinsonism improves, but mild parkinsonism persisted	4 months
11	Shulman et al., 2003	70	M	N/A	AHD	Movement disorder resolved	6 months
12	Weissenborn et al., 2003	35	M	HBV, HCV	HM	Hepatic myelopathy improved	13 years
		40	M	HCV	HM	HM improved	2.5 years
		42	M	HBV, HDV	HM	Hepatic myelopathy improved	9 months
13	Mattarozzi et al., 2004	51.9 (mean)	23 patients in total	N/A	MHE	Selective attention and verbal short-term memory improved	6 and 18 months
14	Papapetropoulos and Singer, 2005	63	F	HCV	AHD	Oro-bucco-lingual dyskinesias resolved post transplant but reappeared 3 months post LT	N/A
15	Klos et al., 2005	52	M	Primary sclerosing cholangitis (PSC)	Cirrhotic patient with basal ganglia T1 hyperintensity	Parkinsonism persisted	1 year
		43	F	PBC	Cirrhotic patient with basal ganglia T1 hyperintensity	Cognitive impairment resolved	1 week
16	Servin-Abad et al., 2006	47	F	HCV	AHD	Confusion, dysarthria, gait instability, choreo-atetotic movement of torso and extremities completely resolved for 11 months post LT and completely resolved after re-transplant	N/A
17	Nardone et al., 2006	Mean 51 (39-64)	3M/2F	PBC, Hepatitis B, alcohol	HM	2 patients with mild hepatic myelopahty improved, whereas 3 patients with more advanced disease did not improve	6 months
18	Pinarbasi et al., 2008	50	M	HDV	AHD	AHD improved	6 months
		48	M	HBV	HM	HM improved	8 months
19	Fernandez-Rodriguez et al., 2010	68	M	Viral	AHD	No improvement in neurological disorder	3-24 months (mean 13 months)
		74	F	Viral	AHD	No improvement in neurological disorder	3-24 months (mean 13 months)
		46	M	Hemochromatosis	AHD	No improvement in neurological disorder	3-24 months (mean 13 months)



fection and acute graft rejection. Our data shows OLT may lead to resolution of AHD; however, AHD may return with worsening of liver disease. We also conducted a review of literature to summarize the effect of OLT on AHD. Our review found a heterogeneous group of case series reported in 19 papers, suggesting that the experience with OLT is variable.

Our study provided further evidence that OLT is a possible effective therapy for AHD-related parkinsonism. It remains unclear the duration of clinical benefit, and little is known about the long term effect of OLT on AHD. Future studies are needed, and will ultimately help to guide the decision of liver transplantation.

Reference:

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2. Servin-Abad, L. et al. Liver transplantation 2006; 12:1161-5.

P-038 POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME (PRES) AFTER LIVER TRANSPLANTATION

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Background: PRES can present in less than 0.4% of recipients of orthotopic liver transplantation (OLT) treated with calcineurinic inhibitors (CNI). It starts with headache, visual disturbances, and cognitive deterioration. The pathogenic mechanism of neurotoxicity seems to be in relation to a failure in the auto-regulation of the blood pressure which results in brain hypo-perfusion and consequent vasogenic edema that can be seen in brain imaging techniques.

Patients/Methods: We present a case of a 60-year old man with alcoholic cirrhosis who underwent OLT, and in the 6th postoperative day started with an intense headache and generalized clonic-tonic seizures associated with cognitive deterioration and disorientation in time and space, as well as an important decrease in visual acuity. The imaging techniques showed symmetric hypodense subcortical areas in the parieto-occipital lobes. In the electroencephalogram we saw a generalized slow cerebral activity. The tacrolimus levels were slightly increased (17.8 ng/ml). Once PRES was diagnosed, tacrolimus immunosuppression was substituted by cyclosporine. The patient improved progressively with complete recovery of all the brain cortical functions.

Conclusion: The early diagnosis and treatment of PRES is very important, and consists in substitution of CNI agent by another one in the early post-transplant period. If we do not substitute the CNI there is a rapid progression of the disease to an irreversible coma.

P-039 ANTIBODY-MEDIATED CHRONIC REJECTION REVERSED BY B-CELL DEPLETING AGENT IN A LIVER RETRANSPLANT RECIPIENT

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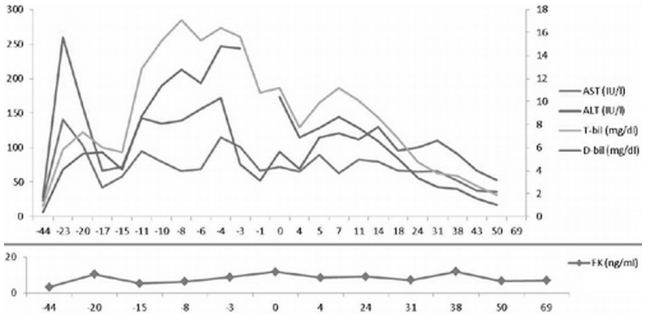
Background: Chronic rejection in liver allograft causes graft failure and is considered mostly irreversible. We reported a case of biopsy-proven chronic rejection which was reversed by anti-CD 20 antibody (rituximab).
Case Report: A 49 year-old man received deceased liver retransplantation abroad for repeated biliary infection causing re-cirrhosis of the 3 year-old graft. The indication of the first liver transplantation was HBV related liver cirrhosis. He was told to have "good matches" with the "donor". The postoperative course was prolonged and complicated with bile leakage through the abdominal wound which resolved by conservative treatment back home. The immunosuppressant regimes were FK 506, mycophenolate mofetil, and prednisolone. The trough level of FK 506 was maintained at 5-10 ng/ml. Acute jaundice (total bilirubin up to 7.3 mg/dl) without signs of biliary obstruction was noted 4 months post retransplant. Elevated biliary enzymes (Alp 1989 U/L, γGT 841 U/L) but only mildly elevation of liver enzymes were noted. Results of two consecutive liver biopsies suggestive of the diagnosis of chronic rejection and small residual bile ducts with cell atypia. Immunostaining shows C4d was weakly expressed in central vein and portal capillaries but not in sinusoidal lining cells. Panel reactive anti-HLA IgG antibody I and II were 1.68% and 73.69%, respectively. The clinical condition was deteriorated with progressive jaundice, coagulopathy, and acute renal insufficiency. Steroid pulse therapy and plasmapheresis partially relieved jaundice temporally only. Therapeutic trial with monoclonal anti CD20 antibody (rituximab) (day 0 in Figure) 50 mg persistently decreased serum level of total bilirubin from 11.2 mg/dl to 1.9 mg/dl in 2 months.



Conclusion: Antibody-mediated chronic rejection should be highly suspected in retransplant recipients. This chronic rejection can be reversed by B-cell depleting therapy such as rituximab.

P-040 HEMOSUCCUS PANCREATICUS (HP) AFTER LIVER TRANSPLANTATION (LT)

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Hemosuccus pancreaticus represents a challenging cause of upper gastrointestinal bleeding (UGB) given its rarity and intermittency. We report a post-LT patient, who presented with gastrointestinal bleeding, acute pancreatitis and splenic artery aneurysm, and discuss the problems and pitfalls of diagnostic workup and management of HP in the immunocompromised patient.
In 2008 a 58-year old man was evaluated for endoscopy negative 7-day melena following recurrent episodes of upper abdominal pain. Elevated serum amylases on admission and diffuse enlargement of the pancreas on CT were consistent with acute pancreatitis. Four years prior, the patient underwent LT with Roux-en-Y hepaticojejunostomy for alcoholic liver cirrhosis. Repeat endoscopy did not reveal any source of UGB, but the whole colon was sheathed with dark blood. MSCT angiography showed one proximal and two distal splenic artery aneurysms and stenosis of hepatic artery anastomosis. Embolization did not succeed due to tortuosity of the splenic artery, wide neck of the major aneurysm and proximity of the other two aneurysms to the splenic hilum. Hematemesis the next day urged repeat gastroscopy that revealed fresh blood from the papilla of Vater. ERCP demonstrated the blind remnant of the common bile and cystic ducts with passable common pancreatic duct, and excluded communications between the pancreatico-biliary tract and blood vessels. During the procedure few blood clots originated from the papilla of Vater, but no fresh blood. Visceral angiography did not reveal bleeding sites. Vasoactive support and red blood cell transfusions stabilized the patient and UGB resolved. Three weeks after the first episode of UGB the patient developed hepatic artery thrombosis with consequent ischaemia, multiple liver abscesses and septic episodes. Percutaneous drainage attempts of the abscesses were unsuccessful. Three months later, the patient was retransplanted and underwent a splenectomy. After 3 years of follow-up the patient remains uneventful.

Clinical Cases – Cardiothoracic – surgical

P-041 DIMENSION COUNTS: AN UNUSUAL CASE OF BLEEDING AFTER CENTRIFUGAL LVAD IMPLANTATION

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Introduction: The causes of perioperative bleeding, following left ventricular device (LVAD) implantation, is multifactorial.
We herein describe an unusual case of late massive hemothorax in a patient with a LVAD (Heartware™ HVAD™) in place and propose a method to prevent this detrimental complication.
Clinical Case: A 45 year old man on inotropic and intraaortic balloon pump support underwent HVAD Heartware placement for end stage heart failure due to dilatative cardiomiopathy. The surgery was straight forward and the patient could quickly start the rehabilitation protocol. Twenty days later, on fully anticoagulation, he experienced a hemothorax with severe blood loss that required urgent thorachoscopic treatment.
Surprisingly, chest wall erosion caused by the pump was found, and an arterial bleeding site was localized and cauterized. The pump had been pushed against the chest wall by the heart and the continuous movement eroded an intercostal artery. The bleeding was controlled and a thick layer of oxidized cellulose was placed between the pump and the chest wall.
The patient recovered and eventually could be discharged.
Conclusion: From this experience we learned an important lesson and changed our clinical pathways with good results. Left ventricular dimension should be very carefully considered during evaluation of a patient for HVAD™ implantation. Given that the pump is set on the left ventricular apex, some room between the heart and the chest wall should be anticipated. If, like in our patient, the left ventricle is so big that it touches the chest wall, a chest CT scan should be consider to study the anatomy, and, if there is no room between the heart and the chest wall, the surgical procedure should include insulating the pump from the rib cage with some sponge like material like the oxidized cellulose.

Islet / cell transplant

P-042 CYTOPROTECTIVE EFFECT OF HUMAN ADIPOSE TISSUE DERIVED REGENERATIVE CELL ON PORCINE ISLET CELLS

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Background: Type 1 Diabetes Mellitus (T1DM) is an autoimmune disease, and the radical therapy of T1DM is exogenous insulin supplement. Recently, stem cells are considered as effective for beta cell replacement therapy for T1DM. We reported that human adipose tissue derived regenerative cell (ADRC) transplantation into peri-pancreatic lesion improved FBS of islet injury nude mouse model induced by Storeptozotocin (STZ). However, this mechanism is still unknown. In this study, we investigated the cytoprotective effect of ADRC.
Materials and methods: After Isolation porcine islet cells, the cells were freeze preserved for 72 hour to make islet injury model (Cold ischemic time: 9h 19min, Yield: 210,304 IEq, Viability: 89%, Purity: 58%, SI 3.44). Coculture between porcine islet and ADRC without cell contact is performed (ADRC+ group). Recovery rate, cell viability and morphology score were measured and compared with control group for quality check of islet cells. And inflammatory cytokine (IL-1β, 6, 8, 10, TNF-α, VEGF) were measured for investigating the paracrine effect of ADRC.
Results: Recovery rate and cell viability were significantly increased in ADRC+ group. (56.3 vs. 22.1% $p<0.01$, 83.4 vs. 65.5% $p<0.05$). ADRC+ group had high tendency for morphology score (6.8 vs. 4.2 p=0.08). IL-6, IL-8 and VEGF in ADRC+ group were significantly increased compared with control group (3500 vs. 0.30 <0.01, 25.7 vs.1.9 $p<0.01$, 889 vs. 18 $p<0.01$).

Conclusions: ADRC had cytoprotection effect on porcine islet cells, and liquid factor might be involved in this effect not cell contact. Our data suggested that ADRC was useful to islet transplantation and maintain islet cells for shipping time.

P-043 IMPROVED THE EFFECT OF ISLET TRANSPLANTATION BY ENDOTHELIAL CELLS COATING AND INFUSION SERTOLI CELLS

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Background: Improving islet vascularization and inhibiting rejection become key points for prolonging islet graft survival. Endothelial cells (ECs) are the basis of islet vascularization and Sertoli cells have the effects nutritional support and immunosuppression. We construct vascularized islet by a method of ECs coating to cnstruct vascularized islet. Sertoli cells were intravenous infused to inhibit rejection in islet transplantation. Thereby, the survival rate could be improved by a decrease of islet graft loss.
Methods: Islets, ECs and Sertoli cells were isolation from SD rats. ECs and islet were co-cultured in culture tube for 2 hr and then transferred to heparin treated petri dish. After successful coated, streptozotocin-induced diabetic rats were divided into three groups before islet transplantation: single islet and ECs coating islets were transplanted in group A and B respectively; group C with Sertoli cells infusion and ECs coating islets transplantation. The meansurvival time (MST), insulin expression and microvessel density (MVD) of islet grafts were measured. The number of lymphocytes and the levels of cytokines in peripheral blood were also measured.
Results: Group C had the longest MST of islet allografts (59.8±7.81 days) followed by groups B (21.3±6.22 days) and A (11.0±4.47 days) ($P<0.05$).Immunohistochemistry showed similar results with MST. Microvessel density (MVD) of group C (17.2±2.6) were significantly higher than those in group A (1.6±1.1) and B (8.0±1.5) ($P<0.05$). The rats in group C had the least CD4+T cells (only18.1±6.1%) compared with other two groups ($P<0.05$). The numbers of CD8+ T cells in rats of groups C (12.2±5.3%) were significantly lower than those of groups A and B ($P<0.05$).
Conclusion: The program of vascularization by ECs coating islet and immune tolerance induction could effectively prolong the survival of islet grafts.

P-044 SEARCHING FOR KERATINOCYTE SPORE-STEM CELLS

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Rationale: Keratinocyte (KC) stem cells are located in the basic epidermal layer and hair follicle bulge. They express the p63 and CD29 antigens and retain DNA label. Moreover, they initiate the transient daughter cell proliferation. This process has been documented for proliferation under normal conditions and in hyperkeratoses. However, it remains unclear how can basic layer KC can crawl upon epidermis-deprived surfaces as wounds and ulcers. We noticed that KC covering edges of ulcers originate not from basic layers but rather from stratum spinosum. The question arouse as to whether these cells are not another form of KC stem cells,the so called spore-stem cells. Aim. To study which KC population covers healing ulcers.
Methods: Study was carried out on 15 patients with long lasting leg venous ulcers. Microscopical glass was laid upon ulcer surface and its edge and kept for 24h. Cells from granulation tissue and ulcer edge adhered to the glass. This procedure was repeated every other day for 10 days. Adherent cells were stained for p63, CD29, PCNA, Ki67 and keratin 6.16 and 17. Viability test based on KC enzymatic activity was done.
Results: Among the whole population of infiltrating granulocytes and macrophages single large cells of a diameter of 20-30 microns with small nucleus resembling by shape those from stratum spinosum and granulosum revealing full enzymatic activity were identified. They were more numerous close to the ulcer edge. They were p63 and CD29-negative. Some of them underwent mitoses, others had two small nuclei. No other keratin-containing KC could be seen.
Conclusions: Large nucleated KC colonize ulcer surface close to its edge but also some of them are dispersed in the ulcer mid portion forming small colonies. The phenotype of these cells was totally different from that of epidermal basic layer KC.

P-045 GLYCATED ALBUMIN IMPAIRS GLUCOSE-INDUCED INSULIN SECRETION IN RAT PANCREATIC β-CELLS

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Background: Glycated albumin (GA) is an Amadori product used as a marker of hyperglycemia. In this study, we investigated the effect of GA on insulin secretion from pancreatic β cells.
Methods: Islets were collected from male Wistar rats by collagenase digestion. Insulin secretion in the presence of non-glycated human albumin (HA) and GA was measured under three different glucose concentrations, 3 mM (G3), 5 mM (G7), and 15 mM (G15), with various stimulators.
Results: Insulin secretion in the presence of HA and GA was 38.2±5.5 and 37.2±2.8 mU/3 islets/h for G3 (P=0.877), 89.6±4.8 and 55.0±5.2 mU/3 islets/h for G7 ($P<0.001$), and 77.2±5.2 and 58.2±5.4 mU/3 islets/h for G15 (P=0.017), respectively. High extracellular potassium and 10 mM tolbutamide abrogated the inhibition of insulin secretion by GA. Glyceraldehyde, dihydroxyacetone, methylpyruvate, GLP-1, and forskolin, an activator of adenylate cyclase, did not abrogate the inhibition.
Conclusion: GA impairs glucose-induced insulin secretion from rat pancreatic β-cells. The mechanism of the impairment involves reduction of ATP-sensitive K-channel-dependent Ca^{2+} response.

P-046 INVASION AND HOMING EFFICIENCY OF INTRAVENOUS INJECTED MARROW MESENCHYMAL CELLS IN INFARCTED MYOCARDIUM RATS MODEL

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Background: The transplantation of mesenchymal stem cells (MSCs) has attracted much attention as a novel therapeutic option for the treatment of acute myocardial infarction. To date, the mechanisms of their mobilization and homing properties are still not well defined. Improving our knowledge on these core processes might elevate the efficiency of stem cell therapy. Our aim is to characterize some key mechanisms of TIMP-1 involved in transmigration and invasion of MSCs.
Methods/Materials: We modified a commercially available self-inactivating lentiviral vector for the delivery of TIMP-1-siRNA into MSCs, MSCs were transfected with lentiviral vector containing either TIMP-1-siRNA and green fluorescent protein (GFP; TIMP-1-siRNA/GFP vector) or GFP alone (control vector).The expression of matrix metalloproteinase (MMP) was analyzed by reverse transcriptase polymerase chain reaction (RT-PCR) and zymography. We used a transwell migration system to study MSCs migration toward stromal cell derived factor-1 (SDF-1).
Results: We demonstrated this modified vector could efficiently transfer TIMP-1-siRNA into MSCs and the TIMP-1 expression of these MSCs was downregulated. Expression of siRNA by lentivirus-based vector confers efficient and stable silencing of TIMP-1. Compared with control MSCs, MSCs transfected with TIMP-1-siRNA showed significantly more ability of migration toward SDF-1.
Conclusions: Transfected MSCs migrate rapidly toward SDF-1 and the migration of MSC and that intravenous injected MSCs were able to home to viable myocardium and preserve systolic function by 4 weeks after ligation.

P-047 THE EXPERIMENTAL STUDY OF AUTOLOGOUS MESENCHYMAL STEM CELLS MOBILIZATION INHIBIT VENTRICULAR REMODELING AFTER ACUTE MYOCARDIAL INFARCTION

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Background: To study the effect of autologous bone marrow mesenchymal stem cells mobilization on ventricular remodeling in acute myocardial infarction models, and to explore the mechanism initially.
Methods/Materials: The models of acute myocardial infarction were established and divided into three groups Group A: control group. Group B: transplanted MSCs 1×10^7 through coronary artery 3 hours after myocardial infarction. Group C: treated with G-CSF after myocardial infarction through subcutaneous injection. MMP-9,TIMP-1 and TNF-α numerus of blood serum were observed in different timepoint. The change of left ventricle pressure was detected with Powerlab and Millar catheter. We also observed the change of each index of cardiac function with MRI., infarction size were measured and the den-

sity of blood vessels in cardiac muscle were detected by the method of vWF immunity histochemistry.
Results: Compared with other groups, the index of group C improved significantly including LVDP, +dp/dtmax and -dp/dtmax and EDWT, SV, aslo, there was significant difference as to the size of myocardial infarction at the end of experimental time. Serum levels of MMP-9 and TNF-α in group C dropped significantly compared with other groups. At the same time, TIMP-1 in group C elevated significantly. Immunohistochemistry study showed that vessels stained with vWF of group C was much more than other groups.
Conclusions: In the acute phase of myocardial infarction, bone marrow stem cells mobilization can reduce MMP-9/TIMP-1 ratio, down-regulate proinflammatory cytokines TNF-α expression and promote angiogenesis in MI area, increase perfusion of ischemic myocardium.

Composite tissues

P-048 VASCULARIZED BONE MARROW TRANSPLANTATION MODEL IN RATS AS AN ALTERNATIVE TO CONVENTIONAL CELLULAR BONE MARROW TRANSPLANTATION – PRELIMINARY RESULTS

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Background: Current protocols for bone marrow transplantation (BMT) involve removing the bone marrow component directly from its donor microenvironment and then injecting such components into the circulatory system of the recipient. Vascularized bone marrow transplantation (VBMT), in comparison with conventional marrow transplants, has the advantage of providing a microenvironment and immediate engraftment of both mature and progenitor hemopoietic cells at the time of transplantation. The aim of the study was to follow the development of microchimerism after allogeneic VBMT vs conventional BMT.
Methods: In one group a VBMT model consisted of a donor Brown Norway (BN) rat hind limb heterotopic transplanted on recipient Lewis rats was used. In the second group a VBMT model consisted of a donor Brown Norway (BN) rat femur heterotopic transplanted on recipient Lewis rats was used. An intravenous infusion of donor bone marrow cells in suspension equivalent to that grafted in the vascularized femur limb was administrated i.v. on recipient rats in the third group. Cellular microchimerism was investigated in recipients of VBMT vs BMT.
Results: Donor-derived cells could be detected in VBMT recipients at 30 and 60 days but not in recipients of i.v. suspension BMC grafting.
Conclusions: VBMT provides a theoretical alternative to conventional cellular bone marrow transplantation by addressing crucial clinical problems such as failure of engraftment or graft versus host disease. It may be possible to develop a new approach for bone marrow transplantation based primarily on a microsurgical procedure (transplantation of vascularized bone marrow flaps).

Allocation

P-049 OLD AND NEW INSIGHTS IN THE EVALUATION OF MARGINAL KIDNEY DONORS: A MONOCENTRIC EXPERIENCE

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Background: The main obstacle to a wider spreading of kidney tranplantation practice, accepted as the best therapy of ESRD, is the disparity between organ demand and supply. The use of Expanded Criteria Donors (ECDs) partially sort out this problem. Which of the clinical and/or histological criteria is the more suitable to allocate ECDs and to predict the outcome is still debated.
Methods/Materials: We provide a comparative analysis between the allocation strategy -clinical and histological- used in our Centre and both Nyberg and Schold scores on a retrospective survey of 520 ECDs histologically evaluated before implantation.
Results: *Histopathologic score (Karpinski):* a tendency towards an association between higher global scores and a worse 5 years organ survival was noted, but statistic correlation was not found.
Nyberg score: 89% of our donors were in class C e D; even if there was a good correspondence with Nyberg score applied *a priori* before histological evaluation ($p<0,001$), no correlation with histological score was found.
Schold score: 96,7% of our donors belongs to classes III, IV, V; correspondence with histopathologic score was absent, a correlation with Nyberg was noted.
A new scoring system: using only some variables of Nyberg and Schold, we developed a multivariate model able to predict an ECD profile without histological data; 3 "increasing-risk" classes were identified on the basis of donor hypertension, age $\geq$65 years, cerebrovascular death, GFR $\leq$77 ml/min.
Conclusions: The dilemma whether clinical scores could replace the histological approach when transplanting ECDs has not yet been solved. We tested 2 of the most recognized scoring systems on a monocentric population, confirming the efficacy of these models and suggesting a "new scoring system" able to define a quality profile of the ECDs without the histological support.

P-050 KIDNEY TRANSPLANTATION FROM LIVING DONORS IN NORTHERN PORTUGAL

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Living donation is the cornerstone of kidney transplantation worldwide. A new law from July 29th, 2007, partially transposed into Portuguese juridical order the Directive 2004/23/EC of the European Parliament and of the Council of 31st March 2004 on setting standards of quality and safety for the donation of human organs, tissues and cells. Previously to this law, living candidates for organ donation only could be third-degree related donors or closer. Since August, 2007, all people can be kidney donors with the usual exceptions.
The aim of this work is to compare kidney transplants from living donors performed in Northern Portugal, before and after August, 2007.
Between February, 2004 and July, 2007, 43 kidney transplants from living donor (LD) were performed in Northern Portugal (10.7% of 402 kidney transplants recorded in that period). While, between August, 2004 and January, 2011, were registered 72 kidney transplants from LD in Northern Portugal (12.2% out of 589 kidney transplants recorded). Chi-Square test (or Fisher exact test when appropriate) and t-student test were used to compare demographic and immunologic characteristics between LD kidney transplants performed before and after August, 2007.
Donors before August, 2007 have an average (standard deviation) of 44 (9.7) years old and 67.4% were female, 39.5% of the recipients have blood type O and 3 were transplanted with HLA full match. Not significant different from donors after August, 2007 with 45.3 (9.6) years old and 70.8% female donors, 38.9% blood type transplanted recipients and 3 HLA full match transplants. After 2007, 17 spouses (15 wives) could be donors for their loved ones as consequence of the new law.
Although the increased number of transplants from LD we do not found statistically significant differences between transplants performed before and after implementation of the law.

Ethics / law / psychosocial / public policy

P-051 NUMBER OF RECIPIENTS LIVING WITH A FUNCTIONING GRAFT: ESTIMATION AND REPARTITION IN FRANCE

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Introduction: These past years, the number of organs transplantations has increased. Patients follow up has represented an increasing in effort for professionals and was not yet quantified.
The Agence de la biomédecine assessed the number of recipients living with a functioning graft according to organ types.
Method: All transplantations until 31-12-2008 have been used. For which an annual follow up is requires in the national data base (Cristal).
The estimation of the number of recipients living with a functioning graft was calculated as:
1. The number of patients alive without graft failure with a follow up less than 18 months post graft
2. For living patients not in (1) (ie follow up dated more than 18 months), the number was estimated by Kaplan Meier estimation.
The evolution of this number is shown between 2000 and 2008 according to recipient's residential French departments together with mapping representations (Arcview) among organs.
Results: This study has showed an important rise of estimated number of living recipients between 2000 and 2008: 47% for kidney, 76% for liver, 12% for heart, 153% for lung and 14% for heart&lungs. This augmentation was observed for each organ with disparities according to departments.

Table 1. Estimated number of recipients living with a functioning graft at 31/12 (CI95%)

Year	Liver	Kidney	Lung	Heart	Heart & lungs
2000	5220 (5218–5221)	19769 (19761–19777)	334 (334–335)	3506 (3505–3508)	166 (165–166)
2008	9164 (9152–9176)	28974 (28946–29000)	846 (845–847)	3931 (3927–3935)	189) (188–189)

Conclusion: The augmentation of number of patients has increased the transplant centers needs to assure the follow up. A reflexion on a professionals networks organisation has to be engaged.

P-052 "I HAD NO END OF PEOPLE TELLING ME NOT TO DO IT": SOCIAL AND PSYCHOLOGICAL PROCESSES IN NON-DIRECTED KIDNEY DONATION- A GROUNDED THEORY APPROACH

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Donation of a kidney to an unknown recipient on the waiting list, (non-directed donation or "NDD"), has been possible in the United Kingdom since the change in law in 2007. There is however little research that aims to understand the process and motivations behind NDD. This qualitative research study was devised to address gaps in the literature. We will interview up to 16 individuals who meet the study's inclusion criteria by donating a kidney through the non-directed organ donor scheme in the United Kingdom. This is a Grounded Theory study, which offers a rigorous, systematic approach to understanding people's subjective experiences. The aim is to provide a "bottom up" conceptualisation of the donor experience. One of the strengths of this study is that it has been developed in collaboration with a donor who has spoken openly about his donation in the media. The interview process involved the donors being asked for their story of the donation process and to elaborate upon the social and psychological processes involved in donation. At the time of submission, the interviews were not complete and preliminary analysis is at an early stage. Initial emerging themes are concerned with: resisting dissuasion from others, others finding it difficult to understand, internal tension of doing something against the norm, loneliness of the process, lack of supportive follow up and the social ripple effect of donation. The results of this study will be discussed in detail alongside implications for clinical practice and areas for future research.

P-053 BARRIERS FOR IMMUNOSUPPRESSIVE MEDICATION-TAKING DIFFER AMONG ADULT KIDNEY, LIVER AND HEART TRANSPLANT RECIPIENTS

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Background: After transplantation, adherence to an immunosuppressive medication regimen is crucial to guarantee good graft function. However, barriers, defined as environmental and personal constraints, often compromise patients' medication adherence.
Aims/Purposes: To identify and compare barriers to immunosuppressive medication adherence among adult heart, kidney and liver transplant recipients, and to explore the construct validity of the barrier questionnaire used.
Methods: Using a comparative descriptive design, we investigated barriers to immunosuppressive medication taking in 440 transplant recipients (58 heart, 268 liver and 114 kidney) using a newly developed 16-item barrier instrument. Exploratory factor analysis (EFA) was conducted to determine the questionnaire's factor structure using an oblique quartimin rotation. Barrier scores among transplant groups were compared using the Kruskal-Wallis test. Covariance analysis (ANCOVA) was used to compare the three groups' factor scores controlling for working status and study site (transplant group).
Results: A 4-factor model (Issues with Medication Management, Cognitive and Emotional Issues, Issues with Medication Administration, and Complexity and Side Effects) emerged. The most frequently reported barriers were: physical side effects (42.7%), forgetfulness (42.3%), feeling depressed or overwhelmed (40.5%), and disruption of daily routines (38.0%). Patients experienced a median number of 2 barriers (range 0-14). Kidney transplant recipients reported significantly more barriers (median=5.0) than heart (median=1.5) and liver (median=2.0) transplant recipients ($p<.001$).
Conclusions: Medication adherence barriers are common among heart, liver and kidney recipients, with more barriers reported by kidney recipients. Adherence interventions need to include interventions designed to overcome barriers to adhering to medication regimens.

P-054 EDHEP, EUROPEAN DONOR HOSPITAL EDUCATION PROGRAM: A SWEDISH PERSPECTIVE

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Background: In Sweden as in the rest of the world there is lack of organs for transplantation. One reason might be the difficult psychological situation for intensive care doctors and nurses dealing with next of kin to dying patients that might donate organs and tissues. In the nineteen's the Eurotransplant Foundation in Leiden in The Netherlands established a program, EDHEP, (European Donor Hospital Education Program) focusing on increasing self- knowledge to personnel in how to approach families. EDHEP was adopted in Sweden 1993, to some extent developed and since then seminars have been performed in all transplant regions yearly.
Methods: EDHEP is a two day seminar focusing on doctors and nurses in intensive care and is situated in a comfortable and relaxed environment.
Eight intensive care doctors and eight nurses is an optimal combination of participants. The seminar is interactive starting with a short introduction about formal regulations, physiology and laws followed by role plays and video clips. The focus is knowledge how people react in difficult situations, empathy training, self- knowledge and specific reactions when somebody looses a near and dear and donation could be the result.
A national committee established 1999 representing seminar moderators, transplant coordinators from transplant units and donor responsible from intensive care make sure that the material is updated.
The material is used by all regions but each region design there own faculty.
Results: So far, 110 courses including 1717 persons have been performed. Positive rewievs predominate although structured evaluation is needed and is now performed.
Conclusion: In Sweden there is an increasing interest for education regarding organ donation.
How to approach next of kin to donors is an important part.
EDHEP seminars convey this by giving the participants increased level of knowledge and self awareness.

P-055 AN ETHICAL ANALYSIS OF THE ROMANIAN DEBATES ON PRESUMED CONSENT

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Background: We attempt of providing a thorough ethical analysis of the Romanian debates concerning various alternatives of defining consent for organ donation after death. Although presumed consent solely does not automatically increase the donation rate, there have been authors claiming that presumed consent may represent a better and more ethical option than explicit consent. As the debate concerning the form of consent is far from being ended in Romania (recent initiatives of the Health Ministry attempt to introduce a form of mandated choice via the new health card), an investigation into the main ethical arguments is more than needed. As there were many voices against presumed consent claiming a religious motivation, a special attention was reserved to this aspect.
Materials/Methods: Besides the analysis of relevant documents (legislative texts, various media documents stating key positions, Church documents), a series of semi-structured interviews with major actors of the debate (transplantologists, representatives of the Christian Orthodox Church, representatives of the Romanian College of Physicians, ANT representatives) were carried on. Questions targeted existing alternatives to and ethical arguments concerning presumed consent, and relevance of religion and religious organizations in legislating health policies.
Results/Conclusion: Interviews revealed a distance between the official position of the Church, that is more nuanced and more open to transplantation, and the various voices of Church representatives, who may not overpass a dogmatic level of argumentation. Another aspect uncovered during the interviews was the issue of who may claim a "property right" over the body after one's death and what ethical and legal consequences are involved here. Fi-

nally, the lack of information of the general public concerning transplantation matters is overwhelmingly affirmed, yet there is not so clear which actors would take the responsibility for carrying on such an information campaign.

P-056 THE EFFORT TO ENLIGHTEN ABOUT LOCAL CITIZEN ORGAN DONATION & TRANSPLANTATION TOGETHER WITH TRANSPLANT PATIENT SOCIETY

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(Introduction) The importance of organ donation and transplantation has not been fully recognized by Japanese civilians. Our urology department has been committed to informing citizens about organ donation and transplantation since 1999. We have established the transplant patient association and recently asked the members to assist us with informing the public about organ donation and transplantation. Here, in this paper, we introduce this voluntary approach and analyze the mechanism of change in the empowerment of the patients association that develops into a voluntary activity.
(Method) The constituent members of this association were transplant patients, kidney donors, transplant doctors, nurses, and coordinators. The activities were as followed: 1. Participation in the gathering held by our urology department for the last 12 years to provide information to the patients awaiting transplant. 2. Participation in the local city festival to educate on the topic of organ donation and transplantation. 3. Participation in social gatherings to ease communication among patients.
(Results) Education in transplantation by the patient society resulted in the issue of a bulletin magazine and monthly informational meetings with patients on the waiting list for organ transplantation.
(Discussion) Members of the society achieved cooperation, mutual understanding, sympathy, and satisfaction through the voluntary enlightenment program by relating their transplant experiences to civilians. We realized that continuation is very important to push this activity. We thought that self-analysis was necessary to the patient's empowerment. However, since we do not yet have an objective standard to analyze this, we need to create an analyzing tool from the point of psychology.

P-057 QUALITY OF LIFE AFTER KIDNEY TRANSPLANTATION (LIVING NON-RELATED REGULATED PROGRAM)

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Background: The International Foundation for Organ Transplant, Inc. (*InFort*), a non-stock and non-profit association, managed by transplant patients or their families, provides postdonation care program for living non-directed nonrelated kidney donors in the form of SSS, Philhealth, livelihood assistance, life insurance and 10 - year medical checkup.
Objectives: To evaluate the socioeconomic profile of the donors and how their donation made an impact on their lives.
Methods: The study was based on the (*WHO-QOL).* 77 of 110 donors (2007-2008) attended yearly health fora and lectures on livelihood assistance (balloon and soap making, hairstyling, meat processing). Questionnaires gathered information on their quality of life postdonation.
Results: All respondents did not regret on their decision to donate. In 97% (75/77), their families were very supportive of their decision. Livelihood assistance was utilized sensibly. Thirty percent (N=23) acquired a house and lot, 26% (20) purchased transport vehicles and 23% (18) started small businesses. Ninety-two percent (71/77) were contented with their lives, and 79% (61/77) declared they have achieved what they have hoped for postdonation. When asked, "kung maibabalik ang panahon, pipiliin mo pa bang magdonate?", 95% would still donate (73/77). Everyone agreed on the importance of their health condition and compliance to regular followup. Usual reason for non-compliance to scheduled check-ups was lack of transportation fare. Some were residing in the province or were just too lazy to come for checkup because they felt healthy.
Conclusion: The InFORT had successfully followed up 70% (77/110) of the non-directed donors. All of them did not regret having donated. 92% (71/77) of them were contented and satisfied with their quality of life postdonation.

P-058 THE HIPPOCRATIC OATH IN THE STUDY OF THE MEDICAL ETHICS OF THE LIVING DONOR HEMI-PANCREATECTOMY

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Background: The study examines the medical ethics of the Oath in relation to the contemporary hemi-pancreatectomy on living donors for pancreatic transplantation.
Material and Methods: The rights of healthy pancreatic donors are examined under the perspective of the ethical precepts and the humanistic concepts of the Hippocratic Oath.In fact focusing on the contemporary treatment of living donor's hemi-pancreatecomy and studying both bibliographical qualitative and quantitative data of the classic pancreatic surgery (for both malignant and non-malignant diseases), the impact of hemi-pancreatectomy on healthy pancreatic donors is examined by: 1) referencing in the current medical data bases (PUBMED) and 2) typing the key words "morbidity-mortality after hemi-pancreatectomy", "morbidity-mortality", "pancreatic resection", "pancreatic regeneration", "pancreatic transplantation".
Results: The study showed that the Hippocratic Oath and the related Hippocratic Aphorisms can be used as an applicable and useful ethical guidance. Its principles in collaboration with the available clinical, laboratory, physiological and biological data, presented in the current medical and surgical bibliography, don't justify the practice of living donor hemi-pancreatectomy for pancreatic transplantation, on a routine basis. Appart from the lack of thorough physiological data about the regenerative ability of pancreas, the complexity of the operational technique makes it hardly reproducible. Also, despite its low mortality ($<$3%), donors' post-operative glucose intolerance and diabetes are rather unacceptable ($>$25%).
Conclusion: The implementation of the Hippocratic Oath into the current theory and practice of the living donor hemi-pancreatectomy, showed that despite its "humanistic" basis and its "effectiveness" doesn't seem fully "beneficial" for the rights of the healthy donors. The lack of certain data about its regenerative basis and its observed high morbidity may make it "unsafe" for the donors underlying the need for new predictive protocols and more specific standards of application.

P-059 BARRIERS TO LIVING DONATION: A QUALITATIVE STUDY OF RECIPIENT ANXIETIES

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Background: Numerous studies demonstrate physical benefits to living over cadaveric kidney donations. However, the psychosocial anxieties of living donor recipients remain understudied, despite many recipients expressing reluctance to accept a living donation. We performed detailed semi-structured interviews to determine the anxieties experienced by living donor recipients and to understand how these might inhibit living donation.
Material and Methods: Fourteen living kidney donor recipients took part in semi-structured interviews at the Renal Outpatient Department, Guy's Hospital. The interviews explored their journey of renal transplantation. They were then transcribed verbatim and analysed using framework analysis.
Results: Framework analysis revealed four key themes: 1. The decision of living donation: All patients expressed hesitancy to approach donors directly. Fear for the donor's health was the main barrier to accepting donations. 2. Relationship change: Donor-recipient relationships only suffered post-transplantation when the relationship was previously unstable. Amongst relationships in general, some recipients expressed concern over disclosing information about their transplant, and some found friendships strained after disclosure. 3. Post-transplantation: Many patients felt dependent on others following the operation and complained of side-effects from medication. This was worse in pre-emptive patients. 4. Perceptions of self, health and the future: Overall little regret was expressed over the choice of living donation. However, complications or inadequate support were related to a more negative outlook.
Conclusion: Throughout the living donation process, kidney recipients remain understandably anxious about the donor, which may inhibit acceptance of donation. Transplant programmes could consider placing greater emphasis on informing the recipient about donor risks and outcomes. This may need to continue after transplantation has taken place. Unstable donor-recipient relationships pre-transplantation often deteriorate further following donation. Additional psychosocial support may be needed for pre-emptive recipients as they experience a greater sense of dependency after transplantation.

P-060 SELF-REGULATORY FACTORS AND MEDICATION ADHERENCE AFTER KIDNEY TRANSPLANTATION: FINDINGS AT 6 WEEKS POST-TRANSPLANT

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Background: Patients who undergo kidney transplantation require a strict, lifelong immunosuppressant regime. Medication non-adherence among this group is estimated to be around 30% and is associated with poorer clinical outcomes (Denhaerynck et al. 2005; Dew et al. 2007). As adherence is a form of behaviour it is likely to be influenced by thoughts and emotions related to that behaviour. This prospective study investigated whether self-regulatory factors are related to medication non-adherence after kidney transplantation.
Methods: Consecutive patients were invited to participate in a face-to-face interview 6 weeks (T1) and 6 months (T2) after kidney transplantation. Adherence was measured using the Basel Assessment of Adherence to Immunosuppressive Medications Scale (BAASIS-interview). Participants also completed self-report measures on illness (Brief-IPQ) and treatment beliefs (BMQ-specific), goal importance, commitment, alignment, conflict, and self-efficacy.
Results: Preliminary results from T1 indicated that, in accordance with the literature, immunosuppressant dose and timing adherence immediately after transplantation was high. Patient ratings of adherence ranged from 80-100%. Adherence to the immunosuppressant regime was reported to be an important goal, for which commitment and confidence in ones ability to adhere (self-efficacy) were high. Patients perceive this goal to be well aligned with other personal goals. The perceived need for the medication was high (M=23.2, SD=2.3) and concerns about medication were relatively low (M=9.8, SD=3.8). High treatment efficacy beliefs were correlated with high perceived necessity of medication while greater concerns were correlated with a greater emotional impact of transplantation ($p<0.05$). Greater goal importance, commitment and self-efficacy were related to higher self-reported adherence ($p<0.05$).
Conclusion: Self-regulatory factors are potentially important targets for interventions aimed at improving adherence among kidney transplant patients.

P-061 SOURCES OF ORGAN TRANSPLANTS IN CHINA

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This presentation would consider both the volumes and sources of organ transplants in China. It would attempt to identify the sources by volume.
Statistics from China are difficult to obtain and unreliable. China has several transplant registries which tabulate data for various organs. None are publcly accessible.
The Hong Kong liver transplant registry used to be publicly accessible but is no longer. There are various statements and articles by Health Ministry officials from time to time which draw on the registries and give data snapshots.
The Ministry of Health of the Government of China claims that the primary source of transplants is prisoners sentenced to death and then executed. China does not publish death penalty statistics and refuses to do so. Various non-governmental organizations, using different methodologies, make death penalty estimates.
China has an organ donation system in its infancy. The presentation would consider the extent to which this system provides organs for transplants.
China does not have a law allowing for sourcing of organs from the brain dead cardiac alive. The presentation will consider the extent to which this happens anyways and the impact the absence of the law has on the volume of transplants.
There have been consistent reports of prisoners of conscience in general and practitioners of the spiritually based exercise regime Falun Gong in particular being killed for their organs. The author will consider the extent to which, if at all, these reports explain the volume of organ transplants.
The overall conclusion will be that there is a substantial discrepancy between the volume of transplants and the sources to which Chinese authorities are willing to admit. This discrepancy requires an explanation.

P-062 ASSESSMENT OF ANXIETY AND DEPRESSION IN KIDNEY TRANSPLANT PATIENTS

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Objective: To assess the prevalence of anxiety and depression in kidney transplant patients.
Material and Methods: Directed Interview. Hamilton Anxiety Scale. Beck Depression Inventory.
Results: Thirty-four patients (18 women and 16 men), with an average age of 43.64 and an average post-transplant period of 42.6 months, were assessed. Of all the patients interviewed, 23 (68 percent), divided into 15 women (44 percent) and 8 men (24 percent), experienced anxiety, while 6 exclusively female patients (18 percent) developed depression.
The age of most female patients with anxiety ranges between 20-30 and 41-50 (28 percent), while there is a greater anxiety percentage in male patients over the age of 50 (19 percent).
Most depressive women are between 20 and 30 years old (18 percent).
As regards work, of the 14 actively employed patients (42 percent), 8 (24 percent) suffered from anxiety, while the remaining 6 (18 percent) had no depression or anxiety symptoms. Of the 10 unemployed patients (30 percent), 2 (6 percent) had depression, 6 (18 percent) had anxiety, and 2 (6 percent) experienced both anxiety and depression. In the remaining 10 underemployed patients (30 percent), including retired people, students and housewives, 2 (6 percent) suffered from depression and 7 (21 percent) from anxiety, while 1 patient had no anxiety or depression symptoms.
Conclusions: The percentage of anxiety is greater than that of depression, and it affects women more than men.
No depressive symptoms were detected in men.
Anxiety was detected in those patients who were actively employed (but no depression), while out-of-work patients experienced both anxiety and depression.

P-063 WHEN MEDIA CAMPAIGNS FAIL – MISCONCEPTIONS ABOUT ORGAN DONATION AND TRANSPLANTATION AMONG THE RURAL MALAY COMMUNITY IN MALAYSIA

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In Malaysia, the demand for transplant organs and tissues exceeds the supply and as a result, the government had launched massive campaigns in various media attempting to educate the population and boost the number of organ donors in recent years. With the support of NGOs, the National Transplant Resource Centre (NTRC) also implemented a number of grassroots events and interpersonal communication activities in order to disseminate information on organ donation in urban and rural areas. To this date, less than 1% of the Malaysian population have pledged to donate their organs from 2006 until 2010. Many Malaysians, especially the members of the majority ethnic group, the Muslim Malays are reluctant to sign up as organ donors. Malaysian health experts assume the existence of particular cultural and religious barriers that prevent this group from becoming organ donors. This study looks at the various campaigns and activities implemented by the government to increase awareness and the percentage of donors among the Malaysian population. By incorporating a qualitative case study, it also investigates the misconceptions about organ donation among a rural Malay community in Kampong Tebuan, Kedah and to find out the reasons for (not) signing up as organ donors. The study unveils the discrepancies between the media messages and campaigns on one hand and the opinions of the Malays on the other. Its findings support the idea that there exist cultural and religious misconceptions that prevent the Muslim Malays from becoming organ donors. For example, the rural Malay community in this study had very little knowledge about the concept of organ donation from Islamic perspectives and was unaware of a *fatwa* issued 40 years ago already which explicitly declared organ donation conformable with Islam.

P-064 TERMS AND SIGNIFICANCE IN TRANSPLANTATION MEDICINE

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Determining and defining human death in age of life-sustaining technologies is a matter of controversy and touch on some of society's deepest human questions.
A great part of controversy seem to be caused by an imprecise, ambiguous, confusing and misleading use of terms.
Medical literature in English language and web sites in Italian language concerning human death, organ donation and transplantation have been studied.
We have found a deep gap between medical use of some terms and their common use.
Terminology in medicine in general and in transplantation field specifically has developed and evolved over time often before much of significance was known about disorders involved.
Brain death used in a specific medical language to describe a clinical condition has been misleading among people not involved in medicine.
More than 40 years have been necessary before White Paper by the President's Council on Bioethics (1) establish that there are no different kinds of death. And 2 years after White Paper the debate about brain death is still open.
Cardiac death or Donation after cardiac death need to be clarified in order to avoid the risk of misleading how it has been for Brain death.
Medical terms often are more than words, describe different and difficult clin-

ical conditions, despite this scientists should never forget patients and their parents, both need to well understand what's happening to avoid confusing and misleading specially if organ donation is required.

P-065 THE DEFINITION OF QUALITY OF LIFE IN SOLID ORGAN TRANSPLANTATION: A PSYCHOLOGICAL QUALITATIVE MODEL

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Quality of life has been extensively discussed in acute and chronic illnesses. However a dynamic model grounded in the experience of patients in the course of transplantation has not been to our knowledge developed.
In a qualitative longitudinal study, patients awaiting solid organ transplantation participated in semi-structured interviews: Exploring topics pre-selected on previous research literature review. Creative interview was privileged, open to themes patients would like to discuss at the different steps of the transplantation process.
A qualitative thematic and reflexive analysis was performed, and a model of the dimensions constitutive of quality of life from the perspective of the patients was elaborated.
Quality of life is not a stable construct in a long lasting illness-course, but evolves with illness constraints, treatments and outcomes.
Dimensions constitutive of quality of life are defined, each of them containing different sub-categories depending on the organ related illness co-morbidities and the stage of illness-course.

P-066 IS THE TRANSLANTATION ETHICS AT THE CROSSROAD?

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Ethical issues in organ transplantation have always been of great concern to the physicians and whole society. Consent is required from the donor for the use of organs for transplantation. The organ should not be either purchased or sold, there should be no mistake in recognition of death, organ allocation from deceased donors should always follow medical criteria. Living donors should be fully informed about the risk, and healthy.
Due to the organ shortage recovery of organs from the donors after cardiac arrest, and extension of the living donor pool are commonly used.
These developments have caused that the ethical principles related to various aspects of transplantation have changed. In certain centers not quite healthy living donors are being used (nicely called extended criteria donors. Organ trade is condemned, but we agree to use as donors the complete strangers (obviously believing in pure altruistic motivation of such donors without the additional incentives}.
Is the autonomy an important value? We restrict the autonomic decision of the donor to sell his/her kidney, at the same time withdrawing from recovering organs from all deceased potential donors when we do not know their autonomic decision.
The dead donor rule still stands, BUT are we not modifying this rule recovering organs in controlled cardiac arrest situation? Organs cannot be sold, BUT the incentives to the donors are allowed. The use of LD is fully justified, BUT do we have the right to use complex living donors. Finally is the trend to consider utility in organ allocation justified? How far shall we get adjusting ethical principles?

P-067 EXPLORING THE ROLE AND RELATIONSHIP BETWEEN THE GIFT, DECEASED ORGAN DONATION AND RELIGION: A CASE STUDY OF POLISH IMMIGRANTS

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Background: The most influential gift theory is gift-exchange theory by Mauss (1954), where the gift relationship carries the obligation to give, receive and repay. Deceased organ donation has been analysed within this framework and is used in encouraging donation through the "gift of life".
The role that religion plays in deceased organ donation is complex, however, most major religions support donation based on religious scripture such as "love thy neighbour". The extent of support is limited due to factors such as divergence of opinion of the definition of death and brain stem death.
Previous research focussing on minority ethnic groups in the UK elicited that religion or religious reasons are factors in deciding to donate, but these are not expanded on. The Polish community, a significant immigrant group since the EU enlargement, has not been represented.
Methods/Materials: A constructivist grounded theory methodology will be used. As an exploratory study, the qualitative research tool, focus groups, will gain a rich insight into the role and relationship between the gift, organ donation and religion. The pilot study and first focus group will include Polish immigrants who attend the local Roman Catholic Church. The grounded theory approach will guide the sample for the next focus groups. It is expected that will be eight focus groups in total.
Results: The pilot study and four subsequent focus groups results and analysis will be presented in September 2011.
Conclusions: The findings will provide a deeper understanding of how religion, gift theory and organ donation interact within the Polish community. By gaining an understanding of this, further studies can explore the interaction of these in other communities or build upon the study to create health campaigns.

P-068 THE MISTAKE OF COMMUNICATION WITH RELATIVES OF HEART-BEATING DONORS: VIDEO MODEL

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Background: The communication about brain stem death and donation could influence the consent rate and psychosocial effect of the donation. The aim of this study was to estimate the communication mistakes with relatives.
Methods: Following lectures the Hungarian Organ Donation Course provides trainings with 5-7 members who played "physicians", "psychologist" and "relatives" in a role play. The 10-12 minutes long communication about brain-dead and donation was recorded by video camera. The 32 video records from 2008 to 2009 (16-16 under age and adult donors) were explored in retrospective way concerning informing the relatives about brain stem death and donation. The typical communication gaps of "physicians" and the common questions of "families" were analyzed by qualitative and semi quantitative examination.
Results: 192 participants (87 men, 105 women) from 53 hospitals were present. The average age of 187 physicians and 5 coordinators was 42 (26-69).
Remarkable mistakes of communication were: expression of the coma and brain stem death used changeable (9.38%); to apply expression to be connected with "life" such as present tense (21.88%), mechanically keep alive (59.38%); organ focused behavior such as organs to be useable (34.38%). The consent of the family was more important for the physicians than the application of the law in 93.75%. The 78.13% physicians emphasized altruism to support donation.
The frequent questions and statements of "relatives" were "heart beats" (100%), "did he really died?" (65.63%), "fear of loss of the integrity of the corpse" (59.38%), "wake up from the coma" (46.88%).
Conclusion: The immediate analyzing of video gap can be called attention to gaps of information process, consequently it can be increased to transplantable organs and it can be influenced psychosocial effects of donation in the long through developing skills.

P-069 ATTITUDE TOWARDS XENOTRANSPLANTATION OF PATIENTS PRIOR AND AFTER HUMAN ORGAN TRANSPLANTATION

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Xenotransplantation is a potential strategy to overcome the shortage of human donor organs. Since this technique has a major medical and psychological impact on patients and their family and friends, the attitude of patients currently waiting for an organ transplantation is important.
Therefore we conducted a survey on the attitude towards xenotransplantation of patients on the waiting list and already transplanted patients. Patients received detailed information before being asked to fill in the questionnaire.
We found that 65% would accept xenotransplantation, irrespective of gender, education level or if the patients were on the waiting list or already transplanted. The most common concern was transmission of diseases or genetic material, followed by psychological concerns and ethical issues. More patients had a positive attitude towards accepting cell or tissue transplantation as compared to whole organs. Pig pancreas islet cell transplantation is generally well accepted, patients with diabetes mellitus show even higher acceptance rates than patients without diabetes.

In conclusion xenotransplantation seems to be well accepted in patients who are potential future candidates for organ transplantation. Informing patients about the current status of research tended to decrease acceptance rates slightly.

P-070 Skype SAVED THE ELPAT CONGRESS

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Introduction: From April 17-20, 2010 the 2nd EU funded ELPAT/ESOT congress on Organ Transplantation: Ethical, Legal and Psychosocial Aspects took place in Rotterdam, The Netherlands. On April 15th an volcanic eruption resulted in cancellation of all flights in Northern Europe. As a result, 122 out of 297registrants were not able to attend our conference. We describe here the impact of the volcanic eruption and how we managed to let the congress proceed.
Methods: The organization convened how we could maintain the programme and decided to use Skype connections.This enabled absent speakers to give a presentation from abroad and it involved on short notice the organization of more technical equipment and technicians. After the congress we drafted a questionnaire that we sent to all (297) registrants.The aim was first to find out how and if registrants could reach and leave Rotterdam, and second to find out how they experienced the Skype presentations, both as presenter and as viewer.
Results: 175 people managed and attend the congress. From Europe 162 people attended (12 countries), including 119 people from The Netherlands and surrounding countries. 13 people (7 countries) came from outside of Europe.
The quality of the Skype presentations was generally considered as good. Both our instructions by E-mail and the help/testing beforehand from the technicians were considered helpful.
On a total of 113 presentations, 34 presentations (20%) were given by Skype and 10 presentations (9%) were taken over by others. 17 presentations (15%) were cancelled. This means that 85% of all scheduled presentations was delivered.
Discussion: Normally it is highly appreciated that experts communicate on the subjects and physically take part in the discussions. Skype is a good solution in an emergency situation, but it does not replace the presence of people.

P-071 TO IMPROVE LOW ORGAN DONATION RATE AMONG ETHNIC MINORITY GROUPS IN UNITED KINGDOM

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Transplants safe lives; however, there is a severe shortage of organs in the United Kingdom (UK) in proportion to people awaiting a transplant. This is more significant among ethnic minority groups in UK.
Therefore a literature review was conducted to identify the reasons for low organ donation rate among ethnic minority groups in UK. Hopefully we can work on those reasons to improving the donation among ethnic minority groups. Both free text and medical subject heading (MeSH) were used to search the electronic databases. Relevant quantitative and qualitative studies were selected and quality assessed using either the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) method or the Greenhalgh's principles.
Ten studies relevant to the review till 2010 were identified. Among these ten studies, four are quantitative studies, others are qualitative studies. Lack of information and awareness or understanding was one of the main reasons identified by most of the studies. Religious stance was another important reason. Others believed that the body should be "intact" after death for judgement day. Lack of confidence or mistrust of the medical authorities and system was another major concern among the studies population. Wishes of the deceased as well as the elder members in the family were important to some groups. Because of the difficulty of topic in relating to death, emotional and passive detachment was presented. Some other reasons had also been mentioned in the ten studies.
The studies also highlighted some initiatives to improve this situation.
The current situation of organ donation is crucial not only for the ethnic minority groups but also for the whole population in UK; however, it is not without hope.

Clinical immunosuppression

P-073 ATG MODE OF ACTION: T-CELL DEPLETION AND FAR BEYOND

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Depleting anti-lymphocyte or- thymocyte polyclonal antibodies have long been used as induction immunosuppressive regimens. We hypothesized that investigating (early) inflammatory parameters like IDO, HMGB-1, IMPDH, CRP and C5b-9 could give predictive information about delayed graft function (DGF), rejection (AR) and long term survival (GS).
Patients and Methods: In a consecutive group of patients transplanted between 10/1989 and 06/1992 (n=324) treated either with quadruple drug induction (QDT, n=238; ATG-F, CsA, AZA, MP) or triple drug (TDT, n=86; CsA, AZA, MP) as immunosuppressive therapy.
Results: There was a significant difference between HMGB-1 in PF vs. DGF (correlation HMGB-1 and DGF r^2=0,718). HMGB-1 in ATG-treated patients at week 1 after transplantation was decreased by 82% whereas elevated by 24% in TDT patients. With IDO we differentiated two groups of patients within the first 2 months: Gr.I (n=42) involved patients showing IDO levels $<$ 4,0 μmol/L, Gr.II (n=46) $>$ 5,0 μmol/L at day 21 and thereafter at least for 3 times. There was no statistic difference in demographic data between both groups. Gr. I showed 1/5/10 year graft survival of 100/89/71% vs. Gr.II with 87/54/31% ($p<0,001$ at year 5 and 10, all data death censored). IDO was already upregulated in the donor, without any predictive value for the outcome. CRP showed no predictive value and IMPDH was significantly higher in pretransplant probes.
Conclusion: Monitoring of IDO is a novel tool of immune monitoring. HMGB-1, already existent in the donor, is supporting the idea of pretreatment to suppress innate immune reactions in the donor. These results are a proof of concept for the preconditioning of donors.
We propose that the results are not independent but represent distinct injury: scaring and inflammation reflecting the cumulative burden of injury over time. "Silencing" inflammation might be responsible for long term outcome.

P-074 IMPACT OF MDR1 AND CYP3A5 GENETIC POLYMORPHISMS ON TACROLIMUS DOSAGE REQUERIMENTS AND ACUTE REJECTION IN CAUCASIAN LIVER TRANSPLANT RECIPIENTS

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Aim: To evaluate the association between CYP3A5 and MDR1 genetic polymorphisms and tacrolimus exposure, dose requirement, and organ rejection as a result of genotype-related underimmunosuppression.
Methods: Using RT-PCR method, 98 caucasian adult liver transplant recipients (24 women & 74 men; aged 54.3 8.3 years) and 81 donors (aged 54.4 17.6 years) were genotyped for CYP3A5 6986A$>$G, MDR1 1236C$>$T, MDR1 2677G$>$A/T, and MDR1 3435C$>$T alleles, and their concentration dose of tacrolimus (C:D)were measured at day 3, 7, and 14, and at 1 month and 3 month after transplantation.
Results: Frequencies of variant alleles among the transplant recipients and donors were similar to those previously described in Caucasian population. Hepatic (donors) CYP3A5*3 alleles 84.3% showed higher blood tacrolimus concentrations per adjusted dose ratio than did those with CYP3A5*1, with no statistical difference (0.195 *vs* 0.099, p= 0.120). A notably decrease on C: D ratio was observed on CYP3A5*1 carriers (present in recipients and donors, n=2) at day 7 after transplantation (0.109 *vs* 0.326, p=0.092). No association was found between rejection incidence and C: D tacrolimus ratio or genotypes (CYP3A5 and MDR1).
Conclusion: The CYP3A5 genotype of the liver seems to be associated with tacrolimus concentration and dose tacrolimus requirement increases for recipients and donors carriers of CYP3A5*1 allele. In liver transplant patients, recipient and donor liver genotypes may act together in determining overall drug disposition, sometimes neutralizing each other, hence the importance of assessing both. Further haplotype analyses are now required to evaluate the clinical impact of CYP3A5 and MDR1 genetic polymorphisms in regard to the clinical outcome in liver transplantation.

P-075 IN-VITRO ASSESSMENT OF T CELL RESPONSE AND CLINICAL STATUS OF TRANSPLANT PATIENTS ON VARIOUS IMMUNOSUPPRESSIVE DRUGS IN KwaZulu-Natal (SOUTH-AFRICA)

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Background: The immunosuppressive therapy in transplant patients is routinely monitored only by drug blood levels and patients clinical status. We have previously established a simplified method of measuring the immune response using bioluminescence to detect ATP production by stimulated peripheral blood mononuclear cells (PBMC). We now monitor the immune response of transplant patients on various immunosuppressive drugs while recording their clinical status and drugs blood levels.
Methods: Thirty eight patients were prospectively studied including 22 on cyclosporine based regimen, 10 on sirolimus based regimen and 6 on tacrolimus based regimen and fifteen healthy controls were studied. Clinical status was monitored monthly and checked against% ATP increase following PHA stimulation of patient PBMC normalized to a% ATP increase in healthy control PBMC, and against drug blood levels tested in accredited laboratories.
Results: Infections were associated with low (<15%) increase in ATP in 89% of cases and with mild ATP increase (15-30%) in 11% and with normal increase > 30% in 0%.
Stable patients expressed low (<15%) increase in ATP in 69% of cases and with mild ATP increase (15-30%) in 23% to normal increase (> 30%) in 8% of cases.
The only patient who had acute rejection had% ATP response of 74%. The drug blood levels were within the recommended range in 73%. They were associated with clinical status only in 2 out 3 cases with drug levels over the limit.
Conclusions: ATP production by stimulated T cells offers a more sensitive association with clinical status of transplant patients than immunosuppressive drugs blood levels. A longer monitoring period will determine whether% ATP changes can predict the clinical manifestations.

P-076 CORRELATION OF EVEROLIMUS EXPOSURE WITH EFFICACY AND SAFETY OUTCOMES IN RENAL TRANSPLANT RECIPIENTS: 24-MONTH UPDATE

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Introduction: The multicenter randomized A2309 study showed that everolimus (EVR) with reduced-cyclopsorine (CsA) achieves comparable efficacy and renal function to MPA with standard-CsA in *de novo* renal transplant recipients (RTxR). Correlations of EVR C0 levels with efficacy and safety events over 12 months (M) indicated EVR C0 range of 3-<8 ng/mL to be the optimal target range in *de novo* RTxRs receiving reduced CsA. The present analysis assessed this association for the 24-M treatment period.
Methods: Time-normalized mean C0 levels were calculated up to the occurrence of an efficacy (treated BPAR, graft loss, death) or safety event (renal function parameters, selected adverse events [AE]), or to the last sampling date if there was no event. Median-effect analyses were performed for the combined EVR arms with time-normalized C0 values divided into quintiles. The proportion of patients experiencing an event in each quintile was determined and logistic-regression analyses were performed.
Results: Incidence of graft loss was inversely related to everolimus C0 values at M12 (median-effect logistic regression p=0.007) and M24 (p=0.004), mainly driven by a higher incidence of graft loss with EVR C0 <4 ng/mL. Higher EVR C0 levels were associated with more proteinuria events at M12 (p=0.004) and M24 (p=0.01), whereas analyses for other renal function parameters (low or decreased GFR or creatinine clearance, high creatinine) showed no clear correlation. Significant direct correlations were observed between EVR C0 and new onset diabetes mellitus (p=0.035), and hypercholesterolemia (p=0.022) at M12 in the combined EVR groups but not for other selected events (wound healing, peripheral edema, stomatitis/oral ulcers, hypertriglyceridemia, low testosterone in men).
Conclusions: These findings confirm that the everolimus C0 target range of 3–8ng/mL is associated with a better benefit-risk ratio when assessed in both EVR groups at M24 post-RTx.

Table 1: Median effect analysis: Incidence of patients with events for different EVR C0 quintiles

	Graft loss		High urinary P/C (≥300mg/g)		High TC (≥6.2mmol/L)	NODM	Wound healing
Quintiles (EVR C0 [ng/mL]) %	M12	M24	M12	M24	M12	M12	M12
1	(<4.4) 8.7%	(<4.6) 11.7%	(<4.6) 52.5%	(<4.7) 61.2%	(<4.0) 68.8%	(<4.4) 9.3%	(<4.4) 36.1%
2	(4.4-5.7) 5.6%	(4.6-5.7) 6.7%	(4.6-5.9) 45.7%	(4.7-6.0) 46.0%	(4.0-5.3) 62.2%	(4.4-5.7) 5.4%	(4.4-5.6) 26.2%
3	(5.7-6.8) 1.9%	(5.7-6.9) 2.7%	(5.9-7.1) 53.6%	(6.0-7.1) 56.8%	(5.3-6.7) 64.4%	(5.7-6.9) 7.5%	(5.6-6.9) 25.5%
4	(6.8-8.5) 2.7%	(6.9-8.4) 2.8%	(7.1-8.8) 56.6%	(7.1-8.7) 63.9%	(6.7-8.7) 64.5%	(6.9-8.5) 9.7%	(6.9-8.7) 31.8%
5	(≥8.5) 1.9%	(≥8.4) 3.7%	(≥8.8) 71.0%	(≥8.7) 73.2%	(≥8.7) 84.5%	(≥8.5) 16.8%	(≥8.7) 46.7%

NODM, new onset diabetes mellitus; TC, total cholesterol; P/C, urinary protein/creatinine ratio

P-077 THYMOGLOBULINE PRE-TREATMENT AND MINIMIZATION OF IMMUNOSUPPRESSION WITH ADVAGRAF IN LIVER TRANSPLANTATION ALLOWS INCREASE OF Treg AND GUIDANCE OF TOLEROGENESIS. PRELIMINARY RESULTS OF A PROSPECTIVE RANDOMIZED TRIAL

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Background: FOXP3+ T regulatory cells have strongly emerged in the mechanisms of tolerogenesis and maybe crucial for an effective therapeutic intervention. We designed a tolerogenic regimen of recipient pre-treatment with Thymoglobuline and gradual minimization of immunosuppression in a Advagraf-based prospective trial in liver transplantation to investigate expansion of Treg in peripheral blood and guidance to reduce IS in selected tolerant patients.
Methods: Thymoglobuline pre-treatment +low-dose Advagraf monotherapy or Advagraf+Certican; IS levels were reduced by half at 6 and 12 months in clinically stable patients. Blood samples for PBMC were collected at LTx, every 3 months and before any reduction of IS, and different T-cell subsets (CD8, CD4, CD25, Treg) were measured by standard flow cytometry. Serial liver biopsies were searched for subtle histological signs of immune activation.
Results: After 1 year 15 patients have been enrolled. From baseline values, Thymoglobuline caused a mild decrease of CD4 and CD8 at T3, and a steady increase until T12 in CD4 (CD4: 334 c/μL, 44%) but not in CD8 (CD8: 171 c/μL, 23%). CD25 constantly increased from baseline (20,3%) to T12 (64,3%) and similarly Treg increased from 9,57% to 12,48% (max 15,48% at T6), and from 31 c/μL to 44,7 c/μL (max 47,3 c/μL at T3). Rejection was absent in all 15 patients despite very low levels of IS (mean ADV/CERT levels first 6 months: 5,0/4,1 ng/ml; months 6-12: ADV/CERT 2,5/1,87 ng/ml). No histological signs of immune activation was found in all liver biopsies examined.
Conclusions: Induction with Thymoglobuline and minimization of IS with Advagraf is safe, allows no rejection and permits expansion of Treg, which may be a “tolerogenic” monitoring tool for guidance of IS reduction.

P-078 PRELIMINARY RESULTS OF GENERIC MYCOPHENOLATE MOFETIL (Myfenax) TREATMENT IN DE NOVO RENAL TRANSPLANT RECIPIENTS

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The aim of the study is to show the preliminary outcomes of renal transplantation (RT) in patients treated with the generic formulation of mycophenolate mofetil (Myfenax, Teva).
Material: 32 patients received Myfenax in the immunosuppressive protocol (23 – with tacrolimus, steroids, 9 - with cyclosporine, steroids). 28 patients were monitored for a period of at least 6 months, 17 for at least 12 months.
Results: Acute rejection (AR) was observed in 5/32 patients (15,6%) and delayed graft function (DGF) in 10 patients (31%). In a comparable period, the frequency of diagnosis of AR and DGF in our unit were 16.6% and 22,1%, respectively. Mean creatinine level and eGFR were 1.33/56 – after 3 months, 1,25/69 - after 6 months and 1,19/66 (mg/dl and ml/min/1.73m2.) - after 12 months.

In the course of observation two female patients died (3 and 13 months after RT due to sepsis and pancreas cancer, respectively) and one patient returned to chronic hemodialysis 8 months after RT (IF/TA). Overall, the dose of Myfenax was reduced in 18 patients on the basis of adverse reactions in the form of diarrhea, anemia, PTDM, mucosal lesions, elevated liver function tests and infections. The pre-reduction MPA mean level was 6.3 mg/l – target level 3-5 mg/l). In 2 cases Myfenax was excluded from the treatment, in one case because of urosepsis and in the second it was changed to everolimus as rescue therapy in IF/TA of the graft after 7,5 months after transplantation.
Conclusion: 1. Myfenax is an effective immunosuppressant in renal transplant patients. 2. In order to confirm its complete biological and pharmacokinetic equivalence with the reference medicine, long-term, randomized observations carried out on larger renal transplant patient groups are needed.

P-079 CONVERSION FROM TWICE-DAILY TACROLIMUS (Prograf®) TO ONCE-DAILY PROLONGED RELEASE TACROLIMUS (Advagraf®) IN LIVER TRANSPLANT RECIPIENTS

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Background: To analyze the safety of a 1:1 dose conversion from twice-daily tacrolimus (Prograf®) to once-daily tacrolimus Advagraf® in liver transplant (LT) recipients.
Methods: This prospective study on 200 of 600 LT, that had LT between 2003 and 2009, examined tacrolimus levels after conversion to Advagraf® therapy. Mean patient age was 53 (38 –65) years.
Conversion occurred at 12 (12 – 85) months posttransplantation, and follow-up was 201 (30–385) days. Levels of tacrolimus, total bilirubin, aspartate aminotransferase, alanine aminotransferase, g-glutamyl transferase, alkaline phosphatase, and creatinine were recorded on the day before conversion to Advagraf and 10 days, 3 months, 6 months after conversion.
Results: Of the 200 patients converted to Advagraf®, 80 (40%) had cirrhosis HCV related, 60 (30%) HBV related, 30 (15%) had alcoholic cirrhosis.
The tacrolimus whole blood trough level at T0 (the day before conversion) was 4.9 ng/mL (3-6.7) with a daily dose of 2 mg (1-5). The mean tacrolimus blood trough levels at T1 (10 days after T0), T2 (3 months after T0) and T3 (6 months after T0) were 4.05 (2.5-5.3), 4.5 (2.5-5.6) and 4.05 (2.5-5.2) ng/mL with mean daily doses of 2.5, 2 and 2 mg, respectively. There was no significant difference between T0, T1,T2 and T3 either for tacrolimus blood trough levels or for tacrolimus daily dosages. Dose adjustment was performed in 16 (8.3%) patients at T1, in 10 (4.9%) at T2, in 2 (1.6%) at T3. Liver and renal function tests remained stable; no episodes of acute rejection. No deaths, only 1 patient was converted to tacrolimus due to hypotension and tremor and 1 patient developed acute leukemia.
Conclusions: A switching policy using a dose ratio of 1:1 from twice-daily tacrolimus to once-daily prolonged-release tacrolimus was safely applied to LT recipients.

P-080 RENAL FUNCTION IN PATIENTS TREATED WITH BELATACEPT-OR CYCLOSPORINE-BASED REGIMENS AT YEAR 3 IN THE BENEFIT AND BENEFIT-EXT STUDIES

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Background: Renal function is an important predictor of long term patient/graft survival. The current analysis focuses on renal function in 2 Phase III studies of belatacept-based immunosuppressive regimens in kidney transplant recipients.
Methods: BENEFIT assessed belatacept in patients receiving a kidney transplant from a living or standard criteria deceased donor; BENEFIT-EXT in extended criteria donor recipients. Each assessed belatacept in more intensive (MI) and less intensive (LI) regimens vs cyclosporine (CsA).
Results: Mean cGFR data over the 3-yr course of BENEFIT and BENEFIT-EXT are listed in Table 1.
The rate of change (mL/min/yr) in mean cGFR from Month 3 to Month 36 was 1.0 (MI), 1.2 (LI), and -2.0 (CsA) in BENEFIT, and was -0.9 (MI), -0.6 (LI), and -1.9 (CsA) in BENEFIT-EXT. By Year 3, more patients in the CsA group in BENEFIT (20%) and in BENEFIT-EXT (44%) had a cGFR <30 mL/min (CKD stage 4 or 5; advanced renal dysfunction) vs those in the belatacept groups (MI/LI) (BENEFIT: 9%-10%; BENEFIT-EXT: 27%-30%). An on-treatment analysis showed that the relative renal function benefit w/belatacept (MI/LI) was ~20-22 mL/min in BENEFIT and ~12-13 mL/min in BENEFIT-EXT at Year 3.
Conclusions: Belatacept was associated with improved renal function, as demonstrated by multiple analyses, which was evident early post-transplant and persisted through 3 yrs. The significance of these findings is further reflected by fewer belatacept patients meeting criteria for advanced renal dysfunction.

Table 1. cGFR in BENEFIT and BENEFIT-EXT over time (ITT analysis)

	BENEFIT			BENEFIT-EXT		
cGFR (mL/min/1.73 m²)	Belatacept MI (n = 219)	Belatacept LI (n = 226)	CsA (n = 221)	Belatacept MI (n = 184)	Belatacept LI (n = 175)	CsA (n = 184)
Month 3	63.1	63.6	51.0	45.1	45.3	37.8
Year 1	65.2	65.4	50.1	44.4	44.8	36.5
Year 2	65.5	65.4	47.9	44.4	42.8	34.9
Year 3	65.2	65.8	44.4	42.7	42.2	31.5

P-081 CLINICAL OUTCOME IN HEART TRANSPLANT RECIPIENTS RECEIVING TACROLIMUS RETARD (Advagraf®)

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Tacrolimus retard (Advagraf®) is a new oral formulation of tacrolimus. It is given once daily, whereas tacrolimus (Prograf®) is administered twice daily. Efficacy and safety of tacrolimus retard in cardiac transplant recipients (CTx) is currently not known. We compared blood trough levels of tacrolimus, kidney function, the occurrence of cardiac rejections, and adverse events in 11 patients who received tacrolimus retard (ADV group) and 11 patients who received tacrolimus (PRO group) during a 6 months follow-up period. Both, the ADV and the PRO group initially receivedthe standard therapy with cyclosporine A (CSA), azathioprine, and cortisone. They were switched over from CSA to one of the two tacrolimus formulations after a median time interval of 12 days (ADV group) and 15 days (PRO group). In both groups, one patient had to be re-converted to CSA due to neurological complications. Tacrolimus trough levels of the remaining patients did not differ between groups and were within the target range (5.0 -8.0 μg/l) during follow-up. Creatinine levels were comparable between groups and did not change significantly. Blood urea nitrogen declined in both groups. However, the decline was more pronounced in the ADV group than in the PRO group (P=0.028). Six cardiac rejections occurred in each group (P=1.000). Sixteen adverse events occurred in the ADV group and 18 in the PRO group (P=0.650). The most frequent adverse events in the ADV group were arrhythmia (n=3), pericardial effusion (n=3), and gastrointestinal complications (n=3).
In conclusion, this small investigation indicates that Advagraf® is as safe as Prograf®, whereas Advagraf® is probably less nephrotoxic than Prograf® in CTx patients.

P-082 IMPACT OF CHANGE TO A PRIMARY IMMUNOSUPPRESSION REGIMEN OF BASILIXIMAB, MYCOPHENOLATE, PREDNISOLONE AND LOW-DOSE TACROLIMUS, ON THE 3 YEAR OUTCOME OF KIDNEY TRANSPLANTATION

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Introduction: Compared with other conventional regimens, immunosuppression with daclizumab, mycophenolate mofetil, corticosteroids, and low-dose tacrolimus (Tac) has been shown to achieve superior renal function and transplant survival one year after kidney transplant (Ekberg H et al, N Engl J Med 2007;357:2562-75). Longer term outcome with this regimen remains uncertain. Our centre's immunosuppression protocol was changed from a ciclosporin (CyA) based regimen to this low-dose Tac regimen in 2007. We present the 3 year outcome for patients transplanted in the year before compared with the year after this change.
Methods: Data were collected from the electronic record for consecutive kidney only transplants between 01/01/06 and 09/11/07.
Results: 131 transplants were performed. 5 were excluded due to transplant loss within 2 weeks. 61 started CyA-based and 65 started the Tac-based immunosuppression regimen. All but 2 patients (both in the Tac group) had 3 year outcome data. The Tac group had a lower average recipient age (41.9 v 48.4 years; p=0.003) and more live donor transplants (32% v 16%; p=0.03). Comparing the Tac group to the CyA group 1 v 8 patients died (p=0.01) and

6 v 6 returned to dialysis (p=0.91) within 3 years. Renal function was better in the Tac group at 1 (eGFR 55.5 v 43.9 mL/min; p= 0.001) and 3 years (51.2 v 38.3 mL/min; p=0.004). More patients switched from the CyA regimen to Tac regimen than vice-versa during the first year (16 v 1; p=<0.001). The results were similar when analysing deceased and live donor transplants separately.
Conclusion: A change to a low-dose Tac primary immunosuppression regimen in unselected patients in our centre resulted in significantly improved 3 year transplant function.

P-083 IMPROVING OR SUSTAINING RENAL FUNCTION OVER 3 YEARS WITH BELATACEPT OR CYCLOSPORINE A (CsA): INSIGHTS FROM THE BENEFIT STUDY

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Background: Patients receiving belatacept had better renal function, similar patient/graft survival, and a higher rate of acute rejection versus CsA through 3 years in BENEFIT. We report the likelihood of sustained/improved glomerular filtration rate (GFR) with belatacept versus CsA.
Methods/Materials: BENEFIT is a randomised, phase III study in adults receiving a kidney transplant from a living or standard criteria deceased donor. Patients received a more intensive (MI) or less intensive (LI) regimen of belatacept, or CsA; basiliximab induction, mycophenolate mofetil and corticosteroids. GFR stage shifts (Modification of Diet in Renal Disease formula) from month 3 to 36 were assessed post-hoc (Stage 1: ≥90 ml/min, Stage 2: 60–89 ml/min, Stage 3: 30–59 ml/min, Stage 4: 15–29 ml/min; Stage 5: <15 ml/min, or return to dialysis, graft loss or death).
Results: Data were available for 181 belatacept LI and 162 CsA patients at months 3 and 36. At month 3, 59% of belatacept and 30% of CsA patients were GFR Stage 1/2 (Stage 4/5: 8% versus 11%). Of patients in Stage 2, 85% receiving belatacept and 67% receiving CsA had sustained/improved stage at month 36. Fifty-nine percent of belatacept patients and 17% of CsA patients in Stage 3 at month 3 had improved stage at month 36; 5/7 belatacept patients (71%) and 3/7 CsA patients (43%) in Stage 4 at month 3 improved by month 36. Two of 7 belatacept patients in Stage 5 at month 3 were Stage 2 or 3 at month 36; 11/11 CsA patients remained in Stage 5. Belatacept LI and MI outcomes were similar.
Conclusion: In standard criteria kidney recipients, early renal benefits with belatacept were more likely to be sustained/improved over 3 years versus CsA.

P-084 EARLY CONVERSION TO A SIROLIMUS-BASED, CALCINEURIN-INHIBITOR-FREE IMMUNOSUPPRESSION IN THE SMART TRIAL: OBSERVATIONAL RESULTS AT 24 AND 36 MONTHS AFTER TRANSPLANTATION

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The SMART study showed that at 12 months posttransplant, early conversion to a calcineurin-inhibitor (CNI)-free regimen with sirolimus (SRL) in combination with mycophenolate mofetil (MMF) resulted in a better renal function compared to a cyclosporine (CsA)-based regimen in combination with MMF.
This in an observational follow-up of 132 patients for additional 2 years with the same endpoints as the core study. At 24/36months 46.4%/40.6% of patients were on treatment in the SRL arm and 71.8%/57.7% of patients in the CsA arm. The SRL and MMF arm continued to have a significant lower median S-creatinine (m24:1.40vs.1.60 and m36:1.40vs.1.60 mg/dl) and a trend towards a higher eGFR (m24:61.95vs.54.66 and m36:60.80vs.53.72 mL/min/1.73m^2) in the ITT analysis. This effect was even more pronounced in patients, who were able to stay on their designated SRL-based therapy for at least 12 months. Multivariate analysis revealed that a CNI-free SRL-based regimen may especially benefit CMV-negative recipients receiving young donor organs with good initial graft function. Patient- and graft survival at 24 months (SRL 99%vs.CsA 97%) and 36 months (SRL 96%vs.CsA 94%) was excellent in both arms. Three late biopsy-proven rejections were recorded in the CsA arm, none in the SRL arm. De novo malignancy developed in 5 patients in the CsA arm, no malignancy was recorded in the SRL arm (p=0.0259). There were no notable differences between groups in late infections or adverse events during follow-up beyond month 12.
Recipients at risk for CMV infection receiving a donor organ with good long term potential may benefit most from a CNI-free SRL based therapy. However, only a subgroup of patients, will be able to tolerate a SRL-based therapy long-term, and will be able to enjoy the respective merits of this regimen.

P-085 SIROLIMUS RESCUE THERAPY AFTER ACUTE REJECTION IN RENAL TRANSPLANT RECIPIENTS – ONE YEAR FOLLOW UP

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Background: Conversion from calcineurine inhibitors (CNIs) to sirolimus (SRL) is proved to be effective in improving long-term graft outcome. SRL treatment of high risk renal transplant recipient (RTR) is still under investigation. Aim: We studied the long-term effects of conversion from CNI to SRL as rescue therapy on RTR after treatment of biopsy proven acute rejections (BPAR).
Patients and Methods: RTR converted from CNI, mycophenolate mofetil (MMF) as 2gm daily and steroid to SRL, MMF and steroid after treatment of BPAR were studied.
Results: Thirty candidates were maintained on CNIs (24 were on cyclosporine-A and 6 on tacrolimus) after receiving ATG (80%) or basiliximab (13.3%) induction therapy. The overall mean age was 35.1±13.5 years, including pediatric and geriatric age groups and patients with multiple co-morbid conditions. Black patients were 63.3%. Mean body mass index (BMI) was 27.8±8 and 33.3% had a BMI >30. Pre-conversion steroid-resistant rejection incidence was 16.7%. Mean time to convert to SRL was 10±18.8 months post-transplantation. Post-SRL rejection episodes were reported in 16.6% with 10% resistance to steroid treatment. Leucopenia, hypercholesterolemia and hypertriglyceridemia increased significantly post-SRL (p 0.031, 0.0001 and 0.007 respectively). Graft and patient survival were 100% each. There were significant improvements in estimated creatinine clearance from 58±22.1to 69.6±22.2 ml/min/1.72 (MDRD formula) at one year (p 0.001). SRL had to be discontinued in 6.6% of candidates mainly due to its side effects.
Conclusion: SRL rescue therapy after treatment of BPAR is proved to be effective as a CNI free regimen for high risk RTR after one year of follow up.

P-086 EVALUATING EFFICACY AND SAFETY OF TWO IMMUNOSUPPRESSIVE REGIMENS IN KIDNEY TRANSPLANT PATIENTS – THREE YEARS RESULTS

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End Points: PRIM.: to determine the acute rejection rate at month 12 and 36. SECOND.: the renal function, as expressed by serum creatinin and the glomerular filtration rate at month 12 and 36. Patient and graft survival rates at month 12 and 36.
Study Design: Group A – daclizumab, tacrolimus, mycophenolate and corticosteroids. Group B – control group tacrolimus, mycophenolate and corticosteroids. Number of patients: 40 patients, 20 for each arm.
Results: *acute rejections* at 12 months- group A one corticosens. rejection,- group B two corticosens. rejections – statistic. not significant. There was no rejections betwen month 12-36 in both groups. *Serum creatinin* at month I was: group A 142±44 umol/l group B 154±42 umol/l, at month 12 group A 133,4±32 umol/l, group B 148,9±44 umol/l (not significant) and at month 36 group A 120,8±31 umol/l, group B 166,2±67 umol/l (significant). *Glomerular filtration* at month I was: group A 1,058±0,38 ml/s group B 0,95±0,28 ml/s, at month 12 group A 1,136±0,38 ml/s group B 1,099±0,25 ml/s (not significant) and at month 36 group A 1,175±0,35 ml/s group B 1,012±0,44 ml/s (not significant). *Patient survival rates* at 12 months were 100% in both groups. At 36 months group A100% group B 90% (Ix suicide,Ix cardiovasc. death- both with functional graft). *Graft survival rates* at 12 months was: group A 95%,

group B 100% (not significant), at month 36 group A 90%, group B 90% (not significant). All tested by F-test.
Conclusion: The follow up has not documented beneficial effect of daclizumab use to the existing standard regimen.

P-087 INTENSIFIED DOSING OF ENTERIC-COATED MYCOPHENOLATE SODIUM ACHIEVES EARLY HIGH DRUG EXPOSURE AND LOWER RATES OF ACUTE REJECTION VERSUS STANDARD DOSING IN DE NOVO RENAL TRANSPLANT RECIPIENTS

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Background: More intensified mycophenolic acid (MPA) dosing in the first weeks post renal transplantation (RTx) may result in more effective rejection prophylaxis. A prospectively planned meta-analysis of data from two 6-month (M) parallel-run studies evaluated the therapeutic benefit of an initially intensified *versus* standard dosing regimen of enteric-coated mycophenolate sodium (EC-MPS).
Methods: 441 *de novo* RTx recipients were randomized (1:1) to receive either Intensified EC-MPS (2 wks 2880 mg/d; subsequently 4 wks 2160 mg/d; followed by 1440 mg/day) or Standard (1440 mg/day) EC-MPS, with concomitant CsA and steroids with or without anti-IL2R induction. Primary endpoint was treatment failure (BPAR, graft loss, death) at M6 post-transplantation. Here we report the results of MPA pharmacokinetic data and a logistic regression analysis.
Results: Mean MPA AUC0-12h >30 g*h/mL was achieved as early as Day 3 in 80.5% of patients with Intensified regimen *versus* 39.0% of patients with Standard regimen. Treatment failure was not significantly different between the groups, but the incidence of BPAR was 13.8% *versus* 19.3% (p=0.034; Intensified *versus* Standard). From logistic regression analyses, more than three HLA mismatches and non-use of induction therapy were associated with higher risk of treatment failure (Table 1). Renal function, gastrointestinal symptom rating scores and safety profiles were comparable between treatment groups.

Table 1. Logistic regression analysis for treatment failure

Variable	Odds ratio	95% CI	p-value
Non-use of anti-IL-2 receptor antibodies	2.480	1.347, 4.565	0.004
HLA mismatches >3	1.892	1.135, 3.153	0.014
Cold ischemia time ≥18 hours	0.385	0.177, 0.839	0.016

Conclusion: An initially intensified EC-MPS dosing regimen in combination with CsA resulted in more rapid attainment of higher MPA exposure and significantly lower rate of BPAR with comparable safety *versus* a standard dosing regimen. Use of IL-2 receptor antibodies was associated with a significant reduction in treatment failure risk across both groups.

P-088 EXTENDED-RELEASE TACROLIMUS THERAPY IN DE NOVO CARDIAC TRANSPLANT RECIPIENTS: SINGLE-CENTER EXPERIENCE

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Background: Non compliance in immunosuppressive therapy is a cause of rejection or lost of the graft. Any formulation which allows simplifies the drug administration should improve the compliance and prevent the rejection. There is experience in conversion from twice-daily Tacrolimus (TD-TAC) to once-daily dose (OD-TAC), but there are not data for extended-release Tacrolimus in de novo heart transplant.
Objective: Describe our initial experience with OD-TAC in combination with induction therapy with Basiliximab, corticosteroids a Mycophenilate Mofetil therapy in patients undergoing de novo heart transplant.
Patients and Methods: In this retrospective, observational, single-centre study, data were obtained for 12 adult recipients treated with extended-release (G1) Tac and 15 patients treated with standard-release Tac (G2). Mean (SD) follow-up in the 2 groups was 8.6 (2.9) months and 20,6 (7,4) months, respectively. The primary characteristics were comparable between the groups.
Results: 3 patients presented 2R ISHLT acute rejection in G1 and 2 in the G2. Mortality was similar, one patient death in G1 and 2 patients from the G2. Renal function in both groups was comparable: serum creatinine concentration 1.37 (0.5) mg/dL vs. 1.11 (0.3) mg/dL at 1st month post transplantation. And 1.41 (0.4) mg/dL vs. 1.32 (0.4) mg/dL. at final follow-up. Tac doses were 4,73 mg/d vs. 5.14 mg/d, and blood concentrations were 11.6 ng/mL vs. 11.5 ng/mL. No differences were found in diabetes, blood glucose levels or HbA1c in both groups at the end of follow up: Glucose: 86.41 mg/dl (21.8) vs. 95.71 mg/dl (28.1), HbA1c: 5.52% (0.4) vs. 5.70% (0.8).
Conclusions: Short-term experience with extended-release Tac therapy in de novo renal recipients confirms its efficacy and safety. Adjusting blood concentrations in the immediate post transplantation period is not more difficult with extended-release Tac compared with the twice-daily formulation.

P-089 BASILIXIMAB INDUCTION CAN TRIGGER SHOCK AND ARDS IN YOUNG RECIPIENTS

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Background and aim: Induction with IL-2R Antagonists (IL-2RA) is recommended to prevent early rejection after renal trans-plantation. IL-2RAs have an excellent overall safety profile. We describe here a life-threatening episode of shock following basiliximab injection and review the literature.
Patient description and literature review.
A 20-year-old patient underwent kidney transplantation consequently to childhood post-diarrheal haemolytic uraemic syndrome. He was given tacrolimus, methylprednisolone and mycophenolate preoperatively. Basiliximab 20 mg iv was given after anesthesia induction. He received no blood transfusions. On POD 1, he developed dis-tributive shock, multiple organ failure, acute cor pulmonale and cardiac arrest that required intensive support. He fully recovered by POD 3, but the graft was lost from cortical necrosis. The patient has since undergone surgery with the same anesthetic drugs without complication. PubMed search yielded 7 similar cases. The total 8 patients were 6 to 21-year-old from various ethnicities. Five were suffering from renal dysplasia. They had no history of allergy or cardiac dysfunction. It was the first transplantation for 6 of them, and the first basiliximab injection for all of them. Other treatments were trivial in the context of anaesthesia. After ini-tially being well during some hours -arguing against an anaphylactic reaction- all developed ARDS. Six required invasive ventilation, three developed cardiac arrest, 3 required huge inotropic support and 2 developed MOF and myocardial depression. All but one patient (deceased) recovered in a few days. Infections or fluid overload could be ruled out by clinical assessment. Although the direct causal role of Basiliximab can not be formally proven in these poly-medicated patients, it is likely because such events have not been reported among patients who did not receive IL-2RAs.
Conclusion: Basiliximab in young kidney recipients can trigger rare but life-threatening shock and ARDS.

P-090 EVALUATING THE IMPACT OF GASTROINTESTINAL EPISODES ON THE HEALTH-RELATED QUALITY OF LIFE OF SOLID ORGAN TRANSPLANT RECIPIENTS: SENSITIVITY TO CHANGE OF THE SIGIT-QoL QUESTIONNAIRE. MYPACIENTE-2 STUDY

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Background: The study aims to evaluate the health-related quality of life (HRQoL) of solid organ transplant (SOT) patients suffering from gastrointestinal episodes (GI) and to assess the sensitivity to change of the SIGIT-QoL questionnaire.
Methods: An observational, multicentre, prospective study. SOT patients (lung, kidney, liver or heart) aged>= 18, who had received the graft between 3-24 months before and suffering from GI episodes, were evaluate at baseline, 1-2 weeks later and 3 months after baseline. Sociodemographic and clinical data: age, sex, SOT type, acute allograft rejection (AAR), GI etiology, Clinical and Patient global Impression scale (CGI-SI&GI and PGI-SI&GI) and the SIGIT-QoL (range: 0-maximum impact to 68-minimum disruption). Intra-

class correlation coefficient (ICC), differences between baseline and last visit (Wilcoxon test), effect size (Cohen's *d*) and the minimal important differences -MID- (using CGI & PGI scores as anchors in General Linear Models) were calculated.
Results: 285 SOT patients were included (62.1% males). Mean age (SD) was 52.65 (11.75) years, time since transplantation was 12.11 (6.76) months, 22.1% suffered AAR and 48.2% of GI were related to immunosuppressant drugs. At baseline, SIGIT-QoL scores (median, Q1-Q3=54.00, 44.00-60.00) showed an impact on patients' HRQoL that diminished 3 months later (SIGIT-QoL=60.00, 54.00-64.00). Differences were found between baseline and last visit in SIGIT-QoL scores (-6.071, $p<0.001$) with a moderate effect size (d=0.571). Moreover, MID of 4.00 points in total scores were found ($p<0.01$). Finally, SIGIT-QoL test-retest reliability was adequate (ICC=0.740-0.892).
Conclusions: GI episodes affect SOT patients limiting their HRQoL. The SIGIT-QoL questionnaire is a specific and brief instrument (17 items) which can provide valid data from patients' HRQoL during clinical practice and is a useful tool for detecting changes in their clinical situation.

P-091 EXTENDED RELEASE TACROLIMUS VERSUS CONVENTIONAL TACROLIMUS IN DE NOVO ORTHOTOPIC LIVER TRANSPLANTATION

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Aim: The extended release tacrolimus (ERT) combine the immunosuppressive effects of conventional tacrolimus (CT) with improved adherence to the treatment owed to the once a day dosage. The aim of this study is to compare the efficacy and security, blood trough levels and doses in both tacrolimus formulations.
Methods: 100 consecutives patients (50 in each group) receiving a first liver transplant with 6 months follow up were analyzed. Immunossuppresion regimen consited on Tac+Esteroid or AntiCD-25+Tac (delayed)+MMF+Esteroid for patients with Pretx renal disfunction. The incidence of acute cellular rejection, and patient and graft survival were collected as efficacy variables. Safety variables, renal function, diabetes mellitus and arterial hypertension de novo were also evaluated.
Results: The incidence of biopsy proven acute cellular rejection (BPAR) was 8% (4 episodes) in the ERT group and 7 episodes (14%) in the CT group. In both groups, none was steroid-resistant and all resolved.
At the end of the study, nine patients (18%) in the ERT group versus 7 (14%) in the CT group developed diabetes de novo and nine patients (18%) arterial hypertension in the both groups. Ten patients (21%) of the ERT group and nine (18%) of the CT group presented a creatinine $\geq$ 1.3 mg/dL.
Two patients discontinued treatment with ERT. Patient and graft survival, at the end of the study was 100% in the ERT group and 98% and 96%, respectively, in the CT group.
Conclusions: Extended release tacrolimus and conventional tacrolimus are effective immunosuppressors in liver transplantation with a low incidence of acute rejection confirmed by biopsy. Both tacrolimus formulations are well tolerate and have the same safety profile. The excellent results of tacrolimus extend release in patient and graft survival make them a very useful drugs in de novo liver transplantation.

P-092 ORAL STATUS OF RENAL TRANSPLANT RECIPIENTS RECEIVING CYCLOSPORIN A OR TACROLIMUS

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Cyclosporin A (CsA) and Tacrolimus (Tac) are two calcineurin inhibitors extensively used to prevent the rejection of allogenic renal transplants (RT). Although Tac and CsA have been associated with similar side effects in respect to nephrotoxicity, neurotoxicity and the induction of a diabetic state, it has been suggested that Tac could be associated with less frequent oral health problems, namely gingival overgrowth.
We aimed to evaluate the oral status of renal transplant recipients receiving CsA or Tac as immunosuppressive agents.
Twenty-eight RT recipients receiving CsA (17 men and 14 women, age 53$\pm$9 years) and 33 renal transplant patients receiving Tac (18 men and 14 women, age 41$\pm$6 years), followed-up in our post-transplant outpatient clinic, were included in the study. The oral health status was evaluated in all patients through oral examination by a physician, blind to the transplantation status and immunossupressive treament.
The groups did not differ on time (months) since transplant (58$\pm$70 vs. 49$\pm$46) and dialysis duration before transplant (47$\pm$30 vs. 43$\pm$27). The mean dosage of CsA was 215$\pm$75mg/day and that of Tac 5.94$\pm$3.49 mg/day. Average blood levels of Tac and CsA in the blood at the time of the study were 9.1$\pm$3.2 ηg/ml and 147$\pm$52 ηg/ml.
The following parameters were evaluated in both groups (mean$\pm$SD, CsA vs. Tac): gingival index: 2.179$\pm$0.116 vs. 2.212$\pm$0.084 (p=0.81); plaque index: 86.643$\pm$2.557 vs. 87.697$\pm$2.242 (p=0.76); gingival overgrowth: 29% vs. 18% (p=0.54); DMF index: 10.71$\pm$1.43 vs. 11.27$\pm$1.35 (p=0.78); teeth brushing habits: 1.75$\pm$0.18 vs. 1.55$\pm$0.17 (p=0.43); unstimulated saliva flow rate: 1.81$\pm$0.24 vs. 2.10$\pm$0.38 (p=0.53); unstimulated saliva pH: 7.11$\pm$0.09 vs. 7.09$\pm$0.09 (p=0.87); stimulated saliva flow rate: 6.167$\pm$0.81 vs. 7.87$\pm$0.98 (p=0.20); stimulated saliva pH: 7.75$\pm$0.09 vs. 7.69$\pm$0.08 (p=0,60).
We conclude that oral health status, namely gingival overgrowth, does not differ significantly between RT recipients receiving CsA or Tac.

P-093 IMPACT OF ONCE-DAILY PROLONGED-RELEASE TACROLIMUS ON HCV-SPECIFIC IMMUNE RESPONSE OF PATIENTS UNDERWENT OLTx COMPARED TO TWICE A DAY TACROLIMUS TREATMENT

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Hepatitis C virus (HCV) RNA recurrence after Liver transplantation is almost always present. We previously found that FK did not induce a severe reduction of immune response compared to other clacineurin inhibitor (ILTS 2009 oral presentation). Aim of the present study was to evaluate if prolonged Realease Tacrolimus had the same effect on HCV specific immune response within 12 months from OLTx.
Methods: 20 HCV+ve patients (20 male and 10 female) underwent OLTx within 1 year and having evidence of HCV recurrence histologically proven. Blood samples were taken and at least on $2\text{-}3\times10^5$ cells per well ELISpot was performed to evaluate HCV IFN-γ specific response before and 7,30 and 90 days after switching from Tacrolimus twice a day to once a day prolonged tacrolimus. Further we also evaluated transaminasis, HCV-RNA and FK trough level.
Results: Results are reported in table, indeed we found no statistical significant difference in HCV- IFN-γ specific response in the evaluated time points during once a day prolonged tacrolimus treatment compared to basal values. Moreover neither transaminasis and HCV-RNA showed differences. No correlation were found among studied parameters.
Conclusion: Once a day prolonged Tacrolimus treatment does not seem to have any impact on HCV IFN-γ specific response and viral load compared to twice a day tacrolimus treatment being safe on HCV recurrence as previously demonstrated for this old formulation. This evidence suggests that the prolonged release ensures not only the same immunosuppressive but also the same properties on immune system network in those having a HCV recurrence.

P-094 IMPACT OF ONCE-DAILY PROLONGED-RELEASE TACROLIMUS ON HCV-SPECIFIC IMMUNE RESPONSE OF PATIENTS UNDERWENT OLTx COMPARED TO TWICE A DAY TACROLIMUS TREATMENT

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Immunosuppressive drugs have important influence on metabolism and related morbidity. Twice a day tacrolimus treatment have been previously associated to some metabolic morbidity after liver transplant. Aim of the present study was to evaluate if switching from Tacrolimus twice a day to prolonged Realease Tacrolimus may determine a difference in metabolism of transplanted patients. 20 transplanted patients (20 male and 10 female) underwent OLTx within 1 year were switched from Tacrolimus twice a day to prolonged released tacrolimus. Blood samples were taken at the following time points: T0 (before switch), T1 (one month after switch) and every three months. Particularly Glucose, triglyceride and cholesterol and glycate haemoglobin were evaluated. All patients had a diagnosed diabetes receiving antidiabetic drugs or insulin treatment. Non Parametric tests were performed.
Results: 12 out 20 patients had a glucose and trygliceride plasma levels, to be statistically significant reduced after one months from switch ($p<.01$) as well as glycate haemoglobin levels ($p<.05$). 6 out 12 patients did not required any antidiabetic drugs 6 months after switch. Those patients under insulin treatment did not show any statistical significant reduction of their glucose levels within six months from switch. FK trough levels were found to be reduced in

the first month after switch ($p < .001$), while after two months no more differences were found.
Conclusion: Once a day prolonged Tacrolimus treatment seems to reduce glucose levels in those patients having diabetes after OLTx and being under oral anti diabetic drugs but not in those under insulin treatment compared to twice a day tacrolimus schedule.

P-095 ANTIBODY-BASED IMMUNOSUPPRESSIVE THERAPY AND IMMUNE RESPONSE TO DECEASED DONOR'S KIDNEY ALLOGRAFT: A SINGLE CENTRE EXPERIENCE

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Background: We aimed at evaluating the efficacy of antibody-based induction therapy in recipients of kidney from deceased donors.
Material/Methods: This study represents a retrospective analysis of induction therapy using biological agents (basiliximab or daclizumab) in firstly and re-transplanted patients (pts) after kidney Tx. A total of 353 consecutive renal Tx from deceased donors were analyzed. All 207 pts of study group underwent antibody-based induction therapy and 146 pts as control group underwent only maintenance immunosuppression. The proportion of highly sensitized pts and re-transplanted pts was significantly greater in the study group than in the control group (24/207 vs 7/146, $\chi 2$= 4.9414, $p<0.05$).
Results: Graft survival rate at 1 year using Kaplan-Meier method was 96.2% in study group and 87.5% in control group. Graft loss due to immunological reason during first year after Tx in pts receiving antibody-based induction therapy was significantly lower than in those pts under triple-drug therapy ($\chi 2$=8.9893, $p<0.05$). The number of pts with the incidence of acute rejection during first year was significantly lower in re-transplanted recipients with antibody-based induction therapy compared with re-transplanted without- induction therapy 6/26 (23%) vs 8/11 (72.7%), respectively, $\chi 2$=4.4295, $p<0.05$.
Conclusions: Our study revealed the efficacy of antibody-based induction immunosuppression on immune response to deceased kidney allograft in early period after Tx even on antibody-based induction therapy.

P-096 MANAGEMENT OF MODERATE TO SEVERE CHRONIC RENAL GRAFT DYSFUNCTION USING mTOR: LONG-TERM RESULTS

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The mTOR protein intervenes in the pathogenic mechanisms of the progression of chronic renal graft dysfunction (CGD); however we have no clinical studies of long-term in patients with moderate to severe dysfunction in our setting.
Methods: From May 2002 until April 2008, we did the conversion from calcineurin inhibitors to sirolimus in 43 patients with a renal biopsy consistent with interstitial fibrosis and tubular atrophy (IF/TA). 8 patients presented immune glomerulopathy (*ig*) associated with IF/TA. Immediately after conversion, the renal function got worse in all of them and the drug was discontinued. 71% of the others 35 presented no immune glomerular sclerosis (*eg*) over the fibrosis area and 57% out of 71% mononuclear inflammation *(egi),* too. Serum creatinine (SCr) and proteinuria/24 hs (Ptnuria) have been measured before the conversion (mean = 2.4±1.11 mg/dL; 0.956±0.78 g, respectively) and, afterwards, annually. Time observation ended in April 2009. Graft survival was represented graphically by Kaplan-Meier curves. Graft loss was estimated using the Cox model (confidence interval = 95%).
Results: 77% of the grafts have survived (range = 6.96 - 1.09 years; mean = 4.23±1.48), with stabilized renal function. HR for graft loss was: 1) Ptnuria >0.8 g/day = 2.56 (p=0.027); 2) SCr >2 mg/dL = 1.83 (p=0.014); 3) when Ptnuria >0.8 g/day was adjusted for (*eg*) = 2.68 (p=0.38); 4) when SCr >2 mg/dL was adjusted for (*eg*) = 2.76 (p = 0.38); 5) when Ptnuria >0,8 g/24hs was adjusted for (*egi*) = 2.83 (p=0.018); 6) and when SCr >2 mg/dL was adjusted for (*egi*) = 1.84 (p=0.024).
Conclusion: The findings of our study confirm that sirolimus can control the progression of moderate to severe CGD.

P-097 PHARMACOKINETICS OF EVEROLIMUS WHEN COMBINED WITH TACROLIMUS IN DE NOVO RENAL TRANSPLANT RECIPIENTS

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Background: The recommended starting dose for everolimus (0.75mg bid) when combined with ciclosporin accounts for the known ciclosporin-induced 2-3-fold increase in everolimus exposure. Subsequent clinical trials assess the use of everolimus with tacrolimus; however, pharmacokinetic information about this combination is sparse.
Methods: The 12-month (M), multicenter ASSET study randomized 228 de novo kidney transplant recipients to receive everolimus, corticosteroids, basiliximab, and either *[Group A]* very-low-exposure tacrolimus (n=109; tacrolimus C0 4-7ng/ml M0-3]and 1.5-3ng/ml M4-12 or *[Group B]* low-exposure tacrolimus (n=119; C0 4-7ng/ml M0-12). Everolimus and tacrolimus C0s were collected at each study visit in all patients; AUC-profiles were collected in a pharmacokinetic substudy at D5 and M1, 3, 12 (N=46).
Results: Tacrolimus C0 was similar in both groups through M3. From M4-12, C0 diverged with an average at M12 of 3.4±1.4 versus 5.5±2.0 ng/ml in groups A versus B. Everolimus dosing started at 1.5mg bid yielding C0 of 3.2±1.9ng/ml. Doses were subsequently increased to 2.2±1.0mg bid from M1-3 yielding C0 of 5.5±2.5ng/ml. In M4-12 there was a slight decrease in dose to 1.7±0.7mg bid without notable C0 change.
In the pharmacokinetic substudy, everolimus C0, Cmax and AUC significantly increased between D5 and M1, plateaued between M1 and 3, and slightly decreased by M12 (Table 1), consistent with the dosing pattern in the full population. C0 was significantly correlated with AUC (slope=12.6; r=0.84; $p<0.001$) similar to the known everolimus/ciclosporin correlation (slope=12.9, r=0.86).

Table 1. Everolimus PK parameters for combined groups A and B

Parameter	Day 5	Month 1	Month 3	Month 12
C0 (ng/mL)	3.8±3.6	5.4±2.6	6.1±2.9	4.6±1.6
Dose (mg bid)	1.5±0.1	2.5±1.4	2.3±1.2	1.9±0.7
Cmax (ng/ml)	14.7±6.0	22.5±12.2	21.2±10.5	15.0±8.2
AUC (ng·h/ml)	69±35	104±43	113±47	83±33

Conclusion: (1) Everolimus doses were 2-3-fold higher in the everolimus/tacrolimus combination than doses known from the everolimus/ciclosporin combination, suggesting no interaction of tacrolimus on everolimus. (2) Use of low-exposure or very-low-exposure tacrolimus did not differentially affect everolimus pharmacokinetics. (3) Tacrolimus did not alter the everolimus C0 and AUC correlation, thereby preserving the basis for everolimus therapeutic drug monitoring.

P-098 DEVELOPMENT OF ANTI-HLA ANTIBODIES AFTER CONVERSION TO AN mTOR INHIBITOR IN STABLE RENAL TRANSPLANT PATIENTS

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Background: New development of anti-HLA antibodies after transplantation, especially donor-specific (DSA) has been related to late appearance of chronic humoral rejection. Conversion to an mTOR-inhibitor with complete calcineurin-inhibitor elimination has been proppossed to avoid long-term nephrotoxicity, but some concerns have recently arised on the risk of underimmunosuppression and increased immunological risk.
Methods/Materials: 185 RT-patients converted to an mTORi in stable phase (after 3-mo post-tx) were retrospectively tested for the early development of anti-HLA antibodies using frozen sera collected immediatly pre-conversion and 3-6 months later. 370 sera have been analized using the ELISA technique. The study is ongoing and the single-antigen analysis (LUMINEX) in order to precissely determine the presence of DSA is planed to be performed and results presented in the congress. Patients were clasified in four groups according to their HLA-ab status for class-I and class-II antibodies: Neg/Neg (before and after), Pos/Neg, Pos/Pos and Neg/Pos (this subgroup suppossed to represent newly developped ab). We evaluated evolution of graft function in the Neg/Pos subgroup.
Results: Seventeen patients without HLA-ab prior to conversion developed HLA-ab (13 class-I, 3 class-II and 1 class-I&II). Class-I and Class-II status of HLA-ab before and after conversion is presented in table 1.
In the subgroup of 17 Neg/Pos patients eigth patients maintain stable renal

Distribution of patients

	Class I	Class II	Any
Neg/Neg	149/185 (80.5%)	166/185 (89.7%)	141/185 (76.2%)
Pos/Neg	7/185 (3.8%)	5/185 (2.7%)	10/185 (5.4%)
Pos/Pos	15/185 (8.1%)	10/185 (5.4%)	17/185 (9.2%)
Neg/Pos	14/185 (7.6%)	4/185 (2.2%)	17/185 (9.2%)

Neg: absence of HLA-ab; Pos: presence of HLA-ab; Any: class-I or class-II ab.

function after mean follow-up of 52-months, 2 patients died with a functioning kidney (neoplasm) and 7 patients lost their graft at 1,2,10,13,16,19 and 64-months post-conversion.
Conclusion: About 9% of patients converted to an mTORi develop anti-HLA antibodies in the first months post-conversion, most of them class-I alone (it remains to demonstrate whether they are DSA). This can be followed by graft damage. Early appearance of de novo HLA-ab should be chequed in the first months after mTORi conversion.

P-099 USEFULNES AND SAFETY OF mTOR IN LIVER TRASPLANTATION

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The mTOR are a new immunosuppressive drugs used in organ transplantation. They could be promising drug because of its potential antitumor effect and the absence of nephrotoxicity. Their most common indications are renal dysfunction in calcineurin inhibitor (CNI) treated patients and tumors.
Objective: To analyze the indication, security and effectiveness of mTOR in a group of liver transplant patients.
Methods: We retrospectively identified patients who were treated with mTOR, and we review in their Charts the indication of liver transplantation, the immunosuppressive treatment, the occurrence of acute rejection and the kidney function before and after the mTOR treatment.
Results: We identified 43 (19.02%) patient on mTOR treatment; 35 men (81.4%) and 8 women (18.6%), with average age of 56.7 (rank 44-68). In a 30% of the patients, the drug was introduced by renal dysfunction, in 23% by recurrence of hepatocellular carcinoma (HCC) or high risk of HCC recurrence in the explanted liver; in 23% by "de novo" tumor, in 14% by neurotoxicity and in 10% by colangiocarcinoma. The IS regime before to introduce mTOR was Tacrolimus (44%); 39% Tacrolimus and Micofenolate-Mofetil (MMF), 12% Neoral and MMF and 5% Neoral. The time average to introduce mTOR was 6.4 months (range 1- 46meses). The ending IS regime was mTOR isolated 73% of the patients, 23% mTOR and CNI and 4% mTOR and MMF. The creatinine and urea level average were significantly smaller after the conversion to mTOR ($p < 0,05$). The acute rejection rate was 6.9% and there wasn't lost of the liver graft.
Conclusions: mTOR are a new effectives and safe immunosuppressive drugs in liver transplant patients. They are very effective to control the renal dysfunction. Other indications are neurotoxicity, "de novo" neoplasm and HCC recurrence. More prospective studies are needed to clarify their effectiveness in the long term.

P-100 EVEROLIMUS AS PRIMARY IMMUNOSUPPRESSION IN KIDNEY TRANSPLANTATION: EXPERIENCE IN CONVERSION FROM CALCINEURIN INHIBITORS

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Background: We analyzed clinical experience with everolimus and identified prognostic factors for a successful conversion in a large and uniform cohort of renal transplant patients.
Methods: We performed a retrospective study of 220 kidney recipients consecutively converted to everolimus after elimination of calcineurin inhibitors. We reviewed demographic data, analytical data, and concomitant treatment. We studied risk factors for proteinuria at 1 year after conversion, loss of renal function, and graft survival.
Results: Baseline GFR was 52.4 (17.8= ml/min compared with 53.4 (20.1) mL/min at 1 year after conversion (p=0.150). Median proteinuria increased from 304 mg/d (IQR, 160-507) to 458 mg/d (IQR, 238-892; $p<0.001$). Risk factors for the development of proteinuria >= 900 mg/d (P75) at 1 year after conversion were age (OR, 0.97; 95%CI, 0.93-1.00), GFR <60 mL/min (OR, 3.37; 95%CI, 1.15-9.89), serum triglycerides >=150 mg/d (OR, 4.35; 95%CI, 1.70-11.17), no treatment with prednisone (OR, 3.04; 95%CI, 1.22-7.59), baseline proteinuria >=550 mg/d (OR, 10.37; 95%CI, 3.99-26.99), and conversion >=35 months after transplant (OR, 5.77; 95%CI, 1.89-17.59). An interaction was observed between baseline proteinuria and time to conversion after transplant: in patients with baseline proteinuria >=550 mg/d, the risk of developing proteinuria >=900 mg/d at 1 year after treatment with everolimus was 77.1% if they were converted after >=35 months post-transplant. However this risk was 29.8% in the subgroup converted before (p=0.02). Actuarial graft survival at 1and 4 years post-conversion was 98.2%, and 86.5%. Baseline proteinuria >=550 mg/d was a risk factor for graft lost in patients converted after the 35th month but not in patients converted before this time.
Conclusions: Conversion to everolimus and elimination of calcineurin inhibitors is safe. Success depends on not making late conversions and not converting patients with high baseline proteinuria.

P-101 DIFFERENTIAL EFFECTS OF CALCINEURIN INHIBITORS ON ARTERIAL FUNCTION

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Background: Cardiovascular complications are the leading cause of death and one of the leading causes of graft failure in renal transplant recipients. Calcineurin inhibitors induce an acceleration of atherosclerotic processes in the arterial wall. There are conflicting data whether cyclosporine (CsA) and tacrolimus (Tac) differ in their deleterious effects on arterial stiffening. The present study combines several measurement techniques in order to provide a global and reliable assessment of the differential effects of calcineurin inhibitors on the gold-standard parameters of arterial function.
Methods: Pulse wave analysis was performed by the SphygmoCor (AtCor®), HEM-9000AI (Omron®), and CR-2000 device (Hypertension Diagnostics®) in 56 stable renal transplant recipients (29 CsA, 27 Tac).
Results: Groups were homogeneous for age, gender, body mass index, time on dialysis prior to transplantation, and graft function. Whereas systolic and diastolic blood pressure, central aortic blood pressure, cardiac index, large and small artery compliance (C_1 and C_2), and pulse wave velocity did not significantly differ between CsA and Tac, augmentation index (AI_{75}) was significantly lower in patients treated with Tac. This finding was consistent as assessed by two different measurement systems ($p<0.05$).
Conclusion: Compared to CsA, Tac has a favorable impact on augmentation index, a strong independent predictor for cardiovascular mortality.

P-102 PREDICTABLE PHARMACOKINETICS (PK), PHARMACODYNAMICS (PD), AND EXPOSURE-RESPONSE (E-R) OF BELATACEPT AVOID THE NEED OF THERAPEUTIC DRUG MONITORING (TDM)

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Background: TDM of calcineurin inhibitors is standard clinical practice due to their narrow therapeutic index with respect to nephrotoxicity, risk of drug-drug interactions (DDI), and high exposure variability. Belatacept (LEA29Y), a first-in-class biologic designed for co-stimulation blockade, is being developed for primary maintenance of immunosuppression in de novo renal transplant recipients (RTR). An assessment of TDM requirements of belatacept in RTR is reported.
Methods/Materials: Belatacept PK was characterized in healthy subjects and RTR. Covariates and exposure variability were evaluated in population PK analyses. PD of belatacept was assessed using CD86 receptor occupancy in Phase 2 (P2) trial data. E-R analyses were conducted with P2 and Phase 3 (P3) trial data.
Results: Belatacept PK is linear and exposure is dose proportional with low day-to-day variability (overall mean CV% [range]: C_{max}, 15% [14–16%]; C_{avg}, 23% [14–27%]; and C_{min}, 47% [19–57%]). Gender, race, age, renal function, serum albumin, diabetes, and dialysis do not affect exposure. C_{min} was maintained $\geq$ 5 years post-transplantation. Belatacept has minimum DDI involving CYP enzymes and binds CD86 in a predictable, concentration-dependent manner: Day 5: 94% Month 12: 65% as C_{min} decreased from ~35 to 4 μg/mL. Target C_{min} was achieved in >75% of patients in P3 trials. Time-to-event E-R analysis in P3 trials found no definitive exposure and acute rejection relationship but did suggest exposures using a less intensive regimen (LI) are associated with lower serious infection rates vs a more intensive regimen,[1] suggesting TDM is unlikely to improve the more favorable clinical profile of LI.
Conclusions: Predictable PK, PD, and E-R of belatacept avert the need of TDM for the LI regimen.
Reference:
1. Grinyo J, Charpentier B, Pestana JM, et al. *Transplantation*. 2010;90:1521-1527.

P-103 RATIONALE FOR BELATACEPT LESS-INTENSIVE (LI) REGIMEN IN RENAL TRANSPLANT RECIPIENTS

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Background: Belatacept (LEA29Y), an intravenous biologic, is a first-in-class co-stimulation blocker being developed for primary maintenance of immunosuppression in de novo renal transplant recipients (RTR). We report an assessment of preclinical/clinical data supporting the belatacept LI regimen recommendation.
Methods/Materials: Target trough concentrations (C_{min}) identified via mixed lymphocyte reaction (MLR) assay and primate transplant model (PTM). Modeling and simulation guided construction of LI and more-intensive regimen (MI) to achieve target C_{min}. LI and MI were tested in a Phase 2 trial (P2) and 2 Phase 3 trials (P3). Integrated efficacy/safety and exposure-response (E-R) analyses were conducted to select the recommended regimen.
Results: 10 mg/mL belatacept maximally inhibited alloresponse in MLR. PTM suggested C_{min} 3–30 μg/mL and up to 1.5 μg/mL to maintain efficacy during initial and maintenance phases, respectively. LI/MI were constructed to achieve different durations of target C_{min} of 20, 5, and 2 μg/mL, and then tested in the P2. Both regimens achieved target C_{min}, except LI Day 14 ($<$20 μg/mL). Numerically higher subclinical acute rejections (AR) were noted with LI. MI and LI (refined Day-5 dosing) were selected for the P3. Patient/graft survival, AR, and renal function preservation were similar for LI and MI; however, there were fewer deaths, malignancies, serious infections, and central nervous system infections with LI. There was no definitive relationship between exposure $\leq$1 year and AR in P3, supporting the lack of additional efficacy with MI vs LI, but did suggest that an average belatacept concentration in the lower 2 tertiles over the first 6 months post-transplantation resulted in fewer serious infections, consistent with P2/P3 results where LI was associated with a more favorable safety profile.
Conclusions: Integrated efficacy, safety, and E-R analyses support the belatacept LI regimen as the recommended regimen in RTR.

P-104 COMPARISON OF THE SIDE EFFECTS OF *DE NOVO* MPAs IN FIRST 3 MONTHS AFTER KIDNEY TRANSPLANTATION: SINGLE CENTER EXPERIENCE

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Mycophenolates (MPA) are the most frequently used immunosuppressive drugs in solid organ transplantation.
Aim: To assess and compare adverse effects of MMF and EC-MPS in first 3 months after transplantation.
Material and Methods: Data collected from patients who received kidney years between 2006-2011 in Gazi University Transplantation Center, Ankara.Totally 100 kidney transplantations were performed.There were 68 *de novo* MMF (group A), and 32 EC-MPS (group B) patients in each group. In group A, mean age was 32,7$\pm$14,3 years old. Twenty nine of the recipients were female and 39 of were male.Transplantations were performed from deceased donor in 32 and from living donor in 36. In group B, mean age was 27,3$\pm$13,2 years old. Fourteen of recipients were female and 18 were male.Transplantations were performed from deceased donor in 19 and from living donor in 13. Immunosuppressive protocol consists of calsineurin based triple regimen.
Results: In group A, we have not seen any side effect of MMF in 49%(n=33) recipients during postoperative first 3 months. Fifty one percent of recipients had following side effects; gastrointestinal 26%, bone marrow 20% and hepatotoxicity 15%. Majority of the GISE is diarrhea (n=16), and dyspepsia (n=2), vomiting (n=2) follows. Majority of BMSE are leukopenia (n=13), and pansitopenia (n=2), anemia (n=1) follows. In groupB, we have not seen any side effect of EC-MPS in 44%(n=14) recipients postoperative first 3 months. Fifty six of recipients had following side effects; bone marrow 26%, gastrointestinal 26% and hepatotoxicity 4%. Majority of the GISE is diarrhea (n=6) and dyspepsia (n=2), floating (n=1). Majority of BMSE is leukopenia (n=8), and pansitopenia (n=1) follows.We have not seen any statistical differences between two groups concerning side effects ($p>0,5$) within 3 months after transplantation.
Conclusion: EC-MPS and MMF demonstrated therapeutic equivalence in *de novo* renal transplant patients. EC-MPS may have less hepatotoxicity, and better GI tolerant.

P-105 EFFECT OF EARLY CONVERSION FROM CALCINEURIN INHIBITORS TO EVEROLIMUS ON RENAL FUNCTION AND MARKERS OF CARDIOVASCULAR DISEASE: DESIGN OF THE ELEVATE STUDY

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Purpose: Chronic calcineurin inhibitor (CNI) toxicity contributes to chronic allograft dysfunction and cardiovascular disease in renal transplant (RTx) recipients. Conversion from CNI to an everolimus/mycophenolic acid (MPA)-based regimen at 4.5 months post-RTx demonstrated improvement in renal function up to 12 months. The effect of an early switch (10-14 weeks post-RTx) to an everolimus/MPA-based CNI-elimination regimen on renal function and cardiovascular parameters is investigated in the ELEVATE study - a multicenter, open label, randomized, controlled, parallel-group trial.
Methods: The primary endpoint of the 24-month-study is renal function (estimated glomerular filtration rate [eGFR]; MDRD4) at Month 12. Cardiovascular parameters are a major study focus: improvement of left ventricular hypertrophy is assessed by left ventricular mass index and the change in pulse wave velocity is measured. In addition efficacy (composite efficacy failure defined as biopsy-proven acute rejection $\geq$IB, graft loss, death or loss to follow-up at Month 12) and safety are assessed. RTx recipients (primary/secondary RTx from deceased or living donors), 10-14 weeks after RTx, are stratified by renal function and previous cardiovascular events and randomized to proceed on standard CNIs (tacrolimus or CsA; b.i.d) and EC-MPA versus everolimus (6-10 ng/mL; b.i.d) and EC-MPA (0.72-1.44g/day; b.i.d). In the CNI to everolimus conversion arm, CNI elimination is carried out either overnight or stepwise over one week. A total of 676 patients will be randomized worldwide. Currently the study is recruiting patients and 12-month results are expected in 2014.
Conclusion: Reducing cardiovascular disease is an unmet need in recipients of kidney allografts. The ELEVATE study investigates potential cardiovascular benefits of an early conversion from CNIs to everolimus in a large cohort of de novo RTx recipients.

P-106 TACROLIMUS SIDE EFFECTS AFTER LIVER TRANSPLANTATION: IS THERE A DIFFERENCE BETWEEN ONCE DAILY AND TWICE DAILY FORMULATION?

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Background: The idol immunosuppression has an uncomplicated therapy scheme with maximal safety and minimal side effects. For this reason we analysed the once daily formulation of tacrolimus compared to the twice daily formulation in terms of side effects and rejections in patients at least 6 months after liver transplantation.
Methods: This prospective observational single centre trial was performed between August 2008 and July 2010. All patients who underwent liver transplantation for any indication in the University Medical Centre Mainz meeting the inclusion criteria were included after informed consent. Patients should be aged over 18 years, in outpatient care of the University Medical Centre and under current immunosuppressive therapy with tacrolimus in the twice daily formulation. Data was collected 6 months under treatment with tacrolimus in twice daily formulation. Then immunosuppression was changed to tacrolimus in once daily formulation, data was again collected for 6 months.
Results: 61 Patients were included. The following parameters were comparable in both groups: Rates of diabetes (18 on treatment with tacrolimus in twice daily formulation vs. 19, p= 1.0), hypercholesterolemia (8 vs. 9, p= 1.0) and hypertension (27 vs. 27, p= 1.0), creatinine (p=0.556), creatinine clearance (p=0.853), cholesterol (p=0.797), HDL (p=0.419), LDL (p=0.302), glucose (p=0.656), uric acid (p=0.818), BMI (p=0.068). Under treatment with tacrolimus in once daily formulation target whole-blood trough levels were significantly lower (p=0.000) and glycated hemoglobin was elevated (p=0.001). There was only one rejection under treatment with tacrolimus in a twice daily formulation (p=1.0).
Conclusions: Immunosuppression with a once daily formulation of tacrolimus is simplified and safe with comparable rejection rates. Due to elevated glycated hemoglobin in spite of equal glucose and lowered target whole-blood trough level we recommend further investigations concerning galenics and glucose metabolism.

P-107 SPECIALIST PHARMACIST ROLE IN HIV-POSITIVE RENAL TRANSPLANTATION

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Introduction: Kidney transplantation in HIV-positive recipients has similar short-term outcomes to those without HIV providing optimal immunosuppression dosing and potential interactions, notably between protease and calcineurin inhibitors, are determined pre-transplantation.
To date, GSTFT transplant unit has performed 14 kidney transplants in HIV positive recipients. We describe our multidisciplinary approach.
Method: All HIV-positive patients are referred to renal pharmacists for medication review before entry onto the transplant waiting list. A drug history is taken and literature reviewed for any known interactions.
An individualised protocol is created detailing immunosuppressant doses, expected interactions, monitoring requirements and dose adjustment advice for antiretrovirals as renal function changes.
All patients on protease inhibitors have ciclosporin profiling performed prior to transplantation. They are started on 10mg BD of liquid formulation (100mg/ml), issued with 1ml oral syringes, educated on using them and advised not to dilute the solution. Ciclosporin levels are measured every 2-3 days with dose adjustment in 5-10mg increments until serum levels are therapeutic (200-300mcg/l). Once within range, ciclosporin dosing is stopped.
Results: We have produced 25 protocols which are updated as new information becomes available.
Fourteen patients have been transplanted successfully. Of the 8 patients profiled on protease inhibition, 2 had successful transplants with appropriate ciclosporin levels achieved during the first week. The range of ciclosporin doses required to achieve a serum level of 200-300mcg/l was 10-35mg BD with no correlation between weight and required dose. The average period of pre-transplant profiling was 2 weeks.
Conclusion: For successful management of HIV-positive transplant recipients, a multidisciplinary approach is mandatory with need for careful interaction screening of all new treatment regimens and heightened clinical vigilance for unexpected toxicities.
Our experience demonstrates the importance of the renal pharmacist as part of the team caring for this uniquely challenging group of patients.

P-108 IMMUNOSUPPRESSION IN HCV-RNA POSITIVE LIVER TRANSPLANT RECIPIENTS

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Influence of immunosuppression (IS) on posttransplant outcome in HCVRNA – positive recipients is still remains speculatiable. No more than one third of transplant centers have special IS protocol for recipients with HCV-infection.Since Feb.2006 we had made 23 LT to 20 HCV-RNA positive patients. 30% of patients died in the first year after LT.1st month IS of 16 recipients included baziliximab/daclizumab induction and was based on tacrolimus (Tac) in 16 recipients.1 recipient had got prolonged form of tacrolimus (Adv). 2 recipients had started with cyclosporine (Cs). In 15 cases we had complement IS with micofenolate mofethyl (MMF). Steroid-free pattern was performed in 15 cases. 2 of 4 recipients who had got steroids participated in clinical trial and it was mandatory term of protocol, two others - had started with Cs and fear of allograft rejection we gave them steroids. Interestingly, but in 5 recipients with 1 B genotype HCV had severe HCV recurrence in early post transplant period.Two of them had Cs+ corticosteroids IS and in three cases IS was steroid free+Tac. In four of these recipients we suspected acute allograft rejection and in spite low RAI (3-6 points) and hi viral load we performed 1 -3 times 3 day pulse – therapy of Metilprednisone and of course get no positive effect in patients status & Lab. data. Only one patient had no any signs of allograft rejection (RAI – 2 points), and that is why she passed such "hard corticosteroid way". Histological assessment also demonstrated fast speed of fibrosis progression (METAVIR F – 0 – 2 – 3) in recipients with 1 B genotype HCV and history of corticosteroids pulse – therapy.In conclusion, our experience confirm that use of corticosteroid boluses has negative influence on graft survival and patient outcome.

P-109 PHARMACOKINETICS AND CLINICAL OUTCOMES OF DE NOVO RENAL TRANSPLANTATION WITH ONCE-DAILY TACROLIMUS EXTENDED RELEASE (TER)

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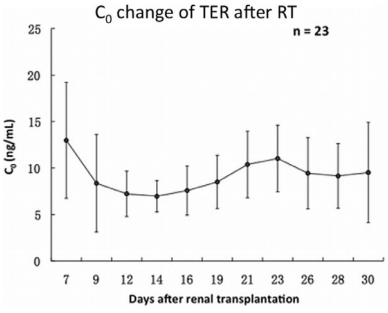
Purpose: Once-daily extended-release formulation of tacroloimus (TER) has been introduced in renal transplantation (RT) lately. We studied precise pharmacokinetics (PK) of TER and clinical outcomes (COs) in de novo RT in Japanese population.
Methods: Twenty-three de novo RT using TER were analyzed by PK and COs. All patients received TER (0.2mg/kg), corticosteroids, mycofenolate mofetil and basiliximab. Pharmacokinetic study was performed by blood sampling at 0, 0.5, 1, 2, 3, 4, 6, 8, 12, 18 hours after TER administration, and were done before and 7, 14, 28 days (D) and 3, 6, and 12 months (M) after RT. COs were evaluated by patient and graft survival, graft function and adverse effects. Biopsy-proven acute rejection (BPAR) and CMV infection were also monitored.
Results: Fourteen recipients were male. Nineteen received kidney from living donor, and four from deceased donor. The mean dose of TER was 0.20 (0.11-0.33) mg/kg to achieve target blood levels according to our protocol. The mean serum creatinine was 3.2mg/dl, 1.75mg/dl and 1.58mg/dl at 7 days, 1 and 3 months after transplant respectively. The average tacrolimus blood trough level (C0) and AUC0-24 were 13.0 ng/ml/407.0 ng/ml hr (D7), 7.0/319.2 (D14), 10.4/403.2 (D21), 9.15/275.9 (D28), 9.13/227.9 (M2), 6.4/223.1 (M3), 7.0/229.0 (M6), 6.0/274.0 (M12), respectively.

Pharmacokinetics of TER in de novo RT

Post op	C0 (ng/ml)	AUC0-24 (ng/ml hr)
Day 7	13.0	407.0
Day 14	7.0	319.2
Day 21	10.4	403.2
Day 28	9.15	275.9
2 month	9.13	227.9
3 month	6.4	223.1
6 month	7.0	229.0
12 month	6.0	274.0
18 month	4.9	

Correlation between C0 and AUC0-24 was excellent (r2=0.81). Dose adjusted blood level of tacrolimus tended to be lower between D12 and D19.



After one month, PK of TER reached stable state. Both patient and graft survival were 100%. We experienced one (4.4%) BPAR (Banff 1A) and 5 (21.7%) borderline changes, but fourteen patients (60.9%) found positive CMV antigenemia during 2-6 weeks after transplant. No severe adverse effects were observed.
Conclusion: We can achieve safe and good RT with TER by appropriate PK monitoring. Some particular pharmacokinetic attention is necessary to pay during 2-3 weeks post de novo RT.

Pre-clinical immunosuppression

P-110 EFFECT OF CYCLOSPORINE A ADMINISTRATION IN PREGNANT RATS ON BLOOD PRESSURE IN THEIR OFFSPRING

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Background: Successful kidney transplantation allows women with chronic

kidney disease stage 5 to get pregnant. The immunosuppressive therapy may influence fetal and postnatal development in the offspring i.e. may cause the hypertension in adulthood. The aim of the study was to assess the effects of exposure to cyclosporine A (CsA) during gestation on blood pressure in the rat's offspring.
Methods/material: Eight pregnant Sprague-Dawley rats were assigned into two groups. In the first group (n=4) CsA (a dose 3 mg/kg/day) were administered. In the second group (n=4) only the corresponding volume of solvent (0.9% NaCl 1 ml/kg/day) were given. The substances were administered from the 10th day after the fertilization till the 7th day after the delivery, subcutaneously, once a day. At 7 and 11 weeks of age in the offspring of both groups (n=65) blood pressure was measured indirectly on tail artery. At the end of experiment (12 weeks of age) both albuminuria and plasma creatinine concentration were measured. Statistical analysis was performed using Student's t-test.
Results: At 7 and 11 weeks of age systolic (SBP) and diastolic blood pressure (DBP) in the offspring of the females treated with CsA during gestation (n=34) was higher compared to the offspring of those treated only with solvent (n=31) (7th week - SBP: 125±5 vs. 117±6 mmHg, $p<0.001$; DBP: 82±6 vs. 77±6 mmHg $p<0.001$; 11th week - SBP: 132±9 vs. 126±7 mmHg, $p<0.05$; DBP: 89±8 vs. 83±7 mmHg, $p<0.001$).
Conclusion: The results suggest that treatment with CsA during pregnancy can lead to hypertension in the offspring.

P-111 BELATACEPT 6-MONTH INTRAVENOUS TOXICITY STUDY IN MONKEYS

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Background: The selective mechanism of action of belatacept (LEA29Y), a CD28 co-stimulation blocker for kidney transplantation, is intended to avoid calcineurin inhibitor nephrotoxicities. This study characterized the toxicokinetic/toxicity profile, including lack of nephrotoxicity of belatacept, in monkeys.
Methods/Materials: Four groups of 5 cynomolgus monkeys/sex received intravenous belatacept doses of 0 (saline control), 10, 22, or 50 mg/kg once/week for 6 months. Necropsies were conducted on 3 monkeys/sex/group following 6 months of treatment, while 2 monkeys/sex/group were retained for a 3-month dose-free recovery period, during which the T-cell-dependent antibody response (TDAR) to keyhole limpet hemocyanin was assessed. Criteria for evaluation included clinical observations, electrocardiograms, clinical and anatomical pathology, and immunologic assessments.
Results: Belatacept was not associated with any drug-related toxicity. Specifically, there was no evidence of nephrotoxicity (normal blood urea nitrogen, serum creatinine levels, and renal pathology), infections, or hyperplastic, preneoplastic, or neoplastic changes in the peripheral blood cells or lymphoid tissues of any monkey. Reversible pharmacologic effects observed consisted of minimal decreases in serum immunoglobulin (Ig) G (no effect on IgM/IgA) levels and minimal/moderate decreases in the diameter and number of lymphoid germinal centers. Functional activity (TDAR) of the immune system was demonstrated after a 2-month recovery period. Exposure to belatacept was dose proportional and was 20-fold higher than exposures observed during the maintenance phase in Phase 3 (P3) trials.
Conclusions: Belatacept up to 50 mg/kg (20x exposure of that in clinical trials) is well tolerated in monkeys over 6 months. No evidence of neoplasia, infections, autoimmunity, or target organ toxicity, including nephrotoxicity, was observed. Absence of nephrotoxicity supports P3 clinical trial results that show steady improvement in renal function in belatacept patients over 3 years post-transplant. Drug-related changes were predictable and reversible. Functional recovery of the immune system was noted at all doses.

P-112 ANTI-CLASS II HUMANIZED ANTIBODY, IMMU-114 SUCCESSFULLY SUPPRESSES ALLOGENEIC IMMUNE RESPONSE

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Background: In this study, we evaluated the immunosuppressive effect of anti-Class II-DR humanized monoclonal antibody, IMMU-114 in the allogeneic mixed lymphocyte reaction (MLR).
Methods: Human peripheral blood mononuclear cells (PBMCs) were isolated from healthy volunteers. 1) PBMCs (1×10^6 cells) (n=5) were cultured for 7 days in the presence of IMMU-114 (Immunomedics, Inc., Morris Plains, New Jersey, USA) or control antibody (Control). Phenotype of PBMCs was analyzed on days 1, 3, and 7 of culture by flow cytometry. 2) Responder PBMCs (1×10^6 cells) (n=8) were co-cultured with irradiated (30 Gy) stimulator PBMCs (1×10^6 cells) (n=8) for 6 days. ^{3}H-thymidine incorporation assay was performed on day 7. 3) Phenotype of responder PBMCs, prepared in experiment #2 was analyzed on day 7 of culture by flow cytemetry. Control antibody and IMMU-114 were used at the concentration of 10 nM in all the experiments.
Results: 1) There were no significant changes in CD3-, CD4-, and CD8-positive T cells, on days 1, 3, and 7. Class II -DR-positive cells on days 1, 3, and 7 were 4.3%, 6.5%, and 2.2% in IMMU-114, and 24.1%, 38.27, and 42.3% in Control, respectively. CD19-positive cells on days 1, 3, and 7 were 1.85%, 1.08, and 1.16% in IMMU-114, and 4.1%, 3.0%, and 3.6% in Control. CD16/56-positive cells were 12.3%, 16.4%, and 7.8% in IMMU-114, and 19.4%, 19.4%, and 19.0% in Control, respectively. 2) Thymidine incorporation rates at 1:1 responder/stimulator ratio were 2254.5±118.1 cpm in IMMU-114, and 22080.7±602.4 cpm in Control, respectively ($P<0.01$). 3) In responder PBMCs, CD3/CD25-positive, activated T cells were 4.6% in IMMU-114, and 7.3% in Control, respectively ($P<0.05$).
Conclusion: IMMU-114 successfully depleted Class II -DR-positive cells from PBMCs, and suppressed proliferation of lymphocytes in the human allogeneic MLR test.

P-113 THE REVERSIBLE REDUCTION OF β-CELL ADAPTABILITY INDUCED BY mTOR INHIBITION IN AN EXPERIMENTAL RAT MODEL

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Recent studies observed an association of Sirolimus (SRL) treatment with new-onset diabetes mellitus after transplantation.
The aim of this study is to determine the effect of SRL on the development of insulin resistance in an experimental rat model.
Zucker lean: (ZL) and *Zucker fatty* (ZO) rats at 6 weeks were distributed randomly into 2 groups, vehicle, SRL (1.0mg/Kg), treated during 12 days. Glucose tolerance test (GTT) and insulin resistance test (IRT) were evaluated at day 0, 12 and 26. The pancreas was collected to perform histological measurements at 12 or 26 days. The proliferation and apoptosis assays were performed by immunofluorescence using Ki67 and TUNEL stain respectively. Langerhans islets were isolated to analyze total insulin content, insulin secretion and gene expression.
Only ZO rats treated with SRL presented a worse GTT, since these animals had problems to reduce the glucose injected at day 12, showing a higher area under the curve (AUC). After withdrawal of the drug, the GTT and IRT were normalized at day 26. Moreover the pancreas weight (PW) was impaired by SRL treatment both in ZL and ZO rats. The ZO rats presented an enlarged islet area compared to ZL group. SRL treatment blocked the proliferation in islets of ZL and ZO rats, and apoptosis was not increased. The insulin content in ZL and ZO was reduced by SRL treatment while insulin secretion was only no affected. Langerhans islets from ZO+SRL rats presented a downregulation of NeuroD1, Pax4, and Insulin-2 genes, while genes related with secretion were no affected.
In conditions that require an adaptive β-cell proliferation the administration of SRL might reveal harmful effects, through the blockade of β-cell proliferation and insulin production but no insulin secretion. These effects disappear when removing the therapy.

P-114 ATG-Fresenius INHIBITS EBV INFECTION OF HUMAN B-CELLS *IN VITRO*

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Background: Post-transplant lymphoproliferative disorder (PTLD) is a severe complication of transplantation and results from uncontrolled proliferation of B-lymphocytes infected with Epstein-Barr virus (EBV). Infection of B-lymphocytes mainly occurs via binding of the viral glycoprotein gp350 to the B-cell surface molecule CD21.
ATG-Fresenius is a polyclonal immunoglobulin derived from the serum of rabbits immunized with Jurkat cells, a human T-lymphoblast cell line. This study sought to investigate whether ATG-Fresenius can impede EBV infection of human B-lymphocytes *in vitro*.
Methods/Materials: B-lymphocytes were isolated from peripheral blood from five donors and were infected with a green-fluorescent protein (GFP)-expressing, recombinant EBV virus stock (EBV-2089) at a multiplicity of infection (MOI) of 0.02. Prior to infection, cells were pre-incubated with different concentrations of ATG-Fresenius (10, 50, 100, 500 and 1000 micrograms/ml) for 30 min at 37°C. Infected B-cells were quantified by flow cytometry three days after infection.
Furthermore, Jurkat T-cells were examined for CD21 mRNA expression by cRNA Microarray and for CD21 surface expression by flow cytometry.

Results: In 5/5 independent experiments ATG-Fresenius dose-dependently inhibited EBV infection of human B-cells. At ATG-Fresenius concentrations of 100, 500 and 1000 micrograms/ml the observed effect was statistically significant and at 500 and 1000 micrograms/ml it was comparable to the inhibitory effect of a monoclonal anti-CD21 antibody and of a monoclonal anti-gp350 antibody. A pre-immunization rabbit control serum did not exert any inhibitory effect.
Analysis of CD21 expression in Jurkat T-cells demonstrated presence of CD21 mRNA and cell surface protein.
Conclusion: These *in vitro* results indicate that ATG-Fresenius may protect B-cells from primary EBV infection after transplantation.

Histocompatibility

P-115 GENETICS DETERMINES LONG OR SHORT-TERM KIDNEY SURVIVAL. RARE CLASS I HLA ALLELES FOUND BY SEQUENCE BASED TYPING

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Short or long-term survival of renal graft is still a mystery. HLA matching effect and antibodies not always explain graft outcome. Current molecular typing is better than serology. Old immunosuppressant schemes were also less effective. Even so, many patients have good graft function after 15-20years.
To understand HLA role at SBT level on long-term renal-graft survival, we called patients transplanted >15 years.
159 patients with renal graft long-term survival >15y, 109 patients with short-term <2y and 16809 BMDonors as Controls. Patients and controls were typed by SBT high resolution for DRB1*, medium/high for HLA-A*, -B*, -Cw*.
102 different HLA-A* alleles/NMDP codes were assigned in the 268 patients, 117 HLA-B*, 113 HLA-C* and 47 HLA-DRB1* showing high polymorphism.
47% HLA-A* are exclusive from patients as 29.9% HLA- B*. From these B*, 63% are long-term. HLA-B* 35DNXN, 44ENWFand 490101 represent 68% of all exclusive.
30% HLA-C* are exclusive from patients. 37.5% HLA-C* assigned in short-term and 26.9% from long-term, are absent in controls.
20.5% HLA-A* and 17.7% HLA-C are shared by short and long-term and do not exist in controls ($p<0{,}00000001$, pc=0.0000001), suggesting a different genetic background associated to renal disease. Frequency of exclusive alleles A* in short-term is higher than in long-term patients (39.9%vs18.2%), RR: 2, suggesting a role not only in the susceptibility to renal disease but also in graft rejection.
DRB1*1101 is significantly more frequent in patients $pF<0.00000001$, OR=234.
Short-term patients without exclusive alleles show homozygosis.
Conclusion: The main genetic difference is at HLA-class I level, seen by SBT. HLA-class I or genes located nearby are candidates to a role, either in renal disease susceptibility or in graft rejection, where antigen presentation and autoimmune response seems to be involved.

P-116 PREDICTIONS IN THE FACE OF CLINICAL REALITY: T-CELL EPITOPE CLASSIFICATION OF HLA-DPB1 MISMATCHES DOES NOT PREDICT SEVERE ACUTE GvHD

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The relevance of HLA-DPB1 matching in hematopoietic stem cell transplantation (HSCT) has been reported. An algorithm for determining DPB1 mismatch permissiveness based on T-Cell Epitopes (TCE) has been proposed (Crocchiolo et al, Blood 2009; 114:1437). According to this algorithm, DPB1 alleles are categorized into groups 1-4 (TCE4) with increasing antigenicity (HLA-DPB1*09:01, *10:01, *17:01), (HLA-DPB1 *03:01, *1401, *45:01), (HLA-DPB1*02:01, *02:02, *101:01), and (others), respectively. Accordingly DPB1 mismatches are classified as permissive (group 1); non-permissive in host vs. graft (group 2); and non-permissive in graft vs. host direction (group 3).
Objective: To investigate the potential of the TCE classification of DPB1 mismatches to predict high-risk HLA allele mismatch combinations responsible for severe acute graft-versus-host disease (aGvHD grades III and IV) published by Kawase et al (Blood 2007;110:2235).
Methods: We classified 16 DPB1 mismatch combinations observed in 549 donor-recipient pairs who underwent HSCT facilitated through the Japanese Marrow Donor Program into their respective TCE4 groups. These combinations included 2 associated with high risk of severe aGvHD (HR >2, $P < 0.005$, observed in 120 pairs) & 14 low risk (HR<1, n=429 pairs). Simulation scenarios were constructed where the recipient's HLA*DPB1 allele was involved in one high risk (combinations #15 & 16) and multiple low risk mismatches (combinations #2, 10, 14 and 4, 7, 8, 13, respectively).
Results: In our analysis TCE classification did not correlate with DPB1 mismatch combinations associated with increased risk of severe aGvHD. In addition, no predictable TCE patterns of association with high or low risk combinations could be distinguished in the simulation scenarios (Table: 1).

Table 1. Lack of association between TCE4 groups and the risk of severe aGvHD

Combination #	Donor-Recipient DPB1	Number of pairs	HR	P	TCE4
1	04:01–04:02	10	0	1.000	1
2	04:02–**09:01**	17	0.33	0.270	3
3	02:01–02:02	47	0.35	0.076	1
4	02:02–05:01	41	0.43	0.152	2
5	04:02–04:01	22	0.45	0.273	1
6	02:01–14:01	28	0.46	0.186	3
7	09:01–05:01	48	0.71	0.457	3
8	04:01–05:01	29	0.73	0.593	2
9	04:01–02:01	46	0.76	0.560	3
10	03:01–**09:01**	15	0.80	0.754	3
11	02:01–13:01	24	0.88	0.803	2
12	04:02–02:01	66	0.88	0.694	3
13	13:01–05:01	25	0.89	0.801	1
14	04:01–**09:01**	11	0.90	0.890	3
15	05:01–**09:01**	71	2.03	0.002	3
16	03:01–05:01	49	2.41	<0.001	2

Conclusion: These results suggest that the TCE algorithm has limited discriminative capacity rendering it ineffective as a strategy for prioritizing donors with DPB1 mismatches.

P-117 *DE NOVO* BUT NOT PREFORMED DONOR-SPECIFIC ANTI-HUMAN LEUKOCYTE ANTIGEN ANTIBODIES ARE PREDICTIVE OF SURVIVAL AFTER LUNG TRANSPLANTATION

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Lung transplantation (LT) is a valid therapeutic option for selected patients with end-stage lung disease. Recently, the development of humoral immune response, particularly antibodies against donor-mismatched human leukocyte antigen (DSA-HLA) has been highlighted. However, their potential role in the pathogenesis of chronic rejection (bronchiolitis obliterans syndrome, BOS) is not well known.
The aim of this study is to determine whether HLA sensitization detected by a high sensitive solid phase assay (LUMINEX®) is an independent risk for transplant survival and BOS. This is a retrospective monocentric study based on 113 adult LT recipients. Serum samples were serially collected before (D0) and after LT (D15, M1, M3, M12 and M24). Anti-HLA Class I and Class II antibodies detection and identification were performed by GEN PROBE® Single Antigen kits. Statistical analyses were performed by SPSS 15.0.
The overall survival of the LT population was of 96%, 89%, 76% and 73% at D15, M1, M12 and M24 respectively. Preformed HLA antibodies were found in 30 recipients (38%), of which 11 were DSA. The preformed HLA antibodies or DSA did not influence survival or BOS frequency ($p> 0{,}05$). After LT, *de novo* anti-HLA antibody were detected in 37 recipients (33%) and 27 patients exhibited DSA. DSA early detected after LT (D15) were mostly directed against HLA Class II antigens (4 Class I, 16 Class II and 7 Class I and II). *De novo* DSA, which were exclusively related to Class II DSA, significantly affected survival ($p<0{,}05$) but were not associated with BOS.
This study shows that survival after LT and BOS are not correlated to preformed HLA sensitization. In contrast, *de novo* DSA Class II are predictive of poor survival after LT with no association with BOS accuracy.

P-118 COMPARING LUMINEX-DEFINED HLA ANTIBODIES WITH FLOW CYTOMETRIC CROSSMATCHES IN RENAL TRANSPLANT PATIENTS

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Background: Deciding which HLA antigens to report as unacceptable mismatches when registering patients for renal transplants can be a dilemma. Ignoring high titre HLA-specific antibodies risks incurring a positive crossmatch (X-match) and delaying organ assignment. Over-reporting unacceptable HLA antigens can compromise the offer of an organ. To address this issue we audited a series of historic flow X-matches performed on patients with Luminex-defined donor-specific HLA Abs (DSA).
Methods: The median fluorescence intensity (MFI) values of DSA as measured with LABScreen® single antigen class I and II kits (OneLambda Inc), was compared with the relative mean fluorescence (RMF) results obtained in 90 flow cytometric X-matches (T and B cell, allo and auto), using linear regression and univariate analysis of stratified MFI levels.
Results: Positive correlation coefficients (R) were obtained between HLA Class I DSA MFIs and T cell and B cell FCXM RMFs (R=0.7 and 0.6 respectively). The computed regression line bisected our current RMF cut-off for a positive T cell X-match at approximately 2,500 MFI and B cell X-match at approximately 3,000 MFI. Univariate analysis of DSAs set at 1000, 1500 or 2000 MFI, revealed a highly significant association between positive T and/or B cell FCXMs and DSAs $\geq$2000 MFI (Chi Square = 16.3, P = 0.00005; Odds Ratio = 7.36). This association was lost when MFIs were stratified at $\leq$1000 or $\leq$1500.
Conclusion: Luminex-defined DSA titres $\geq$2000 MFI show the strongest correlation with positive allo flow X-matches. Thus in our centre, HLA-specific Abs of $\geq$2000 MFI are the most worthy of reporting to the United Kingdom Organ allocation scheme, when registering patients for renal transplants.

P-119 HLA MATCHING REDUCES THE INCIDENCE OF EARLY RENAL TRANSPLANT FAILURE IN SENSITISED PATIENTS

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Introduction: Sensitised patients wait longer for a transplant and national sharing schemes benefit these patients by giving access to HLA compatible transplants within a large donor pool. Furthermore highly sensitised patients (HSP) are often given priority for well matched transplants. We have sought to determine whether HLA matching confers a benefit to sensitised patients.
Methods: Outcome analyses were performed in deceased donor renal transplants, 2000-2008 (n=9,801), grouped by%HLA antibody reaction frequency (%Rf). Four levels of HLA-A,B,DR mismatching have been identified in UK analyses of transplant outcome: Level 1 [000], Level 2 [0DR+ <2Bmm], Level 3 [0DR+2Bmm/1DR+ <2Bmm], Level 4 [1DR+2Bmm/2DRmm]. Cox regression models were fitted to analyse the combined effects of HLA mismatch and other factors (donor/recipient age, recipient sex, cold ischemic time, graft number) in sensitised and unsensitised patients.
Results: 5 year graft survival in non-sensitised patients was superior to that in all groups of sensitised patients, both in first grafts (84% vs. 74-82% p=0.001) and regrafts (83% vs. 75-79%, p=0.002). In the Cox model, recipients of poorly matched (Level 4) transplants had a significantly higher risk of failure than other mismatch groups (non-sensitised patients RR=1.7, 95%CI1.4-2.3; sensitised patients RR=1.7, 95%CI1.1-2.6). However epoch analysis showed that for sensitised patients the increased risk of failure was in the first 3 months (RR1.9, 95%CI1.1-3.5), whereas in non-sensitised patients the effect was later (3 months-1 year: RR2.6, 95%CI1.2-5.5; 1-5 years: RR2.2, 95%CI1.5-3.0).
Conclusion: Poorly HLA matched transplants [1DR+2Bmm/2DRmm] have significantly inferior outcome in sensitised and non-sensitised patients and in sensitised patients the adverse effect occurs early after transplantation, suggesting an antibody mediated effect. HLA matching reduces the risk of early transplant failure in sensitised patients and demonstrates the importance of national allocation in providing well matched kidneys.

P-120 ABO INCOMPATIBLE KIDNEY TRANSPLANTATION WITH CAMPATH INDUCTION

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ABO incompatible (ABOi) kidney transplantation (Tx) is intended to increase the availability of live donor organ Tx. In Russia we have a legislation ban for interfamily organ exchange so ABOi Tx is the only option for recipients with incompatible donors.
From December 2005 to May 2010 we performed 26 ABOi kidney Tx, patients were 0.9 – 34 (13$\pm$9) years old. Campath (23 pts) and Mabtera (3 pts) were used for B-cell depletion, plasmapheresis - for antibody removal. Antibody titer less than 1:8 considered as acceptable. Maintenance immunosupression was CsA or tacrolimus (1:1) and mycophenolates. Since June 2007 early steroid withdrawal was applied. Patients were followed 252-1868 (904$\pm$455) days, protocol biopsies were performed at 1 month, 1 and 3 years. Infrared video records of graft reperfusion were used for detection of early contact of graft endothelium with isoantibodies.
One and two years survival was equal – 92% for grafts and 96% for patients. The rate of acute rejection was 18% at one year and 38% at two years. In 55 analyzed biopsies CADi was calculated. It was 2.0 at one year and 3.1 at two years. When compared with CADi in database (1326 biopsies) of compatible grafts it didn't change from 1 to 2 year and was 2.6 ($p>0.05$ with ABOi).
The kidney worming after reperfusion in the temperature range between 15 and 200C proceeded with speed 10.3$\pm$2.2 and 26.8$\pm$1.8 C/min/1.73 for ABOi and compatible kidneys respectively ($p<0.05$).
We conclude that ABOi kidney Tx leads to satisfactory early results and can be considered as acceptable option in case of absence compatible donors. Meanwhile the reduced speed of warming during reperfusion as well as trend to increased CADi score from first to second year in ABOi grafts may be a signs of not enough control of rejection.

P-121 ANALYSIS OF KIR GENE PROFILES IN RENAL TRANSPLANT RECIPIENTS

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Background: Killer Immunoglobulin-like receptors (KIR) are a group of polymorphic activating and inhibitory cell receptors expressed by natural killer (NK) cells and memory T cells. KIRs are involved in modulating the activity of NK and T cells by binding to their HLA class I ligands. Recipient NK cells have been shown to infiltrate renal allografts and their presence is thought to contribute to rejection (Totterman et al, Transplantation 1989; 47: 817-23).
Methods/Materials: The aim of this pilot study was to determine whether certain recipient KIRs and donor HLA ligand combinations associate with biopsy proven rejection. 73 recipient and donor pairs transplanted between 2006-2009 were HLA (-A, -B, -C, -DRB1*, DQB1*) and KIR (KIR2DL1, KIR2DL2, KIR2DL3, KIR2DL4, KIR2DL5, KIR2DP1, KIR2DS1, KIR2DS2, KIR2DS3, KIR2DS4, KIR2DS5, KIR3DL1, KIR3DL2, KIR3DL3, KIR3DP1, KIR3DS1) typed with commercial HLA and KIR genotyping PCR-SSOP kits (One Lambda), using the Luminex platform.
Results: Full KIR genotype profiles were produced on all recipient and donor pairs. Our initial analysis of KIR gene profiles in this cohort has revealed that a combination of recipients with KIR2DL2 transplanted with donors carrying the HLA-C locus alleles with the C1 epitope (Ser^{77} and Asn^{80}) recognised by KIR2DL2, may associate with rejection (Table1).

Table 1. Patient KIR2DL2 Donor HLA-C1 group combinations in renal transplant rejectors and non-rejectors

KIR2DL2/HLA-C1	Rejectors (n=25)	Non-rejectors (n=48)
Patient/Donor (+/+)	1	17*
Patient/Donor (+/–, –/+, –/–)	24	31

*Chi-Square=8.7, P=0.003, OR=0.08 (CI=0.00 < OR < 0.61).

Conclusion: This pilot study shows that some KIR genes may play a significant role in the rejection of renal transplants. Further studies of KIR gene profiles should be performed in a larger cohort of recipient and donor pairs to confirm the above findings.

P-122 NO EVIDENCE FOR INVOLVEMENT OF DONOR OR RECIPIENT NK-CELL ALLOREACTIVITY IN LIVER TRANSPLANTATION OUTCOME

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Background: Whether NK cells contribute to the immune response to solid organ allografts is still an unresolved issue. NK-cell activation is regulated by binding of killer-cell immunoglobulin-like receptors (KIRs) to specific HLA-ligands. In transplantation, lack of self-MHC on allogeneic tissues may lead

to recipient NK-cell activation and transplant rejection. So far, contradicting results have been reported on the impact of donor HLA-C genotype and KIR-ligand incompatibility on the outcome of liver transplantation (LTX).
Methods: We typed a cohort of 260 LTX donors and recipients for HLA-C/Bw4 and 153 donor/recipient pairs for KIR genes.
Results: We found that donor HLA-C genotype was not associated with graft or patient survival or acute rejection. Additionally, analysis of NK-cell recipient-versus-donor alloreactivity in terms of "missing self" and "missing ligand" models did not predict LTX outcome. As a novel approach we evaluated NK-cell alloreactivity in donor-versus-recipient direction following our previous observations showing transfer of donor NK cells into recipients after LTX (Moroso et al, Liver Transplantation 16; 2010: 895). Given the tolerogenic effects of liver grafts we hypothesized that, similarly to bone marrow transplantation, donor-derived NK cells could protect patients from graft rejection. Our results, however, indicate that donor-derived NK cells do not prevent liver graft rejection nor promote graft survival.
Conclusion: Our observations indicate that recipient NK-cell alloreactivity does not play a substantial role in LTX outcome, and that, in contrast to what was shown in hematopoietic stem cell transplantation, donor-derived NK cells do not contribute to prevention of liver graft rejection.

P-123 POSITIVE LUMINEX IN CADAVERIC RENAL TRANSPLANTATION AND ITS EARLY PREDICTABILITY OF GRAFT FUNCTION, REJECTION EPISODES

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Introduction: Until now a positive immunological crossmatch was considered as a contraindication for renal transplantation. The Luminex crossmatch is highly sensitive on detecting human leucocyte antigen (HLA) antibodies. This study aimed to assess the effect of a positive Luminex and its early predictability of graft function and biopsy proven acute rejection (BPAR) in cadaveric transplantation.
Methods: This study was carried out on a retrospectively collected data of all cadaveric renal transplant recipients between 2007-2009 with 1 year follow-up. During the data collection the investigator was blinded for crossmatch results; graft function was assessed by estimated GFR (eGFR) and rejection episodes. All recipients were on standard tacrolimus/rapamycin, MMF and prednisolone immunosuppression.
Results: All recipients (n= 53) were grouped according to the HLA class I and II results. HLA class I positivity noted in 17 and was negative in 36. Similarly, HLA class II antibody was positive, negative in 12, 41 respectively whilst 7 of them were positive for both. The HLA class I and II positive group did not show any difference in e GFR (P =0.75) after transplantation. HLA class I positive group had higher rejection rate (P =0.04) but not in HLA class II (P = 0.19).
Conclusion: From our study we conclude that HLA class I and II antibody does not affect early and intermediate graft function and HLA class I positivity is an independent risk factor for biopsy proven acute rejection.

P-124 HLA-DQ AND -DP ALPHA/BETA CHAIN ANTIBODIES IN RENAL TRANSPLANTATION

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In kidney transplantation, current HLA class II matching strategies consider DR antigens only. Both a and b chains of HLA-DQ and -DP heterodimers are polymorphic and can elicit a humoral immune response. Preformed HLA class II donor-specific antibodies (DSA) have a deleterious impact on graft outcome and post-transplant development of anti-class II DSA is strongly associated with acute and chronic rejection occurrence.
This study was done to investigate the incidence of anti-DQ and -DP antibodies in 56 kidney transplant (KTx) recipients who developed HLA class II DSA and 145 HLA class II-positive re-transplant candidates. Antibody characterization was performed by using Single antigen bead assay (microbeads coated with 29 DQA1/DQB1, 24 DPA1/DPB1 heterodimers besides DRB1/3/4/5, molecules).
In the KTx group of patients, incidence of anti-DQ/DP DSA was significantly higher than anti-DR DSA (76% vs. 20%, $P < 0.0001$); in 3 patients we only found anti-DQA1 DSA. During the follow up period, graft failure occurred in 14 of the 38 (36.8%) patients who only developed anti-DQ and/or -DP DSA.
Analyzing specificity of HLA class II antibodies detected in re-transplant candidates, 131 of the 145 (90%) patients showed production of anti-DQ and/or anti-DP antibodies. Nineteen percent of these patients had only anti-DQ a/b chain antibodies, 5% had only anti-DP a/b chain antibodies and 7% had both anti-DQ and anti-DP antibodies. It is important to underline that 87% of anti-DQA1/DQB1 positive patients and 98% of anti-DPA1/DPB1 positive patients developed wide antibody patterns due to the recognition of a "public epitope" of the mismatched donor molecule/s.
These data demonstrate the great immunogenicity of mismatched DQA1/DQB1 and DPA1/DPB1 molecules of a kidney transplant and underline the need to consider all the HLA class II molecules in matching strategies especially for re-transplant candidates.

P-125 THE ROLE OF HLA IN CYTOTOXIC T-CELL IMMUNOTHERAPY OF POST-TRANSPLANT LYMPHOPROLIFERATIVE DISEASE

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Epstein-Barr virus (EBV)-specific cytotoxic T-cell (CTL) immunotherapy has been used successfully for the treatment of post-transplant lymphoproliferative disease (PTLD). PTLD occurs in up to 10% of solid organ transplant patients and has a mortality of up to 50%. To ensure recipients worldwide have ready-access to this potentially life-saving immunotherapy, we are currently establishing a GMP EBV-specific CTL bank using lymphocytes from donors resident in areas with low infectious disease risk.
To establish the optimum number of donors required for the bank, low resolution HLA types of 200 apheresis donors were assessed for mismatches against 304 patients on a kidney transplant waiting list. Eleven apheresis donors gave a "low-grade" HLA-A, -B and -DR mismatch for 86.2% of patients. Based on this information, no more than 20 donors will be needed to set up the bank.
To help investigate future PTLD treatment response rates (currently 50% at 6 months) using *ex vivo* generated CTLs, apheresis donors used to set up the bank have been HLA typed for HLA-A, -B, -C, -DRB, -DQB1 and -DPB1 by PCR-SBT and SSOP. The purpose of high resolution typing is to investigate the impact of best HLA-matching on HLA-restricted killing, of least HLA-mismatching (D->R) to reduce recipient sensitisation risk and of least HLA-mismatching (R->D) to reduce GvHD risk. Recent work by others has shown memory virus-specific T-cells to have allo-HLA reactive properties; the implication of these findings will be an important consideration in patient monitoring post-infusion.
Determining the number of apheresis donors required based on HLA type and high-resolution typing of donors and patients could increase response rates, without a corresponding need to increase cell bank numbers. The availability of such a bank has the potential to offer reliable, effective and targeted treatment for PTLD.

P-126 ARE ADDITIONAL ANTIBODIES DETECTED BY LUMINEX SINGLE ANTIGEN TESTING CLINICALLY RELEVANT?

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Background: It is unclear whether kidney transplant recipients with preformed donor-specific HLA antibodies (DSA) detectable only in the highly sensitive Luminex Single Antigen (LSA) assay are at increased risk of graft failure.
Methods: We studied 3,148 patients who received a deceased donor kidney graft between 1996 and 2008. There were 118 patients with graft loss during the first 3 years after transplantation on whom recipient and donor DNA was available for complete HLA typing. We compared the incidence of LSA-detected DSA in these patients with graft failure and matched controls with functioning grafts. All patients were found negative in the less sensitive complement-dependent cytotoxicity and ELISA assays.
Results: When mean fluorescence intensity (MFI) of $\geq$1,000 was used as cut-off for Luminex positivity, 118 patients with graft loss did not show a higher incidence of DSA against HLA-A, -B, -C, -DRB1/3/4/5, -DQA1, -DQB1, -DPA1, or -DPB1 antigens than 118 matched controls without graft loss (for all loci *P* not significant). The incidence of strong DSA (MFI $\geq$2,000 or MFI $\geq$3,000) detected only by LSA was low (for all loci between 0 and 5%) and did not identify unacceptable antigens that were relevant for graft loss within the first 3 years after transplantation.
Conclusion: We conclude that, given currently practiced crossmatch procedures and immunosuppressive regimens, exclusion of donor organs carrying "unacceptable" HLA antigens based exclusively on sensitive LSA antibody testing is not justified. An additional study with posttransplant sera in 64 matched pairs is currently under evaluation and incidence of LSA-detected DSA against mismatched donor HLA will be presented.

P-127 HLA MATCHING BASED ON BOTH NUMBER AND TYPE OF MISMATCHES CORRELATES BETTER WITH GRAFT OUTCOMES IN DECEASED-DONOR KIDNEY TRANSPLANTATION (DDKT)

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Background: Traditionally, the number of HLA mismatches correlates with graft outcomes in DDKT, but this fails to differentiate mismatches conferring poorer prognosis like HLA-DR.
Methods: Death-censored immunologically-mediated graft loss and rate of biopsy-proven acute rejection were analysed retrospectively in 617 ABO-compatible, crossmatch-negative DDKT between 1990-2008 with 2-digit split resolution HLA typing. Different risk stratification models were compared: 1) number of mismatches; 2) MHC class of alleles involved; 3) both isotype and number HLA mismatches (our model); originated from the 27 possible permutations of HLA mismatches ordered in theoretical progressive immunogenicity, leading to 5 clinically applicable risk categories.
Results: A differential immunogenicity of the HLA alleles (HLA-DR>A>B) was identified. Our model defined 5 risk categories and appeared more reliable to predict immunologically-mediated graft loss and rejection rate than the other models. The very low risk group (0DR/0AB) had 100% graft survival and no rejections at 10 years. It appeared to be a gradual increase in the rejection and graft loss rates in the subsequent risk categories: low risk (0DR/1-4AB), moderate risk (1DR/0-4AB), high risk (2DR/0-3AB); being the very high risk group (2DR/4AB) the one with worse graft survival and highest rejection rate (both 66% at 10 years). The difference among the groups was not statistical significant due to sample size. Recipient age and waitlist-time were independent factors affecting negatively graft outcomes.
Conclusions: Our results hint that achieving better HLA matching in DDKT can improve outcomes. Our risk stratification for rejection or graft loss based on HLA matching might facilitate individual immunosuppression tailoring, with the potential of minimising immunosuppression in the lower risk group. In our setting, avoiding very high risk DDKT, and prioritising kidney allocation to very low risk recipients might be desirable.

P-128 SOLUBLE CD30 AND HEPATOCYTE GROWTH FACTOR AS PREDICTIVE MARKERS OF ANTIBODY-MEDIATED REJECTION OF THE KIDNEY ALLOGRAFT

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Background: our retrospective study was aimed to assess the relevance of pre- and post-transplant measurement of serum concentrations of the soluble CD30 molecule (sCD30) and the cytokine Hepatocyte growth factor (HGF) for prediction of the risk for development of antibody-mediated rejection (AMR) in kidney transplant patients.
Methods: evaluation of sCD30, HGF levels and the presence of HLA-specific antibodies in a cohort of 205 patients was performed before, 2 weeks and 6 months after transplantation. Patients were followed up for kidney graft function and survival for two years.
Results: We found a tendency of higher incidence of AMR in retransplanted patients with elevated pre-transplant sCD30 ($\geq$100 U/ml) (p=0.051), however no such correlation was observed in first-transplant patients. Kidney recipients with simultaneously high sCD30 and HLA-specific antibodies (sCD30+/Ab+) before transplantation had significantly lower AMR-free survival compared to the other patient groups ($p<0.001$). HGF concentrations were not associated with the incidence of AMR at any time point of measurement, nevertheless, the combined analysis HGF and sCD30 showed increased incidence of AMR in recipients with elevated pretransplant sCD30 and low HGF levels.
Conclusion: the predictive value of pretransplant sCD30 for the development of antibody-mediated rejection after transplantation is significantly potentiated by the co-presence of HLA-specific antibodies. The role of HGF as a rejection-protective factor in patients with high pretransplant HGF levels would need further investigation.

P-129 ACUTE MEDIATED REJECTION AFTER A KIDNEY TRANSPLANT WITH PREFORMED anti-HLA ANTIBODIES ABOVE THE LEVEL DESCRIBED TO HAVE CLINICAL SIGNIFICANCE: CASE REPORT

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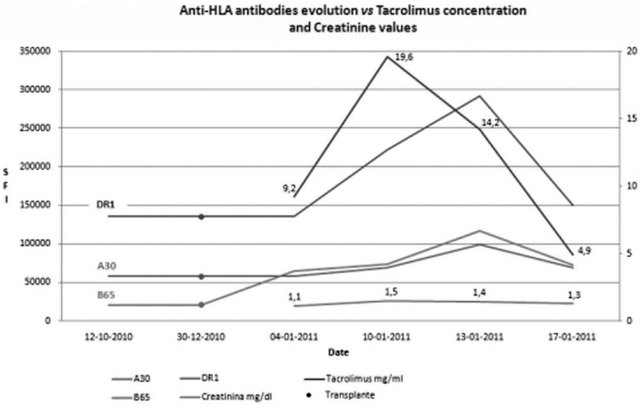
Background: We describe a case of an acute mediated rejection after a kidney transplant associated with low title preformed anti-HLA antibodies, above the Standard Fluorescence Intensity (SFI) *cut-off* value with clinical relevance as described in Mizutani et al. Am J Transplant. 2007;7(4):1027-31.
Methods/Materials: HLA genotyping were determined by PCR-SSP (Olerup), Antibodies anti-HLA by LABScreen SingleAntigen (One Lambda, Inc) and quantification by Quantiplex.
Results: A 60-year-old female patient with Chronic Glomerulonephritis initiated hemodialysis in January 2006 and was registered in a deceased donor kidney waiting list in July 2006, with the HLA genotyping HLA-A*02; B*44,*51; DRB1*13,*14. Preformed anti-HLA antibodies were detected, possibly because of six previous gestations, and antibodies with SFI values above 200000 were taken into consideration as mismatch for a future transplant.
In 30th December of 2010 she received a kidney from a cadaver donor with 59 years-old, with the HLA typing: HLA-A*23,*30; B*14,*27; DRB1*01,*13. Both Crossmatch class I and II were negative for CDC and flow cytometry. The mismatches acquired were A23, A30, B65, B27, DR1 and we assisted a massive antibody response from A30, B65 and DR1, detected previously with values below 200000, as showed in graphic. Creatinine and C4d staining biopsy confirmed the diagnostic and a heavy immunosuppression therapy was started with plasmapheresis, thymoglobulin and tacrolimus.



Conclusion: Monitoring antibodies before and after transplant allows an individual therapy with a more adequate dosage of immunosuppression for each patient, but determining the SFI value for antibodies that represent a clinical threat is still controversial. Should antibodies with very low titles detected by Single Antigen, and not detected by Flow Cytometry, be taken into consideration for transplant?

Immunobiology / basic science

P-130 ENDOTHELIAL NITRIC OXIDE SYNTHASE GENE T-786C POLYMORPHISM IN RENAL TRANSPLANT RECIPIENTS

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Background: Nitric oxide (NO) is a major mediator in vascular biology, regulating regional blood flow. NO and the enzymes required for its production is contribute to ischemia-reperfusion injury. The T–786C functional polymorphism in the promoter region substantially reduces promoter activity of the eNOS gene and compromises endothelial NO synthesis.
Objective: The aim of the present study was to examine the association between T–786C (rs 2070744) single nucleotide polymorphism (SNP) in eNOS gene and the development of acute rejection in renal transplant patients
Methods: Sixty renal transplant recipients (30 patents with episode of acute rejection and 30 recipients without rejection), between June 2008 and March 2010, were included in this study. The polymorphism was determined by PCR-restriction fragment-length polymorphism analysis.

Results: The distribution of the genotypes were TT/TC/CC 60%, 33.4%, 6.6%, and 43%, 46.7%, 13.3% in ARs and non-ARs respectively (P value= 0.28). T-allele frequency were 76.7% and 66.3%; C-allele frequency were 66.6% and 33.3% in ARs and non-ARs groups respectively (P value= 0.09). There were no significant associations between these polymorphisms and acute and chronic kidney allograft rejection
Conclusion: Our findings suggest that polymorphism in T–786C of eNOS gene was not associated with development of acute rejection.

P-131 RAPAMYCIN MAY ALTER THE PERCENTAGE OF THE Treg FOXP3 AND/OR GITR POSITIVE IN ENVIRONMENT OF THE CALCINEURIN INHIBITORS

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In the last decade it has become clear that regulatory T (Treg) cells play a pivotal role in immune regulation through their control of T cell responses. Tregs can induce transplantation tolerance by suppressing immune responses to allograft antigens. The balance between Treg cells and inflammatory cells will determine the occurrence of an immune response. Upon transplantation, strong inflammatory signals, which need to be controlled through the administration of immunosuppressive drugs, are induced in the recipient. Both the generation and the suppressive capacity of Tregs can be substantially affected by different immunosuppressive drugs used in clinical transplantation. The aim of this study was to determine the effect of mTOR inhibitor (rapamycin) in environment of the calcineurin inhibitors (cyclosporin A or tacrolimus), on the induction of Treg and the expression of the transcription factor FOXP3 and GITR receptor – positive and negative (respectively) controlling the suppressive function. Tregs were induced in a two-way mixed lymphocyte reaction (MLR) in the environment of different regimens of immunosuppression. Tregs were identified in MLR cultures by flow cytometry using anti-CD4, anti-CD25, anti-CTLA4, anti-GITR mAbs and anti-PE-FOXP3 staining sets. The immunosuppressive agents used – rapamycin and cyclosporine A or tacrolimus, can control the percentage of regulatory T cells by affecting the expression of the transcription factor FOXP3 and GITR receptor. We observed that single immunosuppressive drugs have decreased the percentage of Treg FOXP3+GITR- cells in vitro. The level of Treg FOXP3+GITR- significantly increased and FOXP3+GITR+ decreased when rapamycin was added to the environment of calcineurin inhibitors. This implied that immunosuppressive therapy based on rapamycin in combination with tacrolimus, a calcineurin inhibitor, may positively affect the modulation of the proportion and function of the Treg subpopulation.

P-132 DIFFERENTIATION OF DENDRITIC CELLS IN IMMUNOSUPPRESSIVE AGENTS *IN VITRO*

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Background: The most important antigen-presenting cells (APCs) are dendritic cells (DCs), which present antigen to T cells. The state of maturation of DCs is crucial for induction of a T-cell lymphocyte response. It was noted that immature DCs play an important role in peripheral tolerance, whereas mature DCs induce a complete immune response.
We have studied the effect of immunosuppressive agents: rapamycin and cyclosporine A on generation of immature DC and the subsequent activation of these cells with LPS.
Materials and Methods: Peripheral blood monocytes of healthy donors were induced by using cytokines: IL-4 and GM-CSF, in the direction of DCs in the presence of rapamycin and cyclosporin A or without drugs. Then the ability of these cells to undergo activation by LPS was evaluated. Immature DCs were identified by the expression of surface molecules: CD11c, HLA-DR (MHC II), CD86 and the absence of CD3, CD4, CD14, CD16, CD19, CD20, CD56 (lin^-).
Results: We have observed a higher percentage in both immature DCs and DCs after activation with LPS, when these cells were differentiated in an environment of cyclosporin A.
Conclusion: We have shown that the environment of rapamycin, in contrast to cyclosporin A, may be conducive to the survival of dendritic cells with tolerogenic properties. The use of rapamycin might be better for modulating the tolerogenic DCs and blocking their ability for activation by exogenous factors such as LPS *in vivo*.

P-133 INTERFERON GAMMA PROMOTES STARVATION-INDUCED AUTOPHAGY BY ACTIVATING THE GCN2-ATF4 PATHWAY

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Background: Tubular epithelial cells must adapt to interferon gamma (IFNγ) produced during acute rejection. During the response to this sublethal stress, cells undergo rapid changes to adapt their metabolism and protect themselves against potential damage. One of the key pathways that mediate stress-induced adaptation and damage control is autophagy. The aim of this study is to characterize the mechanisms of IFNγ induced autophagy in human tubular epithelial cells.
Methods and Results: Human Renal Cortical Cells (HRCCs) exposed to 10 ng/ml IFNγ for 48 hours develop an increased autophagic flux characterized by LC3b conversion and autophagosomes formation.
Autophagy inhibition by RNA interference directed toward ATG5 and Beclin1 significantly reduced cell viability, suggesting that autophagy promotes cell survival during IFNγ-induced stress.
IndoleamineDioxygenase (IDO) was strongly upregulated during IFNγ exposure and tryptophan concentration in the culture milieu, measured by Nuclear Magnetic Resonance, was significantly reduced. Tryptophan supplementation reduced autophagic flux, suggesting that IFNγ-induced autophagy is a consequence of IDO-mediated tryptophan depletion. GCN2, an eIF2α kinase, is phosphorylated following IFNγ treatment. GCN2 activates the eIF2α-ATF4-CHOP pathway leading to autophagy. IFNγ-induced autophagy is significantly reduced by RNA interference directed toward GCN2, suggesting that IFNγ-induced autophagy depends on an intact GCN2 pathway.
Finally, we demonstrate that the tubular expression of the autophagic marker LC3a is strongly upregulated during acute cellular rejection, which is associated with a strong IFNγ expression, in human renal allograft biopsies, compared to controls.
Conclusion and Discussion: In this study, we report that IFNγ induces autophagy in human tubular cells and promotes cell survival. IDO-induced tryptophan depletion mediated by IFNγ leads to autophagy. IFNγ-induced autophagy is dependant on an intact GCN2-eIF2α pathway leading to the upregulation of the autophagy inducers ATF4 and CHOP. Our results also suggest that autophagy is triggered during acute cellular rejection in human.

P-134 IDENTIFICATION OF A NOVEL MICA ALLELE MICA*002:04 BY SEQUENCING BASED TYPING AND CLONE SEQUENCING

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Objective: A novel MICA allele was detected in a Cantonese Han lung cancer patient.
Method: Samples were tested by Sequence Based Typing (SBT) as routine MICA allele typing in a research project supported by Guangdong provincial fund. MICA-PCR DNA fragment was inserted into a pMD-T vector and re-sequenced to confirm the typing results.
Results: The DNA sample of a lung cancer patient was found mismatched in MICA gene bank database. Sequence Based Typing (SBT) and clone se-

Fig 1. The nucleotide sequence of new allele MICA*002:04, compared with MICA*002:01
"M"shows mutation point, highlighted with red lines, "-" indicates the same sequence
Fig 2 The nucleotide sequence of new allele MICA*002:04, compared with MICA*002:01
Mutation point from C→A, highlighted with red lines, "-" indicates the same sequence

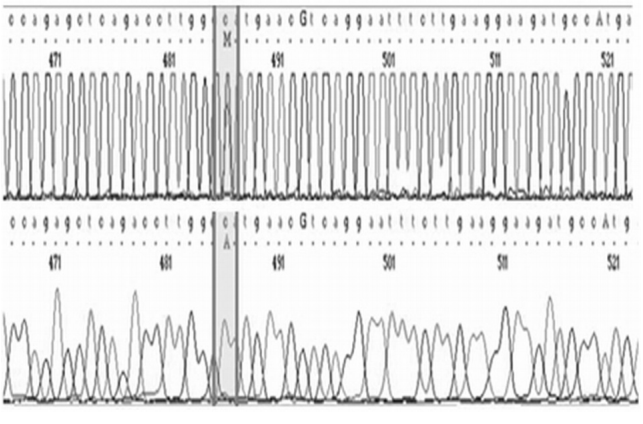
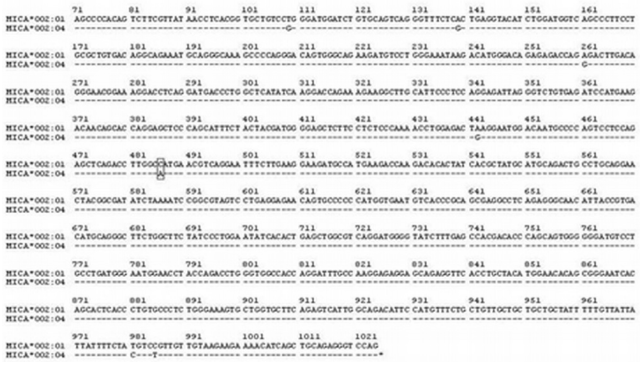


Fig3. New allele MICA*002:04 nucleotide sequence alignments
Mutation point highlighted with red square, dash indicates the same sequence



quence results showed that there was a mutation point at position 486 on exon 3, changing from C→A, resulting in codon 20 changing from GCC to GCA. The amino acid sequence has not been changed since it is a silent mutation.
The sequence of MICA*002:04 allele was submitted to GenBank and its submission number is HM856618.
Conclusion: The name MICA*002:04 has been officially assigned by the WHO Nomenclature Committee in September 2010. This follows the agreed policy that, subject to the conditions stated in stated in the most recent Nomenclature Report (Marsh et al. 2010) names will be assigned to new sequences as they are identified.
Lists of such new names will be published in the following WHO Nomenclature Report.

P-135 IL28B GENE POLYMORPHISM FOR PREDICTION OF EARLY VIROLOGICAL RESPONSE IN ROMANIAN PATIENTS WITH RECURRENT HEPATITIS C AFTER LIVER TRANSPLANTATION

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Introduction: In patients with recurrent HCV infection after liver transplantation (LT), analyses of single nucleotide polymorphisms of IL28B in recipient and donor tissues proved to allow prediction of sustained virological response to PEG-Interferon and ribavirin therapy.
Aim: To investigate IL28B polymorphism in Romanian LT recipients with recurrent hepatitis C during antiviral therapy.
Methods: Twelve LT recipient DNA samples were screened for rs12980275 single nucleotide polymorphism near the IL28B gene in a pilot study.
Results: There were analyzed 2 females and 10 males with a mean age of 52.5±6.9 years at beginning of antiviral therapy and a mean time since LT of 16.3±11.6 months. Distribution of IL28B genotypes were: C/C -1 patient (8.3%), C/T -7 patients (58.3%), T/T -4 patients (33.4%). Nine out of 12 patients had early virological response (EVR). EVR was not associated with recipients IL28B genotype non-T/T. Aminotransferases were significantly higher in genotype T/T patients compared to C/T and C/C patients: AST =285.7±87.4 vs 139.5±20.2 (p=0.04) and ALT= 325.5±84.4 vs 149±28.1 (p=0.03). Although not statistically significant, baseline viral load, necroinflammation score ≥2 and fibrosis stage ≥2 (METAVIR classification) were higher in genotype T/T patients.
Conclusions: Recipient IL28B genotype is not sufficient to predict EVR. Donor IL28B genotype should be also investigated. LT recipients with T/T genotype seem to have a more severe recurrent hepatitis C.

P-136 Tokishakuyaku-san PROLONGED SURVIVAL OF FULLY ALLOGENEIC CARDIAC GRAFTS AND GENERATED REGULATORY CD4+ CELLS IN MICE

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Background: Tokishakuyaku-san (TJ-23), which consists of six kinds of Japanese herbal components, has been used to treat neurodegenerative, immune system and respiratory tract diseases, as well as many gynecologic disorders, with few side effects. This study investigated the effect of TJ-23 on alloimmune responses in a murine model of cardiac allograft transplantation.
Methods: CBA mice (H2k) underwent transplantation of a C57BL/6 (B6, H2b) heart and received oral administration of TJ-23, one of the individual components of TJ-23 or one component missing TJ-23 from the day of transplantation until 7 days afterward. An adoptive transfer study was conducted to determine whether regulatory cells were generated. Histologic and cell-proliferation studies, cytokine measurements, and flow cytometry analyses were also performed.
Results: Untreated CBA mice rejected B6 cardiac grafts acutely (median survival time [MST], 7 days). The majority of CBA transplant recipients given 2g/kg/day of TJ-23 accepted B6 allograft indefinitely (MST, >100 days). CBA recipients treated with 0.2 and 0.02g/kg/day of TJ-23 rejected allografts with MST of 27 and 8 days, respectively. Neither one of the individual components of TJ-23 nor one component missing TJ-23 prolonged allograft survival. Adoptive transfer of either whole splenocytes or CD4+ cells from TJ-23-treated allograft recipients resulted in indefinite survival of allografts in naive secondary recipients for over 100 days. TJ-23 also suppressed proliferation of splenocytes and production of interleukin-2 and interferon-γ. Flow cytometry studies showed that the CD4+CD25+FOXP3+ cell population was increased in transplant recipients given TJ-23.
Conclusion: TJ-23 induced hyporesponsiveness to fully allogeneic cardiac allografts and generated CD4+ regulatory cells in our model. Moreover, one of the individual components of TJ-23 and one component missing TJ-23 are not effective.

P-137 HUMAN B CELL DEVELOPMENT AND ANTIBODY PRODUCTION IN HUMANIZED NOD/SCID/IL-2Rγ^{null} (NSG) MICE CONDITIONED BY BUSULFAN

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Background: Busulfan treatment as a chemotherapeutic agent has been considered an alternative approach in xenograft model because it offers a simple, convenient, effective, and less toxic conditioning regimen.
Materials and Methods: To investigate busulfan effects on the reconstitution of human immune cells and the generation of immune response to foreign antigens, we generated humanized NOD/SCID/IL-2Rγ^{null} (NSG) mice conditioned either busulfan or total body irradiation (TBI) with hCD34^{+} CB cells.
Results: Busulfan resulted in a high survival rate and effective reconstitution of human immune cells including B, T, macrophage and dendritic cells in humanized NSG mice, compared to that of TBI. Moreover, the humanized NSG mice conditioned busulfan showed effective B cell development, and thereby the high production of human antibody against immunized antigen.
Conclusion: Humanized mice conditioned by busulfan provide a powerful and versatile tool for studying the entire process of human B-lymphocyte development and for producing specific human antibodies.

P-138 COMPARISON OF ERYTHROCYTE MEMBRANE FATTY ACID CONTENTS AND LIPID PROFILES IN RENAL TRANSPLANT RECIPIENTS AND DIALYSIS PATIENTS

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Introduction: Alterations of erythrocyte membrane fatty acid (FA) composition play important roles in cellular function. The erythrocyte membrane oleic acid contents are higher in patients with acute coronary syndrome and it contents are also higher in dialysis patients. However, available data of erythrocyte membrane FA contents on renal transplant recipients (KTP) are limited. We investigated the erythrocyte membrane FA contents of KTP.
Methods: In this cross sectional study, we recruited 35 hemodialysis patients, 33 peritoneal dialysis patients, 49 KTP and 33 normal control subjects (CTL). Erythrocyte membrane FA contents were measured by gas chromatography. Comparisons of more than two sets of unmatched data were performed by one-way ANOVA using the Tukey test.
Results: The mean age of the enrolled dialysis patients, KTP and CTL was 56.4±10.1, 48.9±10.4 and 49.5±8.3 years. Mean kidney transplanted duration was 89.8±64.8 months and mean dialysis duration was 49.0±32.6 months. The erythrocyte membrane contents of monounsaturated FA (MUFA) were significantly higher in KTP ($p = 0.001$) and dialysis patients ($p < 0.001$) compared with those found in CTL. The erythrocyte membrane contents of palmitoleic acid were significantly higher but oleic acid were significantly lower in KTP compared with those found in dialysis patients and CTL. The erythrocyte mem-

brane contents of arachidonic acid (p = 0.001), docosahexaenoic acid (DHA) (p = 0.003) were significantly higher and linoleic acid ($p < 0.001$) and omega-6 FA to omega-3 FA ratio ($p < 0.001$) were significantly lower in KTP compared with those found in dialysis patients and those FAs in KTP were similar with those found in CTL.

Comparison of erythrocyte membrane fatty acid contents in renal transplant recipients and dialysis patients

	Dialysis	KTP	CTL	p value
MUFA	18.74±2.27	18.16±1.78	16.24±2.72	0.001
Palmitoleic	1.35±0.86	4.40±0.92	1.78±1.63	<0.001
Oleic	16.92±2.01	13.01±1.34	14.06±2.49	<0.001
Arachidonic	11.05±2.04	12.58±1.67	11.57±3.18	0.001
DHA	6.62±2.20	7.86±1.08	8.21±2.41	0.003
Linoleic	18.10±4.23	12.77±2.84	13.38±2.98	<0.001

KTP: renal transplant recipients; CTL: normal control subjects; MUFA: monounsaturated fatty acid; DHA: docosahexaenoic acid.

Conclusions: FA contents of erythrocyte membrane were significantly different in KTP compared with those found in dialysis patients.

P-139 AN EX VIVO MODEL FOR ASSESSMENT OF ALTERED LUNG FUNCTION DURING LUNG TRANSPLANTATION

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Background: Establishment of a method for the use of isolated perfused rabbit lungs in studies on lung transplantation and organ preservation of marginal donor organs.
Methods: New Zealand white rabbits (2.36±0.35kg) were anesthetized and heparin was administered. After performing a tracheotomy the thorax was opened by midline sternotomy. The pulmonary artery and left atrium were cannulated, the heart-lung-block was excised and transferred to a water-heated artificial thorax chamber. Lungs (n=16) were ventilated with room air (40 breaths/min) and perfused with recirculating, albumin-containing Tyrode-Solution (total volume 400ml, buffered to pH 7.4). The perfusion rate was set at 40-150 ml/min. Furthermore, pulmonary oxygen uptake by the isolated lungs was measured. In another series we preserved lungs for 4h in Perfadex Solution on ice, and thereafter continued ventilation and perfusion to simulate a transplantation situation.
Results: The data after 60min of perfusion were pulmonal arterial pressure 9.58±0.29 cmH_2O, pulmonary resistance 0.04±0.00 cmH_2O/ml/s, pulmonary compliance 1.49±0.01 ml/cmH_2O and lung weight 22.4±2.25 g. Inflow perfusate pO_2 increased from 53.6±4.77 mmHg to 120±11.3 mmHg after passing the lungs. If transplantation was simulated, lungs recovered after 4h, but without reaching pre-transplant control values. After 120min of reperfusion pulmonal arterial pressure increased by 33%, pulmonary compliance was reduced by 46%, pulmonary resistance increased by 67% and lung weight increased by 48%.
Conclusions: Thus, simulated lung transplantation results in a moderate pulmonary dysfunction as can be clinically observed if marginal donor organs are used, so that this setup provides basic requirements for further investigation in assessment of altered pulmonary function after simulated lung transplantation.

P-140 TCR-INDEPENDENT EXPANSION OF FOXp3$^+$CD4$^+$ REGULATORY T CELLS BY CD137 STIMULATION

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We previously demonstrated that in vivo engagement of CD137, a member of TNF receptor superfamily, can delete alloreactive CD4$^+$ T cells through the induction of activation-induced cell death (AICD), thus preventing chronic GVHD in the DBA/2à unirradiated (C57BL/6 x DBA/2)F_1 (BDF_1) chronic GVHD model. In this study, we further showed that in vivo engagement of CD137 was highly effective in triggering AICD of donor CD8$^+$ T cells as well as donor CD4$^+$ T cells in the C57BL/6à unirradiated BDF_1 acute GVHD model. Even though CD137 stimulation facilitated lethal GVHD in mice preconditioned with a higher dosage of total body irradiation, CD137 stimulation rather completely prevented acute GVHD without impairing donor cell engraftment in mice preconditioned with a lower dosage of total body irradiation (100rad). Further analysis showed that engrafted donor T cells followed by CD137 stimulation did not exhibit alloreactivity to host alloantigens, further demonstrating that CD137 stimulation completely removed alloreactive donor T cells from the mature donor T cell pool transferred into the host. Interestingly, CD137 stimulation might induce tolerance to host antigens, since GVHD did not occur in recipient mice that had received anti-CD137 mAb, when GVHD was reinduced. In sum, CD137 stimulation may be used as a GVHD prophylaxis in a parent-into-F_1 GVHD setting.

P-141 TRYPTOPHAN CATABOLITES AS PROGNOSTIC BIOMARKERS FOR THE SEVERITY OF CHRONIC LIVER DISEASES IN POTENTIAL TRANSPLANT RECIPIENTS

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Background: The initial step in the kynurenine pathway is oxidation of tryptophan (Trp) to N-formylkynurenine and is catalyzed by one of two heme enzymes, tryptophan -2,3-dioxygenase (TDO) expressed mainly in liver, and indoleamine 2,3-dioxygenase (IDO), expressed in many tissues and cell types. The role of tryptophan metabolites in chronic liver diseases had not been widely studied. The aim of the present study is to investigate the correlation between tryptophan metabolites [Kynurenine (Kyn), Kynurenic acid (Kyna), Quinolinic acid (Qun)] and the score of end stage liver disease in potential transplant recipients, in order to find biomarkers for the severity of disease.
Method: Ninety-eight cirrhotic liver patients who were categorized in 2 groups according to early (group I, n=56) and late phase (group II, n=42) of end stage liver disease were studied. Trp and its metabolites Kyn, Kyna, Qun were analysed by using tandem mass spectrometry. Kyn/Trp ratio was calculated to estimate IDO/TDO activity. Cytokine levels (IL-1RA, IL-2, IL-4, IL-6, IL-8, IL-10, IL-17, IFN-g, TNF-a, TGF-b $_{1,2,3}$) were determined by Luminex assay. CRP values were estimated by ELISA. Mann-Whitney-U test was used for statistical evaluation.
Results: Serum levels of Kyn, Kyna and Qun, as well as Kyn/Trp ratios were positively correlated with disease severity ($p \leq 0.001$ for all investigations). The levels of cytokine IL-1RA, IL-6, and IL-8, and CRP were significantly increased according to disease severity ($p \leq 0.001$). There were also positive correlations between serum Kyn, Kyna, Qun, Kyn/Trp ratios, CRP, and cytokine levels of IL-1RA, IL-6, and IL-8 ($p \leq 0.003$ for all investigations).
Conclusion: Our results indicate that measurement of Kyn pathway metabolites are useful markers of chronic inflammation and disease severity in potential transplant recipients with end stage liver diseases.

P-142 DONOR PRETREATMENT WITH ANTI-IL-6 DOES NOT REDUCE INFLAMMATORY ACUTE PHASE PROTEINS IN A RAT BRAIN DEATH MODEL

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Background: Kidneys derived from brain-dead donors have inferior outcomes after transplantation compared to kidneys from living donors. Strikingly, early and profound serum levels of interleukin-6 (IL-6) in brain-dead donors are observed. IL-6 is the main regulator of the acute phase response (APR). Neutralizing Il-6 could be an interesting strategy to improve donor organ quality. On the other hand recent studies with IL-6 KO mice show that IL-6 may also serve as a protective protein. The aim of this translational study was to investigate the potential of anti-IL6 treatment to influence expression of renal acute phase proteins (APPs) following brain death (BD).
Methods/Materials: Brain death was induced in rats by inflating an epidurally placed balloon catheter. Four groups were compared: BD+PBS, BD+anti-IL-6 anti-body treatment (2mg/kg), BD+anti-IL-6 (30mg/kg) and sham operated controls. Four hours after BD, blood, urine and tissue were harvested and analyzed. mRNA levels of IL-6 as well as the APP a2-macroglobulin, a-fibrinogen and C3 were measured.
Results: Compared to control, BD kidneys showed significantly elevated IL-6 and a2-macroglobulin mRNA [h1] levels (IL-6 0.55±0.71 vs 0.01±0.00 BD vs control; a2-macroglobulin 1.07±0.66 vs 0.12±0.02 BD vs control)[h2] ($p<0.05$). Anti-IL-6 intervention did not show decreased IL-6 nor decreased APPs. Interestingly anti-IL-6 pretreatment increased a-fibrinogen mRNA levels (3.55±1.34) compared to group of BD with PBS (0.88±1.33) ($p<0.05$).
Conclusions: In conclusion, BD induced upregulation of inflammatory cytokine levels of IL-6 and APP's. Pre-treatment with anti-IL6 antibody did not reduce APP response but rather tended to increase this response indicating a dual role of IL-6 in BD.

P-143 HLA POSITIVITY BY LUMINEX CROSSMATCH AND ITS EARLY EFFECTS IN LIVE DONOR RENAL TRANSPLANTATION

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Introduction: The clinical significance of the presence of anti-human leucocyte antigen (HLA) antibodies prior to renal transplantation remains debatable. This study was done to assess the role of Class I, II HLA antibodies detected by Luminex and its effects on live donor renal transplantation.
Methods: The Luminex is a solid phase assay by using micro-spheres and it is more sensitive on detecting HLA antibodies than conventional tests. This retrospective analysis involved 88 consecutive live donor recipients between May 2007-2009 and with a minimum follow-up of one year following transplantation. The parameters assessed were graft function and biopsy proven acute rejection (BPAR). All recipients had surveillance biopsy at 3 and 11 months following transplantation. The study population divided in to HLA antibodies positive versus negative for Class I and II.
Results: The demographs between the 2 groups showed no difference age, sex, and immunosuppression. Luminex was positive for class I HLA antibodies in 18 whilst 11 for HLA Class II. The HLA class I positive group showed no difference in renal function assessed by eGFR (53±14.98 versus 51±14.98 and p=0.47) or rejection episodes (p = 0.57). Similarly in HLA class II positive group the eGFR (49±14.98 versus 52±14.98 and p= 0.95) and rejection episodes (p=0.72) are statistically not different compare with HLA class II negative group.
Conclusion: Pre-transplant positive HLA class I, II by Luminex does not have any influence on early graft function and rejection episodes within one year in live donor renal transplantation.

P-144 OPTIMIZING LIVER DECELLULARIZATION FOR ORGAN ENGINEERING

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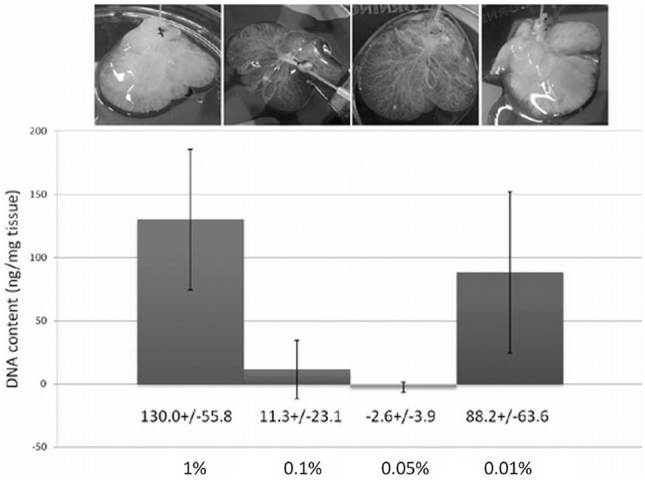
Background: Several groups have recently used sodium dodecyl sulfate (SDS) perfusion to decellularize the heart, lung, and liver to obtain an extracellular matrix (ECM) that maintains adequate organ architecture and microvascular network. This ECM can then be recellularized to restore organ function. However, no study has examined how various concentrations of SDS affect decellularization and the resulting ECM. Our work investigates the optimal SDS concentration for most efficient removal of cellular components while causing minimal damage to the ECM, which may also help improve recellularization. We hypothesize that improved maintenance of the ECM may help direct appropriate localization and homing in complex organs with multiple cell types.
Methods: Livers were harvested from male B6 mice (15-17 weeks) and perfused with PBS through the portal vein at constant pressure (44.8 mmHg, 30 min). The organs were subsequently perfused with SDS at the following concentrations: 1% (n=3), 0.1% (n=4), 0.05% (n=2) or 0.01% (n=3). Perfusate samples were collected every 10 min for DNA quantitation. After a final wash with PBS (30 min), DNA content in the ECM was quantified, and histological analysis was performed.
Results: Paradoxically, highest concentration of SDS (1%) did not result in fastest decellularization. Histological analysis demonstrated copious depositions of cell-free DNA, which was confirmed by quantitation. 0.01% SDS was not effective at decellularizing the livers. Both 0.05% and 0.1% SDS efficiently decellularized the livers with minimal DNA deposition.



Conclusions: The efficiency of organ decellularization using detergent solutions may not be linearly correlated with detergent concentration. Careful optimization is key to obtaining the highest quality "ghosts." We are currently investigating the effect of varying concentrations on the retention of extracellular matrix proteins that carry homing and differentiation signals that may be critical to recellularizing complex organs with multiple structures and cell types such as the liver.

P-145 RESPONSES TO NON-POLYMORPHIC HLA CLASS 1 DERIVED PEPTIDES ARE MEDIATED BY CD4+ T EFFECTOR MEMORY CELLS

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Background: We have recently described that renal transplant recipients' peripheral blood mononuclear cells produce γ-interferon in response to peptides derived from the non-polymorphic α3 domain of class 1 HLA. These responses to cryptic self-epitopes are associated with chronic allograft dysfunction. The cell surface phenotype of responding cells was shown to be $CD3^+CD4^+CD25^+CD127^+$.
Methods and Materials: We now further refine this phenotypic definition.
The responses to HLA derived peptides were then further investigated using two agents (Shk peptide and PAP-1) that inhibit kv1.3 K^+ channels. Kv1.3 K^+ channels play a role in T effector memory cell activation.
Results: $CD4^+CD25^+CD127^+CD45RO^+CCR7^-$ T lymphocytes added to γ-interferon ELISPOT assays containing 5×10^5 PBMC's, result in an upward titration of response in the presence of specific (HLA derived) but not control peptide (n=10, $p<0.005$). This was not observed when titrating equivalent numbers of $CD4^+CD25^+CD127^+CD45RO^+CCR7^+$ or $CD4^+CD25^+CD127^-CD45RO^+$ $CCR7^{+/-}$ T lymphocytes, into these cultures (n=10, $p<0.005$).
γ-interferon production, to these HLA derived peptides, measured in the ELISPOT assay was significantly inhibited by both Shk ([50nM], n=20, $p<0.0001$) and by PAP-1 ([1 & 5 mM], n=20, $p<0.001$). There was however no significant inhibition of responses to PPD antigen or anti-CD3.
Conclusion: If responses to HLA derived cryptic self-epitopes that are associated with chronic allograft dysfunction are also representative of pathogenic T lymphocyte responses to transplantation antigens, then our observations suggest that targeting T effector memory cells may have therapeutic utility in counteracting chronic rejection.

P-146 CONVERSION TO ONCE-DAILY TACROLIMUS IN RENAL TRANSPLANT RECIPIENTS LEADS TO HIGHER P38 MAPK ACTIVITY IN T LYMPHOCYTES

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Introduction: A new modified-release, once-daily formulation of tacrolimus (TACOD; Advagraf®), has recently been approved for the prevention of acute rejection after kidney transplantation. The pharmacokinetic profile of TACOD is different from that of the conventional twice-daily formulation, Prograf® (TACBID). The tmax is delayed but also C0 concentrations are lower after 1:1 mg conversion. Therefore we studied the pharmacodynamics of the two formulations and potential differences therein after conversion from TACBID to TACOD.
Materials & Methods: Patients (n = 16) treated with TAC and mycophenolate mofetil, and who were at least one year after renal transplantation were converted from TACBID to TACOD on a 1:1 mg basis as part of a clinical trial. TAC predose concentrations were measured before and after conversion by immunoassay. In addition, whole blood was collected before and three months after conversion and stimulated with PMA/ionomycin. T-lymphocyte activation was studied by phosphoflow cytometry measuring phosphorylated P38 MAP kinase (MAPK; the activator of Nuclear Factor of Activated T cells, IL-2, and IFN-γ).
Results: A total of thirteen patients were included for the present analysis. After conversion, the mean TAC predose concentrations decreased: 6.0 ng/mL vs. 5.5 ng/mL. With regard to P38 MAPK activity, the opposite effect was observed: after conversion to TACOD, the P38 MAPK median fluorescence intensity was 12.0% higher in CD4+ T-lymphocytes (P = 0.012) and 18.9% higher in CD8+ T-lymphocytes (P = 0.016).
Conclusion: Conversion of TACBID to TACOD on a 1:1 mg basis leads to lower TAC predose concentrations and higher P38 MAPK activity. This reflects the overall lower immunosuppressive state of patients on the TACOD formulation and suggests that close monitoring is necessary when patients are switched from the conventional to the new TAC formulation.

P-147 MANNOSE RECEPTOR DEFICIENCY PROTECTS MICE FROM ISCHEMIC-REPERFUSION INJURY AND NEPHROTOXIC NEPHRITIS

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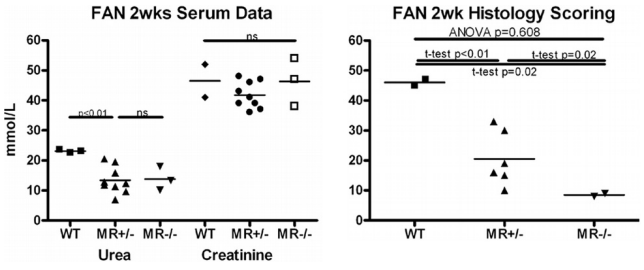
Background: A series of inflammatory and immunological cascades are initiated at the time of graft revasculisation. Ischemic-reperfusion injury (IRI) leads to significant downstream immunological effectes mediated by macrophages. Mannose receptor (MR) is expressed on macrophages and provoks pro-inflammatory cytokine production. As a result, MR deficiency is associated with protection from glomerulonephritis. Their role in IRI and nephritis will be further investigated.
Methods/Materials: MR deficent mice were provided by Rockefeller University. Homozygous knockout mice have been bred to provide experimental mice in the Biological Services Unit at Hammersmith Hospital. Mice used in this study are 8–12 weeks of age. The IRI was induced by clamping left renal artery for 40 minutes and sacrificed after 48 hours of reperfusion. Folic acid (FA) 240mg/kg was injected intraperitoneally with vehicle ($NaHCO_3$) to evaluate the role of MR in the nephrotoxic model. All animal protocols are approved by Home Office regulations. Serum and urine biochemistry were measured at time of sacrifice. Histological scoring of the degree of tubular injury and further immunohisochemistry were analysed.
Results: In the IRI model, the serum and urine biochemistry were similar between wild type (WT) and MR deficient mice. Our preliminary result in histological scoring showed MR deficient mice are protected from IRI. In the FA nephritis model, serum urea level are higher in WT mice comparing to that of MR+/– ($p<0.01$) and MR–/– ($p<0.01$).



Tubular injury score are higher in the WT than MR+/– and MR–/– mice ($p<0.01$ and p=0.02, respectively).
Conclusion: MR deficiency may protect mice from ischemic-reperfusion and folic acid nephrotoxic injuries. Further macrophage phenotypic experiments are warrented to support this hypothesis.

P-148 CCR1 AND CCR3 EXPRESSION IN FINE-NEEDLE ASPIRATION BIOPSY SAMPLES FROM KIDNEY TRANSPLANTS

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Background: CCR1 and CCR3 are chemokine receptors which are associated with activated Th1 and Th2 cells, respectively. CCR1 is further expressed in monocytes-macrophages and neutrophils while CCR3 is further expressed on eosinophils and basophils. We studied CCR1 and CCR3 expression in fine-needle aspiration biopsy (FNAB) samples in kidney transplants (KTx).
Methods: Fifty-five KTx were studied, all from cadaver donors treated with calcineurin inhibitors (CNI), mycophenolate mofetil and prednisolone. They were divided into two groups, I (n=27), rejection-free for the first year post-KTx, and II, acutely rejecting (AR) cases (n=28). AR was confirmed by an independent pathologist reading a classical biopsy following Banff 97 criteria. Every patient consented in FNAB study, done on day 7 in I and on rejection day in II. After cytocentrifugation each cytoslide was kept at -80°C until further testing. We used a mouse IgG_{2B} anti-human CCR1 (R&D) diluted at 8 μg/ml and a rat IgG_{2A} anti-human CCR3 (R&D) diluted at 15 μg/ml using avidin-biotin enzyme complex. Every positive cell was counted as well as every kidney parenchymal cell and every negative lymphocyte and monocyte-macrophage.
Results: No significant difference was observed for demographic characteristics of KTx in I and II. No significant correlation was found between CCR1 and CCR3 with either CNI levels or with creatinine. CCR1 and CCR3 were up-regulated, respectively in II in number of cells (P=0,074, P=0.019), in positives/renal cells ratio (P=0.146, P=0.004) and in positive/negative mononuclear cells ratio (P=0.045, P=0.001).
Conclusions: CCR1 and CCR3 are up-regulated in acute rejection, but surprisingly CCR3 association with rejection was stronger than that of CCR1. This suggest that modern acute rejection is a Th1 and Th2 process but with a predominance of Th2 role. CCR1 and CCR3 expression do not seem to be highly modulated by CNI.

Heart

P-149 PLACENTA GROWTH FACTOR AS A MARKER OF CARDIAC ALLOGRAFT VASCULOPATHY SEVERITY IN HEART TRANSPLANT RECIPIENTS

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Cardiac allograft vasculopathy (CAV) remains to be one of the most serious complications after heart transplantation (HTx). Placenta growth factor (PlGF) has been shown to be an independent biomarker of adverse outcome in patients with coronary artery disease. The study was aimed to investigate the relationship between PlGF levels and coronary lesions severity in heart transplant recipients.
Methods: Eighty heart recipients, 71 men and 9 women, aged 45.5±10.1 years were followed for 6.5 (1-18) years after HTx. Immunosuppressive therapy included steroids, cyclosporine (or tacrolimus), and mycophenolate mofetil. Quantitative angiography was made to assess coronary anatomy. Plasma concentrations of PlGF were measured using ELISA.
Results: CAV was diagnosed in 30 patients and was classified as mild, moderate, or severe on the basis of ISHLT 2010 recommended nomenclature for CAV. PlGF levels were significantly higher in recipients with CAV compared with patients without CAV (22.6±5.3 pg/ml, n=30 vs. 12.5±4.8 pg/ml, n=50, $p<0.05$). Patients with moderate or severe CAV had significantly higher PlGF levels (30.1±4.2 pg/ml, n=18) than those with mild CAV (18.4±5.3 pg/ml, n=12, $p<0.05$).
Baseline PlGF levels at 6 months after HTx were higher in recipients who developed mild (14.6±4.1 pg/ml) and moderate or severe (16.6±5.7 pg/ml) CAV compared with those who did not (11.5±2.2 pg/ml, $p<0.05$ and $p<0.05$ resp.). Prospectively evaluated PlGF levels from six months to follow-up (6.0±2.0, 5.5±1.7 vs. 5.8±3.0 years) were significantly higher ($p<0.05$ resp.) among recipients who developed moderate or severe CAV compared with those with mild CAV and normal angiograms (+13.5 vs. +3.8 and +0.8 pg/ml).
Conclusions: Our results suggest that elevated plasma levels of PlGF are associated with angiographic evidence and severity of CAV. The increase in PlGF during follow-up of HTx is a predictor of the development of CAV.

P-150 PROFILE OF HEART TRANSPLANT RECIPIENT WITH DYSLIPIDEMIA IN THE ERA OF THE UNIVERSAL USE OF STATINS – CROSS-SECTIONAL STUDY

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Background: Effectiveness of statins used in orthotopic heart transplant (OHT) recipients to avoid acute rejection (AR) during the 1st year after surgery and coronary vasculopathy (CAV) thereafter was established in prospective randomized trials, giving the ground for the universal use of this group of drugs independent of the lipid disturbances presence.
Aim: Aim of the study was to describe the occurrence of dyslipidemias in OHT recipients after introduction of guidelines suggesting the use of statins in all individuals able to tolerate this therapy.
Methods: Medical records of all OHT recipients undergoing routine clinical check-up between January and June 2010 were screened for the presence of dyslipidemia (total cholesterol >5 mmol/L, LDL-cholesterol >3 mmol/L, triglycerides >1.65 mmol/L, HDL <1 mmol/L in the serum). Study group consisted of 322 pts. (265 M/57 F, 53.6±12 y/o, 7±4 y. after OHT, coronary artery disease (CAD) before OHT in 113/35% pts., no. of AR episodes 1.9±1.9, CAV diagnosed in 77/24% pts., arterial hypertension in 299/93% pt., diabetes in 89/28% pts., treated with cyclosporine-A/tacrolimus/mycophenolate/everolimus/sirolimus/azathioprine/prednisone/statins - 42/36/56/22/7/3/15/77%). Results of typical clinical, ultrasound, and biochemical evaluations were analyzed statistically to create profile of pts. with dyslipidemias.
Results: At least 1 dyslipidemia was observed in 212/66%, hypercholesterolemia in 121/38%, high LDL in 135/42%, hypertriglyceridemia in 110/34%, and low HDL in 48/15% pts. Typical pt. with dyslipidemia was prone to be older, with CAD before OHT, hypertensive, overweight, and obese, with higher

HbA1C when diabetic, treated less frequently with tacrolimus but achieving higher level of it, more often receiving everolimus. Similar profiles were constructed for all dyslipidemias.
Conclusions: Despite almost universal use of statins dyslipidemias are present in 2/3 of OHT recipients. It is related to typical atherosclerotic risk factors, however the influence of immunosuppressants is also significant.

P-151 DTCM-GLUTARIMIDE SUPPRESSES IFN-γ AND AMELIORATES CARDIAC ALLOGRAFT ARTERIOSCLEROSIS IN MICE

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Background: Transplant arteriosclerosis (TA) remains an unresolved problem to a long graft survival. Allo-antigen specific immunity plays a major role in TA, but non-specific reactions also contribute. Indeed, importance of IFN-γ has been previously shown. Also, vascular inflammation and remodeling including vascular smooth muscle cell (VSMC) proliferation are essential for pathogenesis of TA. 3-[(dodecylthiocarbonyl)methyl]-glutarimide (DTCM-G) is a newly developed agent that has been shown to inhibit activation of T cells and macrophages.
Aim: Effect of DTCM-G on cardiac allograft vasculopathy (CAV) was investigated using a mouse heart transplant model.
Methods: A MHC class II disparate B6.CH-2bm12 (Bm12)-to-C57BL/6 (H-2b: B6) mice cardiac transplant model was utilized. Cardiac recipient was given intraperitoneally either vehicle (n=8) or DTCM-G at 40 mg/kg/day (n=8). Animals were sacrificed 4 weeks later, and the degree of CAV was assessed.
Results: DTCM-G treatment significantly ameliorated CAV as indicated by the graft arterial disease (GAD) score (0.68±0.26 vs 1.64±0.22, $P<0.05$), arterial luminal occlusion (14.8±16.4 vs 36.3±16.3%, $P<0.05$), and intra-graft cellular infiltration of both CD4+ (14.7±2.0 vs 35.7±1.5 cells/HPF, P=0.005) and CD8+ (12.7±0.9 vs 25±2.6 cells/HPF, P=0.005) cells as compared to those of vehicle control. At 2 weeks after transplantation, population of the splenic CD4+CD154+ (1.74±0.07 vs 2.68±0.49%, $P<0.05$) and IFN-γ producing (5.0±1.7 vs 20.9±2.2 spots/500000 cells, $P<0.05$) cells against donor antigens were significantly reduced by DTCM-G administration. In addition, IFN-γ mRNA expression of cardiac allograft was down-regulated. Further, DTCM-G significantly suppressed proliferation of B6 mouse VSMCs in vitro in a dose-dependent fashion when supplied at a dose of >5 μg/ml (n=3).
Conclusion: DTCM-G suppresses allo-immune responses and intra-graft IFN-γ expression, and ameliorates CAV formation. Inhibitory effect of DTCM-G on VSMCs may also contribute to attenuation of vascular remodeling.

P-153 HEART TRANSPLANTATION IS FEASIBLE IN PATIENTS WITH IMPAIRED RENAL FUNCTION

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Objective: Impaired renal function (RF), defined as a glomerular filtration rate (GFR) of 40 ml/min/1.73 or less, is considered a contraindication to heart transplantation (HTx). We reviewed our experience of HTx in patients with severely impaired RF including those in the need of renal replacement therapy (RRT) in the intensive care unit (ICU).
Methods: 464 HTx procedures were performed (mean age 42±17, 354 male) between 1984 and 2009. GFR was measured systematically in all patients with either the 51Cr-EDTA- or the Iohexol-clearance methods. Survival was compared between patients with preoperative GFR <40 (n=29, Group 1) and >40 (n=371, Group 2). Two patients were on hemodialysis and 10 patients had a simultaneous kidney transplant (KTx) in group 1. Survival was compared between those needing postoperative RRT in the ICU (N=83) and those without (n=340).
Results: There was no significant difference in long-term survival between group 1 and 2. No significant difference in long-term survival was observed regardless of how GFR data was stratified (excluding children <17; stratifying GFR <30: >30 and <60: and >60; conditional survival on 1 week or 1 year). Furthermore, there was no significant difference in long-term survival for patients in need of temporary RRT compared to those without. Logistic regression analysis showed that Diabetes Mellitus, preoperative ventricular assist device and preoperative GFR were independent predictors of renal failure at one year following HTx in a multivariate model. In contrast, previous cardiac surgery and age were independent prognosticators for death within one year.
Conclusion: Patients with impaired RF preoperatively and those in the need of RRT early postoperatively had similar long-term survival compared to patients with normal preoperative RF. However, to acheive acceptable outcome after HTx in patients with impaired RF some will require a simultaneous KTx.

P-154 HEART DONATION AND TRANSPLANTATION IN SAUDI ARABIA

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Objective: To evaluate the practice of heart retrieval, transplantation and outcome in Saudi Arabia.
Methods: The study was applied for all donors and recipients of heart donation and transplantation from the year 2000 to 2010. The data includes donor's age, gender, and cause of brain death (BD) to include its ICU stay which then correlated with the outcome of heart transplantation.
Results: There were 2,459 declared death by brain function criteria in which families were approached for organ donation during the study period. Consent for heart donation were obtained in 689 (28%) cases, and out of these, 103 (15%) were transplanted as whole heart and 316 (46%) cases were used as a source for valves. The remaining 270 (39%) cases were not retrieved due to medical, technical reasons and donor/recipient incompatibility. The data for 103 whole heart transplant recipient shows that the donor's mean age is 32 years, while the recipient mean age is 34 years. The outcome of the transplant reveals that 75% (77 out of 103) of them are still active, 24 died and 2 lost follow up. Evaluation of the 77 active cases indicates that 6 of them are in "good" condition, 68 in "good" condition and 3 cases with "good". The mean follow up post transplant period for the cases was 31.6 months. The actual patient survival at two and five year was 81.8% and 78.2% respectively.
Summary: The heart transplantation outcome in Saudi Arabia is excellent compared to international data. However, more efforts are needed to increase the acceptance rate of heart retrieval and transplantation.
Keywords: Patient Survival, Heart transplantation, Saudi Arabia

P-155 IMMUNOSUPPRESSIVE THERAPY IN LONG TERM HEART TRANSPLANTS: 5 YEAR SURVEY ON 56 PATIENTS WITH MORE THAN 10 YEAR FOLLOW-UP

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Background: Gold standard treatment of long-term survivors (>10 years) after heart transplantation is still unclear. Mycophenolate and Everolimus have been advocated to reduce CNIs-exposure. Long-term survivors are often very stable patients. This study aimed to describe changes in treatment and outcome of 56 patients surviving more than 10 yeas prospectically followed-up for 5 years.
Methods: Between January 2005 and December 2010 56 out of 143 transplants done between 1988 and 1996 were followed-up at our centre. Outcomes and drug treatments of those patients were prospectively entered in a dedicated database for cost-analysis.
Results: 39 patients survived all the study period; 7 patients developed chronic graft failure. Echocardiography showed good graft function in 30 patients, only 3 patients die with graft failure. Renal function significantly worsened in survivors (mean creatinine in the 2005 1,81±0,47→2,25±1,19 $p<0,0001$). Dyalisis was necessary in 5 patients; only 1 patient survived. Drug Regimens during the study is showed in table 1. Mycophenolate was prescribed in 19 patients, Everolimus to 8 patients (3 for renal dysfunction, 2 for neoplasm, 3 for CAV). Patients switched to Everolimus for CRF needed dyalisis after a mean of 18 month while only 2 needed dyalisis when treatment remained unchanged. No data were collected about proteinuria. Patients switched for neoplasms and CAV had better outcome. CSA was significantly reduced during the observation period in all patients unrespective to the antiproliferative drug.
Conclusions: This study shows changes in immunosuppressive strategy in long-term survivors after heart transplantation. Graft performance is not the matter. Changes in immunosuppression are uncommon and due to concomitant diseases. CAV and PTLD are the most effective indication to everolimus. Switch to everolimus for renal dysfunction after so long time of CNI assumption was not useful.

P-156 "NON WORKING BEATING HEART" A NOVEL METHOD OF MYOCARDIAL PROTECTION DURING HEART TRANSPLANTATION

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Background: We attempt to reduce the ischemic time during implantation of the donor heart in the bicaval/bipulmonar orthotopic position using normothermic beating heart and thus facilitate the transplanted heart adaptation to the recipient.
Methods: Already in cardiopulmonary bypass, the aorta anastomosis was done first, allowing the coronary arteries to receive blood flow and the recovering of the beats. The remainder anastomosis is performed on a beating heart in sinus rhythm. The pulmonary anastomosis is the last to be done. This metothodology was applied 1n 10 (2,85%) subjects: 7 males, age 16-69 years (mean 32.7), aortic systolic pressure between 90-100 mmHg (mean 96), pulmonary systolic pressure between 25-65 mmHg (mean 46,1), pulmonary vascular resistence between 0.9-5.0 wood (mean 3.17), transpulmonary gradient between 4-13 (mean 7.9) and 8 male donors, age 15-48 years (mean 27.7), weight 65-114 kg (mean 83.1) with causes of brain damage: encephalic trauma in 5, hemorrhagic stroke in 4 and brain tumor in 1.
Results: The ischemic time ranged from 58 to 90 min (mean 67.6) and 8 donors were in hospitals of Sao Paulo and two in distant cities. All grafts assumed the cardiac output after the implant requiring low-dose inotropic therapy and mantained these conditions in the postoperative period. There were no deaths and all were discharged. The late evolution goes from 1 to 11 months with 1 death ocurred after 4 months due to sepsis.
Conclusion: It is a small sample, but, besides reducing the ischemic time of the procedure, allows the graft to regais and mantain their beats without pre or after load during implantation which entails the physiological recovery of the donated heart.

P-157 EVALUATION OF EFFICACY AND SAFETY OF DE NOVO ADVAGRAF IN CARDIAC TRANSPLANT PATIENTS: EARLY RESULTS OF AN OBSERVATIONAL STUDY

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Background: Advagraf (tacrolimus extended-release capsules) has been tested in de-novo liver and renal transplant recipients. In Cardiac transplantation there exists only data on conversion of tacrolimus to advagraf. The aim of this analysis was to evaluate efficacy and safety of de novo use of advagraf in cardiac transplant patients.
Patients and Methods: 10 patients received advagraf after ATG induction therapy, 8.1±3.3 days after cardiac transplantation. Mean patient age was 40.1±16.4 years. All patients received also mycophenolate and steroids. Follow-up was 4.4±1.7 months. Dosages, tacrolimus drug levels (tac) and creatinine (crea) levels were recorded 1,2 weeks and 1 to six months post transplant. Clinical events were defined as acute rejection, infection type, new onset diabetes mellitus (NODM) and renal dysfunction.
Results: Six-month survival was 100%. Two patients were converted to cyclosporine due to NODM 1 and 3 months post transplant. No rejection episodes were recorded during follow-up. Two infections were documented 6 months after transplant (bacterial pneumonia and CMV infection). Advagraf starting dose was 6.2±1.9mg/d. Crea before start was 1.14±0.34mg/dl. First measured tac levels at steady state (5 days post drug start) were 7.8±3.7ng/ml. Until the end of the first month advagraf was slowly increased to 10.1±1.9 mg/d with tac levels of 10.7±2.8ng/ml and crea of 1.22±0.31mg/dl. Three and six month drug doses were 9.3±2.11 and 8.2±0.8 mg with corresponding tac levels of 11.2±2.9 and 11.2±1.3 ng/ml. Crea was 1.47±0.22 and 1.49±0.32 mg/dl. There were no events of renal failure.
Conclusion: Advagraf de-novo therapy shows acceptable efficacy and safety early after cardiac transplantation. ATG induction therapy might be responsible for a low risk of acute rejection despite lower early tac levels.

P-158 CLUSTER TRANSPLANTATION FOR SHORT BOWEL SYNDROME DUE TO COMBINED THROMBOSIS OF THE SUPERIOR MESENTERIC ARTERY AND CELIAC TRUNK

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Background: The treatment of the short bowel syndrome (SBS) due to thrombosis of the superior mesenteric artery (SMA) can be achieved by an intestinal transplantation (IT), but in patients who also develop chronic thrombosis of the celiac trunk, the cluster transplantation (CT) is considered as the only therapeutic approach.
Clinical Case: We present the case of a 38-year old woman who underwent surgical operation for an acute mesenteric thrombosis due to chronic thrombosis and who required the resection of 150 cm of small intestine. In the angio-CT scan, a chronic thrombosis of the celiac trunk and SMA was demonstrated with an important vascular redistribution with collateral branches that originated directly from the aorta. In a second surgery, an aortomesenteric bypass was done in order to improve the blood flow of the remaining small intestine, but 140 cm of small intestine had to be resected because of the thrombosis of the bypass. Because of association of celiac trunk thrombosis, and considering the risk of ischemia of other abdominal organs, a CT was indicated. The implant of the graft was done including stomach, duodenum, pancreas, small intestine, and liver. The patient presented a torpid postoperative period requiring 80 days of ICU stay, but had a good evolution afterwards with normal function of all transplant grafts: normal liver function, normoglucemic state, good oral intake and regular intestinal habit with a biopsy of the intestinal graft (day 86) with no signs of rejection.
Conclusion: The CT is a valid therapeutic option for the treatment of SBS due to combined chronic thrombosis of the SMA and celiac trunk.

P-159 ROLE OF HCV POSITIVE DONORS IN HEART TRANSPLANTATION

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Aim: To verify the impact of HCV positive donors in heart transplantation, our experience was reviewed.
Matherials: Among 73 patients (15 females, 20%, 58 males 80%, aged 18 to 69 years, mean 54±12y) affected by dilated cardio myopathy, 42% vs. other 58%, p.v. 0.1) undergone to heart transplant between April 2008 and February 2011 35 patients, 48%, were on emergency conditions (NYHA class IV: 100%; preoperative IABP: 100%; preoperative mechanical assistance: 80%; preoperative mechanical ventilation: 91%; noradrenalin at a mean dosage exceeding 0.1 g/kg./h. or simultaneous infusion of two inotropic drugs,100%).
In 13 candidates, 18%,Group 1, G1, organs were retrieved from HCV positive donors (4 females, 9 males, mean age 21±6). Seven donors were HCV RNA positive.Remaining 26 candidates, Group 2, G2, had organs from HCV negative donors.
Entire population had the same triple drugs immunosuppressive therapy. Patients were follow up from 38±12 to 1±1 month in G1 and from 29±13 to 1±0.2 month in G2, p.v.: 0.1.
Results: Are summarized in Table 1.

Table 1. Results

Variable	Group 1 (13 HCV pos. donors)	Group 2 (26 HCV neg. donors)	p.v.
30 days survival rate	90%±6	91%±4	0.1
30 months survival rate	89%±5	88%±1	0.1
30 months freedom from any Infection requiring hospital admission	35%±2	41%±4	0.1
30 months freedom from acute rejection	29%±5	31%±7	0.1
30 months freedom from chronic rejection	45%±4	61%±9	0.1
30 months freedom from renal failure	68%±3	71%±11	0.1
Freedom from HCV infection in negative HCV pts receiving organs from HCV pos. but RNA pos. donors	25%±5		
Freedom from HCV infection in negative HCV pts receiving organs from HCV pos. but RNA neg. donors	80%±15		

Conclusion: Use of HCV positive donors is controversial. Chronic rejection freedom may be reduced by donor's drug addiction. Our limited experience seems to indicate that they may play a positive role in emergency conditions.

P-160 IMMUNOSUPPRESSION AND RENAL FAILURE (RF) IN HEART TRANSPLANTATION: 3 YEARS EXPERIENCE

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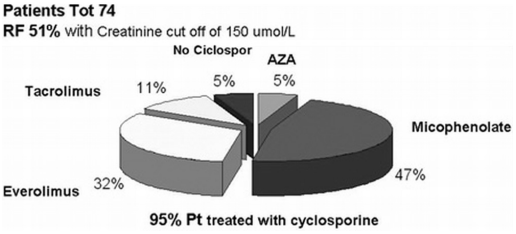
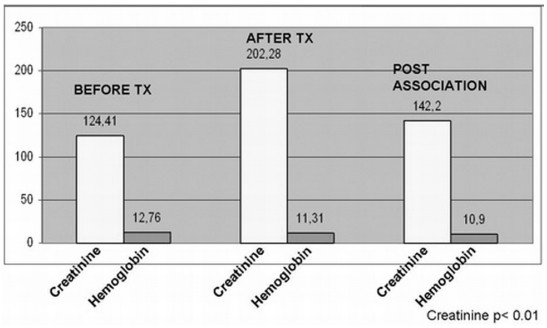
Introduction: In organ transplantation the benefit of a new organ has been reduced by the necessity of by using of immunosuppression therapy to control rejection, having to face the side effects of therapy.
We have reported the renal function at 3 years after cardiac transplantation in patients treated with calcineurin inhibitors. In particular, we have focused on the reduction of renal function due to the need of the immunosuppressive therapy with Cyclosporine or Tacrolimus. For this reason, we have tried to reduce the dosages of these drugs with the introduction of a second immunosuppres-

sant such as Mycophenolic Acid, Azathioprine and Everolimus, to achieve adequate immunosuppression reducing nephrotoxicity. We show the experience of the heart transplant center of Padua.
Materials and methods: We have analyzed, in all the patients transplanted in our center between 2007 and 2009, the levels of creatinine and hemoglobin before and after transplant during monotherapy with Calcineurin inhibitors and the creatinine and hemoglobine during calcineurin inhibitors associated with another immunosuppressant after reducing the dose of cyclosporine.
Results and Conclusions:

- The combination Calcineurin inhibitors with a second immuosuppresant can improve Renal Failure
- The most commonly used immunosuppressants in combination are Everolimus and Mycophenolate (33%-47%)
- Hb showed a decrease after TX and also after pairing.



Immunosuppression in heart transplantation with RF (creatinine ≥150 mg/L).



Comparison of creatinine and Hb in patients treated with calcineurin inhibitors before TX, after TX and in association with other immunosuppressant therapy.

- The association has allowed us to reduce the plasma levels of C0-C2 respectively on average values of 150-450, while maintaining a good immunosuppression and delaying the progression of RF (creatinine: 142 μmol/L < cut off 150 μmol/L)
- The reduction of plasma level of cyclosporine thanks to the combination drugs, has not increased the number of rejection (monitoring with Endomyocardial Biospy)
- Heart has a lower immune-tolerance compared to kidney and liver, greater compared to lung.

P-161 QT INTERVAL PARAMETERS ALTERNATION IN PATIENTS RECEIVED RENAL TRANSPLANTATION

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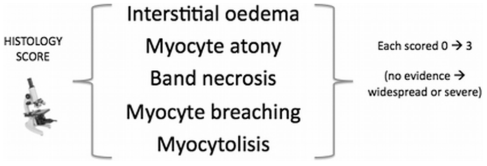
Background: Cardiovascular disease is still the most common causes of mortality in patients with end stage renal disease and renal transplantation (RT). Prolongation of QT-max and QTc dispersion are risk factors of cardiac arrhythmias and mortality. This study evaluated the changes of QT parameters after hemodialysis and RT and correlation between these changes and serum electrolytes.
Methods and materials: Mean serum electrolyte and 12 lead ECG were recorded immediately before and after the last dialysis session and also 2 weeks after kidney transplant in 34 patients underwent kidney transplant. Each QT interval was corrected for patient heart rate using Bazett's formula. The differences of QT parameters (QTd, QTcd, QTc max) between groups (pre hemodialysis (pre-HD), post hemodialysis (post-HD), post renal transplantation (post T) was compared. Correlation between QT parameters changes and serum electrolyte and acid –base alternation were analyzed.
Results: Among patients, the corrected maximal QT interval (QTc max) decreased significantly after transplantation comparing the time of pre –HD (p=0.002) and post-HD (p=0.003). Mean of QTc max decreased significantly between pre-HD, post-HD and post-T (p=0.001). Only increased corrected calcium (P=0.008) and decreased phosphor (p=0.009) level in the group of pre-HD and post T have significant differences.
Conclusion: In RT recipients, QT max was shorter than hemodialysis patients. This alteration significantly was correlated with corrected serum level of calcium and phosphor.

P-162 PRESERVATION OF DONATION AFTER CARDIAC DEATH HEARTS USING OXYGENATED, HYPOTHERMIC MACHINE PERFUSION

Omar A. Mownah[1], Muhammad A. Khurram[1], Christopher Ray[1], Joaquim Majo[1], Noel M. Carter[2], John Brassil[1], Robert Peaston[1], Kelly Phillipson[1], Susan Stamp[3], John H. Dark[1], David Talbot[1]. *[1]Transplant Surgery, Freeman Hospital, Newcastle upon Tyne, United Kingdom; [2]Faculty of Applied Science, University of Sunderland, Sunderland, United Kingdom; [3]Institute of Cellular Medicine, Newcastle University, Newcastle upon Tyne, United Kingdom*

Background: Expanding the donor pool by sourcing hearts from Donation after Cardiac Death (DCD) may stem the annual decline currently seen in heart transplantation. Optimal preservation of the procured DCD heart would be imperative to mitigate the deleterious effects of prolonged warm ischaemia. One possible technique is preservation by oxygenated, hypothermic machine perfusion (OHMP).
Methods: Hearts from 5 pigs (mean weight 31.2kg) were explanted after 10 minutes of warm ischaemia and immediately flushed with cold AQIX RS-I® (a novel preservation solution). The hearts subsequently underwent OHMP with RS-I on either a modified *ex vivo* reperfusion rig (n=3) or on the ORS LifePort® (n=2). Oxygenation of the RS-I was achieved by direct introduction of O2 (0.5L/min). Perfusion pressure was maintained at 10-15mmHg at a temperature of 4-8°C.
Coronary sinus effluent was regularly sampled for measurement of Fatty Acid Binding Protein (FABP) and lactate. Hearts were weighed before and after OHMP. Following 6 hours of OHMP, biopsies were taken for histological analysis.
Results:



		% age Weight gain	FABP 1 hour	FABP 3 hours	FABP 6 hours	Histology Score	Lactate (mmol/L)
Modified *ex vivo* rig	1	18.3	417	532	740	4	1.12
	2	11.8	258	703	1387	10	1.48
	3	29.0	332	732	1484	4	1.12
LifePort®	1	34.0	67	309	443	3	0.615
	2	34.3	75	317	608	4	0.96

Mean pO_2 level in the perfusate was 84.3kPa.
Conclusions: Customised hypothermic machine perfusion with oxygenation can safely be used to preserve DCD-sourced hearts. In both circuits high pO_2 levels were maintained, with low lactate levels measured in the coronary sinus effluent.
OHMP performed on the LifePort®, which is custom designed for machine perfusion, was more practical, with less difficulty controlling the perfusion pressure and temperature. The reduced lactate and FABP levels when using the LifePort® reflect this. Furthermore, histology demonstrated only mild interstitial oedema with mild contraction bands present after 6 hours on the LifePort®, with no severe damage found. The relatively high weight gain found in both groups can be explained by the lack of colloid present in the perfusate.

P-163 AN EX VIVO MODEL FOR REANIMATING PORCINE HEARTS SOURCED FROM DONORS AFTER CARDIAC DEATH

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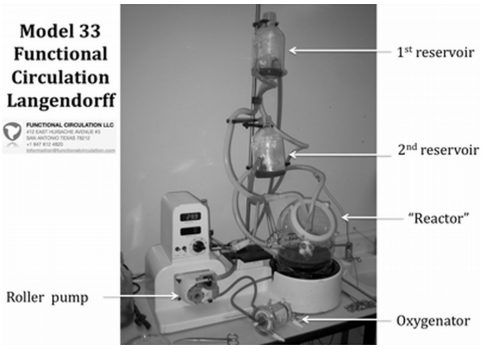
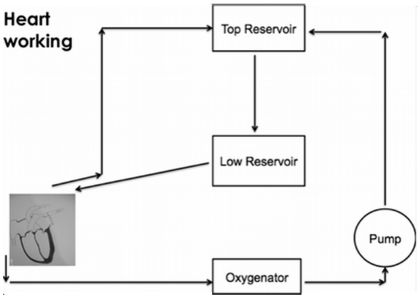
Background: *Ex vivo* reperfusion of organs sourced from Donation after Cardiac Death (DCD) offers the opportunity of organ resuscitation as well as functional testing. This technique is now established clinical practice for DCD lung transplantation. We have extended these practices to reperfuse DCD-sourced porcine hearts.

Materials/Methods: A Functional Circulation Model 33® rig was modified using 2 reservoirs and an inline, hollow fibre oxygenator (Chalice Medical®).



The circuit comprises an autoclaveable glass chamber within which the heart is positioned. Donor blood (heparinised, leukocyte-depleted) is combined with Aqix RS-I® solution (a novel preservation solution) and maintained at 37°C using a water bath. Initially, blood is pumped to the top reservoir via the oxygenator.



With adjustment of the column height, the pressure at the aortic root leading to the coronaries can be varied. Once ventricular contractions are sufficient to sustain the circuit, the lower reservoir feeding into the left atrium is introduced into the circuit by releasing the preplaced clamps. This permits formation of a left-sided working heart model. Inotropic support is infused via a 3-way connector in the oxygenator. Safe defibrillation can be performed in the reactor.

Results: The circuit facilitated excellent oxygenation with mean pO_2 levels of 80-90kPa. Furthermore, the heat exchange allowed controlled rewarming of the heart. In total 20 porcine DCD hearts were reperfused in Langendorff mode using the circuit described, with successful reanimation of 12 hearts.

Conclusions: This circuit can be used successfully to reperfuse and reanimate DCD hearts. Explantation of the heart followed by this method of *ex vivo* reperfusion offers practical advantages and, significantly, removes potential ethical barriers to reanimating DCD hearts *in vivo*.

P-164 THE EXPERIMENTAL STUDY OF INDUCING IMMUNETOLERANCE BY USING TLR4 MONOCLONAL ANTIBODYS IN TAT CARDIAC ALLOGRAFTS

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Background: This study was designed to investigate the effect of TLR4 monoclonal antibodies (Toll like receptor 4 monoclonal antibodies,TLR4mab)on the recipient immunoloregulation in the model of Wistar to SD rat cardiac allotransplantation. The mechanisms of rejection in allotransplantation will be explored in the model.

Materials and methods: Donor (SD rat) and recipient (Wistar rat) were divided randomly into two groups. Group A (control group); Group B (TLR4mAb Group): The recipients were injected with TLR4mab 100ug/kg in abdomen before preoperative 24hs and every 48 hours afte transplantation. The mean survival time (MST)and the pathology of grafted hearts were observed.The expression lever of TNF-α, IFN-γ,IL-2,IL-10 and TGF-β1 in peripheral blood were assayed by ELISA. The expression of NF-κB in donor heart were observed as well.

Results: (1) MST :Group A: 5.6±0.89d; Group B: 25.2±3.40d. (2) The expression lever of cytokine in the recipient's peripheral blood in Group B is significantly lower than in Group A ($P<0.05$), such as TNF-α, IFN-γ, IL-2,IL-10. (3) The protein expression lever of NF-κB was markly decreased in Group B applied with TLR4mab.

Conclusions: (1) Using TLR4mab can prolong the survival time of allograft through inhibiting the secretion of the related cytokine factors such as IL-2, IL-10, IFN-γ. (2) Using TLR4mab can affect the expression level of NF-κB.

P-165 THE METABOLIC SYNDROME ONE YEAR AFTER HEART TRANSPLANTATION DOES NOT AFFECT 10 YEAR SURVIVAL BUT ISCHEMIC HEART DISEASE BEFORE TRANSPLANTATION INCREASES THE RISK OF METABOLIC SYNDROME

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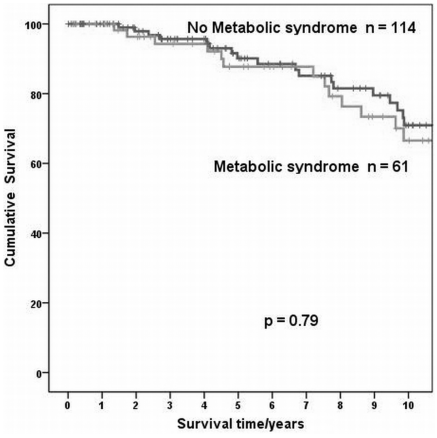
Objectives: The metabolic syndrome (MetSyn) is associated with cardiovascular morbidity, mortality in the general population. The purpose of this study was to assess the impact on survival in a group of patients with MetSyn one year after heart transplantation (HTx).

Methods: A retrospective cohort study of 175 patients alive one year after HTx between 1993 and 2008 at the Sahlgrenska Transplant Institute. The factors contributing to the MetSyn were determined at one year after HTx by the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) criteria with BMI instead of waist circumference.

Results: According to the NCEP-ATP III criteria 61 (35%) HTx recipient had MetSyn one year after HTx. However, MetSyn had no significant impact on survival during ten year follow up after HTx.



Within the study groups, high blood pressure was present at a rate close to 100%. No association was found between gender or age and the development of MetSyn. The presence of ischemic heart diseas (IHD) before HTx increased the risk by 2,75 for developing MetSyn one year after HTx.

Conclusion: Patients with IHD before transplantation runs higher risk of developing MetSyn one year after HTx and special attention should be taken to the contributing factors of the metabolic syndrome in this group. MetSyn had no significant impact on survival during the first ten years following HTx. Further analysis on cardiovascular end points will be studied. Data will be updated.

P-166 THE ROLE OF SERUM ALBUMIN (SA) IN THE PREDICTION OF MALNUTRITION IN PATIENT AT LEAST ONE HEART TRANSPLANTATION (HTX)

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Introduction: Malnutrition after heart transplantation (HTX) causes and aggravates coronary artery disease and heart failure. The risk for malnutrition is often underestimated by conventional measurements like the body mass index (BMI) or the subjective global assessment (SGA). This study aimed to compare the capacity to predict malnutrition of the BMI, SGA and serum albumin (SA).

Materials and Methods: Recipients at least 1 year after HTX were included in the analysis. BMI, BIA, SA and SGA were determined; risk factors for hyponutrition and concomitant diseases (diabetes mellitus, renal insufficiency, hypertension) were assessed. All measurements were correlated. The BIA was considered as reference standard, a phase difference (PD) below 4 degrees was regarded as cut off. All parameters were compared with respect to their prognostic accuracy regarding the cut-off.

Results: 60 recipients (47 male, 13 female) were analysed. The prevalence of malnutrition among the assessment procedures was: SGA 6,6% (4/60), BMI 8,3% (5/60), SA 31,6% (19/60) and BIA 48,3% (19/60). PD values did not correlate with BMI (r=0,118; p=n.s.) or the SGA (r=0,289; p=n.s.), but good with SA (r=0,458; p=0,001). Multivariate analysis yield SA as superior predictor for malnutrition as compared to the BMI. ROC analysis showed an AUROC of 0,716 for SA as compared to 0,693 for BMI in the prediction of existing malnutrition as defined by the PD.
Discussion: In the presented analysis daily used parameters for malnutrition did not show as much power in predicting an existing alimentary deficiency for heart recipients as did serum albumin.

P-167 INDUCED IMMUNE TOLERANCE TO CARDIAC ALLOGRAFTS BY INTRATHYMIC INOCULATION WITH ALLOGENEIC SPLEEN CELLS AND WHOLE-BODY -RADIATION IN THE PIG

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Purpose: Validation of the pig as an experimental animal model for the study on inducing the immune tolerance to cardiac allografts by intrathymic inoculation (IT)with allogeneic spleen cells and whole-body irradiation (WBI).
Material and Methods: In the group A, without IT and WBI, heterotopic cardiac transplant were performed in recipient pigs. In the group B and group C, the evolution of the lymphocyte and its subsets CD_4, CD_8 count was followed for up to 14 days after irradiation in pigs exposed to whole-body γ-radiation at the dose of 2 Gy. In the group B, synchronously, allogeneic spleen cell was injected into the thymus of the recipient pig. Then HCT was performed in pigs of the group B and C 2 weeks after pretreatment. Survival time of cardiac allografts was determined by palpation of donor heartbeat in the abdomen. In each group, recipient serum was harvested in order to analyze IL-2 and IL-10 after transplant.
Results: Survival time of donor heart in the group C was significantly longer than that in group the A and the group B. The level of IL-2 of recipients in the group C was much lower than that of in the group A and group B after transplantation 1$\sim$4 days ($P<0.01$).
Conclusion: WBI could eliminate most of lymphocytes, especially CD_4 T lymphocytes in the peripheral blood. Pretreatment with IT and WBI in the outbreed pig could induce “TRANSIENT” immune suppression, but not the “permanence” immune tolerance in the rodent.

P-168 INCORPORATION OF THE DONOR DNA IN TO THE RECIPIENT LYMPHOID CELLS AFTER ALLOGENEIC TRANSPLANTATION

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Background: Passenger cells, normal constituents of whole organs, migrate from the graft create microchimerism which is suggested to be essential for sustained survival of allografts. The process of DNA transfer between mammalian cells remains not well understood. In our previous study we found donor Sry-PCR product in recipient tissues. This product was detected in splenic macrophages and DC’s, but was absent from hepatocytes and parenchymal cells. It has been suggested that donor DNA may play a role in rejection having influence on tolerance.
Aim: In our study we tried to assess the amount of *Sry* gene in different recipient tissues after allogeneic heart transplantation with and without immunosuppression (FK506).
Material/Methods: In allogeneic combination male rats BN served as donors and female rats LEW as recipients. Genomic DNA was extracted from the recipient blood and tissues at different times after grafting. *Sry* was detected using Real-time PCR. Relative amount levels in the different samples were calculated by using the comparative C_T method with *Gapdh* as internal control.
Results: The relative amount of *Sry* gene was high in all female tissues 30 days after heart transplantation with immunosuppression, with highest values in blood, liver, spleen and lymph node. Thirty days after heart transplantation without immunosuppression the relative amount of *Sry* gene was in all tissues lower than with immunosuppression.
Conclusion: Detection of donor male DNA isolated from female blood and tissues suggests its spontaneous transport into recipients. Its higher levels in immunosuppressed recipients point to cytotoxicity of anti-rejection drugs.The question remains open whether long-lasting presence of donor DNA may have any relevance to the rejection or tolerance process.

P-169 BOTH HEART FAILURE AND DIABETES INTENSIFY DEPOSITION OF ADVANCED GLYCATION END (AGE) PRODUCTS IN CORONARY VESSELS, BUT LOCALIZATION IS DIFFERENT

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Background: Disturbed glucose metabolism is an important but unlikely the sole factor leading to AGE formation. A potential influence of heart failure on AGE amount and distribution in myocardial tissues and coronary vessels is poorly recognized.
Aim: Aim of the study was the assessment of advanced glycation end product (AGE) deposits in unaffected myocardial vessels in heart failure patients with and without diabetes mellitus type 2 (DM2) undergoing transplantation.
Material and Methods: 134 hearts explanted at a time of transplantation were under investigation: 14 hearts from subjects with ischemic cardiopathy and DM2; 8 hearts from subjects with dilated cardiopathy with DM2; 67 hearts from subjects with ischemic cardiopathy w/o DM2; 47 hearts from subjects with dilated cardiopathy w/o DM2. They were compared with 14 hearts of individuals with DM2 who died of non-cardiac reasons and 20 donor hearts discarded due to non-medical reasons (control group). AGE localization was determined immunohistochemically in tissue sections. A semi-quantitative scale was used to assess reaction intensity in arteries, arterioles, capillaries, venules and veins.
Results: Both heart failure and DM2 intensify accumulation of AGEs in coronary vasculature. Both types of cardiomyopathy increased AGE accumulation in intramyocardial veins more than in arteries. The presence of DM2 significantly increased AGE in arterioles and capillaries, especially when coexisting with cardiomyopathy. The type of cardiopathy did not influence a pattern of AGE accumulation in myocardial vessels.
Conclusions: Deposition of AGEs is enhanced by both heart failure and DM2. However, chronic heart failure increases AGE deposition mostly in veins, while DM2 promotes AGE accumulation in arterioles.

Donation / retrieval

P-170 IS HCV (+) A CONTRAINDICATION TO BE RECIPIENT OF LIVING DONOR?

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Introduction: There is an increasing number of patients in waiting list and stable number of liver grafts from brain death donors. Consequently, there is an increase rate of mortality of patients in the waiting list.
Patients and Methods: There were 47 patients transplanted with grafts from living donors (all OLT performed between May 1995 and July 2008). These patients were divided in 2 groups that were compared: Group A includes 13 recipients with HCV-cirrhosis, and Group B includes 34 patients with negative HCV infection.
Results: The mean age of the series of 47 recipients was 38.7 years (51.2 years in Group A; p=0.023). Gender: 28 were males, and 19, females.
The overall rate of intraoperative and postoperative complications was 59.6%: 61.5% in Group A, and 58.8% in Group B; p=0.87). Three of these complications were small-for-size (1 case in Group A). The overall rate of re-OLT was 23.4% (11 cases): 3 cases in Group A, and 8 cases in Group B).
The mean recipient survival in group A was 2271 days, and in group B was 2949$\pm$787 days (p=0.206). The 1-, and 5-year actuarial recipient survivals of Group A were 84.6% and 68.4%, respectively, and 88.2% and 85.1, respectively, in Group B. The mean graft survival was 1614 days in group A, and 2174 days in group B (p=0.244).The 1-, 3, 5, and 10-year actuarial graft survivals in Group A were 69.2%, 53.8%, 46.2%, and 30.8%, respectively; whereas in group B they were 70.6%, 67.4%,67.4%, and 62.2%, respectively, at the same periods.
Conclusion: The use of liver grafts from living donors for patients with HCV-cirrhosis is associated with worst patient and graft survivals in comparison with other OLT indications.

P-171 HAND ASSISTED RETROPERITONEOSCOPIC LIVE DONOR NEPHRECTOMY – 230 CASES SINGLE CENTRE EXPERIENCE

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Introduction: Live donor nephrectomy can be performed using various techniques. In our unit we have adopted the Hand Assisted Retroperitoneoscopic (HARS) approach since 2005. The aim of this study was to review the results from the first 230 cases including right side, complex anatomy and obese donor cases.
Methods: Between 2005 and 2010, 230 HARS nephrectomies were performed. Prospectively collected data were analysed using SPSSv17.
Results: There were 115M and 115F donors. The mean age was 48 (min18, max76) and the mean BMI was 26kg/m2±3.5 (SD) [18kg/m2 - 38kg/m2]. 41 (18%) donors had BMI>30 kg/m2. There were 202 (88%) left and 28 (12%) right side neprhectomies. 109 cases (48%) had complex anatomy. The overall mean operative time was 136±45 min (SD), for simple anatomy 128±44 min (SD) and for complex 144±45 min (SD). Warm ischaemia time (WIT) was 97±43 seconds (mean ±SD), cold ischaemia time (CIT) was 63±35 min (mean ± SD) and the median blood loss 20ml (IQR=50). The median postoperative stay was 2 days (IQR=1). The incidence of minor and major complications was 5.2% and 2.6% respectively. There was no significant difference between left and right side nephrectomies with respect to age, sex, BMI, operative time, blood loss, WIT, CIT, complex anatomy and length of stay. Similarly, there was no significant difference in these parameters between donors with a high BMI (>30kg/m2) and those with a low BMI (<30kg/m2). Complex anatomy operations had a significantly higher blood loss (median 10ml versus 20ml, p=0.042) and CIT (56±26 versus 72±42 minutes [mean ±SD], p=0.003) than those with simple anatomy.
Discussion: HARS live donor nephrectomy is a safe technique, offering low incidence of complications to donors and a short hospital stay. This technique is suitable for complex anatomy, right side nephrectomy as well as obese donors.

P-172 DIFFICULTIES OF ORGAN TRANSPLANTATION COORDINATORS DURING PERFORMING THEIR JOB

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This study covers totally 64 people, who are working as active transplantation coordinator. This descriptive type study was performed with an questionaire between 22 February-15 May 2010.
35,9% of the coordinators were nurses, 54,7% were doctors, 4,7% were health care officer, 1,6% were social service officer and 3,1% were anestesia technician. The avarage rutime of coordinators was 4±4 years (min:0,5, max: 25). 82,8% of them were working in a potentially donor hospital; 17,2% in organ transplantation centre. Exclusively 53,1% of them were volunteers. The others were assigned to this position by the hospital management. 92,2% of the coordinators considered themselves appropriate for the position, the others did not. However, 32% indicated that their position did not provide professional satisfaction.
According to the survey, the major challenges were thougth to be due to; Inadequate support of the management (73.4%), Insufficient education of the coordinators (60,9%) and Reluctance because of inadequate salary (52%).
The suggestions of the coordinators were as follows; 1) To increase the awareness of the managers and provide their support, 2) Training organizations of the ICU and emergency service teams, 3) Salary regulations, 4) Public awareness activities.
According to our study; prominant problems for the coordinators seem to be that inadequate support, lack of education and inadequate wage. These results show that the organ transplantation coordinators do not have enough information about their profession and they can't earn enough money.Therefore through a process of organ transplantation coordinators should be adequqte training and remuneration policies should be established. Organ transplantation needs a multidisiplinary approach. In this context, relevant to all disciplines, managers and the community will be informed and keep their interest up activities should be held constant.

P-173 TRENDS IN THE QUALITY OF KIDNEYS OFFERED AND TRANSPLANTED IN RECENT YEARS. HOW MARGINAL IS A MARGINAL DONOR? ARE MARGINAL DONORS THE NORM? AND WHAT IMPACT THEY HAVE ON RENAL ALLOGRAFT FUNCTIONS? A SINGLE CENTRE ANALYSIS

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Background: Organ shortage has led to the increased use of so called marginal donors. Kidneys which were previously considered suboptimal are now being routinely accepted and used for transplantation. These so called Expanded Criteria Donor (ECD have demonstrated to convey a 70% or greater risk for graft loss for transplant recipients relative to an ideal donor kidneys.
Methods: A retrospectively analysis on the outcome of kidneys transplanted from "expended and beyond" criteria donors was performed over the last decade starting from January 2001 to December 2010. We analysed the impact of these donor variables on long and short term allograft outcome and survival. T-test is used to compare different groups and Kaplan-Meier estimator is used for graft survival analysis
Results: There were 234 cadaver renal transplants within this period with a distribution of HBD=155, NHBD=79. The overall 1 year Survival was 91% (213/234) with 92% (142/155) for HBD and 90% (71/79) for NHBD and a 2 years survival of 84% with 86% (134/155) for HBD and 80% (63/79) for NHBD. There is no significant change observed between different categories of donor kidneys. One of the major risk factor for graft loss is a combination of pre-existing hypertension and raised serum creatinine levels in non heart beating donor kidneys age above 60 years.
Discussion: These results demonstrate that in recent years the number of NHB extended criteria donors has significantly increased and careful selection of the donors can lead to better graft survival. This study can be used as a mile stone to conduct nationwide analysis to see the outcome of these kidneys on a broader scale.

P-174 ANALYSIS OF CONSENT RATES FOR ORGAN DONATION IN THE UK

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Introduction: In 2003, a national UK audit of deaths in ICUs was established to identify the potential for organ donation and determine factors impacting on consent. In 2008, as a result of the Organ Donation Taskforce recommendations in the UK, a new organ donation infrastructure was agreed which resulted in central employment and a doubling in number of Donor Transplant Coordinators (DTCs).
There has been no real increase in the proportion of families giving consent for organ donation since 2003, although the number of families approached has increased. This study seeks to understand factors associated with higher family consent rates.
Methods: In the year ending September 2010, 2,088 families were recorded as being approached about donation from donors meeting criteria identifying them as potential donors. The possible association with consent rate of a number of factors was investigated using binary logistic regression modelling. Factors considered included patient demographics and the nature and timing of the approach.
Results: Of the 2,088 patient families approached about donation, 58% consented (63% for donors after brain death (DBD) and 53% for donors after circulatory death (DCD)). Analysis was based on DBD and DCD patients combined. The consent rate was higher for white patients ($p<0.0001$), those with trauma-related deaths ($p=0.03$), where families expressed an interest in donation prior to approach ($p<0.0001$) and where the patient had expressed a wish to donate ($p<0.0001$). Consent was more likely for approaches made prior to neurological tests, although omission of patients not tested because of lack of consent may account for this. Finally, involving a DTC in the formal approach was an important factor ($p<0.0001$) indicating significantly higher consent rates.
Conclusions: This study is important in identifying a highly positive impact of a DTC being involved in the approach to families for consent to organ donation.

P-175 PROPOSED MODEL FOR PATIENT RESPONSE OUTCOME MEASURES (PROM) IN LIVE DONOR NEPHRECTOMY BASED ON DONOR RESPONSES

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Background: Patient Response Outcome Measures (PROMs) are a means of collecting information on the clinical quality of care as perceived by the patients themselves. In 2007, the UK National Health Service implemented plans to assess all elective procedures using a questionnaire answered by the patient.

The aim of this study was ascertain key questions that may affect the perceived outcome for kidney donors following donation.
Method: An anonymous questionnaire assessing peri-operative and post-operative care was sent to all donors who had undergone donor nephrectomy at our unit from January 2004 to December 2009. The responses were by quantitative and qualitative means using 5 point Likhert scale and free text boxes.
Results: There were 98 donors in the given time period with 51 returning the questionnaire. Donors rated nursing and doctor attitudes towards them as excellent or good in 72% and 81% cases respectively. 1 in 3 felt nursing care was excellent.
Over 90% of donors experienced severe sleep disturbance following donation. Noise accounting for most complaints. 8 donors felt that not being cared for on the same ward as the recipient was an issue. Emotionally most donors felt that this was a positive experience (n>30) with comments used as feeling proud, delighted and brilliant, however 1 in 5 felt weepy, let down and isolated after surgery.
Physical symptoms included constipation (affecting 76% of donors) and tiredness, however pain relief was not an issue, with 55% reporting no or mild pain.
Conclusion: Most donors are happy with the care and their outcome. However this questionnaire has identified a group of patients who feel isolated and upset following donation and emotional support is required for donors not just prior to donation but also following donation.

P-176 THE DUTCH TRAINING "COMMUNICATION ABOUT DONATION"

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Backround: Approaching relatives of a potential donor for donation is not a daily routine for professionals in the hospitals. These conversations always take place in emotional and stressful circumstances for the relatives, obviously demanding a lot of the professionals. Therefore, the Dutch Transplant Foundation developed a training "Communication about Donation" (CrD), with financial support of the Dutch Ministry of Health, to facilitate professionals in acquiring skills to guide families in the decision-making process.
Methods/Materials: The CrD training can be seen as a follow up of the European Donor Hospital Education Programme. The objective of developing a new training was to meet the current educational standards and the time constraints of the target groups. The CrD training is therefore developed 1) according to the "blended learning" principle, where digital training comes prior to the training in practice, 2) the duration of the practical training is reduced by half, 3) the training can be given in any local hospital, after a psychologist passes the Train the Trainer course.
Results: After the CrD training was completed in 2007, the training was implemented in local hospitals during the following three years. Our main target groups were physicians, medical residents, and critical care nurses. In total 118 CrD trainings were given to 916 professionals in 38 hospitals: 78 physicians, 422 medical residents, 286 nurses, and 75 other professionals. In addition, 77 psychologists followed the "Train the Trainer" course, to ensure that the CrD training will permanently be organised in local hospitals.
Conclusion: By developing and implementing a new training that meets the current educational standards and time constraints, we achieved the main objective to facilitate our target groups (two out of three). Data on the results of the CrD training will be shown at the ESOT congress.

P-177 URINE NGAL AS A BIOMARKER FOR EVALUATION OF DECEASED KIDNEY DONORS

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Background: Urine neutrophil gelatinase associated lipocalin (NGAL) is a biomarker of acute kidney injury, which could be helpful in evaluation of deceased organ donors (DD). The aim of this study is to evaluate the usefulness of NGAL detection in DD.
Methods/Materials: Study included 55 consecutive kidney transplantations (KT) from 31 DD performed in a single center from 01.01.2010 till 31.12.2010, where donor urine NGAL (DNGAL) analysis results were available (donor age 47,7+8,7, recipient age 45,7+13,2 years). Recipients were followed-up for 30 days. DNGAL levels were analyzed compared with donor serum creatinine (DSCr) and in association with other donor factors, "zero" biopsy (ZB) results, and early posttransplant outcomes (incidence of delayed graft function (DGF), acute rejections (AR), early graft loss, recipient SCr (RSCr) at the end of the follow-up).
Results: DNGAL correlated with DSCr ($p<0.001$) and in posttransplant period it was associated with higher incidence of DGF and higher RSCr level ($p<0.05$).
DNGAL >130 ng/ml was observed in 6 DD (12 KT), and DSCr >0,15 mmol/l in 8 DD (16 KT). Presence of elevated DNGAL comparing with DSCr was more predictive for DGF (p=0.030 vs. 0.237), however less predictive for RSCr level (p=0.050 vs. 0.010). Both parameters failed to show association with DD demographical and clinical data, results of ZB and graft loss and AR in posttransplant period.
In 2 DD (4 KT) there was elevated DSCr with normal DNGAL, showing the possibility of chronic kidney injury, that later was approved by ZB and resulted in elevated RSCr in all cases.
Conclusions: Urine DNGAL is useful for the detection of acute kidney injury in donors and prediction of DGF and worse graft function. Study must be continued to evaluate the role of DNGAL in conjunction with other factors.

P-178 CURRENT STATUS OF THE POTENTIAL DECEASED DONOR IN NEUROSURGICAL INTENSIVE CARE UNIT: A MULTI-CENTER EXPERIENCE FROM KOREA

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Background: The shortage of donor organs is the main problem to be solved in Korea as well as other countries. To evaluate the potential deceased donor (PDD) and to extend the donor pool, we retrospectively reviewed brain-dead patients who expired without organ donation in neurosurgical intensive care unit (NICU).
Methods: From January to December 2008, PDDs who expired without organ donation in NICU were recruited from 52 secondary or tertiary referral hospitals in Korea. In total, data of 2,288 PDD cases were collected from the questionnaire, of which 1,980 cases were eligible for analysis.
Results: There were (59.1%) males and (39.9%) females with a mean age of 57.6±18.0 years (the 5th decade, 21.2%; the 6th decade, 21.0%). The most common cause of PDD was cerebrovascular accident (n=1,034; 52.2%). Glasgow coma scale was 3 in 23.1% and 4 in 12.1%. Craniotomy was performed in 996 patients (50.3%). Sepsis was diagnosed in 276 patients (14.0%). Microorganism was confirmed in 200 patients (10.1%). Diagnostic procedure for assessment of brain death was performed in 194 patients (9.8%). The mean duration of NICU stay was 12.7±31.6 days. The seroprevalence of HBsAg and HCVAb was 1.7% and 0.6%, respectively. The mean AST/ALT level at admission and at brain death were 80.9±344.9/49.0±162.1 and 308.6±1,485.2/142.5±596.3 IU/L, respectively. The number of patients with normal total bilirubin level was 1,497 (75.6%) at admission and 597 (30.2%) at brain death. Urinary protein test was normal in 1,221 patients (61.7%) at brain death. Of the 1980 PDDs, 19 patients (1%) donated the organs for transplantation.
Conclusion: Only small number (1%) of PDD in NICU donated the organs in Korea. Continuous and active donor action is needed to increase organ donation from PDDs.

P-179 A MODEL OF "NON TECHNICAL SKILLS" IN ICU AND ORGAN DONATION

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Background: The ANTS System (Anaesthetist "Non Technical Skills") is able to reduce the risk of errors in anaesthesia. This System includes four behavioural markers: "Task Management", "Task Management", "Task Management" and "Task Management", and is also effective in the Intensive Care Unit (ICU).
Organ Donation (OD) is a specific task of ICU. To manage crisis situations, emotions, relationship, communication, explanation of brain death, notwithstanding managing families' mourning reactions and proposing organ donation, the operators need not only the abilities of the ANTS system, but also new and specific skills.
The aim of this study is to evaluate the use of Notechs in ICU and OD, to define a hierarchy of the importance of Notechs and to verify the adequacy of a specific new NTS model for this context (NOTSOD System – Non Technical Skills in Organ Donation), including two new abilities: "Emotional Awareness" and "Communication/Relationship".
Materials and methods: A 1-year research-action programme, involving doctors and nurses, was set up; through group discussion, conducted according to Aberdeen University's methodology, 7 cases of "near miss incident" were analysed.

Results: 1. Operators considered the use of Notechs in ICU as "poor" or "marginal", except for "Situation Awareness" (23%) and "Decision Making" (28%) which were considered "acceptable". 2. Overall they considered all the four Notechs of ANTS System "important" or "very important" in ICU. 3. They recognized the importance of "Emotional Awareness" and "Communication/Relationship" in OD and evaluated adequate the NOTSOD System.
Conclusion: To ensure greater efficiency, safety and humanity to patients, relatives and health carers, the implementation of a Model of Notechs in ICU and OD is very important. To include specific training in medical and nursing education represents an innovation which could improve the quality of care, reduce risk of error and increase safety.

P-180 FOR KIDNEY TRANSPLANTS, IS IT POSSIBLE TO OFFER NON HEART-BEATING DONORS LOCATED MORE THAN 30 MINS AWAY?

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Time constraints for taking an organ in a non-heart-beating donor are very strict and, in particular, require less than 150 min between patient's collapse and the setting of an extra-body circulation (hot ischemia). We wanted to see if a remote "pre-hospital" department could respect this time restriction.
Population: For 2 years, we followed all patients accepted by an organ removal center in an area near Paris located 15 to 45 mins from this center.
Results: 27 patients have been supported for cardiac arrest and admitted for transplants from non-heart-beating donors (mean age 41 - 19 to 50 years old). Essential times (minutes) are summarized below:

	Min	Mean	Max	Max advisable	Cases outside recommendations
No-flow	0	10	21	30	0
Low-flow	91	140	159	120	15
Warm ischemia time (WIT)	133	149	170	150	6
Cardiac arrest – Local physician	7	18	40		
Time before decision	27	35	75		

11 patients have been transplanted. Reasons for not taking organs were: 4 families refused, 4 because of previous antecedents, 2 cases of heart resuming and 5 pre-hospital support errors (no schedule, technical errors).
Transport time varied from 27 to 55 min (mean: 42 min) and don't seem to influence donor's quality. The major delay is linked to making the decision to remove organs by a local physician.
Conclusion: When located between 30 min and an hour from a specialized organ removal center, it is completely possible to offer non-heart-beating donors. The essential limitation is related to the local physician decision-making process.

P-181 CAUSES OF REJECTION OF POTENTIAL LIVING DONORS FOR LIVING-RELATED LIVER TRANSPLANTATION

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One of the most important problems in liver transplantation programs is represented by the shortage of organs due to the increasing number of patients on the waiting lists, which is not matched by an increase of available cadaveric donors. For this reason many patients die while awaiting a liver transplant. In order to better cope with this growing problem, living donor liver transplantation programs have been developed.
The aim of the study is to evaluate the most frequent causes that lead to the rejection of potential living donors from donating a liver fragment.
Material and methods: We evaluated 39 potential donors were in order to establish the possibility of donating a liver fragment for 16 patients with end stage liver disease. The standard protocol of investigations was applied including compatibility of the ABO system, normal psychological and psychiatric examinations, absence of liver or systemic disorders.
Results: Of the 39 potential liver donors, only 9 (26.47%) were considered elligible for donation. 9 (23.07%) were found to be HBV carriers, 1 (2.5%) presented multiple hepatic cystic masses, 1 (2.5%) presented lung tumor, 3 (7.69%) presented macrovesicular steatosis $>$ 20%, 5 (12.82%) were rejected after psychological evaluation, in 3 potential donors (7.69%) hepatic volumetry contraindicated donation due to the risk of small-for-size syndrome, 1 (2.5%) presented an anatomical variant of the hepatic artery which did not allow for hepatic resection, and 4 (10.25%) had biological profiles which suggested Wilson disease.
Conclusions: the fact that for each recipient for living donor liver transplantation it is usually necessary to evaluate several potential donors. The screening of potential donors is costly and time-consuming, while medical contraindications of donation are frequently encountered.

P-182 CHANGING RELATIONSHIPS IN KIDNEY DONATION

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Introduction: Kidney transplantation from a live donor is increasingly being performed as the preferred treatment option for endstage renal disease. We hypothesized that increased use of living donors in renal transplantation might have influenced the pattern of relationship between living donors and recipients.
Methods: We included all kidney donations in Norway until December 31, 2010. Donor relationship and donation date were obtained from the Norwegian Renal Registry. We divided our entire experience into four periods; 1963-79, 80-89, 90-99 and 00-10, to estimate changes in relationship between donor and recipient.
Results: There were 2594 kidney donations during 1963-2010 (table 1). Mean donor age was 47.7$\pm$12.4 and 41.9% were male. Mean recipient age was 41.4$\pm$16.9 years, increasing throughout the period. The proportion of unrelated donors increased from 7.7% in 1980-89 to 25.0% in 2000-10. The proportion of parents as donors decreased from 39.0% in 1963-79 to 24.4% in 2000-10. The proportion of sibling donors also decreased from 58.1% in 1963-79 to 32.8% in 2000-10. Offspring constituted 3.1% of donors in 1980-89, increasing to 13.6% in 2000-10. The mean age of offspring donors have been fairly unchanged at 36.5 years.

Table 1. Donor relationship to recipient by different time periods

Relation	All donors (n=2594)	1963–1979 (n=246)	1980-1989 (n=598)	1990-1999 (n=768)	2000–2010 (n=982)
Sibling (%)	982 (37.9)	143 (58.1)	247 (41.3)	278 (36.2)	314 (32.0)
Parent (%)	832 (32.1)	96 (39.0)	251 (42.0)	245 (31.9)	240 (24.4)
Offspring (%)	233 (9.0)	NA	18 (3.0)	81 (10.5)	134 (13.6)
Other relative (%)	118 (4.5)	7 (2.8)	36 (6.0)	27 (3.5)	48 (4.9)
Spouse (%)	345 (13.3)	NA	44 (7.4)	124 (16.1)	177 (18.0)
Friend (%)	84 (3.2)	NA	2 (0.3)	13 (1.7)	69 (7.0)
Donor age	47.7 (12.4)	46.1 (13.2)	48.4 (13.9)	47.9 (12.2)	47.5 (11.4)
Recipient age	41.4 (16.9)	35.0 (14.2)	38.5 (16.2)	42.5 (17.1)	44.0 (17.2)

Conclusion: The relationship between kidney donors and recipients have changed over decades.
This may be partly explained by a higher proportion of older kidney recipients, The increasing proportion of kidneys being passed from offspring to parents should be viewed with caution, as the long-term consequences of kidney donation are not yet fully elucidated.

P-183 LIVING DONOR RENAL TRANSPLANTATION IN DONORS WITH INCIDENTAL NEPHROLITHIASIS

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Introduction & Objectives: The routine use of cross-sectional imaging in the assessment of potential kidney donors has led to the increased detection of incidental urinary tract calculi. The presence of such stones is no longer regarded as a contra-indication to donation in the appropriately assessed patient. We report our experience of living donor renal transplantation in donors with incidental nephrolithiasis.
Methods: All living donor nephrectomies performed in our department from December 2004 to October 2010 were analysed using a prospectively maintained database. All donors were imaged pre-operatively with a triple-bolus multi-detector computed tomography. Patients with incidental stones were identified and their pre-operative stone burden, treatment plan and operative details collected. All donors and recipients were contacted post operatively to determine the presence of any stone related complications. Our policy has been to preferentially remove the stone containing kidney for transplantation.
Results: Incidental calculi were identified in 10/167 kidney donors (6%). Stones were identified; bilaterally in 2 patients, right side in 5 and left side in 3. The average stone size was 4mm (Range 2-8mm). Living donor nephrectomy was performed on the stone carrying kidney in 8/10 cases (80%); this was not possible in 2 cases due to challenging vascular anatomy. Stone removal using flexible ureteroscopy (1 in-vivo, 2 ex-vivo) was performed prior to transplantation in 3 cases. At a median follow up of 24 months 10/10 recipients were symptom free with reported no stone related complications. 1/10 donors experienced post operative loin pain, whilst 0/10 reported any complications requiring intervention.
Conclusion: Living kidney donation in the presence of incidental urinary tract calculi in appropriately assessed patients appears safe. In our experience transplantation in this cohort of donors results in a low rate of stone related morbidity in both donors and recipients.

P-184 5 YEAR FOLLOW-UP OF INTERNATIONAL CLASSIFICATION OF DISEASES (ICD) BRAIN DEATH RELATED DIAGNOSTICS AT IN-HOSPITAL DISCHARGE, BRAIN DEAD (BD) DETECTED PATIENTS AND BD ORGAN DONORS (OD)

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Background: Catalonia is a region in Northeastern Spain with 7.5 M inhabitants. Its organ donation and transplantation per million population (pmp) rates are among the highest in the world, as is the case for the whole of Spain. Nevertheless, the large number of patients awaiting an organ transplant obliges us to ensure accurate case detection and valid donor retrieval with quality assurance programs and close data follow-up.
Methods: Since 90% OD are BDOD, minimum Data Set Model (MDSM) with *exitus* at in-hospital discharge records were checked for the occurence of ICD brain death diagnostic related codes. All "acute service" hospitals in Catalonia were checked from 2005, since organ extraction authorized hospitals are included in these. MDSM validated record availability has a delay of 6 months approximately. For this reason, 2010 is not considered.
Results: Yearly, around 3000 records with *exitus* at in-hospital discharge contain one or more ICD diagnostics related to brain death. BD cases detected (CD) were between 300 and 350 and actual donors (AD) varied from 200 to 250. As expected, the big picture shows parallel lines for the 3 distributions over the years. However, 2008 and 2009 do not follow strict parallelism. In 2008 *exitus* and DC increased while AD decreased. In 2009 *exitus* almost did not vary, but DC rose slightly while for AD there was an unexpected increase.
Conclusion: The number of actual donors not only depends on total number of *exitus* due to brain death related causes, but also on diverse factors along the donation process. Among these, we would mention as an exemple and key factor the number of family refusals.

P-185 ESTABLISHING A BRAIN DEATH DONOR MODEL IN PIGS

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Several factors influencing organ quality and recipient survival after multiorgan donation and transplantation are still unknown and difficult to investigate in humans. Therefore the need for an animal model that imitates human conditions might be useful not only to be able to monitor pathomechanisms of brain death and biochemical cascades in the organisms after brain death but also to be able to investigate novel strategies to ameliorate organ quality and functionality after multiorgan donation. Therefore the aim of this study was to establish a brain death donor model in pigs.
15 pigs were used for these experiments in accordance with the Austrian animal law. Brain death was induced by inserting a catheter into the intracranial space after trepanation of the skull and augmenting intracranial pressure until brain stem herniation occurred. Intracranial pressure was monitored continuously and after 60 min brain death diagnostics was performed by a neurologist including EEG examination and clinical examination. Donor care was performed according to standard guidelines and after 24 h of brain death and intensive care multiorgan donation was performed.
60 min after brain death induction neurological examination and EEG examination confirmed brain death.
It is feasible to induce brain death in a pig model by inserting a catheter after trepanation of the skull. According to standard guidelines brain death diagnostic was performed, 0 line EEG occurred in all animals 60 min after brain death induction. Using this method, a suitable brain death donor model could be establish that will enable us not only to investigate in detail effects and pathophysiology after occurrence of brain death but also to evaluate new strategies to ameliorate organ quality and even to enlarge the donor pool for multiorgan donation.

P-186 ESTABLISHING A NON-HEART-BEATING DONOR (NHBD) MODEL IN PIGS

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Introduction: Due to the lack of human donor organs, several strategies to expand the organ donor pool are under investigation. During the last years a lot effort has been emphasized on the characterisation of non-heart beating donors (NHBD). In order to be able to evaluate organ quality in terms of cell viability, histological and immunohistochemical changes and the occurrence of oxidative stress that is known to negatively impact on graft survival after transplantation, a large animal model would be useful. Therefore, we aimed to establish a NHBD animal model in pigs in our laboratory.
Methods: We simulated non-heart beating donation Maastricht II and III in 24 pigs. Cardiac fibrillation is induced by using 9 V direct current. After different time-spans (1 min – 10 min) of ventricular fibrillation with no cardiac output mechanical and medicamentous reanimation is performed according to the protocols for 30 min prior to multi-organ donation. A neurological status is performed. Blood samples are taken at defined time points, tissue samples are stored in liquid nitrogen and embedded in paraffin and treated for further analysis. Oxidative stress is monitored determining CP and MPO using ELISA. Tissue quality is assessed by ATP measurement and routine histological and immunohistochemical analysis is performed.
Results: We succeeded in establishing a NHBD pig model in our laboratory by inducing cardiac fibrillation. Up to now, only NHBD donation according to the Maastricht criteria II and III is performed, but establishing of all Maastricht criteria NHBDs seems to be feasible.
Discussion: Using a NHBD model in pigs will enable us to characterize NHBD donor organ quality more precisely and means for amelioration of storage condition and donor treatment can be evaluated more detailed in a large animal model.

P-187 ORGAN DONATION IN JAPAN: A LONGITUDINAL STUDY OF QUALITY OF LIFE OF LIVING LIVER DONORS

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Background: In Japan, the number of cadaveric organ donation has been minimal and the most patients in need of liver transplantation underwent living donor liver transplant. The purpose of this study was to longitudinally explore the quality of life (QOL) and health status of living donors after the donation. The phase 1 study was done in 2002 which measured QOL of living liver donors (n=46) by utilizing a QOL tool, the Short Form 36® (SF-36®) and a researcher made questionnaire. This study showed that the majority of donors (69%) said they completely recuperated from the operation, while 32% said they did not. Moreover, living donors scored lower on the SF-36® than their controls when measured within a year after their surgery, and donors who were more than two years post-surgery had higher scores meaning their health status and QOL was better than those within a year after surgery.
Methods: For this phase 2 study, the same living donors were invited to participate. The same QOL tool, SF-36®, and the questionnaire were used and the change in their QOL and health status over seven years were examined.
Results: There were no donor deaths in the donor population, though nine donors were admitted to a hospital for a variety of reasons. The majority of donors (61.9%) said they had completely recuperated, while 12 donors (33.3%) said they still had some symptoms. The donors who scored lower on the SF-36® from the phase 1 study scored higher for this phase 2 study. However, many still have minor complications and some lost their income or changed their job after this surgery.
Conclusion: This study indicates that most living liver donors see themselves as having recuperated well, though some still had long-term problems.

P-188 EFFECT OF OXIDATIVE STRESS AND ENDOTOXIN ON HUMAN SERUM ALBUMIN IN BRAIN-DEAD ORGAN DONORS

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Albumin binds and detoxifies endotoxin in healthy people. Oxidative stress leads to protein oxidation and thus to impaired binding properties of albumin. This, in combination with increased gut permeability leads to appearance of endotoxin in systemic circulation and impaired organ function. We hypothesise that these processes occur in brain-dead organ donors.
Endotoxin was determined with an adapted limulus amoebocyte lysate assay, albumin fractions and binding capacity by HPLC. FlowCytomixTM was used for determination of cytokine levels and RT-PCR for analysis of tight junction protein (TJP) mRNA expression.
Eighty-four brain-dead organ donors were enrolled and categorized by the length of intensive care unit (ICU) stay. Albumin binding capacity was reduced and oxidative modification was increased in donors compared to controls. Endotoxin positivity in 16.7% of donors was associated with decreased binding capacity in donors and worse survival of recipients. Lengths of ICU stay increased albumin oxidation. TJP expression in duodenum showed a trend towards lower expression in endotoxin positive donors.
We conclude that oxidative stress and systemic endotoxemia are present in brain-dead organ donors what might affect recipient survival. High endotoxin levels might be due to increased gut permeability and decreased albumin binding capacity facilitated by higher albumin oxidation.

P-189 DONOR MANAGEMENT ON LINE: SEVEN YEARS OF REGIONAL EXPERIENCE

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In Lazio, up to 2004, donor management was made by phone and fax. In fact when there was a Potential Organ Donor (POD), the Hospital Coordinator (HC) had to fill in a paper model in which all the clinical data were reported and sent it to Transplant Regional Center of Lazio (CRTL) by fax. Then CRTL evaluated POD suitability and communicated these informations to Transplant Centers by fax again and all that happened during a long lasting period. Seven years later this situation has been totally changed. In 2004 CRTL started to use a software program called Gedon (GEstione DONatori, donor management), that replaced paper forms, proving to be day by day a real timesaver. After having instructed all the parts involved in a donation process about how to use this system, CRTL can see the results of this work, knowing that many changes improved on the software during last seven years. Now, when there is a brain death process, HC inserts all the clinical data regarding the POD on Gedon and CRTL, in real time, let them clear to the Transplant Centers. CRTL also attach scanned files, as original blood group or original viral panel of POD for example, reducing in this way the risk for error. This program allows a wider management of transplant network of Lazio. In fact Gedon software is divided into four groups: Organ Donors Management on-line (since 2004); Brain-damaged Register, patients with brain damages deceased inside Intensive Care Units (since 2006); Tissue Donors management on-line, connected to Eye Bank of Lazio (since 2007) and to the Muscoloskeletal Tissue Bank of Lazio (since 2010); ER admittances consulting on-line (since 2009). So that CRTL has a real time picture of brain damage regional care system.

Infections

P-190 CLINICAL UTILITY OF A QUANTITATIVE AND FUNCTIONAL FLOW CYTOMETRY ASSAY FOR CMV-SPECIFIC CD8 T CELL IMMUNITY IN TRANSPLANT PATIENTS

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Background: We have validated a multiparametric diagnostic flow cytometry assay for quantitative and functional evaluation of CMV-CD8 T cell immunity using CMV peptide-specific MHC class I tetramers (HLA A1, A2, B7, B8 and B35).
Method: Functional CMV-CD8 T cell competence was determined by assessing cellular activation (IFN-gamma) and surrogate markers for cytotoxic function (CD107a/b). The data was collated as a CMV-CD8 T cell Immune Competence (TIC) score (0 to5). To preclude the possibility that the lack of CMV-specific CD8 T cell response was due to over-immunosuppression, a parallel global assessment of CD8 T-cell immune competence (GLIC) was performed after mitogenic stimulation. The cohort was segregated into 4 groups based on Recipient (R) and Donor (D) CMV-serostatus. The patients were also divided into 4 groups based on the time of enrollment in the study and CMV CD8 T cell immunity was determined at each time point.
Results: There was no statistically significant correlation between the TIC score, GLIC, T cell counts, CMV viremia or infection in any of the 4 groups, though this could be related to the small sample size in each group. There was only a moderate linear correlation between the ALC and total CD3 T cell count in the R+D- and R+D+ group (R^2= 0.56 and 0.53 respectively). These data suggest that the ALC cannot be solely relied upon to provide evidence of lymphocyte subset dysregulation in immunosuppressed patients.
Conclusions: Most clinical tests have focused on evaluating viral parameters and there has been relatively little emphasis within the clinical diagnostic laboratory on assessing CMV-specific host immune competence. The multiparametric flow test described above provides an opportunity to quantitatively and functionally assess the CMV-specific CD8 T cell immune response.

P-191 DE NOVO RENAL ALLOGRAFT FEMALE RECIPIENTS, BUT NOT MALE ONES, SHOW INCREASES IN URINARY TRACT INFECTION (UTI) INCIDENCE AND RELAPSES AFTER URETERAL STENTING

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Introduction and Aims: Stenting of the extravesical ureteroneocystostomy has become the standard for reestablishment of urinary tract continuity in kidney transplantation (KT). Double J stenting decrease urological complications but some authors have reported a higher incidence of UTI. We evaluated the impact of stenting use in the incidence of urological complications and UTI after KT.
Methods: UTI in the early KT (within 10 days post-KT) and the UTI risk of relapses within 3 months of follow up were studied. Frequent relapses were considered 2 or more UTI episodes. A retrospective study of consecutive KT performed in our hospital between August/2007-August/2010 was undertaken. Antibiotic prophylaxis was limited to cephalosporin just before the KT and ciprofloxacin just before stent removal. No *pneumocysitis-jiroveci* prophylaxis with cotrimoxazol is used in our unit.
Results: 114 KT were evaluated (70 men/44women), mean age was 54.9$\pm$12.9 years. Fixty-six percent of KT had a stent and median time to stent removal was 4-weeks. We found an important reduction in urological complications in the stenting group (16% vs 4.5%). Male recipients did not show significant differences in UTI risk or frequent UTI relapse risk. However, in female, the use of ureteral stenting increased both early UTI (RR 1.6 [1.02-2.30], $p<0.05$) and the UTI risk of relapses (RR 2.06 [0.73-5.88], p=0.08). Most common isolated bacterial in urine culture were E.coli 41.7% (39.4% resistant betalactamases-producers), Enteroccous 17.4% and Klebsiella 16.4%. Only 9.6% of patients had positive blood-culture test.
Conclusions: Ureteral stenting after KT decreased urological complications but increased both early UTI and the risk of frequent UTI relapse. This was only significant in women, not in men. UTI antibiotic prophylaxis is advisable in the female recipient, but appears to be unnecessary in men.

P-192 CLINICAL STUDY OF RENAL TRANSPLANTATION IN PATIENTS WITH HEPATITIS C

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Objective: To explore clinical strategies improving renal transplantation effect in patients with hepatitis C virus (HCV) infection.
Methods: Patients were divided to HCV infection group (n=106) and control group (n=137) according to the results of serum HCV antibody and HCV-RNA. Patient in HCV infection group received preoperative treatment of viral hepatitis before transplantation (n=106), strengthening the postoperative hepatotherapy treatment (n=106) and application of low-dose calcineurin inhibitor (CNI) (n=66) or CNI-free (n=40) immunosuppressive programs after transplantation. We compared patient and graft survivals, incidence of acute rejection episodes and CNI dosages in two groups.
Results: The recipient/renal survival rates of 1, 3 and 5 years were 93.3%/92.4%, 82.1%/80.2% and 79.2%/78.3% respectively which have no sig-

nificant different with those in control group (P>0.05). The incidences (12.62% vs 10.87%) were not significantly different between HCV infection and control groups (P>0.05). CNI dosages in 66 HCV infection patients were significantly lower than that in control group 1 year after transplantation (2.07 vs 2.66 mg/kg·d).
Conclusion: Rational use of immunosuppressive agents, especially regimen with a relatively low liver toxicity, is the key for successful kidney transplantation in patients with hepatitis C and their health and survival.

P-193 HEPATIC ABSCESS. A STRANGE COMPLICATION OF OLT

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Introduction: Infections after liver transplantation are an important cause of mortality and morbidity. Liver abscesses are a rare complication after orthotopic liver transplantation with an incidence in the only chart reported of 2,6% and a mortality rate of 42%.
Methodology: We made a retrospective study of orthotopic liver transplantation recipients (OLTR) between January 2000 and December 2010. We selected 9 OLTR diagnosed of liver abscess from a chart of 732 OLTR and 101 liver abscess in the community.
Results: We present a chart with a mean age of 56.33 years (SD 9.097), 7 men and 2 women. The percentage of diabetic patients was 55.6%. The most common clinical signs were fever (88.9% of cases); followed by hepatomegaly (66.7%) and nausea with the same percentage, right hypochondriac (55.6%), anorexia (44.4%), jaundice (44.4%) and loss of weight (44.4%).
The origin of the abscess in transplanted patients was biliar in 88.9% (in opposition to the 47.6% of the general series) and the only one of non-biliary source was a tumor. The most important problem was the ischemic cholangiopathy which was present in 8 of 9 patients.
The bacteria which were most frequently isolated were E. Coli and Klebsiella pneumoniae, representing the 55.5% of the germs.
The most common treatment was catheter drainage and antibiotic therapy in six cases; two were resolved with antibiotics and only one required surgical treatment, which consisted of retransplantation.
The actuarial survival rates for these patients were 77%, 46.7% and 31.1% at 1,3 and 5 years.
Conclusion: Liver abscess is a bad prognostic factor in liver transplanted patients.
The ischemic cholangiopathy is one of the most decisive factors in its pathogenesis.
Liver retransplantation is the best option that involves a long-term survival.

P-194 INFECTIONS IN KIDNEY TRANSPLANTATION: INCIDENCE, TYPE AND LOCATION. A PROSPECTIVE STUDY

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Infection after renal transplantation remain an important cause of morbidity and mortality.However, its real incidence and the causes for admission are poorly understood.
Material and Methods: We prospectively analyzed all hospital admissions due to infections and infection complications during admission in all kidney transplants performed at our Institution between January 2000 and December 2008.
The sample consisted in 416 kidney transplant patients (256 men and 159 women) with a mean age of 51,45±14.45 years and mean follow up of 60 months.We analyzed: Inmunossupression,time since transplant, type, location, causative organism, origin (nosocomial or outpatient) and severity of the infection. Statistical data were analyzed with SPSS 15.0
Results: During admission for transplantation 44 (10.5%) patients had 55 infections, 33 (75%) in the urinary tract and the rest from other causes, amongst these 3 (7,5)CMV infection and 5 (11.3%) in the surgical wound. Only two patients had bacteremia.
After transplantation has been 304 incomes for infections in 146 patients. 69 have had one, 44 two, 18 the and 15 over three. 5 patients (1,2%) died for infection. Nosocomial infections represent 16.7% of the infections in the first year, 4.2% between 2-5 years and 10.5% of those that occur later. The number of patientes admissions does not increase nosocomial origen.
41% of infections were from urine, 21% pulmonary, 21% abdominal, 5% skin and the rest from other causes. 47% of infections are bacterial, 13% viral and 5% fungal. In the first year admissions for viral infections are 21.4% of the total, dropping to 7% in subsequent years.
The probability (Kaplan Meyer) to be free of infections income is 80.2% in the fist year, and 51.5% at 10 years.
Conclusions: Noscomial infections are more common in the first year post-transplant.
Remains a significant cause of viral and fungal infections.

P-195 INDIRECT EFFECTS OF CYTOMEGALOVIRUS INFECTION IN KIDNEY TRANSPLANT RECIPIENTS

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Background: Cytomegalovirus (CMV) infection affects clinical outcomes after renal transplantation (RTx) through both the direct effects of CMV disease and indirect effects. Our aim was to evaluate the association CMV infection and acute rejection (AR) with graft failure under the current immunosuppressive regimens.
Patients and Methods: From June 2002 to December 2009, 108 consecutive adult kidney recipients were included in this study and followed until December 2010. All patients were monitored with qualitaive pp65 antigenemia until 1 year after transplantation. Antiviral therapy was initiated when antigenemia became positive, defined as more than 5 of 100,000 leukocyte nuclei. From August 2006, recipients received prophylaxis with valganciclovir for 3-6 weeks, followed by preemptive regimen. We compared the clinical outcomes of the 5 recipient groups, divided based upon the occurrence of AR and/or CMV infection within the first 12 months after RTx. Group1; without AR or CMV infection (n=56), group2; with AR alone (n=14), group3; with CMV infection alone (n=18), group4; with AR preceding CMV (n=8), and group5; with CMV preceding AR (n=12).
Results: The mean follow-up was 1529.6±814.7 days. The overall death-uncensored graft survival was 90.7%. Thirty-eight patients (35.2%) presented CMV infection and 25 (23.1%), CMV disease. The incidence of AR was 31.5%. CMV infection was not found to be risk factor of AR. The graft survival of each group was as follows; group1; 96.4%, group2; 92.9%, group3; 83.3%, group4; 87.5%, group5; 75.0% (p=0.096). The mean serum creatinine level (mg/dl) 1 year after RTx was below; group1; 1.15±0.31, group2; 1.40±0.27, group3; 1.33±0.39, group4; 1.64±0.58, group5; 1.72±0.50 (p=0.005).
Conclusions: These results showed that CMV infection in the presence of AR was associated with poor outcomes after RTx, especially in cases with CMV preceding AR.

P-196 AGE AND SEX AS RISK FACTORS FOR CMV-INFECTIONS AFTER LUNG TRANSPLANTATION

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Purpose: Opportunistic infections after organ transplantation are a major problem. Cytomegalovirus (CMV) is the most prevalent opportunistic infection in patients after lung transplantation (LuTX). Therefore, a better risk classification is urgently needed.
Methods and Materials: We retrospectively reviewed all consecutive 690 patients (317 female, 373 male, mean age: 46 16) who were lung transplanted at the Medical University of Vienna between 01.2000 and 01.2010. The impact of age and sex on CMV-outcome (freedom from PCR- proven viremia and clinical disease after LuTX) was analyzed by Kaplan- Meier curves and Log Rank tests.
Results: Median freedom from CMV- viremia was 362 days (range: 32-3648 days) and median freedom from clinical CMV- disease was 846 days (range: 64-3673 days) for all patients. When patients were divided into two groups by mean age, older patients had the significant worse outcome with regard to viremia (young vs. old: 1-year freedom from viremia: 79% vs. 65%; 3-year freedom from viremia: 77% vs. 55% and 5 year freedom from viremia: 70% vs. 54%; Log Rank: p<0.001) but no significant difference was found in freedom from disease. Furthermore, female recipients had the significant longer freedom from viremia (female vs. male: 1-year freedom from viremia: 75% vs. 65%; 3-year freedom from viremia: 67% vs. 58% and 5 year freedom from viremia: 65% vs. 58%; Log Rank: p=0.019) and freedom from disease (female vs. male: 1-year freedom from disease: 95% vs. 88%; 3-year freedom from disease: 93% vs. 87% and 5 year freedom from disease: 93% vs. 87%; Log Rank: p=0.020). Beside these findings, CMV-donor/recipient antigen status had a significant impact on CMV-outcome.
Conclusions: These findings could help to define risk groups and to schedule tailored prophylaxes for lung transplanted patients.

P-197 RATE OF URETERIC STRICTURE IS INCREASED IN THE PRESENCE OF BK VIRAEMIA WITHOUT NEPHROPATHY

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Background: BK virus is a polyoma virus which may cause viraemia post kidney transplant with or without clinical nephropathy. Urothelial inflammation in the donor ureter has the potential to affect ureteric vascularity and healing of the anastomosis. This study addresses the hypothesis that BK viraemia may have a role in post transplant ureteric dysfunction and the development of strictures.
Methods: Clinical and demographic data from 140 consecutive renal transplant patients over 2 years, were compiled prospectively. All patients were screened for BK viraemia by PCR. The incidence of radiological hydronephrosis and clinically significant hydronephrosis was compared between patients manifesting BK viraemia in the year following transplant and the group with no viraemia.
Results: 36 of 139 patients developed detectable viraemia. 1 case was excluded due to early vascular thrombosis. None manifested biopsy proven BK nephropathy. The incidence of radiological hydronephrosis was 16.7% in the BK viraemic group and 3% in the no viraemic group (p=0.01). The incidence of clinically significant hydronephrosis was 10% in the BK viraemic group versus 1% in the no viraemia group (p=0.04).
Conclusion: BK viraemia, without nephropathy, is associated with both radiological and clinically significant post-transplant hydronephrosis, independently of known risk factors.

P-198 DONOR URETER CULTURES IN RENAL TRANSPLANTATION

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Background: Routine microbiological analysis of ureters obtained during organ retrieval for transplantation have revealed an incidence of unexpected contamination with pathogenic and non-pathogenic organisms. We hypothesised that there would higher numbers of culture-positive ureters in donation after cardiac death (DCD) grafts compared to donation after brain death (DBD) and living donor (LD) grafts and that recipients of grafts with culture-positive ureters would be more likely to develop a UTI.
Methods: Between January 2005 and May 2009, 358 kidney-only transplants were identified which had routine ureter cultures: DCD=181, DBD=123 and LD=54. Since June 2009, recipients of grafts with culture-positive ureters have been treated with antimicrobials. During this period, 196 transplants were performed: DCD=96, DBD=48 and LD=52.
UTI and ureter infection rates were analysed using Newcombe's method for 95% confidence intervals (CI).
Results: Prior to June 2009, culture-positive ureters occurred in 13.8% DCD, 7.3% DBD and 7.4% LD grafts. There was no statistically significant difference between donor groups.
Since June 2009, culture-positive ureters occurred in 14.6% DCD, 10.4% DBD and 0% LD grafts. There were significantly more culture-positive ureters in DCD (CI=0.0565 - 0.2300) and DBD (CI=0.0136 - 0.2217) grafts, compared to LD grafts.
Prior to antimicrobial treatment, 42.1% developed a UTI in the culture-positive group compared to 18.1% in the culture-negative group, which was statistically significant (CI= -0.4014 - -0.0901). Following use of antibiotics, rates of UTI fell to 26.3% in the culture-positive group compared to 13.0% in the culture-negative group. The incidence of UTI was no longer significantly higher in the culture-positive group (CI=-0.0229 - 0.3618).
Conclusion: Culture-positive ureters are more common in grafts from deceased donors, but no difference exists between DCD and DBD donors. Culture-positivity confers a risk of developing UTI in the recipient. Antimicrobial treatment in such recipients, reduces, but does not eliminate, the risk of developing UTI.

P-199 URINARY TRACT INFECTIONS IN RENAL TRANSPLANT RECIPIENTS

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Introduction: Urinary tract infections (UTIs) are most common infections in renal transplant recipients and are considered a potential risk factor for poorer graft outcomes.
Aim: To evaluate incidence, clinical manifestations, microbiology, risk factors for UTIs and the influence of UTIs on long-term renal graft function.
Patients and Methods: We analyzed urine cultures with reference to clinical data of patients who received a renal transplant at Gdansk Transplantation Centre between January and December 2009 during a 12-month follow up.
Results: We studied 1170 urine cultures and clinical data from 89 renal transplant recipients, including 58,4% of male gender, with mean age of 48±14 years. We observed 151 episodes in 49 patients, consisting of asymptomatic bacteriuria (65%, *n* = 98), lower UTIs (13%, *n*=19) and upper UTIs (22%, *n* = 34) including five cases of bacteremia. Nearly 48% of UTIs were diagnosed during the first month post-transplant. Most frequently isolated uropathogens were *Enterococcus faecium* (33%, *n*=24) and *E.coli* (31%, *n*=23). Beginning from the second month bacterium most frequently found in urine cultures was *E.coli* (65%, *n*=51). Risk factors for posttransplant UTIs were female gender and a history of acute rejection and/or CMV infection. All patients with vesico-ureteral reflux or strictures at the uretero-vesical junction suffered from recurrent UTIs (*n*=7). The evolution of renal graft function did not differ significantly between patients with and without UTIs.
Conclusions: UTIs are a frequent problem after kidney transplantation. Most common form of UTI is asymptomatic bacteriuria. *Escherichia coli* and *Enterococcus faecium* are predominant pathogens. Exposition to greater immunosuppression due to episodes of acute rejection or as a result of CMV infection is a risk factor for UTIs. Vesico-ureteral reflux or strictures at uretero-vesical junction are risk factors for recurrent UTIs. UTIs do not impair long-term graft function.

P-200 BKV VIREMIA IN A WELL-MATCHED KIDNEY TRANSPLANT POPULATION

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Background: Polyomavirus-associated nephropathy (PyVAN), predicted by high-level BKV-viremia, has been rare in our well-matched kidney transplant population mainly on cyclosporine-based immunosuppression. We characterized patients with BKV-viremia and PyVAN in our population.
Methods/Materials: Among 104 adult kidney only transplantations 2007-2009 with graft survival over 1 year followed up at at Helsinki University Hospital nephrology clinic, 88 were screened for BKV-viremia by quantitative plasma PCR in parallel with BKV-viruria during the first posttransplant year (mean 2.7 times, range 2-4). PyVAN was diagnosed from allograft biopsies with histopathological characteristics and immunohistochemical detection of SV40 T-antigen. BKV-viremia or PyVAN were treated with reduction of immunosuppression. Furthermore, all positive BKV-viremias from the whole country analyzed in Helsinki University Hospital Department of Virology were identified.
Results: Viremia was detected in 6/88 (7%) patients and monitored subsequently; 3 were low-level viremias (<5,000 copies/ml) of short duration (<2 months); PyVAN was diagnosed in 2 patients (2%) with persistent high-level BKV-load (peak viral loads 11,400 and 89,100 copies/ml). One patient had peak viral load of 10,100 copies/ml, but only transient viremia and no PyVAN. BKV-viruria was seen in 17/88 (19%) patients. From patients followed at other nephrology units in Finland, 15 additional cases of BKV-viremia were identified: 7 with persistent high-level BKV-loads (range 11,040-1,100,000 copies/ml, presumptive PyVAN), and 8 with low-level BKV-loads (range 520-2,500 copies/ml) of short duration. After reduction of immunosuppression, no grafts were lost due to PyVAN. Only one patient with PyVAN had sustained low-level viremia (for >1 year), and was unable to clear viremia, although graft function stabilized with reduction of immunosuppression.
Conclusion: Although relatively rare in our population, BKV-viremia may occur, and monitoring of viral loads is essential. Reduction of immunosuppression was successful and no grafts were lost due to PyVAN.

P-201 LYMPHOPROLIFERATIVE DISORDER OF THE CENTRAL NERVOUS SYSTEM AFTER RENAL TRANSPLANTATION: SINGLE CENTER EXPERIENCE IN JAPAN

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Objective: Post-transplantation lymphoproliferative disorder (PTLD) of is a rare complication of solid organ transplantation or bone marrow transplantation and is mostly associated with an Epstein-Barr virus infection. The central nervous system (CNS)-PTLD is fatal complication for renal transplant recipient, but the clinical characteristics are not well recognized. We analyze CNS-PTLD at Kitasato University hospital for 38 years.
Patients and methods: From 1972 through 2010, 475 kidney transplants were performed at our institution. 4 (0.8%) recipients developed PTLD and 3 (0.6%)

were CNS-PTLD. Data on clinical course, immunosuppressive regimen, CMV infection, EB virus infection, treatment and prognosis were compiled from the institutional database. Patients were 1 male and 2 female. Average age was 37 to 51 (mean, 42.3 years). CNS symptoms developed 24 to 300 months (mean, 148 months) after transplantation. All patients received immunosuppressive (1 cycrospoline and 2 Tacrolimus), therapy. Radiographically, all lesions enhanced either homogenously or in a ring-enhancing pattern. Two patients had multifocal tumor. Cerebral biopsy was performed to establish diagnosis for 1 patient. Only steroid was continued after diagnosed for CNS-PTLD for all recipients. One patient's renal function turned worse and needed HD. The tumors were in remission 3 months after treatment for all patients. Median follow up was 15 months; there was no CNS symptom for all patients.
Discussion: SNS-PTLDs in renal recipients were rare and carried good prognosis for our follow up. Although early onset is common for PTLD after transplantation, 2 of 3 patients had long course after transplantation and had received minimum immunosuppression. Prognosis depends on a appropriate diagnosis, prompt reduction of immunosuppression, and careful long-term follow-up for recipients patients.

P-202 IMPACT OF RITUXIMAB INDUCTION THERAPY ON CMV INFECTIOUS DISEASE IN ABO INCOMPATIBLE KIDNEY TRANSPLANTATION

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(Objective): Cytomegalovirus (CMV) infection frequently occurs in renal transplantation (RTx) with many adverse effects. Recently rituximab (RXM) induction is becoming a gold standard in ABO incompatible RTx (ABO-I). The purpose of this study was to evaluate the impact of RXM induction on CMV infection in ABO-I.
(Method): 359 live renal transplantations were performed in our department between 2002 and 2008. They were divided into 204 ABO compatible RTx (ABO-C): Group A, 63 ABO-I without RXM: Group B, and 62 ABO-I with RXM: Group C. CMV-I was defined as an indication of ganciclovir treatment for CMV and incidence rates and risk factors of CMV infection were compared between them.
(Result): The graft survival rates of Group A, B, and C were 94.2%, 93.6%, and 93.9% at five years, respectively. 65 patients (31.9%) developed CMV infection in Group A, 33 (52.4%) in Group B, and 21 (33.9%) in Group C. There were significant differences of CMV infection incidence rate between Group A and B (P= 0.0101; Fisher's exact test), and Group B and C (P=0.030) with no significant difference between Group A and C (P=0.500). Although D+/R- (preoperative presence of CMV-IgG in donor/recipient), steroid pulse treatment, and old donor (60 years old or more) were risk factors of the CMV infection in the univariate analysis, RXM was not a significant risk factor.
(Conclusion): CMV infection incidence rate in Group C was comparable with that in Group A, and significantly less than that in Group B. And RXM was not a significant risk factor of CMV infection. We conclude that RXM can be used as an induction in ABO-I without increasing the risk of CMV infection with excellent graft survival rate.

P-203 INVASIVE MYCOSIS INFECTIONS AMONG KIDNEY TRANSPLANT RECIPIENTS

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Invasive mycotic infections (IMIs) are a major cause of morbidity and mortality (30-100%) among kidney transplant patients (KTP) with an incidence ranging from 2% to 25% in the six first months post-transplantation. Candida and Aspergillus are responsible for 80% of them, being Cryptococcosis the third most common invasive fungal infection, having also a high mortality rate.
Methods: Retrospective analysis of 180 charts was performed to evaluate IMIs among KTP from January 2003 through December 2010. *Immunosuppression: Induction* with Thymoglobulin® 167P and Simulect®13P. *Maintenance Immunosuppression:* Tacrolimus-Sodic Mycophenolate-Esteroids 135P, Tacrolimus-Sirolimus-Esteroids 30P, Belatacept-Mycophenolate Mofetil-Esteroids 10P, Cyclosporine-Micophenolate Mofetil-Esteroids 5P. Trimethoprim-Sulfamethoxazole and Ganciclovir were used as infectious prophylaxis
Results: 13 IMIs were identified among 12 KTP. In 4KTP symptoms appeared six months after transplantation while in the others, after the first year. 2KTP, having the same cadaveric donor, acquired invasive surgical wound aspergillosis infection. Both died. The preservation fluid was cultured, being negative.1KTP had lung aspergillosis concurrently with cutaneous histoplasmosis. 1KTP acquired paranasal sinuses histoplasmosis. 1KTP had lung histoplasmosis. 7KTP developed invasive cryptococcosis, 2KTP presented lung cryptococcosis (one relapsed under fungal treatment). 4KTP acquired brain cryptococcosis, two of them died. 1KTP had osteoarticular and brain cryptococcosis, which is an atypical combination.1KTP with brain zygomycosis died. Biopsy, mycological cultures and other complementary methods were used to carry out diagnosis. Amphotericin B was used as first-line treatment in all KTP followed by azole derivatives.
Conclusions: In our series the most frequent fungus infection was Cryptococcosis, with an occurrence of 58.3% and a mortality of 28.5%. Aspergillus represented 25% with a mortality of 66%. Histoplasmosis incidence was 25%. The highest mortality was caused by aspergillosis. The KTP having brain lesions showed the worst evolution. The over-all mortality was 41.7%. New immunosuppressant and immunomodulatory viruses favour the opportunistic infections such as mycosis.

P-204 IL-33 INDUCES DEFENSE MECHANISM AGAINST *Candida albicans* THROUGH RAPID RECRUITMENT AND ENHANCED FUNCTION OF NEUTROPHILS

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IL-33 is a recently identified member of the IL-1 family that signals through ST2 and is implied in the recruitment of neutrophils, the first and crucial line of defense against *Candida albicans* infection. In the current study, we found that IL-33 decreased mortality of mice infected with *C. albicans*. At the very early stage after infection, IL-33-treated mice displayed increased neutrophil influx into the peritoneal cavity as well as production of higher level of IL-6 which was believed as a regulator of granulopoiesis in vivo. Moreover, neutrophils of IL-33-treated mice were more potent to phagocytize *C. albicans* than those of control mice. In contrast, IL-33 markely decreased the phagocytosis activity of macrophages. The fungal growth in blood and peritoneal cavity (PEC) at 4 hour after infection was significantly lower in IL-33-treated mice, indicating an effective fungal clearance in these mice. To confirm the role of neutrophils, they were depleted *in vivo* with anti-Gr-1 antibody (RB6-8C5). Neutrophil depletion abolished the fungal clearance effect of IL-33 in *C. albicans* infection, which highlighted the role of neutrophils in this context. Taken together, our results suggest a previously undescribed effect of IL-33 in fungal infection through the rapid recruitment and functional enhancement of neutrophils.

P-205 ISONIAZID PREVENTIVE THERAPY FOR POSTRENAL TRANSPLANT TUBERCULOSIS: A SYSTEMATIC REVIEW

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Objectives: To systematically evaluate published randomized controlled trials (RCTs) on the efficacy and safety of isoniazid preventive therapy (IPT) in renal transplant recipients.
Methods: Electronic databases of Medline, Embase, and Cochrane Library (up to April 2010) were searched to identify relevant publications. Two reviewers independently applied the study selection criteria, examined study quality and extracted data. Data were expressed as risk ratios with 95% confidence intervals, and all statistical analyses were performed using Review Manager 5.0.
Results: Three RCTs met our selection criteria, including 657 patients (300 versus 357). IPT versus control: Posttransplant TB (P=0.09), extrapulmonary TB (P=0.38), TB-related deaths (P=0.25), and hepatitis (P=0.78) were not significantly different. None of the 3 RCTs reported serious adverse effects related to IPT.
Conculsions: Based on current evidence, IPT cannot be recommended as routine practice for preventing post renal transplant TB, even in countries where TB is endemic.
References: Wang XD, Zhuang J, Xie LB, Li MY, Lu YP. Isoniazid preventive therapy for postrenal transplant tuberculosis: a systematic review. Rev Med Microbiol 2011; 22(1):5-11.

P-206 EVALUATION OF HUMAN CYTOMEGALOVIRUS (CMV) SPECIFIC T-CELL RESPONSES PREDICTS EARLY AND LATE ONSET CMV INFECTION IN A COHORT OF KIDNEY TRANSPLANT RECIPIENTS

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Background: Monitoring post-transplant antiviral immune recovery is an appealing strategy to detect kidney transplant recipients (KTRs) at risk of developing early (<100 day) and late (>100 days) episodes of post-transplant CMV infection and disease.
Methods: We employed both Interferon gamma (IFN-g) ELISPOT and CMV Quantiferon (QTF) tests to detect CMV specific T-cell immune recovery in a cohort of 150 KTRs.
Results: Both ELISPOT and QTF tests are able to detect CMV specific responses in KTRs. Patients displaying >100 ELISPOT or >2 IU QTF are protected from CMV infection.
Conclusion: Both ELISPOT and QTF tests possess predictive value for assessing patients at risk of CMV infection.

P-207 IMPACT OF CONTAMINATED PRESERVATION FLUID ON CADAVERIC KIDNEY ALLOGRAFT TRANSPLANT – 5 YEAR EXPERIENCE

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Introduction: Contamination of organ preservation fluid (OPF) is common, with a reported incidence of 2.2% to 28%. Undetected, such contamination may lead to septicaemia and mycotic aneurysm.
Materials and Methods: From January 2006 to December 2010 we analyzed culture reports of all samples of preservation fluid from deceased donor kidney transplants for microbial contamination and the subsequent clinical course of the recipients. All patients with positive cultures were treated with an extended (10-14 days) period of antibiotics.
Results: Two hundred and seventy nine patients were transplanted during the period with 191 (68%) samples submitted for microbiological analysis. Gram stain was positive in only 3 patients. However on culture 39 (20.4%) grew at least one organism. The two commonest contaminants were Staphylococcus 14 (35%) and E.coli 11 (28%). Mixed growth and Candida was grown in 4 (10%) and 2 (5%) respectively. On follow up; 13/279 patients developed septicaemia during the postoperative period of which OPF positive group had only 4 septicaemic episodes and two secondary haemorrhage following ruptured anastomotic mycotic aneurysms. Both required nephrectomy and candida was the identified organism in both cases. No other graft losses occurred related to sepsis and no patient deaths occurred.
Conclusion: Contamination of preservation fluid occurs frequently. Gram stain is not a sensitive indicator of bacterial contamination of preservation fluid. OPF culture has sensitivity 43%, specificity of 80%, positive predictive value 0f 0.14 and a negative predictive value of 0.95%. Fungal contamination may be potentially life-threatening and if detected warrants aggressive therapy. These findings demonstrate the importance of microbial surveillance of perfusion media to detect nosocomial infection to guide antibiotic chemotherapy.

P-208 IS ISONIAZID SAFE IN LIVER TRANSPLANT PATIENTS ON THE WAITING LIST?

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Introduction: Isoniazid (INH) is recommended as a tuberculosis prophylaxis in non-liver transplant recipients. However, for pre-liver transplant recipients there is a great reluctance to carry out this procedure due to the risk of precipitating further hepatic decompensation.
Method: Retrospectively we analyzed the records of the candidates for liver transplantation submitted to a PPD test (tuberculosis skin test) between 2008 and 2010. Patients with no respiratory symptoms, PPD test $\geq$ 10mm and normal chest radiography received 300 mg of isoniazid per day for six months. The patients on tuberculosis prophylaxis were submitted to liver blood tests and clinical evaluation monthly. We analyze MELD score and Child-Turcotte-Pugh (CTP) classification.
Results: 191 patients on the liver transplant (LTx) waiting list were submitted to a PPD test. Thirty-four (17.8%) patients had PPD test result over 10 mm and were prescribed INH. Of these, 21 (61.8%) patients received INH for six months and 13 (38.2%) for one to three months. Among these 6/34=17.6% had MELD score over 20. MELD score was 16$\pm$4.80 (10-33) and 15 patients had extra points due to special situations with MELD score 24$\pm$4.52 (13-33). CTP A classification was observed in 7 (20.6%); B in 20 (58.8%) and C in 7 (20.6%) patients. CTP with average of 9$\pm$1.96 (6-15). The main cause of end-stage liver disease was hepatitis C (14= 41.2%), hepatitis C and alcohol (4=11.8%), hepatitis C and CHC (14= 41.2%), alcohol (39=20.4%) and others (2=5.8%). Twenty-one (55.9%) of them were submitted to LTx and post-transplantation mortality was 21% without any association with INH administration. No patients showed any clinical decompensation or laboratory abnormalities.
Conclusion: Tuberculosis prophylaxis with INH was safe for liver transplant candidates.

P-209 CMV INFECTION AFTER HEART TRANSPLANTATION IN RELATION WITH DIFFERENT IMMUNOSUPRESSION

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Background: During the past 3 years changes were occurred in immunosuppressive regimens after heart transplantation at our hospital. Predominantly we use tacrolimus as a maintance immunosupression instead of cyclosporine. However, we were afraid of higher incidence of infection complications due to this new aggressive immunosupression. This is a retrospective study of the incidence of CMV infection in relation to the type of immunosuppressive regimen.
Methods: CMV infections complications were analyzed in 116 patients, who underwent heart transplantation from January 2005 till December 2008. Preemptive treatment of CMV infection was applied in all patients. In 84 patients maintenance immunosupression included cyclosporine, mycofenolat mofetil and corticosteroid therapy while the rest 32 had immunosupression included tacrolimus placed cyclosporine. We followed up all patients for 2 years.
Results: In the group with cyclosporine 56 of 84 patients (66,7%) developed CMV infections vs. 23 of 32 patients (71,9%) in tacrolimus group (p=0,59).

Incidence of CMV infection

Imunnosuppresion	CMV replication without symptoms	CMV syndrome	CMV tissue invasive disease
Cyclosporine (N=84)*	48pts (57,1%)	13pts (15,5%)	10pts (11,9%)
Tacrolimus (N=32)*	22 pts (68,7%)	2 pts (6,3%)	4 pts (12,5%)
p	0,25	0,18	0,93

*CMV infection occurred repeatedly in some patients.

The most often CMV infection occurred during first 100 days after heart transplantation. Asymptomatic CMV viraemia was detected later after Htx in cyclosporine group while in tacrolimus group the later posttransplant period was associated with higher occurrence of CMV syndrome. The incidence of CMV infection wasn't correlated with the incidence of acute rejection.
Conclusion: our data did not assigned significant differences in the incidence of CMV infection in relation with immunosupression. During the preemptive treatment the incidence of CMV infection was high in both groups.
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P-210 A COMPARATIVE STUDY OF GANCICLOVIR VS. ACYCLOVIR FOR CYTOMEGALOVIRUS INFECTION TREATMENT IN RENAL TRANSPLANT RECIPIENTS

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Background: Cytomegalovirus (CMV) prophylaxis still did not adequately prevent CMV infection in patients after renal transplantation (RTx). We compared the efficacy and safety of intravenous ganciclovir with those of intravenous acyclovir in treating CMV infection including CMV seropositive patients and CMV disease patients to explore an effective therapy method of treating CMV infection after RTx.
Methods: 852 renal transplantation recipients including CMV seropositive and CMV disease patients received antiviral therapies of intravenous acyclovir or comprehensive anti-infection solution mainly with intravenous ganciclovir. Effect, time, acute allograft rejection and safety were analyzed during the antiviral therapy.
Results: The total effective rates were higher with ganciclovir in both CMV seropositive patients (98.96% vs. 84.90%) and CMV disease patients (96.29% vs. 50.36%). Ganciclovir curtailed antiviral therapy duration significantly in both CMV seropositive patients (15.0$\pm$2.3 days vs. 16.0$\pm$3.4 days) and CMV dis-

ease patients (19.7±3.1 days vs. 21.5±4.0 days). The acute allograft rejection incidences were significantly lower with ganciclovir in both CMV seropositive patients (8% vs. 14%) and CMV disease patients (11% vs. 22%). Except for the higher incidence of anemia leucopenia and anemia with ganciclovir the safety profile was similar with both drugs.
Conclusion: Comprehensive anti-infection solution mainly with intravenous ganciclovir could effectively treat CMV infection, shorten time course of therapy and decrease acute rejection.

P-211 HEPATITIS C VIRUS (HCV) GENOTYPE MISMATCH IN RENAL TRANSPLANTATION AND HCV GENOTYPE CONVERSION

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Background: Kidney transplantation between hepatitis C virus (HCV) infected donors and recipients is generally admitted because of the worldwide donor shortage. However, the impact of transplantation between various HCV genotypes remains controversial.
Methods and patients: We investigated the clinical courses of 4 cases of cadaveric kidney transplantation between different genotypic HCV carriers, which were performed in 2007 and 2010. The HCV genotypes before and after kidney transplantation were examined in both retrospective and prospective manners. HCV genotype was also determined for 27 patients with end stage renal disease (ESRD) on the transplantation waiting list of our center.
Results: All recipients were HCV genotype 1b, of whom 1 received transplantation from a genotype 2a donor and 3 received transplantation from genotype 2b donors. In the former case, liver aminotransferase began to elevate 1 month after transplantation, after which a liver biopsy revealed acute hepatitis. In addition, HCV genotype was found to be converted from 1b to 2a on post-transplant day 17. However, such conversion was not found in the other 3 patients, while slight hepatic dysfunction was noted in 2. The HCV genotype of the 27 ESRD patients was 1b in 21 cases (77.8%), 2a in 2 (7.4%), and 2b in 2 (7.4%), while no genotype was found in 2. The HCV genotypic incidence was the same between the ESRD patients and general population in Japan. The possibility of transplantation between different genotypes was calculated to be 43.32%.
Conclusion: HCV infected recipients have a risk of acute hepatitis as a consequence of superinfection following transplantation from a kidney donor with a different HCV genotype. HCV genotype mismatches occur approximately in half of transplantation cases involving HCV infected donors and recipients. Thus, it is important to prospectively determine genotype in these cases.

Kidney

P-212 PULSATILE PERFUSION PRESERVATION FOR EXPANDED-CRITERIA DONORS KIDNEYS: IMPACT ON DELAYED GRAFT FUNCTION RATE

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Background: Expanded criteria donors (ECD) kidneys are a potential solution to organ shortage, but exhibit more delayed graft function (DGF) and worse long-term function. Pulsatile Perfusion Preservation (PPP) has been proposed to decrease injury in this type of kidneys. We conducted a prospective controlled study aiming to evaluate the impact of PPP on DGF rate.
Methods: Inclusion criteria were: 1. ECD definition (any brain-dead donor aged >60 years or aged 50-60 years with at least 2 of the following: history of hypertension, terminal serum creatinin level ≥1.5 mg/dL, death resulting from a cerebrovascular accident, 2. Donor prolonged reversible circulatory arrest (>20 mn), 3. previsible cold ischemia time longer than 24 hours. In each pair of kidneys, one organ was preserved with PPP and the other organ was preserved in static cold storage.
Results: From February 2007 to September 2009, a total of 22 donors (44 recipients) were included. Mean donor age was 57.8±15.1 years. Sex ratio was 15M/7F. Mean weight was 78±16.5 Kg and mean height 172±12 cm. BMI was 26.3±4.3 Kg/m2. Death was mainly due to cerebrovascular causes (n= 14, 64%) with a frequent history of hypertension (n= 10, 45%). Terminal donor serum creatinine was 103.8±50.3 μM. Recipients were comparable in the two groups with respect to demographic and immunological data.
The rate of DGF was significantly lower (9% vs. 31.8%, p = 0.021) in the PPP group. At one and three months, renal function was comparable in the two groups, as expressed by serum creatinine and estimated GFR (MDRD).
Conclusion: Pulsatile Perfusion Preservation significantly reduced DGF rate in ECD kidney transplantation. Long term outcome needs further evaluation.

P-213 HAS LONG-TERM SURVIVAL OF KIDNEY TRANSPLANT STABILIZED NOWADAYS? PROJECTED HALF MEAN LIFE

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Background: To compeer the outcomes at the recent time using the classical survival methods we needed a long follow up of the patients that we don't have. Therefore there is not yet a consensus if renal transplant outcomes has improving or has been stabilized along the time. We compeer the survival at recent time using a non-classical test of survival: the mathematics projection of the real survival to calculate the projected half mean life of the renal graft.
Methods/Material: All transplant recipients of a renal graft alone in our centre until 2005 has been selected and followed at least for three years. Demographic, clinical and analytical variables have been recorded for each patient. Projected half mean live has been calculated from 156 observed real survival data (firsts three years post-transplantation) or from 128 observed data (excluding first six months post-trasplantation), using the most adjusted mathematics' equation to these data.
Results: 778 kidney graft's recipients were included and divided in four quartiles depending on the moment of the transplantation (approximately 1979-1989, 1989-1996, 1996-2000 y 2000-2004). The most adjusted mathematics equation was the potential equation at Q1 and Q4 of the 156 observed data and a second grade polynomial equation at Q2 and Q3 of the 156 observed data or always in the analysis of 128 observed data. Using these equations, the kidney graft survival initially improved (Q1-Q2) and lastly was stabilized (Q3-Q4). Classical methods of survival and real half mean life confirmed these results.
Conclusions: Ø Nowadays, kidney graft's survival has been stabilized, regardless of the survival test used.
Ø Projected half mean life based on a high number of observed data after the six months post-transplantation is an adequate method to compeer renal graft outcomes of recent times.

P-214 DOES RETROPERITONOSCOPIC NEPHRECTOMY INCREASE THE RISK FOR LYMPHOCELE FORMATION?

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Retroperitonoscopic approach for donor nephrectomy can be associated with increased risk of fluid collection or lymphocele formation as it creates a potential extraperitoneal cavity. We present our study to evaluating the risk of collection formation after retroperitonoscopic hand assisted donor nephrectomy.
Methods: Forty-seven donors who had surgery in between April and October 2010 at John F Kennedy Hospital were consented to have doppler ultrasound evaluation one month after the procedure. The avarege age was 46. Female to male ratio was 29/18. Seven donors had right nephrectomy. All donors had hand assisted retroperitonoscopic nephrectomy requiring hand port and two trocar insertion. Paramedian incision and pfannenstiel incision (n=3) was performed for hand port. Suction drainage was not used. Non of the donors had bleeding or any other major complication during the surgery. Doppler ultrasound evaluation was performed by the same radiologist to screen the operation site for fluid collections. The screen was performed in between 20 to 33 days after the procedure (mean 30 days).
Results: The ultrasound screen revealed that two donors had hematoma at the paramedian hand port incision. One donor had superficial seroma under the skin incision. One donor had seroma (size of 2x1x4 cm) at the left nephrectomy site. The fallowing ultrasound evaluation performed for this patient showed that the retroperitoneal seroma had disappeared 40 days after the initial screen. The rest of the ultrasound screens were completely normal.
Conclusion: Laparoscopic donor nephrectomy rarely causes a collection as it is an intraabdominal procedure but chylous ascites after laparoscopic nephrectomy was defined in literature before. Retroperitonoscopic approach creates a potential extraperitoneal cavity therefore can be more likely to cause lymphocele. Even if we have not seen lymphocele formation in our series, we be-

lieve that meticulous lymphatic dissection should be performed especially in retroperitonoscopic nephrectomy.

P-215 THE EXPERIENCE OF EXPANDED CRITERIA DONORS; KIDNEY TRANSPLANTATION IN SAUDI ARABIA: 2008-2010

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Objective: To identify and analyze the use of Expanded Criteria Donors (ECD) and the outcome of kidney transplantation in the Kingdom of Saudi Arabia.
Methods: This is a retrospective study of all deceased donor transplantation from the year 2008 to 2010 investigating the impact on graft, patient survival and graft function of ECD kidneys compared to Standard Criteria Donors (SCD).
Results: Out of the 433 kidney transplants in the year 2008-2010, the number of ECD kidneys transplanted were 68 (16%), out of which 7 kidneys were from $>$ 60 years old donors; 43 kidneys from serum creatinine $>$ 133 umol/L or 50-59 years old with CVA/HTN and 18 kidneys were from donors with serum creatinine doubled at harvesting with cases of CVA/HTN. Moreover, it showed significant difference in the mean age group (39 years vs. 48 years). Furthermore, as the causes of brain insult, 38% of SCD were due to trauma while only 1 case (.02%) for ECD. There was increase number of days from the mean period of transplantation to discharge from 19 days for SCD and 32 days with ECD. The mean serum creatinine at discharge was doubled between the 2 groups. In comparison kidney recipients, who had delayed graft function also doubled between SCD 16% and ECD 36%. On the other hand, episodes of acute rejection are significantly increased from 5% in SCD to 20% in ECD group.
Conclusion: The use of Expanded Criteria Donors is an acceptable method to use in specified category for kidney transplantation in Saudi Arabia. The outcome of marginal kidney transplantation is comparable to international data.

P-216 IMPACT OF THE DETERMINATION OF HLA ANTIBODIES IN KIDNEY TRANSPLANT OVER TEN YEARS OF MONITORING

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Objective: The goal of this study was to determine the prevalence of anti-HLA antibodies and the clinical outcome in patients with functioning renal graft over ten years.
Patients and Methods: We measured the presence and the levels of class I and II anti-HLA antibodies by microbead technology (Luminex) in 120 patients with functioning renal graft over 10 years.
Results: The average time of transplantation was 15, 4$\pm$3, 7 years. 25% of the patients studied, had anti-HLA antibodies. The presence of anti-HLA antibodies was associated with worse serum creatinine levels (p 0,03), lower glomerular filtration rate (p 0,02) and increased proteinuria (p 0,00). Antibodies were measured one year after the first determination in patients with positive anti-HLA antibodies. The elevation of these antibodies did not influence the evolution of renal function or degree of proteinuria. (Cr in patients with increased antibody titers compared with those who remained stable was 1, 53 mg/dl vs. 1, 9 mg/dl - p 0.33).
Conclusions: Our study show that in patients with functioning renal graft over ten years, the presence of anti-HLA antibodies was 25%, and this was associated with the development of chronic rejection, worse renal function and greater proteinuria levels, regardless of the evolution of antibody titers at one year. The determination of HLA antibodies could be useful in the management of transplant patients.

P-217 LAPAROSCOPIC RE-INSERTION/EXCHANGES OF PERITONEAL DIALYSIS CATHETERS (PDC) USING THE MODIFIED "Y"-TEC SYSTEM

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Background: The trend towards insertion of peritoneal-dialysis-catheters (PDC) has moved from open surgery towards laparoscopic or peritoneoscopic approaches. We present the Leicester experience, describing the modified "Y"-TEC® technique to deal with problems that could be encountered during re-insertions/exchanges.
Methods: Retrospective analysis of patients undergoing PDC insertions from September 2007 to April 2010. All patients undergoing a laparoscopic PDC insert using a modified'Y'-TEC® technique under general anaesthetic were included.
Results: A total of 112 patients were analysed. The mean age was 56 years, while BMI 27. Total insertion included 83 while the remaining 29 were exchanges of PDC. The mean cumulative follow up period was 258 days. Of these 85 had undergone previous abdominal operations. 42 patients underwent division of adhesions and 5 paraumbilical hernia repairs.
33 patients developed flow problems which were mostly in patients undergoing division of adhesions. Of these 6 were repositioned, 10 exchanged leaving 3 which could never be used. In the long run 5 patients developed hernias and 18 patients developed exit site infections, while 29 episodes of peritonitis were documented. 7 (6.25%) deaths were documented, 6 related to peritonitis and one due to intracranial haemorrhage and none related to the immediate post operative period. All patients were permitted for immediate PD, 19 developed leaks and only 4 persisted after a period of rest.
Conclusions: The series presented shows the successful use of the technique described, allowing the PDC to be inserted and tunnelled out through the well-planned working 5mm port-site, thereby keeping the incisions to minimum. In addition the working ports can be used to deal with possible problems encountered in re-do surgery such as an extensive laparoscopy especially with previous peritonitis, assessing feasibility of PD, biopsy the peritoneum for encapsulating-peritoneal-sclerosis (EPS), dealing with adhesions and replacing/exchanging displaced PDC.

P-218 UROLOGICAL COMPLICATIONS AFTER RENAL TRANSPLANTATION

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Introduction: Urological complications can affect the outcome of kidney transplantations by increasing the morbidity and mortality, including the lost of the graft. The aim of this study is to determine the incidence of urological complications, in our centre.
Materials and Methods: A series of 650 consecutive renal transplantations were performed between 1st of October 2004 and 28th of February 2011. The mean age: 26.2 years old. Renal grafts were obtained in 486 cases (74.7%) from living-related and in 164 cases (25.3%) from cadaveric donors.
Results: The overall incidence of complications was 7.84% (51 cases). We recorded 21 ureteral stenosis (3.23%), 15 ureteral fistulas (2.3%), 10 lymphoceles (1.53%), two hematoma with ureteral obstruction (0.3%) and three cases of clot obstruction (0.46%). For the patients with ureteral stenosis (21 cases) the most common surgical treatment was vesicoureteral re-anastomosis 14 cases (2.15%). In seven cases (1.07%), we performed double pigtail stenting. For ureteral fistulas ureteral stenting was performed in eight cases (1.23%), six vesicoureteral re-anastomosis (0.92%) and one ureteropyelostomy (0.15%). Peri-graft collection with obstruction of the ureter was diagnosed in 10 cases. Percutaneous drainage was successful in four cases (0.61%) and open surgical peritoneal fenestration was performed in the other six cases (0.92%). Two patients developed hematoma with secondary ureteral obstruction, solved by percutaneous drainage in one case (0.15%) and open surgical evacuation and drainage in the other (0.15%). For the cases of ureteral clot obstruction (3 cases), a double pigtail ureteral stent insertion after endourological clot removal was successful.
Conclusions: Urological complications related to leakage or stenosis can be treated minimally invasive by ureteral stent insertion or by surgical vesicoureteral reimplantation. Early diagnosis and treatment will help maintain renal graft function. In our study, graft survival after successful treatment has been similar for all the patients.

P-219 YOU'RE WELCOME: SUPPORTING YOUNG ADULTS WITH KIDNEY DISEASE

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Background: Amongst young adults with long term conditions like kidney disease concordance issues are well recognised. Adjustment issues after transfer from paediatric to adult units can have great personal and financial cost. In one UK study, 35% (7 of 20) of young patients transferred to adult renal care lost their transplant kidney within 36 months. In addition, young adults presenting directly to adult renal services with progressive kidney disease also frequently have major issues with denial and concordance.
Methods: NHS Kidney Care has developed a new national project, "Supporting Young Adults with Kidney Disease". This involves those transferred from paediatric services and those presenting in young adulthood; those who have had, or are awaiting a transplant, and those on dialysis. Approaches focus around:

1. The appointment of key workers working across the adult-paediatric kidney interface, in addition to primary care and social care settings
2. Self assessment of trusts using the You're Welcome criteria to develop holistic patient care. You're Welcome is a national quality framework led by the Department of Health, designed to help providers and commissioners transform health services by improving acceptability, accessibility, quality and choice for young people aged under 20.
Results: Five project groups around England have been approved to be part of this project. They have successfully agreed service models, project definitions and appointed key workers. The impact of their work on patient outcomes is being externally evaluated using qualitative and quantitative methodology. Examples of how project groups have used the You're Welcome criteria and self-assessment tool to improve services will be reported.
Conclusion: You're Welcome criteria can support service redesign to meet the needs of young adults with kidney disease including those preparing for transplant and those who have received their transplant. Recommendations include transferable learning for other conditions.

P-220 CINACALCET IMPROVES ENDOTHELIAL FUNCTION IN RENAL TRANSPLANT RECIPIENTS WITH PERSISTENT HYPERPARATHYROIDISM

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Background: Calcimimetic cinacalcet is a well known drug for the treatment of hyperparathyroidism. Beside its favorable effect in reducing serum parathyroid hormone and calcium level, some experimental data shows direct beneficial effect of calcimimetic on vasculature. In this study we tried to evaluate the effect of cinacalcet on hyperparathyroidism, calcium level and endothelial function in kidney transplant recipients with persistent hyperparathyroidism.
Methods: This prospective, clinical study included 11 patients (aged 39 to 64 years) with a persistent hyperparathyroidism, a serum creatinine <200 μmol/L, stable kidney graft function and they were more than one year since transplantation. During the 6m observation period, in which the stability of measured parameters was determined, and in the 12m treatment period (cinacalcet 30 mg/day) we followed serum concentrations of calcium, intact parathyroid hormone (iPTH) and creatinine, intima-media thickness (IMT) of common carotid arteries (by the B-mode ultrasound technique) and endothelium dysfunction, which was evaluated by ultrasound measurement of the endothelium-dependent dilatation of the brachial artery, induced by reactive hyperaemia test.
Results: During the treatment period, the serum calcium decreased significantly from 2.50 ± 0.12 to 2.32 ± 0.12 mmol/L ($P<0.01$). Serum iPTH decreased significantly from 247 [range, 199-362] at time 0 to 198 [range, 165-233] ng/L after 1m of treatment ($P<0.05$), but increased slightly thereafter. Renal function remained stable during treatment period. After 12m of cinacalcet treatment endothelium-dependent vasodilatation significantly increased from 7.0 ± 4.6 to 12.9 ± 5.6% ($P<0.05$). Endothelium-independent vasodilatation did not change during 12m of treatment. There were no significant changes in IMT of common carotid arteries.
Conclusion: Treatment of posttransplant hyperparathyroidism with cinacalcet was effective, resulting in decreased calcemia and at least transiently decreased iPTH. Cinacalcet treatment resulted in a significantly improved endothelial function and might therefore reduce the risk for cardiovascular events.

P-221 KIDNEY TRANSPLANTATION FROM LIVING DONORS OVER 60: DONOR AGE DOES MATTER

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Living donor kidney transplantation from donors over 60 years has become more frequent. There are only few analyses of donor and recipient renal function in the living donor old-for-young setting. We analyzed all consecutive living donor kidney transplants from donors over 60 years of age performed in two centers between Jan 1, 1999 and Dec 31, 2009, study the impact of donor age on recipient and donor kidney function after living donor transplantation.
94 transplants from donors over 60 years (mean donor age 65; 60-76; mean recipient age 49) were analyzed. 22 organs were lost at 29.8 months (including death of 8 patients with a functioning graft at 28.7 months). Donor GFR (MDRD) at 1 and 5 years was 54 and 58 mL/min. 341 living donor kidney transplants from donors under 60 years (mean donor age 45; 28-59; mean recipient age 39) were also analyzed. Donor GFR was 61 and 62 mL/min at 1 and 5 years. 80% of older donors had GFR below 60 mL/min at one year. 51% of younger donors presented GFR <60. Recipients of older organs had GFR of 47 and 42 mL/min at the respective time points. Young recipients ($<$ 60 years; n=62) of older organs presented GFR of 46 and 43 mL/min at 1 and 5 years. Recipients of young organs had GFR of 59 and 54 mL/min at 1 and 5 years (1 year: $p<0.001$; 5 years: p=0.03).
Kidney transplantation from living donors in their 7th or 8th decade of life to young recipients is feasible and safe for the carefully selected donor, however, is associated with lower recipient kidney function compared with younger organs. Thus, precautions should be taken to preserve kidney function especially in the old-for-young setting.

P-222 SAFE CONVERSION OF STABLE KIDNEY TRANSPLANT RECIPENTS FROM TWICE-DAILY TACROLIMUS (Prograf) TO ONCE-DAILY MODIFIED RELEASE TACROLIMUS (Advagraf)

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Non-compliance to immunosuppressive therapy in solid organ transplantation recipients is a preventable but major factor leading to acute graft rejection and eventually graft loss. The modified release formulation of Tacrolimus (Advagraf) was developed to provide a once-daily dose, thus improving adherence to prescription.
Methods: This open-label, single centre study was performed to analyze the safety of a 1:1 milligram dose conversion from Prograf twice-daily to Advagraf once-daily. Ninety-eight eligible patients were asked to participate the study. More than 6 months after renal transplantation, they all had stable renal function and had received a constant dose of Prograf twice daily for more than 1 month before the conversion. A baseline control of renal function parameters, together with Tacrolimus dose and level, was performed the day before and one month after the switch to Advagraf.
Results: Eighty (81.6%) patients gave their consent to switch. The most commonly adduced reasons for not participating were distance from the transplant center for the first month controls and their supposed greater confidence in Prograf.

Mean values of renal function and Tacrolimus doses/levels

	Serum creatinine (mg/dl)	Creatinine clearance (ml/min)	Daily Tacrolimus dose (mg)	Daily Tacrolimus dose (mg/kg)	Tacrolimus through levels (ng/ml)
Pre-switch	1.75	56.86	3.86	0.065	6.32
Post-switch	1.68	59.17	3.88	0.061	6.26

There was no significant difference between the pre- and post-conversion values of any parameter considered.
Only 1 out of 80 patients returned to Prograf because of the impossibility of reaching therapeutic Tacrolimus levels after the switch to Advagraf. No serious adverse events were encountered following conversion.
Conclusion: Only 1/5 of informed patients refused to switch from Prograf to Advagraf due to the two reasons reported above. In the study population the results provided evidence to support a safe 1:1 milligram dose conversion from Prograf twice a day to Advagraf once-daily in nearly the whole population of stable renal transplant patients.

P-223 OPEN PROSPECTIVE STUDY TO EVALUATE CARDIOVASCULAR RISK FACTORS AND RENAL FUNCTION IN TWO DOSAGE REGIMENS OF TACROLIMUS (TAC) COMBINED WITH MYCOPHENOLATE MOFETIL AND STEROIDS IN RENAL TRANSPLANT PATIENTS

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Background: Calcineurin inhibitors cyclosporin and (TAC) are the most potent immunosuppresants. TAC is considered less nephrotoxic, but may be an important factor of chronic graft dysfunction. The aim of the study was to evaluate kidney function and cardiovascular risk profile in two groups of low immunological risk kidney allograft recipients receiving two TAC dosages.
Material and method: Low immunological risk patients were randomly assigned to two TAC based treatments (Group I (n=14)-standart dose, Group II (n=15)-reduced dose). Primary study endpoints were: 1. Occurrence of cardiovascular events (cardiac death, myocardial infarction, stroke), 2. Acute rejection episodes, 3. Graft function at 12 and 24 months. Secondary endpoints were: patient and graft survival and incidence of PTDM.
Results: Patient demographics were not statistically different between groups. The trough levels of tacrolimus were significantly higher for group I for 1, 3, 6 and 12 months post transplant and fell within desired range according to study protocol. There were no significant differences between groups in patient and graft survival or rate of cardiac events. The AR rate was very low but there were more AR episodes in Group II. Graft function measured as serum creatinine

levels did not differ between groups. The same applies to PTDM incidence. Office blood pressures were numerically higher in group I and this difference reached significance at some time points.
Conclusions: Immunossupression based on low dose of tacrolimus seems to be safe in the group of low immunological risk patients but in the 24 month follow-up does not offer any clear-cut benefits in terms of potential nephrotoxicity or cardiovascular risk. Such approach could not be recommended even in the low risk population until further data is available.

P-224 SINGLE CENTRE EXPERIENCE IN LIVING DONOR KIDNEY TRANSPLANTATION (LDKT)

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Background: Available data show that living donor kidney transplantation (LDKT) is a viable option in transplantation characterized by better short and long term results compared to cadaver KT (CKT). In Poland number of LDKT is very low and accounts for between 2 and 3% of all KT performed.
Material and method: All LDKT performed in our centre between 1999 and 2010 were identified and data collected. There were 29 LDKT during this period, which accounts for 3.33% of all KT.
Results: Most (82,7%) were living related KT. Mean recipient age was 34,4±12,8 years and mean donor age was 48,5±7 years. Most donors were women (17 - 62%). In 3 cases the LDKT was a second transplant. Mean number of HLA class I and II mismatches were 2,18±0,98 and 0,93±0,6 respectively. Mean total ischemia time was 3,22±1,74 hours. 4 recipients (13,7%) received ATG induction and 7 (24,1%) daclizumab induction. 27,6% of recipients were placed on cyclosporin based immunosuppression and remaining 72,4% on tacrolimus. 69% received mycophenolate mofetil. All recipients received steroids. Delayed graft function was observed in 3 cases and in 4 cases acute rejection was diagnosed.
One year patient and graft survival were both 100%(98 and 83 for CKT. Five year patient and graft survival were 100% and 89,6%, respectively, compared to 83 and 69 in CKT. The mean serum creatinine levels at 1, 6 months, 1 and 5 years after KT were 1.59±0.4, 1.51±0.3, 1.51±0.4 and 1.49±0,3 mg/dl, respectively.
Conclusions: Our results confirm excellent outcomes reported previously in LDKT. This form of KT should be actively promoted in our country.

P-225 IMPACT OF CYP3A AND ABCB1 POLYMORPHISMS ON TACROLIMUS DOSE-ADJUSTED TROUGH CONCENTRATIONS AMONG RENAL TRANSPLANT RECIPIENTS IN KOREA

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Background: Tacrolimus is a substrate of cytochrome P450 3A (CYP3A) and P-glycoprotein (P-gp), encoded by the CYP3A and ATP-binding cassette subfamily B member 1 (ABCB1) genes, respectively. This study was aimed to investigate the impact of CYP3A and ABCB1 polymorphisms on the tacrolimus pharmacokinetics and clinical outcomes in renal transplant recipients in Korea.
Methods: We retrospectively analyzed data from a cohort of 63 renal transplant recipients receiving tacrolimus. CYP3A4*4, CYP3A4*5, CYP3A4*18, CYP3A5*3, ABCB1 C1236>T, ABCB1 G2677>T/A and ABCB1 C3435>T polymorphisms were genotyped and correlated to dose-adjusted tacrolimus trough concentration on month 1, 3, 6 and 12 after transplantation.
Results: Frequencies of variant alleles among the renal transplant recipients were CYP3A4*4 0.0%, CYP3A4*5 0.0%, CYP3A4*18 1.8%, CYP3A5*3 77.0%, ABCB1 C1236>T 60.3%, ABCB1 G2677>T/A 57.1% and ABCB1 C3435>T 34.1%. Patients with the CYP3A5*3 alleles showed higher dose-adjusted tacrolimus concentrations for 12 months and higher trough levels until 6 month after transplantation. ABCB1 polymorphisms were not associated with tacrolimus concentrations. In a multivariate analysis, the presence of at least one CYP3A5*3 allele was significant independent variables affecting dose-adjusted tacrolimus concentrations. Glomerular filtration rate (GFR), acute rejection and opportunistic infection were not affected by CYP3A5 polymorphisms. CNI toxicity which showed higher tendency in patients with CYP3A5 *1 alleles, might be associated with higher tacrolimus dose/kg.
Conclusions: The CYP3A5 genotype is a major factor in determining the dose requirement for tacrolimus, and genotyping may be of value in individualization of immunosuppressive drug therapy for renal transplant patients.

P-226 RENAL TRANSPLANTATION FOLLOWING AORTO-ILIAC RECONSTRUCTION IS A SAFE A STRATEGY

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Introduction: Renal transplantation is considered the treatment of choice for end-stage renal disease. However, the association of occlusive aorto-iliac disease and chronic renal failure is frequent and aorto-iliac reconstruction may be necessary prior to renal transplantation. This retrospective study reviews the results of this operative strategy.
Material and Methods: Between January 2001 and June 2010, 309 patients underwent renal transplantation at our institution and 8 patients had prior aorto-iliac reconstruction using prosthetic material. There were 6 men and 2 women with a median age of 62 years (range 51-70). Five aorto-bifemoral and 2 aorto-bi-iliac bypasses were performed for stage II (n=5), stage IV (n=1) and aortic aneurysm (n=1). In one patient, iliac kissing stents and an ilio-femoral bypass were implanted. 4 cadaveric and 4 living donor renal transplantations were performed with an interval of 2 months to 10 years after revascularization. The results were analysed with respect of graft and patients survival. Differences between groups were tested by the log rank method.
Results: No complications and no death occurred in the post-operative period. All bypasses remained patent during follow-up. The median time of post transplantation follow-up was 46 months for all patients and 27 months for patients with prior revascularization. In the revascularized group and control group, the graft and patient survival at 1 year were respectively 100%/96%, 100%/99% and at 5 years 86%/86%, 86%/94%, without significant differences between both groups.
Discussion: Our results suggest that renal transplantation following prior aorto-iliac revascularisation with prosthetic material is safe and effective. Patients with end-stage renal disease and concomitant aorto-iliac disease should therefore be considered for renal transplantation. However, caution in the interpretation of the results is indicated due to the small sample size of our study.

P-227 CONVERSION TO EVEROLIMUS: TO BELIEVE OR NOT BELIEVE?

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Introduction: Immunosupression with calcineurin inhibitors (CNIs) in renal transplantation is associated with chronic graft dysfunction, increased cardiovascular risk and malignancies. Everolimus (EVR) appears to permit a CNI-sparing regimen among stable kidney recipients.
Aim: To analyse the efficacy and safety of conversion from CNIs to EVR.
Material and Methods: Retrospective registry-based study of 151 patients converted from CNIs to EVR between 2006 and 2010 in a Renal Transplantation Unit. The reasons for conversion included: “clinical decision” (72.2%), malignant tumours (10.6%), chronic graft dysfunction (7.3%), adverse reactions (6.6%) and CNI biopsy-proven nephrotoxicity (3.3%).
Results: 151 patients (69.5% male; mean age 50.23±12.7 years) were converted to EVR 37.02±49.77 months after transplantation date, 34% during the first 6 months. At baseline, eGFR-MDRD 57.4±22.14 ml/min/1.73m^2; 139 patients (92.1%) had 24-hour proteinuria <300mg, 11 (7.3%) 300-3000mg, and 1 (0.66%) nephrotic-range proteinuria. 68.9% patients presented with dyslipidaemia and 49.0% arterial hypertension.
During the follow-up, 18 patients (11.9%) were reconverted to CNIs (4 due to nephrotic syndrome, 4 due to acute rejection, and the remaining cases due to infections and other side-effects of EVR), 2 patients died with a functioning graft and 2 patients lost graft function.
At the final evaluation of the remaining 129 patients, after 17.81±9.96 months of follow-up, eGFR-MDRD rose to 65.47±23.01ml/min/1.73m^2. 29 (22.5%) had proteinuria 300-3000mg/day and 1 (0.8%) nephrotic-range proteinuria. Percentage of patients with dyslipidaemia and hypertension rose to 77.5% and 65.9%, respectively. Other reported side-effects included oedema in 5.4% and recurrent oral ulcers in 0.7%.
Conclusion: Renal function improved significantly after conversion. Although side effects are common, most were mild and withdrawal of EVR was necessary in a low percentage of cases. The increase in incidence of hypertension needs further clarification. EVR appears to be an effective and safe alternative to CNIs as maintenance therapy in selected kidney transplant recipients.

P-228 THE INFLUENCE OF OBESITY ON RENAL TRANSPLANT OUTCOMES – A PAIRED KIDNEYS ANALYSIS

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Background: Obesity is significantly increasing worldwide. It also affects people with end stage renal disease who are potential kidney recipients. The aim of the study is to evaluate the effect of obesity on surgical and non-surgical complications after kidney transplantation.
Methods: We analyzed 300 recipients from our transplant center. In this group we found 29 patients who were obese (BMI>= 30). To avoid influence of donor factors we analyzed those 29 patients with their pairs. In each pair kidneys were transplanted into one obese and one non-obese patient.
Results: The groups were similar in gender. The age of the obese group was slightly higher than non-obese (53,6 vs 46,2 years). The rates of acute rejection and delayed graft function were similar in both groups. The mean serum creatinine level at the time of discharge was similar in both groups and the obese group had a lower mean serum creatinine at 1 year but the difference was not significant. The length of hospitalization was longer in obese group (26 vs 21 days) and this group had more surgical complications (58,6% vs 44,8%) which was statistically significant. Numbers of reoperations were equal in both groups because complications which occurred in non-obese group were mostly of minor consequence like wound breakdown and wound infection.
Conclusion: 1. 10% of patients who undergone kidney transplantation in our center were obese. 2. There were no difference in the rate of delayed graft function and acute rejection between obese and non-obese group. 3. There were more surgical complications in the obese group and also the length of hospitalization was longer in this group.

P-229 ESTIMATING MODEL OF GRAFT FUNCTION IN KIDNEY TRANSPLANT RECIPIENTS

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Background: The study aims to estimate the probability of loss of function of kidney transplant in the long-term period after transplantation.
Methods: We analyzed 238 patients who survived more than one year with a functioning transplant. To predict the subsequent duration of the well-functioning of allotransplant the prognostic significance of 15 baseline clinical and sociodemographic characteristics on the results of the survey one year after transplantation was investigated.
In constructing of regression model of prognostication the result was considered positive if the recipient lived for more than 3 years from the time of transplantation.
Results: Over three years with functioning graft had been living 168 (70,6%) kidney transplant patients. Analysis of β-coefficients of the generalized regression model showed that three characteristics can be deemed the most significant ($p < 0{,}001$) for the forecast: blood creatinine and haemoglobin level, as well as degree of proteinuria.
On a dedicated set of features predictive model was created. After model training decision - rejection threshold was optimized. The value Ycrit = 0,435 is obtained. If as a result of calculation within the created model Y value is less than Ycrit, a negative result is predicted and otherwise a positive result is predicted. Received predictive model using these factors is described by the equation:
Y: $= -0{,}967 \times X_1 + 0{,}00955 \times X_2 - 0{,}143 \times X_3$, where X_1 – creatinine (mmol/l), X_2 – haemoglobin (g/l), X_3- proteinuria (g/l) one year after transplantation. On the test set sensitivity of the model was 85,4%, specificity was 92,0%.
Conclusions: Values of creatinine, haemoglobin and proteinuria one year after transplantation is most associated with the termination of functioning of the transplant in the long-term periods and can be used to subsequent prognostication of kidney transplant function.

P-230 PREGNANCY IN KIDNEY TRANSPLANT: RESULTS IN 2 NORTH EAST ITALY TRANSPLANTATION CENTRES

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Objective: evaluate the gestations of transplant patients (pts), analyzing outcomes and complications as well as long term evolution of renal function.
Methods: Retrospective study investigating the outcome of 18 pregnancies in 16 renal transplant pts. Variables analyzed: Type of nephropathy, pts age when dialysis started, age of transplantation, time between dialysis and transplant and between transplant and baby birth. Immunosuppressive therapy, type of delivery, baby weight, Apgar score and mother and baby follow up were also considerate.
Results: In 16 pts were diagnosed: chronic pyelonephritis (4pt), post partum cortical necrosis (1pt), IgA GN (5pt), diabetic nephropathy (3pt), unknown nephropathy (3pt) All received a cadaveric donor kidney, and calcium antagonists and alfamethyldopa for high blood pressure. Immunosuppressive theraphy: Prednisone, AZA and CyA in 9 pt, Prednisone and FK in 7 pt. Renal function was good before, during, after pregnancy: Delivery: Caesarean section (100%). Mother complications: Non Nephrotic Proteinuria (1), Urinary Tract Infection (1), Preeclampsia (4), Internal Placenta Detachment (1) and Spontaneous Abortions (2). Foetal complications: IUGR (2), ARDS (1), Klinefelter Syndrome (1) and 4 Preterm Births. In 2 cases the child weight was lower when compared to the gestational age and 5 babies were admitted to neonatal intensive care unit. Mother' s follow up: no acute rejection. Breastfeeding discouraged due to the transmission of the immunosuppressive medications into breast milk. We did not observe any significant disease in child' s follow up.
Conclusions: The majority of pregnancies in renal transplant pts have a good outcome, but with increased incidence of preeclampsia, reduced gestational age, and low birth weights confirming that pregnancy after kidney transplant, though possible, carries an elevated risk and patients therefore to be referred to highly specialized centres where nephrologists, obstetricians, intensivists and neonatologists providing surveillance and treatment.

P-231 MANAGEMENT OF LOCALIZED PROSTATE CANCER BY RETROPUBIC RADICAL PROSTATECTOMY IN KIDNEY RECIPIENTS

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Introduction:
Association between prostate cancer and kidney transplantation still has an unknown incidence despite the increased transplanted patients screening. In young patients with localized adenocarcinoma, radical prostatectomy or external radiotherapy represent the treatments of choice. The technique and outcomes of retropubic radical prostatectomy (RRP) in 12 kidney recipients are reviewed.
Methods: Between 1995 and 2010, we performed RRP in 12 kidney recipients. The mean age was 64±6 years [52-72]. The interval from renal transplant to RRP was 88±73 months [9-241]. PSA level was 8,83±5,45 ng/ml [4,6-24,22] and clinical stage was T1 in 8 patients and T2 in 4 patients.
Patients underwent a standard RRP with minor modifications: graft's ureter was first identified and bladder neck was not preserved. An ureteral stent was placed to facilitate posterior dissection.
Results: Operative time was 162±30 min [120-210], and estimated blood loss 730±380 ml [300-1500]. Hospital stay duration was 4,8±1,4 days [3-8]. Uretral stent was removed at day 7.
Histological findings were 9 pT2 and 3 pT3. Gleason score was ≤6, between 7 and 8 and ≥ 9 in 9, 2 and 1 cases respectivly.
A pT3 patient with positive surgical margins received adjuvant external radiotherapy.
A pT2 patient, Gleason 9, showed a metastatic evolution and was placed under hormonotherapy.
With a follow-up of 55±38 months [5-127], none of all other patients had evidence of biochemical recurrence.
All patients were continent, even if one needed an artificial urinary sphincter.
None of the patients had impairment of their graft function.
Conclusions: Renal graft is not a contraindication to RRP. Our surgical approach was slightly modified by the graft. Operation time and recovery period were comparable to non-transplanted patients, as were the functional and oncological results.

P-232 LEFT VENTRICULAR HYPERTROPHY AFTER KIDNEY TRANSPLANTATION

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Introduction and Aims: Kidney transplantation is a preferred method of renal replacement therapy. However kidney transplant recipients (KTRs) are at higher cardiovascular risk when compared with general population. Left ventricular hypertrophy (LVH) contributes to cardiovascular morbidity and mortality. The aim of this study was to assess LVH prevalence during first post-

transplant year, and possibly determine the correlates of left ventricular mass index (LVMI), including the role of NT-proBNP.
Methods: 39 KTRs (M:K=20:19, median age 44), free of valvular defect, were followed-up prospectively. Echocardiography (in accordance with ASE Committee Recommendations 2005), ambulatory blood pressure monitoring (every 15 and 30 mins during the day and night, respectively), NT-proBNP concentration (by ELISA) and standard blood tests were monitored. LVH has been defined as LVMI>95 g/m^2 in women, and >115 g/m^2 in men. General mixed models were used for statistical analysis.
Results: LVH was present in 19 of 39 (49%) KTRs at the time of transplantation and this proportion remained fairly constant during follow-up. LVMI, adjusted for gender, was associated with duration of dialysis therapy prior to transplantation (each additional month on dialysis resulted in expected mean LVMI increase by 0.15g/m^2, P<0.03). LVMI had also a negative correlation with estimated GFR (increase in GFR by 1 mL/min resulted in expected mean LVMI decrease by 0.3 g/m^2, P<0.03). NT-proBNP declined significantly during follow-up (134.7 vs. 84.4 pg/mL, P< 0.02), but no relation with LVMI has been found. However KTRs with LVH were expected to have higher NT-proBNP, as compared to age- and gender-matched KTRs with normal LVMI (133.6 vs. 85.5 pg/mL, P<0.02).
Conclusions: LVH is constantly present in every other KTRs during first post-transplant year.
Prolonged dialysis therapy prior to transplantation and poor graft function are the most prominent predictors of LVH after transplantation.
NT-proBNP isn't useful as a marker of LVH.

P-233 A YEAR AFTER THE DONOR/RECIPIENT SERVICE SPLIT – ONE RECIPIENT TEAM'S EXPERIENCE

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In October 2009 the transplant co-ordinator team divided into 2 separate teams - for multi-organ donation and kidney recipients. The recipient team remained at their local hospital within the renal department. A year on from this split is a good time to reflect on the impact this has had on the renal recipient team and the service we provide.

Clinics/Activations and Transplants

	November 2008–October 2009	November 2009–October 2010
Surgical Clinic Appointments	336	391
Co-ordinator Clinic Appointments	72	63
Ad hoc Appointments	51	97
Numbers in local work-up for listing	121	163
Number on Transplant Waiting List	411	421
Renal Transplants performed	107	117

Results: There has been an increase in the number of patients seen in the numerous clinics we support along with increased numbers in work-up for transplant wait-listing. There has been a slight increase in the number of patients we have on the kidney transplant waiting list. Over the year there has been almost a 10% increase in the number of kidney transplants performed at our centre.
There has been an increase in workload: clinics included but mostly the on-call. This has impacted on the day-to-day worklaod both when calls come in overnight and during the day.
Targets (for Living Donor Programme) have impacted on and been impacted upon by recipient team workload when there were staffing issues.
The development of the post-transplant specialist nurse has been great help and benefit to the renal recipient team and patients who have designated support after their transplant
Conclusion: There have been many challenges for the team over the last year. With the changes and developments made we are looking to provide a service that supports patients throughout the transplant journey. Changes - including more people for on-call (to maintain 1:5 rota) and addition of extra administration and untrained health professional support will help develop the service further.
We are a small, strong team providing a supportive environment for each other, other staff, patients and their families.

P-234 DONOR SPECIFIC ANTIBODIES (DSA): CAUSES AND CONSEQUENCES

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Introduction: The presence of antibodies pre and post transplant has been associated with chronic rejection and graft loss. But there are few prospective studies analyzing the prevalence of donor specific antibodies (DSA) as well as the factors that may cause its appearance after kidney transplantation.
Materials and Methods: We conducted a prospective study on 151 consecutive kidney transplant. All of them have been analyzed by Luminex technique the presence of DSA (Class I, Clas II and MICA) pretransplant and between 6 and 12 months after transplantation. All patients received immunosuppression with tacrolimus, MMF and prednisone. 32% of patients also received induction with basiliximab or thymoglobulin.
We examined the prevalence of DSA and the influence of the donor, the surgery or the receptor factors have in their appearance. We also studied the evolution of the graft analizyng renal function and proteinuria every three months during a minimum follow-up period of two years.Thirteen patients who lost the graft within six months were excluded.
Results: We have found DSA in 22 patients (15.9%). 16 Class I, 17 Class II and 3 MICA
Relevant data is shown in Table 1.

	DSA (N=22)	No DSA (N=116)	p
Male sex	12	82	0,05
HLA missmatch >3	15	81	ns
DR missmach >2	9	54	ns
Cold ischemia	15,6±4,3	17±4,6	ns
pretransplant antibody titers	7,4±13	1,5±5	0,006
Induccion treatment	8	37	ns
2 tx	4	10	ns

We have found no significant differences between patients with and without DSA in renal function after one year and two years of monitoring.
In patients with DSA quotient proteinuria creatinine at six months were 0,79±0,3 and increases to 1,4±0,8 mg/mg at two years. In patients witout DSA proteinuria were 0,27±0,04 mg/mg at six months and 0,4±0,2 at two years. P<0,05
Conclusions: With current immunosuppression:
Donor specific antibodies appear in 15% of patients
The appeareance of DSA posttransplantation is more common in patients with nonspecific antibodies pretransplant
After two years of following the presence of DSA is not associated with renal function alteration.However, there is elevation of proteinuria

P-235 NEW ONSET DIABETES MELLITUS AFTER TRANSPLANTATION: RISK FACTORS AND CONSEQUENCES

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New-onset diabetes mellitus after transplantation (NODAT) is a heterogeneous condition of abnormal glucose tolerance with a variable onset, duration, severity and consequences.
The purpose of this study is to evaluate the prevalence, risk factors and consequences of NODAT in Latvian renal transplant (RT) population.
Materials and methods: All living RT recipients at Renal transplantation centre of Latvia (n = 454), transplanted between June 1976 and December 2009 were included in the study. Details on the following items were collected on the basis examination of medical records: demographic characteristics, diabetes-related factors, renal function, biochemical analysis, immunosuppresive regimens (IR), infections. Patients were classified in to 3 groups: group 1 comprised patients with NODAT, group II – post-transplant impaired fasting glucose (PT IFG) patients and group III – control group without NODAT. Diabetes was diagnosed in accordance with WHO guidelines, i.e. on the basis of at least two consistent blood glucose measurements.
Results: NODAT developed in 42 of 454 (9%) recipients, but PT IFG was diagnosed only in 7 of 454 (2%) recipients. The greater risk of developing of NODAT associated with a recipient age>40 years (RR=1.29; 95% CI: 0.71-1.78; P=0.003), BMI>25kg/m2 (95% CI: 1.00-1.9; p=0.028), elevated triglicerides level > 1.7 mmol/L (RR=1.31; 95% CI: 1.04-1.92; P=0.04), hepatitis C infection (RR=1.47; 95% CI: 0.92-1.72,; P<0.001), treatment with rapamycin (RR=1.26; 95% CI: 0.72-2.20; P<0.001) and prednisolon (RR=1.11; 95% CI: 1.02-2.07; P<0.001). We did not observed negative impact of NODAT on graft survival.
Conclusion: The reasons for relatvely low prevalence of NODAT are associated with the abscence of tacrolimus based IR and that all of studied population were Caucasians.

P-236 DOUBLE KIDNEY TRANSPLANTATION IN A SINGLE-CENTER

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Background: Use of organs from marginal donors is a current strategy to expand the donor pool. Its efficacy is universally accepted among data from multicenter studies. The aim of this study was to evaluate possible significant differences between a monocenter versus multicenter studies.
Patients and Methods: Between 1999 and 2008, we performed 59 double kidney transplantation (DKT). Recipient mean age was 63±5 years. Mean HLA-A, -B, and -DR mismatches were 3.69±0.922. Donor mean age was 69±7 years and mean creatinine clearance was 69.8±30.8 mL/min. Proteinuria was detected in three donors (5%). Mean cold ischemia and warm ischemia times were 1130±216 and 48±11 respectively. The right and left kidney scores were 4.18±2 and 4.21±2, respectively.
Results: Thirty patients (51%) displayed good postoperative renal function; 22 (37%), acute tubular necrosis with postoperative dialysis; 3 (5%), acute rejection episodes; 4 (7%), single-graft transplantectomy due to vascular thrombosis; 1 (2%), a retransplantation; 5 (8%), a lymphocele; 3 (5%) vescicoureteral reflux or stenosis requiring surgical correction. Cytomegalovirus infection was detected in five patients (8%). Three patients (5%) displayed de novo neoplasia. Three patients showed chronic rejection (5%), while a cyclosporine-related toxicity occurred in 7 recipients (12%). Nine patients (15%) developed iatrogenic diabetes. Patient and graft survivals after 3 years from DKT were 93% and 86.3%, respectively. We applied successfully a widespread score to allocate organs to single kidney transplantation or DKT.
Conclusions: In our experience the score is suitable for the organ allocation but it may be overprotective, excluding potentially suitable organs for a single transplantation.

P-237 ASSESSING OUTCOME OF ARTERIOVENOUS FISTULAE (AVF) IN RENAL HAEMODIALYSIS PATIENTS WITH AN INDWELLING TUNNELLED DIALYSIS CATHETER (TDC)

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Aims: The Kidney Disease Outcome and Quality Initiative (K/DOQI) guidelines define standards for dialysis access and clearly state autogenous vein arteriovenous fistulae (AVF) are vascular access of choice associated with superior long-term patency and low complication rates compared to TDC. In regards to the probability of patency rates, there are currently no guidelines stating preference between ipsi-lateral or contra-lateral AVF formation in relation to an indwelling TDC.
Methods: A retrospective case note review of 40 consecutive patients, were analysed after a 6 month follow up period. Group 1 included AVF with ipsi-lateral TDC (n=22) and Group 2 included AVF with contra-lateral TDC (n=18). The primary and 6 month patency rates as well as complication profile were assessed.
Results: Demography of both groups showed no difference for mean age (65±14 and 65±15 years) and patients having hypertension or diabetes. All AVFs were brachio-cephalic with a sex ratio (M:F; 12:10 vs. 12:6). The primary patency rate in weeks was less for Group 2 vs. Group 1 (12±8.6 vs. 15±6.3, P=0.0703), three AVF failed to develop in each group. While 13 AVF were patent for Group 2 vs. 12 for Group 1 at 6 months. Group 1 numerically showed a higher rate of other complications (wound infection 3:0, Stenosis 3:2, Steal 2:0 and Bleeding 2:0).
Conclusions: Every attempt should be made to create an AVF on the contra-lateral side of a TDC, ensuring the TDC is removed as soon as AVF is viable, thus achieving K/DOQI practice guidelines.

P-238 IS INTRAVENOUS IMMUNOGLOBULIN AN EFFECTIVE TREATMENT FOR ACUTE ANTIBODY-MEDIATED REJECTION?

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Background: IVIg is one of a number of treatments used for acute antibody-mediated rejection (AMR), yet is costly and difficult to source. Its efficacy may be due to an anti-idiotypic effect, or down-regulation of antibody production. We developed a protocol including IVIg and plasma exchange for the treatment of acute AMR, and report our results.
Methods: A total of 14 patients were treated with IVIg for suspected acute AMR over a 1 year period from May 2009 to May 2010. Acute AMR was diagnosed by evidence of acute tissue injury on biopsy consistent with acute AMR, or the presence of circulating donor specific antibody (DSA) in association with renal dysfunction. IVIg was given at a total dose of 2g/kg over 2-5 days. Plasma exchange (PEX) was also given for 5 days, unless considered inappropriate by the treating clinician. Successful outcome was defined as a functioning graft with stable serum creatinine at 6 months post treatment.
Results: A total of 24 courses of IVIg were given for the treatment of acute AMR in 14 patients. In 8 out of 14 (57%) patients treatment was successful, 3 of whom required 2 courses of treatment. One patient had a graft nephrectomy secondary to surgical complications. 2 of the 5 patients in whom treatment was unsuccessful were HLA incompatible transplants with early rejection and received 3 and 4 courses of treatment respectively. 2 other patients in whom treatment was unsuccessful had treatment initiated on the basis of a rise in DSA without clear evidence of acute AMR on biopsy.
Conclusions: IVIg is an effective treatment for biopsy confirmed acute AMR supported by the presence of DSA and/or C4d+. Repeated courses (>2) may not be effective in HLA incompatible transplants and consideration should be given to alternative strategies in these patients.

P-239 IMPACT OF DONOR KIDNEY SIZE ON ALLOGRAFT FUNCTIONS IN LIVING DONOR RENAL TRANSPLANTS: DOES SIZE MATTER?

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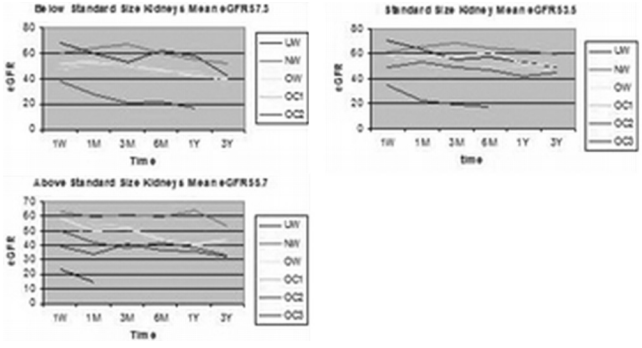
Background: Nephron mass has been identified as one of the non-immunological factors that may have some impact on long-term graft survival and function. In addition, the impact of recipient weight on patient and graft survival has been the subject of some controversy, particularly with the evolving obesity epidemic within the United Kingdom. We aimed to analyse the impact of the size of donor kidney, an indirect marker of nephron mass on short and long term renal allograft function following live donor transplantation (LDT).
Methods: A retrospective analysis was performed of all the first LDT in a single unit over a 5 year (Jan 2005 to Dec 2009: 241 patients). Kidney size was defined as standard if between 10 and 13cm and 5 to 7.5cm wide as per pre-determined standards, whilst smaller or larger kidneys were classified into separate groups. Recipients BMI (kg/m2) was calculated and classified according to the World Health Organization: under weight (16.5-18.4), normal (18.5-24.9), over weight (25-29.9), obese class I (30-34.9), class II (35-39.9) and class III (>40). Graft survival was used as a primary endpoint.
Results: 222 patients were eligible for inclusion. This data indicates that the short and long term graft survival is poorer in recipients with extremes in body habits (both low and high BMI) irrespective of the size of the donor kidney. There is also a trend towards improved graft survival in patients who receive larger kidneys.



Conclusion: This study suggests a role for careful consideration and discussion in patients with higher BMI's who may be receiving kidneys from small donors, and therefore with associated smaller allografts, or in those in which there is a large BMI disparity between donor and recipient.

P-240 ERECTILE DYSFUNCTION AMONG PATIENTS WITH END STAGE RENAL DISEASE: A COMPARISON STUDY BETWEEN HAEMODIALYSIS, CONTINUOUS AMBULATORY PERITONEAL DIALYSIS AND RENAL TRANSPLANT PATIENTS

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Introduction: The prevalence of erectile dysfunction (ED) among patients with end-stage renal disease (ESRD) in Malaysia is not known and is not included as a quality of life indicator in Malaysia National Renal Registry.
Objective: To determine the prevalence of ED in a single center ESRD population receiving different modalities of renal replacement therapy.

Methods: A cross sectional study was conducted between January till June 2009 amongst patients receiving haemodialysis (HD), continuous ambulatory peritoneal dialysis (CAPD) and renal transplantation (RTx) in Serdang Hospital. Patients whom were recently transplanted, initiated on HD or CAPD (<2 months) and acutely ill were excluded. Presence and severity of ED were assessed using self-administered International Index of Erectile Function-5 (IIEF-5) questionnaire.
Results: There were 50 HD, 31 CAPD and 18 renal transplant patients included in this study. The mean age was 54.4±12.3 years with 57.6% having diabetes (DM) and 24.2% having ischaemic heart disease (IHD). The prevalence of ED in our study was 83.8% with its severity further illustrated in Table 1.

Table 1. Severity of erectile dysfunction among different cohort of ESRD patients

Severity of ED, n (%)	IIEF-5 score	HD	CAPD	RTx	All
No ED	22–25	5 (10.0)	6 (19.4)	5 (27.8)	16 (16.2)
Mild ED	17–21	9 (18.0)	3 (9.7)	3 (16.6)	15 (15.2)
Mild to Moderate	12–16	9 (18.0)	2 (6.5)	5 (27.8)	16 (16.2)
Moderate ED	8–11	5 (10.0)	5 (16.1)	0 (0)	10 (10.1)
Severe ED	1–7	22 (44.0)	15 (48.4)	5 (27.8)	42 (42.4)

Increasing age ($p<0.0001$), having DM ($p<0.0001$), IHD ($p=0.029$) and haemoglobin (Hb) level ($p=0.027$) were significantly associated with lower IIEF-5 score. Duration on dialysis or post-transplantation, calcium-phosphate products and use of beta-blocker showed no significant association. Comparatively renal transplant patients had significantly higher mean IIEF-5 score at 15.11 vs. CAPD at 9.97 ($p=0.046$) and vs. HD at 10.22 ($p=0.027$). There were no significant difference in mean IIEF-5 score between CAPD and HD. In age-controlled analysis, Hb <13g/dL was associated with poorer IIEF-5 score.
Conclusions: ED is extremely prevalent among ESRD patient and those had undergone RTx appear to have better sexual health. Increasing age, diabetes, ischaemic heart disease and anaemia were associated with higher prevalence of ED.

P-241 EARLY BEDSIDE REMOVAL VERSUS LATE CYSTOSCOPIC REMOVAL OF URETERIC STENTS FOLLOWING RENAL TRANSPLANTATION; DOES IT MAKE A DIFFERENCE?

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Introduction: Major urological complications (MUC; ureteric leak/stenosis) continue to be the "Achilles heel" of renal transplantation. Routine stenting of the allograft ureter has been shown to significantly reduce MUC. However, stenting also increases the incidence of urinary tract infections (UTI) and requires invasive cystoscopy for removal.
Methods: A prospective randomized study was carried out, comparing late cystoscopic stent removal with early bedside removal. A standard 5 French 12 cm ureteric stent was used in all cases. Group-1 underwent conventional stenting with subsequent cystoscopic stent removal at 4-6 weeks post-transplant as a day case procedure. Group-2 (new method) had the ureteric stent tied to the tip of the urinary catheter intra-operatively. The urinary catheter along with the attached stent was removed at the bedside on day-07, prior to discharge. Both groups were observed prospectively for MUC and UTI.
Results: There were 41 (Group-1, 19; Group-2, 22) transplants between January to September 2010. The mean follow up was 16 (range 4-40) weeks. No MUC were encountered during this period. There were 5 (12%) culture proven UTI with ultrasonic evidence of graft pyelonephritis; 4 in Group-1 and 1 in Group-2 ($p=0.2$). There were no other stent related complications.
Conclusion: Tying of the ureteric stent to the urinary catheter intra-operatively and early bed-side removal appears to be as safe and as effective as the conventional method of ureteric stenting. Its greater convenience and economy due to the avoidance of a readmission for cystoscopy is an added advantage. Further, though not statistically significant, there was a potential decrease in post-transplant UTI. Continuation of this study to obtain greater numbers and longer follow up may result in establishing the newer technique as the preferred one.

P-242 SERUM PARAOXANASE 1 ACTIVITY PREDICTS ARTERIAL STIFFNESS IN RENAL TRANSPLANT PATIENTS

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Introduction: Paraoxanase 1 (PON 1) has been shown to protect from atherosclerosis by modification of lipoproteins. It's activity decrease in dialysis patients but are restored after transplantation. Whether it affects arterial stiffness is unclear. In this study we aimed firstly to investigate the effects of PON 1 on arterial stiffness in renal transplant patients.
Patients and Methods: Seventy renal transplant recipients were enrolled. Arterial stiffness was measured by using Syphmocor device. PON-1 activity was assessed by the rate of enzymatic hydrolysis of paraoxon to p-nitrophenol.
Results: Mean age was 39.0±9.6 years and 5.7% of the patients were diabetic. Post-transplant follow-up was 46.7±37.9 months. Eighyty-five percent received anti-hypertensive and 12.9% antihyperlipidemic medication. Mean PON1 activity was 75.9±52.4 U/L. PON1 activity was negatively correlated with systolic and diastolic blood pressure, mean arterial pressure, LDL-cholesterol and carotid-femoral pulse wave velocity (c-f PWV). Mean c-f PWV was 8.10±1.39 m/s. Cf-PWV was positively correlated with age, systolic and diastolic blood pressure, mean arterial pressure, proteinuria and negatively correlated with PON1, PON1/HDL ratio and creatinine clearance. In lineer regression analysis, PON1 was a predictor for cf-PWV in a model that included age, gender, diabetes, mean arterial pressure, urine protein level, creatinine clearance and PON 1.
Conclusion: Reduced PON1 activity is significantly associated with increased arterial stiffness. The results of this study show a possible role of PON1 for arterial stiffening in renal transplant patients.

P-243 STUDY OF FACTORS AFFECTING GRAFT AND PATIENT SURVIVAL WITHIN FIVE YEARS OF RENAL TRANSPLANTATION

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Objectives: Analysis of factors affecting graft and patient survival in living donor kidney transplantation.
Methods: Study included 554 patient who had undergone renal transplantation between 2002 and 2006 in our institute. Multivariate analysis was carried out using Cox logistic regression.
Results and Coclusions: Male: Female ratio was 6:1. The average age in recipients was 33.6±10.3 and 42.36±11.27 years in donors. First degree relative donors were 420 (76.4%) and second order relative and spouse comprised 23.6% cases. Overall graft survival (death censored) at 1, 3 and 5 years were 94%, 90% and 79%. Mean time of graft loss was 33±11.05 months (range 17 – 56 months). Commonest cause of graft loss was chronic allograft nephropathy (CAN) (47.8%) followed by non-compliance (19.5%). Significant factors predicting graft loss included episodes of acute rejection ($P < 0.001$), BKV infection ($p < 0.0001$), presence of CAN ($p= 0.06$) and cyclosporine based therapy in comparison to tacrolimus ($p = 0.07$). Overall patient survival at 1, 3, and 5 year was 92%, 87% and 83% respectively. Mean time to death was 18±19.05 months (range 0-76 months). Commonest cause of death was septicemia (66.7%). Death was more common in the elderly recipient (> 50 year) ($p = 0.02$), unrelated donor transplant ($p =0.01$), presence of pre-($p = 0.02$), or post-transplant diabetes mellitus ($p= 0.07$), occurrence of opportunistic infection ($p = 0.03$), CMV infection ($p < 0.0001$), disseminated fungal infection ($p = 0.002$), post transplant hepatitis C infection ($p = 0.05$), post transplant tuberculosis ($p = 0.03$) and presence of multiple co-morbid illness ($p = 0.004$).

P-244 EARLY PROGRESSION OF AMYLOIDOSIS IN A RENAL TRANSPLANT RECIPIENT WITH FAMILIAL MEDITERRANEAN FEVER

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Background: Recurrence of amyloidosis in renal transplant recipients with familial Mediterranean fever (FMF) within the first year posttransplantation is unusual. Adequate dose of colchicine is effective in delaying amyloidosis progression in these patients.
Case Report: A 34 years old male who is known to have FMF for more than 15 years. He developed renal failure due to secondary amyloidosis. He was on hemodialysis for 6 months till he received live unrelated renal transplant which is functioning normally. There were no acute attacks of FMF for 3 years before transplantation. He was on 0.5 mg colchicine once daily which was continued after transplantation. His immunosuppressive regime was antithymocyte globulin as induction and prednisolone, mycophenolate mofetil and CsA as maintenance therapy. After 2 months he presented with severe myopathy and muscle biopsy showed evidence of toxic myopathy most likely due to cyclosporine when it was initiated in addition to colchicine. CsA was changed to sirolimus and colchicine was stopped. He was gradually improving apart from residual chronic myalgia requiring oral analgesics. Prednisolone dose was reduced gradually to 5 mg daily. Eight months posttransplantation he was readmitted with acute attack of FMF. He was restarted on colchicine 0.5mg twice daily which was tolerated. He improved temporarily but few weeks later he had recurrent acute attack of FMF with severe diarrhea. Colonoscopy was done and biopsy showed multiple colonic amyloid deposits. His clinical condition

stabilized when colchicine dose was increased to 1mg twice daily and serum creatinine continued to be normal.
Conclusion: Amyloidosis secondary to FMF is a slowly progressive disease in RTR. This may be accelerated if colchicine treatment is interrupted during the first year post-transplant.

P-245 EFICACY AND SIDE EFFECTS OF H1N1 VACCINATION IN RENAL TRANSPLANT AND DIALYSIS PATIENTS

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In 2009 influenza A H1N1, responsible for the first influenza pandemic since 41 years, was discovered. Similar to seasonal flu, immunocompromised patients seem to be at higher risk of infection. Therefore we vaccinated 31 renal transplant patients of our outpatient clinic (mean age 58.6 y +13.5, 35.5% females, on the average 11.6y +7.5 y after transplantation) with the pandemic vaccine Pandemrix in November 2009. Efficacy of vaccination under immunosuppressive therapy (antibody response rate, measured by hemagglutination inhibition assay (HI)), adverse events on transplant function and acute rejection (AR) rate were determined.
We compared the antibody response rate of renal transplant recipients with the efficacy of vaccination in 47 dialysis patients (mean age 58.9 +16.8, 27.5% females). Immunoprotection was stated with an H1N1 titre>40, achieved in 98-100% of 16 healthy controls. Serum samples were taken 4 weeks after vaccination and after 6-9 months, serum creatinine was determined 1 week, 4 weeks and 6 months after vaccination. AR episodes were monitored. Immunosuppression consisted of dual or triple therapy including CsA/tacrolimus, MMF/azathioprin and steroids.
Only 50% of transplant patients responded sufficiently to vaccination, in contrast to 81% of dialysis patients, behaving similarly to the general population. This difference in response was highly significant ($p < 0.0005$). Serum creatinine and GFR were stable in transplant patients during follow up (s-creatinine 1.7mg/dl, GFR 50 ml/min). AR episodes did not occur. Within the transplant population responders and non responders were not significantly different with respect to age, gender, time after transplantation, immunosuppressive medication or CD4 cell counts.
In renal transplant patients booster vaccination seems to be necessary to improve protection against H1N1 infection. This should be recommended, especially as AR or impairment of renal function were not observed under single shot Pandemrix vaccination.

P-246 COMPLICATIONS OF KIDNEY TRANSPLANTATION FROM DONORS AFTER CARDIAC DEATH (DCD)

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Background: The growing demand for renal transplants has resulted in the increased utilisation of DCD kidneys. Here, we report a single unit experience of DCD transplantation, the rate of infectious, medical and surgical complications and their association with DGF.
Methods: Observational analysis of all DCD transplants performed in our unit during a 5-year period. All patients received ATG induction and tacrolimus maintenance immunosuppression with mycophenolate mofetil and prednisolone. Subcutaneous sodium heparin and valgancyclovir prophylaxis was used routinely. Infectious, surgical and medical complications occurring within 6 months after transplantation were analysed.
Results: 80/514 (15.5%) patients received DCD kidneys. Median follow-up time was 29.8 [2-73.8] months. The median donor and recipient ages were 47 [17-68] and 51.5 [19-72] years. 55 (73%) patients experienced DGF. *Infectious complications* were: urinary tract infections: 47 (58.8%); pneumonia: 11 (13.8%); clostridium difficile associated diarrhoea: 4 (5%); wound infection: 26 (32%); bacteraemia: 5 (6.3%); CMV infection-PCR positive: 8 (10%). *Medical complications* were: acute cardiovascular: 12 (15%), cerebrovascular: 1 (1.3%) and venous thrombo-embolic events: 0. *Surgical complications* were: fluid collections 20 (25%), ureteric leak: 3 (3.8%), hydronephrosis: 5 (6.3%), renal artery stenosis: 4 (7.2%), renal vein thrombosis 1 (1.3%). There was no association between the occurrence of DGF and the incidence of any of the above complications. Seven (9%) recipients experienced acute rejection episode. All the 8 re-transplanted patients experienced UTI (p=0.03). Longer cold ischemic time was associated with increased incidence of renal artery stenosis (p=0.003).
Conclusions: In this preliminary analysis a significant number (>50%) of DCD recipients experienced an infectious complication during the first 6 months post transplant with a low rate of biopsy proven acute rejection. The widespread use of ATG induction in this recipient group may have contributed to these observations.

P-247 UROTENSIN II LEVELS IN PATIENTS WITH CHRONIC KIDNEY DISEASE AND KIDNEY TRANSPLANTS

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Backgrounds: Urotensin II is a potent vasoactive peptide that has been implicated in the pathophysiology of many diseases. There is no study reporting the role and level of this peptide in recipients of kidney transplant. So we aimed to study the plasma levels of urotensin II in this group of patients.
Methods: The plasma urotensin II levels were analyzed in 110 subjects, who were divided into three groups; group 1 (35 kidney transplant recipients), group 2 (36 patients with chronic kidney disease), and group 3 (39 healthy controls) (Table 1).

Table 1. Characteristics of the participants

	Group 1	Group 2	Group 3	P-value
N	35/110	36/110	39/110	NS
Age (years)	37.4±13.8	36.8±6.8	38.3±5.6	NS
Sex (F/M) (n)	12/23	14/22	18/21	NS
Creatinin (mg/dL)	1.10±0.20	5.98±1.52	0.75±0.23	0.001[1], NS[2], 0.000[3]

NS, not significant. [1]Comparing Group 1 with Group 2. [2]Comparing Group 1 with Group 3. [3]Comparing Group 2 with Group 3.

Results: Analysis of logarithmic transformation of urotensin II, i.e., log (urotensin II ×1000) levels, with a one-way analysis of variance yielded a P value of 0.001. Post-hoc analysis showed significantly higher log (urotensin II ×1000) levels in group 1 than groups 2 and 3 (P = 0.001 and 0.017, respectively) (Table 2). One of the important feature of this group subjects was that they were on immunosuppressive drug treatment, i.e., calcineurin inhibitor (28 patients on cyclosporine and 7 patients on tacrolimus), azathioprine (7 patients) or mycophenolate (28 patients), and prednisolone (30 patients) because of renal transplantation.

Table 2. Comparision of Log(UII×1000)levels between male and females

Groups	Log(UII×1000) levels (Total)†	Gender	No. of cases	Log(UII×1000) levels Mean ± SE
1	3.0035±0.60478	Male, Female	23,12	3.0686±0.67444, 2.8787±0.44153
2	2.6403±0.29595	Male, Female	22,14	2.7468±0.22989, 2.4730±0.31798
3	2.7400±0.24080	Male, Female	21,18	2.7607±0.27365, 2.7158±0.20089

UII, plasma urotensin II level (ng/mL); SE, Standard error of the mean. †One-way analysis of variance (ANOVA) test's p value was 0.001.

Conclusions: High urotensin II levels in recipients of kidney transplant could be drugs-related (immunosuppressive drugs), and may be of practical importance that may be used to improve the long term outcomes of the patients.

P-248 EFFECTS OF CONVERSION FROM TACROLIMUS TO TACROLIMUS EXTENDED-RELEASE ON TREATMENT ADHERENCE IN KIDNEY TRANSPLANT PATIENTS

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Background: Adherence to immunosuppressive therapy is a critical issue for graft survival in kidney transplant patients. Tacrolimus extended-release (TAC-ER) is a once-daily formulation to reduce the frequency of administration for patients using a twice-a-day tacrolimus (TAC) regimen. We hereby report the results of a questionnaire survey before and after the conversion on treatment adherence with calcineurin inhibitors (CNIs).
Patients and Methods: A total of 322 outpatients in the maintenance phase visiting our hospitals answered a questionnaire on treatment adherence. Treatment of CNIs was converted from TAC to TAC-ER in 58 patients. Changes in treatment adherence before and after the conversion were also analyzed using questionnaire survey to examine whether improved adherence can be obtained.
Results: The survey demonstrated nonadherence in 6.6% patients. The adherence rate was lower for the evening dose than the morning dose and de-

creased with time following transplantation. After the conversion from TAC to TAC-ER, 59.5% patients answered that the frequency of nonadherence decreased, and 94.8% patients answered that they would prefer a reduction in the dosing frequency.
Conclusion: In the questionnaire survey, conversion to once-daily TAC-ER improved treatment adherence in short term. Long term survey and prospective investigation of the relationship between nonadherence and clinical outcomes are necessary.

P-249 THE PROGNOSTIC IMPACT OF DONOR-SPECIFIC ANTIBODY (DSA) LEVELS TO PREDICT SEVER ACUTE ANTIBODY MEDIATED REJECTION IN LIVING KIDNEY TRANSPLANTATION

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Objective and Method: Kidney transplant candidates with donor-specific antibody (DSA) have increased risk of acute antibody-mediated rejection (AAMR).We performed 164 patients who received a living donor kidney graft between 2009 and 2010. In all patients pre T-cell complement dependent cytotoxicity crossmatch (CXM) tests were negative, screening pre-transplant panel-reactive antibody (PRA) tests were positive in 23 cases, and DSA tests were positive in15 cases. We studied to correlate the risk of AAMR, and graft survival with the baseline DSA levels (sensitive Luminex single-antigen flow beads tests).
Result: We defined DSA positive as that mean fluorescence intensity (MFI) of greater than or equal to 800 was used as a cutoff for Luminex positivity. 11 patients with DSA positive had no rejections and succeeded in living kidney transplantation. But 4patients with DSA positive had sever acute antibody mediated rejections. 4 graft functions were excellent immediately after the operation, but the urine output declined rapidly on post-operative day (POD) 1, we could not detect the diastolic arterial flow on Doppler sonography. We treated them with plasma exchange (PEX), intravenous MP pulse therapy, and rituximab. Their urinary excretions increased beginning on POD 7-21, while s-Cr levels decreased gradually and reached 0.9-1.1 mg/dL on POD 14-32. Treatment for rejection was transiently successful. Now all graft functions were excellent 1year after transplantation. In all 4 cases, the incidence of pre-strong DSA (MFI $\geq$3000) detected by Luminex single-antigen flow beads tests. All cases were husband-to-wife spousal kidney transplantation with histories of pregnancy.
Conclusion: The baseline DSA level correlates with risk of early alloantibody-mediated allograft injury. With current protocols, very high baseline DSA patients had high rates of AMR, but had good short-term allograft survival by highlighting the need for improved therapy for these cases.

P-250 THE IMPACT OF HUSBAND-TO-WIFE SPOUSAL RENAL TRANSPLANTATION ON ACUTE REJECTION IN TERMS OF DONOR-SPECIFIC ANTIGEN

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(Background): Spousal renal transplantation (SRT) is increasing in Japan. The risk of SRT on acute rejection is not fully understood.
(Methods): We performed 164 live renal transplantations between 2009 and 2010. ABO incompatible cases and DSA positive recipients were inducted with rituximab. Risk factors of acute rejection (AR), graft survival rates and creatinine (Cr) values were analyzed.
(Results): Of 164 donors, 76 (46.3%) were spouses, 63 (38.4%) parents and 18 (11.0%) siblings. Pre-operative PRA were positive in 22 cases (13.4%) and DSA in 15 (9.1%). Of 76 SRT, 32 were husband-to-wife (HtoW) with 7 (21.9%) DSA positive cases, while 44 were wife-to-husband (WtoH) with 2 (4.5%) positive DSA (p=0.021). Multivariate Cox regression revealed that positive PRA (RR: 18.2, p = 0.00006) and HtoW SRT (RR: 34.9, p = 0.047) were significant risk factors of AR. Donor age, ABO incompatibility, SRT and regraft were not significant. 1-year graft survival rates of SRT and non-SRT were 94.8% and 100%, respectively (p=0.16). Those of HtoW and WtoH were 100% and 90.8%, respectively (p=0.21). Average Cr of HtoW at 1 year was 0.73 mg/dl while that of WtoH 1.21 mg/dl and that of non-SRT 1.59 mg/dl ($p < 0.00001$).
(Conclusion): HtoW SRT was a significant risk factor of developing AR, though SRT itself was not, with significantly more DSA than in WtoH. However both graft function and survival rate of HtoW were comparable or even better than WtoH and non-SRT. We conclude that HtoW SRT carries a higher risk of AR with a higher rate of DSA that could be managed by current protocol therapy for rejection with good prognosis.

P-251 BENEFITIAL EFFECT OF UBIQUINOL, THE REDUCED FORM OF COENZYME Q10, ON CYCLOSPORINE-INDUCED NEPHROTOXICITY

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Introduction: Our previous animal study suggested that cyclosporine (CyA) nephrotoxicity was partly due to some oxidative stress. As one of dietary supplements, ubiquinol, the reduced form of coenzyme Q10 (r-CoQ10), has recently gained attention for its anti-oxidative potential. The aim of this study is to evaluate renal preservation effect of r-C0Q10 on CyA nephrotoxic rats.
Methods: Ten-week-old male Wistar rats were divided into three groups (ten animals each). Group 1 received a medium only. Group 2 received 30 mg/kg/day (i.e. experimentally nephrotoxic dose) of CyA only. Group 3 received both 30 mg/kg/day of CyA and 600 mg/kg/day of r-CoQ10. Both CyA and r-CoQ10 were given orally for four weeks. Daily urinary albumin secretion (u-Alb), serum creatinine (s-Cr) level, and urine 8-Hydroxydeoxyguanosine (u-8-OHdG) level were measured and compared among those three groups.
Results: U-Albs of groups 1, 2, and 3 were 2.8$\pm$0.5, 41.3$\pm$7.2, and 20.6$\pm$3.8 mg/day respectively. S-Cr levels of groups 1, 2, and 3 were 1.0$\pm$0.2, 1.8$\pm$0.4, and 1.5$\pm$0.4 mg/dl respectively. U-8-OHdGs of groups 1, 2, and 3 were 6.8$\pm$2.6, 9.2$\pm$3.1, and 7.2$\pm$2.8 mg/ml Cr respectively. U-Alb, s-Cr, and u-8-OHdG were all ameliorated by r-CoQ10.
Conclusion: R-CoQ10 may have potential for preventing CyA-induced nephrotoxicity. R-CoQ10, one of anti-oxidants, might contribute to the elongation of renal graft survival.

P-252 SLOW EARLY GRAFT FUNCTION: A NEGLECTED ENTITY AFTER RENAL TRANSPLANTATION

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After renal transplantation, early graft function (EGF) can be divided into delayed graft function (DGF), slow graft function (SGF) and immediate graft function (IGF). DGF is well documented. However SGF, a relative new entity, is poorly understood and not well documented. The aim of this study was to document and assess risk factors for developing SGF, and assess the impact on long-term renal function.
The records of all patients undergoing renal transplantation at our institution between 2004 and 2008 were included in the study. The following definitions were used: IGF = sCr <150umol/l on D5; SGF = 150<sCr<450umol/l on D5; DGF = sCr>450umol/l on D5 or dialysis in 1st week. Good early graft function (GEGF)=IGF and poor early graft function (PEGF) = SGF + DGF.
121 patients (77 males,44 females; mean age 39 years, range 14-67) were included in the study. There were no differences in donor factors between GEGF and PEGF, except for CIT which was significantly different (12 vs 16 hours; p=0,013).The 1 year sCr in the IGF was significantly lower than the DGF group (126 vs 169umol/l; p=0,022) and the SGF group (126 vs 160umol/l; p=0,04). The 1 year sCr in the DGF and SGF groups were similar.The 1 year sCr in the GEGF was lower than the PEGF group (126 vs 166umol/l; p=0,01). PEGF was associated with longer hospital stay (20 vs 14 days;p=0,0005).
SGF does not behave like IGF but rather like DGF, and should be included as part of PEGF. The latter has significantly worse long-term function.

P-253 HEPATITIS B REACTIVATION FOLLOWING KIDNEY TRANSPLANTATION: INCIDENCE AND RISK FACTORS

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Background: Limited data is available on the risk of hepatitis B virus (HBV) reactivation in patients with resolved HBV infection undergoing renal transplantation.
Methods: We retrospectively reviewed the charts of all adult patients who underwent kidney transplantation between January 1995 and December 2007. Diagnostic criteria for resolved HBV infection were: HbsAg negative, anti-HBc Ab positive, anti-HBs Ab positive or negative, and normal liver enzymes. HBV reactivation was defined as HbsAg reversion with serum HBV DNA >2,000 IU/mL.
Results: Ninety three patients were included. Mean age was 53 ($\pm$12) years, and 61% were male. Mean duration of follow-up was 6.5 ($\pm$3.5) years. Four patients experienced HBV reactivation 3 within the first year following transplantation. Graft survival was not affected by reactivation. Immunosuppression therapy was similar in patients with and without reactivation. The incidence of acute rejection was significantly higher in patients with HBV reactivation (p = 0.005). Two patients with HBV reactivation (50%) were born in North Africa and 2 were Caucasian, compared to 72% Caucasians and 10% North Africans in the group without reactivation ($p<0.05$). HBV genotype D was identified in

two patients with reactivation and genotype A in one. Among the 4 patients with HBV reactivation, only one (25%) was anti-HBs Ab positive before transplantation, compared to 82% of patients without reactivation (p = 0.03). In this patient, anti-HBs Ab titre decreased progressively and HBsAg reversion occurred when anti-HBs Ab disappeared.
Conclusion: HBV reactivation occurs after renal transplantation with an incidence of 0.7 per 100 patient-year. This intervenes mainly in the first post transplantation year. Ethnic background, acute rejection episodes, and absence of anti-HBs Ab before transplantation appear as risk factors for reactivation. Patients with resolved hepatitis B but without protective anti-HBs Ab should receive vaccination.

P-254 DONOR KIDNEY WEIGHT TO RECIPIENT BODY-WEIGHT RATIO IS AN IMPORTANT RISK FACTOR FOR LONG-TERM OUTCOME OF LIVING DONOR KIDNEY TRANSPLANTATION

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Background: The functional nephron mass of allograft may affect the long-term outcomes of kidney transplant (KT). This study evaluated the effect of the donor kidney weight to recipient body-weight ratio (Kw/Rw) on the graft function and long–term graft survival.
Methods: We investigated whether there is any association between Kw/Rw and long–term graft survival after a follow-up of more than 10 years. Patients were transplanted between 1996 and 2000, allowing relatively long-term follow-up. Only adult-to-adult living KT whose graft survived at least 1 year were included in order to diminish the influence of technical and immunologic failure. A 123 consecutive KT immunosuppressed with cyclosporin and underwent a first KT was studied. According to the Kw/Rw, patients were divided into three groups: "low" (Kw/Rw $<$ 2.85), "middle" (2.85 $\leq$ Kw/Rw $<$ 4.04), and "high" ($\geq$4.04). The following variables were compared: demographic factor, graft survival, mean creatinine levels.
Results: Among three groups, the mean serum creatinine level at 1month, 6month and 1year after transplantation was significantly lower in patients with a high Kw/Rw ratio than in those with a middle or low ratio, but serum creatinine level at 3, 5 years did not differ significantly. This result was due to removal from the data set of patients with a high creatinine level whose grafts failed between 3 and 5 years. Graft survival rates at 5 and 10 years post-transplant were 88.8%, 79.5% in "low" group, 93.4%, 87.4% in "middle" group, 100%, 91.8% in "high" group. A statistically significant association between Kw/Rw ratio and graft survival was found.
Conclusion: The Kw/Rw ratio was an important factor of long-term graft survival and early graft function. However, It does not significantly impact later renal function

P-255 KIDNEYS FROM DECEASED DONORS WITH OLIGURIA ARE FEASIBLE FOR KIDNEY TRANSPLANTATION

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Background: Kidneys from deceased donor with oliguria have not been widely used. We compared the outcomes of recipients with kidneys, received from donors with oliguria at the time of organ procurement and without oliguria.
Methods: Deceased donors and recipients of the kidneys between January 1999 and December 2009 were reviewed. The studied group was defined as having received standard criteria donor (SCD) kidneys or extended criteria donor (ECD) with oliguria at organ procurement, but the control group was defined as having received SCD kidneys without oliguria
Results: The studied group included 32 recipients whose terminal serum creatinine level ($P<0.001$), estimated glomerular filtration rates ($P<0.001$), and deceased donor scores ($P<0.001$) were higher than those of the control group. Delayed graft function (P=0.027) and primary non-function (P=0.019) occurred more often in recipients with kidneys from donors with oliguria than in recipients with kidneys from donors without oliguria, so the period of hospitalization in the studied group was longer (P=0.014). However, the serum levels of creatinine in both groups were comparable, except for three months in the first year posttransplant. There was no statistically significant difference in graft survival.
Conclusion: Deceased donor with oliguria or increased terminal serum creatinine level at organ procurement appear to be poor predictors of outcomes in the early posttransplant period, but kidneys from deceased donor with oliguria should not be precluded for transplantation. The present study suggests that it is acceptable to use kidneys from selected deceased donors with oliguria or high terminal serum creatinine level.

P-256 HORMONAL DIFFERENCE IN BETWEEN FEMALE KIDNEY TRANSPLANT RECIPIENTS AND HEALTHY WOMEN WITH ENDOCRINOLOGIC PROBLEMS IN GYNECOLOGY

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Backgrouds: There is little information in the literature about endocrinologic problems after female kidney transplantation. The purpose of the this study was to describe the endocrinologic symptoms of gynecology and identify the hormonal difference in between female kidney transplants and healthy women with same endocrinologic problems in gynecology.
Methods: Thirty one women of reproductive age who underwent renal transplantation took part in this study. These patients were defined as study group, and control group was healthy women with same endocrinologic problems in gynecology mated adjusted age and symptoms (study: control = 1: 3).
Results: The mean age and body mass index of study participants at the time of interview was 33.3 years (range, 17-48) and 21.5kg/m^2 (range, 14.6-33.3), respectively. The mean interval of endocrinologic problems in gynecology from kidney transplantation was 32.2 months. Symptoms of patients were infertility (n=7), menometrorrhagia (n=7), amenorrhea (n=3), dysfunctional uterine bleeding (n=7), and others. The levels of estrogen and FSH in study group were higher than those in control group, but the levels of progesterone and LH in study group were lower ($P<0.05$). There was no difference in prolactin and TSH between two groups.
Conclusion: We found that the levels of estrogen and FSH in female kidney transplant recipients were higher than healthy women with same endocrinologic problems in gynecology, but progesterone and LH were contrary.

P-257 DEEP VEIN THROMBOSIS IMMEDIATELY AFTER KIDNEY TRANSPLANTATION

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Background: Lower extremity (LE) deep vein thrombosis (DVT) is a common problem in patients undergoing major surgical procedures. But a few data are available on the incidence of LE DVT after kidney transplantation (KT). Most studies were designed retrospectively and came from Western countries. The aim of our prospective study was to evaluate the incidence of LE DVT within 3 month after KT in Korean.
Methods: 93 consecutive patients were included. Among them 25 recipients received KT from deceased donor. In this study the frequency of LE DVT during the first 3 months after KT was evaluated using serial duplex ultrasound (DU). The DU was performed on preoperatively, postoperative days (POD) 7, 14, 28, and 90. All patients were screened before KT for a hypercoagulable state. At the end of surgery, closed suction drains were left in place. And we used only graduated elastic stocking for DVT prophylaxis
Results: LE DVT occurred in 3 patients (3.2%). All DVT developed same side of transplant. The diagnosis was made at POD 1, 14, and 28, respectively. In 2 of them the DVT was asymptomatic and diagnosed at the calf veins by routine scheduled DU. The other one patient required thrombectomy of external iliac vein. All three patients received a KT from living donor and had no history of previous DVT. Interestingly, Factor Va Leiden mutation and prothrombin gene 20210A mutation were not found in our patients.
Conclusion: The incidence of DVT without DVT prophylaxis in this study was relatively lower than that of Western population and we could not found Factor Va Leiden mutation and prothrombin gene 20210A mutation. These findings suggest that these inherited thrombophilic factors have to be considered as the main cause of a different incidence of DVT between two groups.

P-258 SHORT-TERM RESULTS OF ABO-INCOMPATIBLE LIVING DONOR KIDNEY TRANSPLANTATION: COMPARISON WITH ABO-COMPATIBLE GRAFTS

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Background: ABO incompatible (ABOi) kidney transplantation (KT) is increasingly preformed but detailed comparative data with ABO compatible (ABOc) KT about patients and graft survival, graft function, and complications are still scare. The present study was aimed at these issues.
Methods: In this retrospective study, we compared 12 consecutive ABOi living donor KT to 50 ABOc living donor KT used same maintenance immunosuppressive regimen with respect to preoperative demographic factors, immunologic risk factor, patients and graft survival, postoperative renal function (serum creatinine, estimating glomerular filtration rate, and urine protein-to-creatinine

ratio), acute rejection, infectious, medical, and surgical complications, duration of hospital stay and episode of re-admission rate until 90 days after KT.
Results: Baseline characteristics were similar among two groups except positivity of panel reactive antibody (12% in ABOc group vs. 42% in ABOi group; P= 0.029). There were no significant differences of patients and graft survival, postoperative renal function, acute rejection, infectious, medical, and surgical complications, and episode of re-admission. Although there was no statistical difference, bleeding complications were more common in ABOi group (25% vs. 6%, P=0.08, respectively). The preoperative and total hospital stay in ABOi group was significantly longer than in ABOc group (P=0.001).
Conclusions: We concluded that ABOi KT is a viable and safe option for patients whose only donor is blood incompatible despite the longer preoperative hospital stay for preparation.

P-259 CLINICAL RELEVANCE OF POST TRANSPLANT DE NOVO HLA ANTIBODIES AFTER LIVING DONOR KIDNEY TRANSPLANTATION

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After kidney transplantation (KTx) HLA antibodies (Abs) are supposed to cause an inferior long-term outcome. 1 year after KTx we analysed serum of 21 patients for HLA Abs by luminex technology. The group included 6 ABO-incompatible (ABOi) and 15 ABO-compatible transplants. 7/21 patients had received previous allografts (2 liver, 5 kidney). Clinical outcome (acute rejection, kidney function after 1-year) was correlated with antibody development.
One year after KTx, 11/21 patients were positive for MHC class I (6/21) and/or class II (10/21) Abs. In patients with first transplant de novo antibodies occurred in 5/14 patients. They were donor specific (DSA) in 4/5 cases. In patients with previous grafts 6/7 were positive for HLA Abs, most of them were DSA for the previous graft. Only 2/7 patients showed de novo Abs against the actual graft.
Kidney function of patients with and without Abs was similar after 1 year (s-creatinine 1.81 vs. 1.87mg/dl). However, for DSA positive patients (actual graft, 6/21) there was a tendency to worse renal function (s-creatinine 2.09 vs. 1.74 mg/dl). Remarkably 3/6 patients with DSA required treatment for acute rejection, while only 3/15 patients without DSA were treated for rejections.
The detection of HLA Abs by luminex was frequent and DSA against the actual allograft were detectable in 6/21 of patients. In our cohort, MHC class II Abs were more frequent then class I Abs. Patients with DSA seem to have more acute rejections, but there was no clear correlation with the 1-year kidney function in this small cohort of patients. Therefore the question arises which DSA are detrimental, beneficial or neutral? To answer this question a longer follow up and a higher number of patients need to be analyzed in detail.

P-260 HLA-C MISMATCH AFFECTS SHORT-TERM RENAL TRANSPLANT FUNCTION

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Background: HLA compatibility has long been considered pivotal to successful outcomes in kidney transplantation. UK kidneys are allocated based on HLA-A, -B and DR matching with a difference of 21% in 10-year survival between best and worst match categories. This suggests other immunological differences may contribute. Increasing evidence implicates emergent anti-HLA antibody with long-term graft loss and often these antibodies are against HLA antigens not considered in the match grade such as HLA-C and –DQ. This study assesses the effect of HLA-C and –DQ on clinical outcomes in renal transplantation.
Methods: Demographic, clinical and biochemical data for kidney transplant recipients from January 2007 to March 2009, were collected prospectively in an electronic database supplemented by clinical record review. HLA-C and –DQ matched grafts were compared with matched controls for outcome measures alongside other potential confounding demographic factors using linear regression analysis (SPSS).
Results: 149 renal transplantations occurred during the study period. Mean time from transplant was 34 months (16-49 months). No significant difference in graft/patient survival was evident for HLA-C or DQ mismatched grafts, However HLA-C matched grafts had better creatinine/eGFR levels at 1-year post-transplant than their mismatched counterparts [mean creatinine 111 vs 131 ($p<0.003$), eGFR 55 vs 47 ($p<0.001$)]. HLA-C matched patients also have less rates of acute rejection (8.2% vs 17.6% mismatched grafts; $p<0.08$).
Conclusion: These results suggest mismatching for HLA-C may have a direct effect on short-term graft function and acute rejection incidence. Modern immunosuppressive regimens may dampen any clinical effect within the early years post-transplant but given the expanding evidence linking antibodies to donor HLA to long-term outcomes, further studies with expanded patient numbers and longer follow-up are required to assess the magnitude of any HLA-C or –DQ effect on emergent anti-HLA antibody and longer term outcomes.

P-261 THE QUALITY OF LIFE IN LIVING DONOR KIDNEY TRANSPLANTATION

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Purpose: The safety and the impact on quality of life (QOL) was increasingly important concept in living donor kidney transplantation. The purposes of this study were to evaluate the QOL of living kidney donors utilizing the SF-36 questionnaires, to indentify factor for impediment of the QOL after donation and to provide basic materials necessary for instituting a guidelines for health management and additional support after kidney transplantation.
Methods: The subject of this study was 70 living donors kidney transplantation performed in our center from 1990 to 2010. These data have been collected from May to July in 2010 by donor characteristics and SF-36 (version 2). We analyzed and evaluated the collected data through T-test, frequency analysis, ANOVA and scehffe's test by employing a statistics package SPSS 17.0.
Results: The donors were more prevalent in female (60.9%), and average age is 45.4 ± 12.0 years. The relations to the recipients were 20 siblings (29.0%), 17 parents (24.6%), 13 spouses (18.8%). The characteristics related donation were the return of pre-donation activities (72.5%), no visit to a hospital and pharmacy after donation (69.6%), decision of donation in propria persona (97.1%), Most donors were satisfied with their donation (92.8%) and no regrets of donation (87.0%). The QOL of all subjects showed average scores of 71.89.
Conclusions: The overall QOL of living kidney donors showed lower scores (48.56 ± 5.45) compared to average scores (50) of the healthy population in the USA. Especially, the scores for PCS (52.87) on the SF-36 were higher than the scores for MCS (44.25). However, most living kidney donors were satisfied with their donation and showed smoothly physical recoveries despite of their lower QOL. Therefore, systematic and continuous management after transplantation as well as preoperatively appropriate information and counsel for living kidney donors is needed.

P-262 COMPARISON OF SERUM CYSTATIN C AND CREATININE AS A MARKER FOR EARLY DETECTION OF DECREASING GLOMERULAR FILTRATION RATE IN RENAL TRANSPLANTATION PATIENTS

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Background: There are many markers that assessment of transplanted renal function, recently serum cystatin C (CyC) is reported a more sensitive marker for the early detection of decreasing glomerular filtration rate (GFR).
Materials & Methods: We compared CyC with Cr and 24-hour urine creatinine clearance (CrCl) in 72 adult renal transplant recipients from 2001 to 2008. CyC-based GFR was estimated by the formula of Thierry Le Bricon and Cr-based GFR was estimated by the formula of Modification of Diet in Renal Disease II (MDRD II). We compared these as accuracy, bias, precision and sensitivity by post-transplantation period.
Results: Classifying by CrCl level with <30, <60, <90, and ≥90 ml/min/1.73 m^2, the Cr-based GFR had the accuracy of 0.48, 0.27, 0.69, and 0.33 within 30% of the reference, accuracy of 0.71, 0.906, 0.963 and 1.00 within 50% of the reference, and precision (mean absolute percentage error) of 7.57, 10.03, 14.52 and 31.33 ml/min/1.73 m^2. By CrCl level, the CyC-based GFR had the accuracy of 0.31, 0.60, 0.55 and 0.33 within 30% of the reference, accuracy of 0.35, 0.79, 0.93 and 0.67 within 50% of the reference, and precision of 15.03, 14.80, 17.91 and 34.79 ml/min/1.73 m^2. Sensitivity to detect a GFR below 60 mL/min/1.73 m^2 was higher for CyC (0.96, 1 and 0.95) than for the Cr (0.77, 0.75 and 0.82) in receiver operating characteristic (ROC) curve ($p=0.0165$, $p=0.3985$, $p=0.0350$).
Conclusion: CyC is more sensitive indicator than Cr for early detection of low GFR (CrCl$<$60 ml/min/1.73 m^2). And CyC-based GFR underestimates GFR at CrCl$\geq$60 mL/min/1.73 m^2, therefore development of CyC-based GFR formula and double monitoring of Cr, CyC would be needed.

P-263 PREGNANCY IN KIDNEY TRANSPLANT PATIENTS

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Introduction: Pregnancy is currently considered yet another benefit of renal transplantation (KT).
Aim: To analyze the viability of pregnancy in KT and the consequences on renal function,as well as the complications in the patients and the newborns.
Material and Methods: We undertook a retrospective study analyzing all pregnancies between 1986 and 2010 in KT. Evaluation was made of different variables related with renal function, as well as other related with the birth and the newborn.
Results: We studied 24 pregnancies in 20 KT. Their mean age was 29±5 years and the mean time since the transplant was 4.5 years (0.8-12). At the time of pregnancy, 17 patients were receiving steroids and a CNI. Two azathioprine plus steroids and one patient, who had an unplanned pregnancy, was receiving tacrolimus and MMF, which was immediately withdrawn. The GFR was 59±15 ml/min. Twelve patients had well controlled hypertension and no proteinuria. The renal function and proteinuria remained stable during the pregnancy. There was a significant increase in blood pressure at the end of the pregnancy and it was necessary to raise the dose of CNI to maintain suitable levels.

	Basal	Month 3	Month 6	Delivery	Month 3
Creatinine (mg/dl)	1.18	1.0	1.2	1.3	1.2
Systolic BP (mmHg)	128	126	127	139	140
Diastolic BP (mmHg)	78	78	79	88	89
Cyclosporine dose (mg/d)	162	190	204	198	162
Cyclosporine levels (ng/ml)	168	122	135	154	190

No acute rejection was detected. One had gestational diabetes and two preeclampsia. Pregnancy reached term in 20 cases and there were four miscarriages. Cesarean section was required in 12. Delivery was at 36.9 weeks (34-41) and the weight of the newborns was 2.7 kg (1.5-3.6). One patient, who had been advised against pregnancy due to the high risk of complications, had a miscarriage at week 22 and died due to cardiac arrest during induction of the birth. 18 children were born healthy. One was born with esophageal atresia and other had multiple malformations.
Conclusions: Pregnancy in KT is safe if the renal function is correct before becoming pregnant, there is no proteinuria and the blood pressure is well controlled. In these cases, the maternal complications are similar to those of the general population and we detected no increased risk of graft loss.

P-264 REDUCTION IN PROTEINURIA AFTER DUAL BLOCKADE OF THE RENIN-ANGIOTENSIN SYSTEM (ARB II-ALISKIREN) IN KIDNEY TRANSPLANT PATIENTS

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Introduction: Renin-angiotensin system (RAS) blockade has cardioprotective and renoprotective effects in the general population,but whether dual blockade using angiotensin receptor blockade (ARB) plus a renin inhibitor (aliskiren) can minimize severe proteinuria in kidney transplant recipients remains undetermined.
The aim of this study was to analyze the efficacy and safety of dual blockade of the RAS with an ARB and aliskiren in kidney transplant patients with important proteinuria and creatinine $\leq$ 2.5 mg/dL.
Material and Methods: We prospectively studied 25 patients (mean age, 56 years; 65% men) who received a cadaveric renal transplant between 1990 and 2008; 60% were receiving immunosuppressive therapy with a calcineurin inhibitor, 40% with a mammalian target of rapamycin and 85% with mycophenolate mofetil. All were being treated with high-dose ARB II due to high grade proteinuria (range, 1-6.5 gr/24h), with a poor response. Accordingly, 21 patients also received aliskiren and 4 who were receiving an ACE inhibitor were switched from this to aliskiren. The mean follow-up was 15 months.
Results: Proteinuria decreased at 3 months by 40% and at 6 months by 60%, as well as a significant reduction in mean blood pressure figures. Renal function remained stable,as did the serum potassium concentrations.
Conclusions: Dual blockade of the RAS with an ARB II and aliskiren had an additive effect in the reduction of severe proteinuria and blood pressure in kidney transplant patients. No relevant adverse effects were detected in renal function,anemia or serum potassium concentrations.This might contribute to prolonging long-term kidney graft survival.

Effect of aliskiren on renal function, proteinuria, mean blood pressure, hemoglobin and serum potassium concentrations

	Baseline	3 months	6 months
MDRD 4 (ml/min/1.73)	38.1±17.1	35.3±18.7 / p=0.4	38.5±17.8 / p=0.1
Creatinin (mg/dl)	1.7±0.6	1.9±0.8 / p=0.09	1.7±0.7 / p=0.1
Mean Blodd P ressure (mmHg)	100±14	75.4±9.5 / p=0.001	74.1±8.9 / p=0.001
Potassium (mEq/L)	4.4±0.6	4.6±0.7 / p=0.2	4.6±0.6 / p=0.1
Hemoglobin (g/dL)	12.4±1.3	12.8±4.7 / p=0.1	12±0.8 / p=0.1
Protienuria (g/24h)	2.1±1.2	1.1±0.7 / p=0.001	0.9±0.5 / p=0.02

MDRD, Modified diet in renal disease.

P-265 JC POLYOMAVIRUS: DOES IT CAUSE NEPHROPATHY IN RENAL TRANSPLANT PATIENTS?

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Introduction: BK polyomavirus (BKV) reactivation characterized by active viruria occurs in 23-57% of renal allograft recipients and BKV-associated nephropathy in as many as 8% of renal allograft recipients. Only a few cases of nephritis have been attributed to JC polyomavirus (JCV), and just limited information is available with respect to JCV replication in kidney transplant patients and its impact on graft function and survival.
Aim: To determine the prevalence of BKV and JCV replication, the risk factors associated with viral reactivation and their implication in the development of polyomavirus nephropathy (PVN) in renal transplant patients.
Material and Methods: The study included 186 kidney transplant recipients transplanted between 2005 and 2009 with a follow-up of one year. If the PCR in urine was positive, PCR was performed in blood. If this was positive or renal dysfunction was present, renal biopsy was performed.
Results: Viruria was positive in 72 cases (39%) and viremia in 12 (6.5%); of these, 3 patients (1.6%) developed PVN. In the patients with viruria, BKV was detected in 47% and JCV in 46%; both were detected in 7%, though both the viremia and the nephropathy were caused by BKV in all cases.
Conclusions: In renal transplant patients the incidence of BKV and JCV viruria is similar, though in our series the JCV serotype did not cause viremia or PVN. Whilst further studies are required to corroborate these data, in our experience JCV does not have the ability to cause PVN.

P-266 HISTOLOGICAL FINDINGS IN RENAL TRANSPLANT PATIENTS WITH PROTEINURIA

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Introduction: Proteinuria is a factor with a poor prognosis for graft survival.
Aim: To study the histological lesions associated with the presence of proteinuria in renal transplant (RT) patients and analyze the influence of these and other parameters on graft survival.
Material and Methods: We undertook a retrospective study of RT that had a biopsy due to proteinuria between 2006 and 2009.Data were collected on demographic,analytical and histological characteristics.
Results: We analyzed 49 RT biopsies (65% men, mean age 52±13 years).The time from transplant to biopsy was 6.5±5.3 years.At this point,90% were receiving treatment with a CNI and 13% with mTor;80% were receiving MMF.All the cases had proteinuria 2.4 g/24h (1.2-3.2) and in 56% it was also associated with worsening GFR (MDRDa 30±15 ml/min).In 14% the sample was insufficient to determine a glomerular pathology,51% had glomerular disease (40% transplant glomerulopathy,48% glomerulonephritis,12% diabetic). IFTA was present in 85% (33% mild,27% moderate,25% severe).Arteriolar hyalinosis was present in 60%.30% lost their graft (11±9 months after the biopsy).The GFR at the time of biopsy was worse in those who returned to dialysis than in those who retained their function (MDRDa 22±7.5 vs. 34±15 ml/min; p=0.006).The proteinuria was also greater in those who lost their graft (4.1±3.4 vs. 2.1±1.6 g/24h; p=0.007).The absolute increase in risk of graft loss was 34% in those who had moderate-to-severe IFTA versus those who had mild IFTA (RR 4; CI 1.1-15); p=0.01. The severity of the arteriolar hyalinosis or the glomerular pathology did not influence graft loss.After the biopsy, the dose of ACE inhibitors/ARA was increased in 90%, and 30% had a change in their immunosuppression.
Conclusions: In RT patients who have a biopsy due to proteinuria,graft loss is associated with GFR and the amount of proteinuria at the time of the biopsy,as well as with the degree of IFTA.

P-267 RESTROSPECTIVE ANALYSIS OF INDUCTION THERAPY (IT) FOR KIDNEY TRANSPLANTATION IN A SINGLE CENTER POPULATION OVER 17 YEARS

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Background: IT, either antithymocite globulin (ATG) or anti-IL-2 receptor antibodies (Basiliximab – B), is a recognized tool able to reduce acute rejection (AR) rate, mostly valuable in retransplanted and sensitized patients. Moreover it can delay the introduction of calcineurin inhibitors, particularly when using marginal kidneys.
Methods and Materials: We adopted IT only for high-risk patients up to 2000. Afterwords all patients were IT treated (mostly with B; ATG only for high PRA patients). We review and analyze graft and patient outcomes with the two IT over the period 1995-2007 in 1255 patients.

Demographics

	Basiliximab (n=771)	ATG (n=54)	No IT (n=429)	p
M/F	487/284	34/20	279/151	n.s.
Donor age	52±17	41,6±17,6	40,5±16,7	n.s.
Recipient age	51,5±12,4	44,2±12	46,7±11,8	<0,001
% retransplants	10,5	31,5	10,7	<0,001
% PRA>20%	13,1	72,5	26,6	<0,001
% DGF	22,7	37,7	40,2	<0,001
Median f/up (months)	51 (0-132)	118 (0-170)	126 (0-172)	<0,001

Results:

Clinical results

	Basiliximab	ATG	No IT	p
% AR (total)	16,4	20,4	24,2	<0,003
% AR 12 months	13,4	17,6	19,3	<0,03
% infectious deaths	1,7	7,5	3,8	<0,008
% tumors	9,8	15,4	14,8	<0,02
% 10 yrs organ survival death censored	82	67	76	0,03
% 10 yrs patient survival	83	81	85	0,4

Conclusions: IT is significantly associated with lower AR incidence on short and long term compared to no induction, particularly in B patients, but also in ATG patients. Remarkable is the safety profile of B in terms of lower infectious and neoplastic complications compared to ATG.
In our opinion these data, together with a good 10 years organ survival in both groups, support the current use of IT in all patients, preferably with ATG only in the high-risk populations.

P-268 SEVERE NEUROLOGICAL COMPLICATIONS (SNC) IN KIDNEY TRANSPLANTATION (KT)

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Introduction: Neurological complications are common after KT, associated with high morbidity and mortality.They may be related to calcineurin inhibitors (CI) toxicities, opportunistic infections, cardiovascular events, metabolic and electrolytic disorders and neoplasmas.
Aim: Retrospective analysis was performed to evaluate SNC among KT patients (KTP) from January 2003 through December 2010.
Material and Methods: We reviewed 180 records from cadaveric KTP. Immunossupression; 167P received Thimoglobulina ® and 13 Simulect® as induction. 135P utilized Tacrolimus- Sodic Mycophenolate-Esteroids, 30P Tacrolimus-Sirolimus-Esteroids, 10P Belatacept-Mycophenolate Mofetil-Esteroids, 5P Cyclosporine-Micophenolate Mofetil-Esteroids. Trimethoprim-Sulfamethoxazole and Ganciclovir as infectious prophylaxis.
Results: 22 KTP developed SNC.
Infection: 9P (40.9%) acquired: Toxoplasmosis 1P, Cryptococcosis 5P, Zygomicosis 1P. Herpetic Encephalitis 1P, Guillain Barre Syndrome (CMV+) 1P. Three patients died from Cryptococcosis, Zygomicosis and Herpetic Encephalitis respectively.
Severe CI toxicity: 7P (31.8%) had tacrolimus toxicity, 5P improved with tacrolimus interruption, two died, one due to intracerebral hematoma (tacrolimus level >30 ng/ml) and the other from seizures which did not respond to tacrolimus withdrawal or to anticonvulsant treatment.
Stroke: 1P (4.5%) who died due ischemic stroke.
Malignancy: 1P (4.5%) developed a brain lymphoma.
Electrolyte disturbance: 2P (9.09%) had this disturbance accompanied by encephalopathy at the early post-transplant period. RMG was carried out on one of them showing a hyperintensive lesion in hippocampus. Both improved after electrolytic correction.
Rejection encephalopathy: 1P (4.5%) developed sensory symptoms during an acute rejection episode, treated with polyclonal antibodies, he was not under CI, improving after treatment was stopped.
The incidence of SNC was 12.2% and its overall mortality was 3.3%.
Conclusions: Our results differ from international literature, which state that neurotoxicity related to immunosuppressant is the most common neurologic complication. However, in our Institution prevalence of infectious disease was the most frequent. It may be caused by immunosuppression or our geographical location.

P-269 SERUM HOMOCYSTEINE THIOLACTONASE AND PARAOXONASE ACTIVITY IN RENAL TRANSPLANTED PATIENTS

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Homocysteine thiolactonase (HTLase) protects against homocysteinylation,therefore a potencial contributing factor to atherosclerosis. Previous studies have demostrated decreased paraoxonase (PON1) activity in haemodilaysed and renal transplanted patients, however HTLase activity has not been investigated. We aimed to determine the paraoxonase and HTLase activities and to clarify the relationship between HTLase activity and some cardiovascular risk factors, such as homocysteine, cystatin C and asymmetric dimethylarginine (ADMA) in dialysed and transplanted patients and healthy controls.
114 haemodialysed (age: 65.51±13.4 years) and 80 renal transplanted (age:49.01±14.00 years) and 54 healthy controls (54.36±13.78 years) were involved in the study.We investigated BMI, in fasting serum urea, creatinine, cystatin C, homocysteine, glucose, lipids, total proteine, albumine concentrations. The serum paraoxonase and HLTase activities were measured spectrophotometrically, ADMA level was determined with sandwich ELISA method. Both dialysed and transplanted patients has significantly lower HTLase activities compared to the control group ($p < 0.001$).Significantly lower HTLase and PON1 activities were found in dialysed patients compared to the transplanted group ($p < 0.05$).There were significant negative correlations between HTLase activity and ADMA levels in the whole study population ($p < 0.001$).Significant positive correlations were found between paraoxonase and HTLase activities in the whole study population ($p < 0.001$).Multiple regression analysis showed that only paraoxonase activity and homocysteine, cystatin C levels are independent predictors of HTLase activity.
The HTLase activity may be a new predictor of cardiovascular risk in renal failure, however, it may modulated by other risk factors. Measurement of HTLase activity can be recommended in future studies on transplanted and dialysed patients.

P-270 CONVERSION TO EVEROLIMUS IN PATIENTS WITH NEPHROTOXICITY INDUCED BY CALCINEURIN INHIBITORS. ONE YEAR EVOLUTION AS PER BASELINE BIOPSY FINDINGS

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Introduction: The use of calcineurin inhibitors (CNI): tacrolimus and cyclosporine is generally associated to histopathological findings of nephrotoxicity. Proliferation signal inhibitors (PSI) like everolimus were developed with the aim of nephrotoxicity avoidance or improvement but the adequate patient selection for the introduction of PSIs is still under discussion. This report describes the evolution of 65 patients belonging to the Argentinian Everolimus Registry in Kidney Transplant Recipients (AER) who replaced tacrolimus by everolimus due to nephrotoxicity or other reasons.
Materials and Method: The AER is a local database designed to register the experience with everolimus (de novo or after conversion) in renal transplant recipients. Sixty five patients, having baseline biopsy data, were converted from CNI to everolimus and followed during twelve months. Patients were retrospectively identified in three groups as per their renal biopsy findings and

posterior renal function evolution: A- (9) pure nephrotoxicity. B- (38) IFTA I/II/III and C- (18) transplant glomerulopathy, C4d(–). A retrospective analysis using descriptive statistics was performed.

Results:

Baseline and 12 months MDRD and proteinuria

Group	N	Age (years)	Conversion Time post transplant (months)	MDRD (ml/min)		Proteinuria (ml/min)	
				Baseline	12 Months	Baseline	12 Months
A	9	38±12	22±14	46±11	56±0.0	1.1±0.8	0.1±0.0
B	38	46±16	37±15	49±21	48±20	0.4±0.7	2.0±1.9
C	18	46±12	36±12	42±13	38±15	0.4±0.8	0.6±1.0

Everolimus doses and levels were 1.8±0.5 mg/day and 4.4±1.8 ng/ml for Group A, 1.9±0.6 mg/day and 3.9±1.8 ng/ml for group B and 1.6±0.4 mg/day and 3.9±0.5 ng/ml respectively for group C.

Conclusions: In this twelve month follow up conversion from CNI to everolimus the group of patients with pure nephrotoxicity showed stabilization of renal function and even an improvement. For the other group of patients, IFTAI/II/III and transplant glomerulopathy, the intervention was ineffective in terms of renal function improvement. Proteinuria worsening was only observed in IFTA group.

P-271 RENAL VESSEL MULTIPLICITY AND ITS IMPACT ON PERIOPERATIVE AND LONG-TERM DONOR OUTCOMES FOLLOWING LIVING-DONOR NEPHRECTOMY

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Introduction: Live donor kidney transplantation is consistently superior to deceased donor transplantation. Multiple renal vessels present a technical challenge to the operating surgeon and might, it is hypothesised, herald greater risks of perioperative and long-term complications for the donor.

Methods: Data from 386 living-donor nephrectomies, utilizing the "mini-open" technique, were collected over five years at one of the United Kingdom's largest renal transplant units. Intra-operative data and post-operative outcomes (up to 5 years) for multiple and single vessel donors are analysed, compared and reported.

Results: Of the 261 donors satisfying the inclusions criteria, 30 (11%) had multiple renal arteries in the kidney to be removed. Total operation time was not significantly different between those with a single artery (125±49 mins) and those with multiple arteries (120±48 mins, P=0.75). Warm ischaemia time and estimated blood loss were also found not to vary significantly between groups. Total length of hospital stay was not significantly longer for those with multiple arteries (4.9±1.4 days) as compare to single vessel donors (5.3±1.4 days, P=0.43). Peri-operative and long-term (mean = 19 months) complication rates were also not significantly different between groups, with pneumonia and wound infection constituting the commonest postoperative complications for both.

Conclusion: Our unit's experience is that donor nephrectomy is safe in donors with multiple vessels and does not result in higher rates of major perioperative complications. Long-term follow-up data show good outcomes for these donors. While these results are encouraging, we advocate careful selection of multiple vessel donors with appropriate pre-operative education and counselling, and can only recommend their inclusion in centres similar to our own, specialising in marginal donor transplantation.

P-272 UROLOGICAL COMPLICATIONS FOLLOWING RENAL TRANSPLANTATION- A SINGLE CENTRE EXPERIENCE

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Background: Urological complications, in particular urinary tract infection (UTI) are common and debilitating effecting graft survival and patient morbidity. The study aimed to assess the incidence urological complications and their effects on early and intermediate graft function.

Method: The study was carried retrospectively enrolling all consecutive renal transplant recipients from 2007-2009 with 1year follow-up. The parameters used to assess graft function were eGFR, positive urine culture, and rejection episodes. All recipients received standard unit protocol immunosuppression. Every recipient had a ureteric stent (US) at transplantation, which was removed 4-6 weeks postoperatively.

Results: Among the 112 consecutive renal transplant recipients (live-donor: n = 82, cadaveric: n= 30) 52 of them had no UTI (46.42%). 1-3 episodes of UTI occurred in 29 (25.91%) while more than 3 episodes occurred in 31 (27.67%). All recipients were thus grouped in two arms based on number of episodes of UTI, Group 1 (<3 episode of UTI/year) and Group 2 (>3 episodes of UTI/year). Graft function at 1 year showed no difference between the groups (p=0.95), while episodes of acute rejection were significantly higher in Group 1 (p=0.0016). The incidence of UTI between men and women were no different. The incidence of UTI reduced significantly after removal of the US before (n=41) and after (n=26); (p=0.034)]. Major urological complications (MUC) included urinary leaks (n=4), ureteric stricture (n=1) and stone disease causing ureteric obstruction (n=2).

Conclusion: The incidence of UTI following renal transplantation did not affect early/intermediate graft function following adequate treatment. Having less than 3 episodes of UTI increases the susceptibility to acute rejection and this may relate to less immunosuppressive burden. The single most important predictor for a UTI was a US, thus warrants a randomized controlled study to assess early removal of a US and its association with UTI and MUC.

P-273 IMBALANCE OF MMPs/TIMPs SYSTEM IN RENAL TRANSPLANT RECIPIENTS WITH CHRONIC ALLOGRAFT INJURY

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Renal allografts continue to be lost after the first year of transplantation due to chronic allograft injury. Excessive accumulation of extracellular matrix (ECM) results from overproduction and/or defective ECM degradation by proteolitic enzymes, among which metalloproteinases (MMPs) play the major role. Tissue inhibitors of MMPs (TIMPs) inhibite both latent and active MMPs and should be investigated simultaneously (TIMP-2 is the potent inhibitior of MMP2, whereas TIMP-1 forms a complex with MMP-9).

The aim of the study was to assess the potential of MMPs/TIMPs system in renal transplant recipients (RTR) beyond 1 year of transplantation in context of chronic allograft injury or proteinuria.

Material and methods: Plasma and urine MMP-2/TIMP-2 and MMP-9/TIMP-1 were assessed by ELISA in 150 RTR, male 66%, aged 49,2±11,5 years, at mean 73,4±41,2 months (range 12-240) after kidney transplantation and in 37 healthy volunteers, male 54%, aged 48,4±14,1 years. Patients were divided into subgroups, according to graft function (sCr < 1,5 mg/dl and sCr > 1,5 mg/dl) and proteinuria (yes/no).

Results:

Metalloproteinases and their inhibitors in RTR

	sCr		Proteinuria		Controls
	≤1,5 mg/dl	>1,5 mg/dl	NO	YES	
Number of subjects	n=79	n=71	n=106	n=44	n=37
pMMP2	208±46	226±56	208±41	238±67	248±41
pTIMP2	85±20	101±26	88±17	103±33	74±29
uMMP2	0,2±0,9	1,2±3,7	0,06±0,2	2,1±0,3	0,1±0,4
uTIMP2	4,9±9,9	10,1±27,7	5,0±11,8	13,1±32,6	2,1±2,6
pMMP9	160±175	133±109	146±154	150±135	70±44
pTIMP1	140±49	179±63	148±49	186±72	87±16
uMMP9	2,6±15,1	1,6±5,0	2,4±13,3	1,5±4,6	0,1±0,4
uTIMP1	1,9±3,3	3,2±5,2	2,0±3,2	3,9±6,1	1,3±3,9

Mean plasma and urine MMP2/TIMP2 and MMP9/TIMP1 concentrations (ng/ml); urine MMPs and TIMPs/urine Cr ratios were calculated to standardize the samples.

1. In RTR (compared with controls) plasma MMP-2 activity was significantly decreased ($p < 0.001$) but pMMP-9 and pTIMP-1 were increased twofold in RTR ($p < 0.001$) with nearly stable pMMP-9/pTIMP-1 index.
2. Urine MMPs and uTIMPs were increased in RTR, especially in patients with impaired graft function or proteinuria.

Conclusion: Our study revealed the imbalance between plasma and urine MMPs/TIMPs activities in renal transplant recipients, more evident in patients with graft failure or proteinuria, probably due to increased intrarenal production and excretion, but the proteolitic effect may be diminished by enhanced uTIMPs concentrations.

P-274 VARIATION OF THE KIDNEY GRAFT VESSELS DURING LAPAROSCOPIC LIVING DONOR NEPHRECTOMY (LLDN): SURGICAL MANAGEMENT AND IMPACT ON EARLY GRAFT FUNCTION

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Background: In living donor kidney transplantation (LDKT), the presence of anatomic variations of the donor renal vessels may constitute a relative contraindication, particularly for LLDN. The aim of our study was to review our results of LDKT when such anatomical variations were present.

Methods: LDKT performed since 2004 were reviewed. In this group, we analyzed the incidence and the type of anatomic variations of the donor renal vessels and the techniques used for vascular reconstruction. We compared graft outcomes in normal donor anatomy (NDA) versus abnormal donor anatomy (ADA) groups.
Results: 53 LDKT using LLDN were reviewed, vascular reconstruction were performed in 28 cases (53%) included 20 arteries and 8 veins. Following number of the renal arteries were presented respectively after left and right LLDN: 1 artery (N=23 and N=10), 2 arteries (N=8 and N= 4), 3 arteries (N=3 and N=2), 4 arteries (N=3 and N=0).
The anastomose of the polar artery with principal renal graft artery (N=14), creation of the common arterial trunk (N=5), use of the recipient inferior epigastric artery (N=2) were done.
The donor right renal veins were extended using donor gonadic vein in 6 patients. One left renal vein was extended with saphenous vein. One orthotopic left kidney was performed.
No differences were observed between NDA and ADA for operative duration, cold and warm ischemic time, urological complications and creatinine levels. The primary graft non function and the arterial reversible thrombosis appeared in one case ADA and NDA respectively.
Discussion: Anatomic variations of the donor renal vessels are frequent. Adequate surgical management, i.e. back table vascular reconstruction, allows obtaining similar results than those observed in case of normal anatomy and increases the donor pool.

P-275 eGFR AND 1-HOUR BIOPSY ARE BETTER PREDICTORS OF DECEASED KIDNEY TRANSPLANTS WITH USING IN-SITU-COOLING DOUBLE-BALLOON CATHETERS SYSTEM

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Introduction: The worldwide shortage of deceased donor kidneys for transplantation has become a serious issue in the past decade. However, both the availability and feasibility of kidneys from deceased donors is still unclear. The aim of the present study was to estimate availability of deceased donor kidney with using our cooling system, and find better evaluation method to estimate donor kidney function rather than using donor Cr.
Methods: We studied 129 deceased renal transplant recipients who received kidneys from non-heart-beating donors (Maastricht Donor Categories III and IV). In order to minimize warm ischemic kidney damage, we performed in-situ cooling with specially designed double-balloon catheters. Donor 1-hour biopsies were analyzed with Remuzzi's evaluation system.
Results: The donor Cr and estimated donor glomerular filtration rate (eGFR) levels at admission were 0.3 - 2.1mg/dl (average 1.0) and 25-136 ml/min/1.73 (average 67). The recipient Cr and eGFR levels at discharge were 0.3 - 5.3 (average 1.8) and 9-100 (average 100).
Recipients were classified according to eGFR at discharge: <25 for the poor function group (PF: n=32) and >25, the good function group (GF: n=95). The GF had higher eGFR levels at admission than the PF (p=0.005), although there was no statistically significant difference in Cr levels of donor (at admission and before death) between those groups. Pathologically, the GF had less glomerular global sclerosis, tubular atrophy, and arterial/arteriolar narrowing than the PF in one-hour biopsies. (p=0.0000001, 0.003, 0.0002). Histological scores of interstitional fibrosis was not associated with kidney function.
Conclusions: In conclusion, our kidney transplants had excellent renal function with double balloon catheter system. Although donor Cr levels were not a useful measurement for our analysis, eGFR and 1-hour biopsy were and should be used for donor evaluation.

P-276 DISTRIBUTION OF RENAL HISTOPATHOLOGY FINDINGS IN GUILAN PROVINCE, NORTH OF IRAN DURING 2001 TO 2006

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Background: Glomeronephritis is the third most common cause of end stage renal disease. Epidemiological data of renal disease is population based and has great geographic variability. The aim of this study was to a five -year survey of histopathological findings frequency of renal biopsy performed in Guilan province.
Methods: In a retrospective cross sectional study, 397 renal biopsy which recorded in department of nephrology in Razi Hospital of Rasht, capital city of Guilan province from August 2001 to September 2006, were reviewed. Data consisted of age, gender and histopathological diagnosis. The data were analyzed by SPSS version 16.
Result: Among patients, 248 (62.46%) cases were male and mean age was 39.52 ± 17.75 (range: 2-84) years. Overall, frequency of Glumerolonephritis, non- Glumerolar disease and normal pattern was 268 (67.50%), 80 (20.15%) and 49 (12.34%) of biopsy specimens respectively. Focal and segmental glomerosclerosis (FSGS; 17.38%) was the most common pathology, followed by membranous glomerulopathy (MGN; 12.59%),minimal change disease (MCD; 9.82%), systemic lupus erythemato nephritis (SLEN; 9.82%), tubulointerstitial nephritis (TIN; 7.55%) and IgA nephropathy (IgAN; 3.02%). Frequency of histopathological findings was significantly related to sex and age. SLE-GN, MGN, IgAN were significantly more frequent among female patients ($P<0.05$); FSGS, MCD, SLE-N were significantly more frequent among patients under 40 years ($P<0.05$).
Conclusion: In our study, FSGS was the most common pathology. The frequency of MGN, SLE-GN and MCD, to a greater extent, was similar to other studies; conversely, IgAN was much lower than other studies.

P-277 LIVING DONOR KIDNEY TRANSPLANTATION IN CROSSMATCH-POSITIVE PATIENTS ENABLED BY PERITRANSPLANT IMMUNOADSORPTION AND ANTI-CD20 THERAPY

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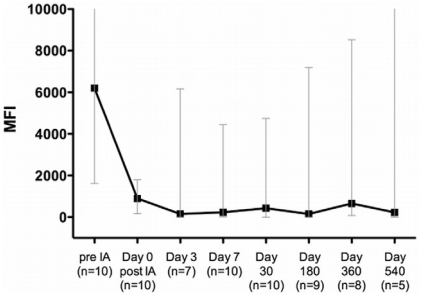
Background: Living-donor kidney transplantation in crossmatch-positive patients is a challenge that requires specific measures. We analyzed the efficacy of a desensitization protocol based on repeated peritransplant immunoadsorption.
Methods: Ten patients with positive CDC and ELISA crossmatch results (n=9) or negative crossmatch results but strong donor-specific antibodies (DSA) in Luminex and ELISA testing (n=1) were desensitized using immunoadsorption (IA) to enable living donor kidney transplantation. Patients in addition received anti-CD20 antibody together with basiliximab (n=6) or thymoglobulin (n=4) induction. IA was continued in the early posttransplant period and accompanied by HLA antibody monitoring and protocol biopsies.
Results: After a median of 10 pretransplant IA treatments, all patients were desensitized successfully and transplanted. Median mean fluorescence intensity (MFI) of Luminex-DSA before desensitization was 6,203 and decreased after desensitization and immediately before transplantation to 891.



Patients received a median of 7 posttransplant IA treatments. At last visit, after a median follow up of 19 months, 9 out of 10 patients had a functioning allograft and a median Luminex-DSA of 149 MFI; serum creatinine was 1.6 mg/dl, MDRD-GFR 54 ml/min/1.73m^2, and protein to creatinine ratio 0.1. Reversible acute antibody-mediated rejection was diagnosed in 3 patients. Infectious complications were infrequent. One allograft was lost during the third posttransplant year due to glomerular thrombi in a patient with systemic lupus erythematosus and antiphospholipid syndrome.
Conclusions: We describe a treatment algorithm for desensitization of living donor kidney transplant recipients that allows the rapid elimination of DSA with a low rate of side effects and results in good graft outcome.

P-278 ATTITUDES AND PRACTICES TOWARDS RENAL TRANSPLANTATION IN SICKLE CELL SYNDROMES AMONGST UK TRANSPLANT CENTRES

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Introduction: Patients with Sickle Cell Disease (SCD) are at increased risk of developing renal failure. The renal morbidity in patients with Sickle Cell Trait (SCT) is not established. The outcome for patients with SCD or SCT receiving

renal allografts has been reported with variable success. There are no UK guidelines concerning renal transplant recipients with SCD or SCT. Similarly, there are no guidelines regarding donor nephrectomy in patients with SCT or SCD. The aim of this study was to ascertain current UK practice regarding renal transplantation in donors and recipients with sickle syndromes.
Methods: Thirteen UK transplant centres were contacted and invited to complete an e-mail based questionnaire in October 2010. A further e mail was sent to non-responders. All responses were anonymous and centres not identifiable from their reply.
Results: Ten of thirteen centres (77%) responded to the questionnaire. All ten centres would perform renal transplantation in recipients with SCD or SCT if an appropriate graft was available. Only 2 (20%) centres questioned had a formal policy to screen potential donors for sickle syndromes. However all centres would consider utilising a graft from a donor with SCT, including living related donation.
Conclusion: Although donors are not consistently screened for sickle syndromes, the UK transplant centres involved in this study would be happy to consider potential living related donors with sickle cell trait but not sickle cell disease. Patients with SCD or SCT would be considered as transplant recipients provided an adequate kidney was available. These findings suggest that attitudes and practices regarding sickle cell syndromes and renal transplantation are similar to transplant centres in the United States [1].
Reference:
1. Reese PP, Hoo AC, Magee CC. Screening for sickle trait among potential live kidney donors: policies and practices in US transplant centres. Transpl Int. 2008 Apr;21(4):328-31.

P-279 RESTARTING A LIVING DONOR KIDNEY TRANSPLANT PROGRAM IN KENYA: 24 TRANSPLANTS PERFORMED IN LESS THAN ONE YEAR

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Introduction: Kidney transplant (KT) allows improved survival in patients with end-stage renal disease (ESRD) compared with dialysis. Moreover, transplant is cost-effective and leads to better quality of life. This is particularly true in developing countries, were limited access to dialysis makes KT the sole therapeutic valid option.
Aims: The aim of the project was to restart the living donor KT program in Kenya to ameliorate ESRD management and patient care in the country.
Methods: The Kenyatta National Hospital (KNH) is the national referral hospital in Nairobi and treats patients from all the country. The KT program started in 1984 and continued with up and downs until year 2000, since then KTs have become episodic, mainly due to poor results. Presently around 150 patients are under dialysis at the KNH, around 50% of them are suitable for KT. Novartis Pharma Spain and Kenya, as part of its Social Corporate Responsibility, initiated INTERLIFE, a Public-Private partnership between Novartis and KNH. INTERLIFE is a 5-year KT exchange program between Kenya and Spain aiming to build a reference center for KT in Kenya by upgrading processes and training experts. The first year focused on improving surgical expertise and post-transplant management. The KT team was trained in practical and theoretical aspects through exchange meetings and "in situ" training by the first Spanish KT team collaborating in the project.
Results: From March to November 2010, 24 living donor KTs have been successfully performed by the KNH KT team. During the congress, first-year results will be presented.
Conclusions: Within the first year of implementation of this project, the living donor kidney program at the KNH has successfully restarted allowing a better ESRD patient management and care in a developing country.

P-280 IMPACT OF LOW SERUM ADIPONECTIN LEVELS ON ARTERIAL STIFFNESS IN NEW ONSET DIABETES AFTER RENAL TRANSPLANTATION

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Background: New onset diabetes after transplantation (NODAT) is recognized as a potent risk factor of cardiovascular events in renal transplant recipients. Adiponectin, a recently discovered adipocytokine, has attracted great attention because of its anti-atherogenic properties. The purpose of this study was to determine whether serum adiponectin levels in renal transplant patients are associated with arterial stiffness related to NODAT.
Methods: A total of 90 previously non-diabetic patients who underwent renal transplantation between 1999 and 2009 were enrolled. The mean age and post-transplant follow-up duration were 44.3 years and 42 months, respectively. We evaluated their diabetic risk factors, lipid profiles, and serum adiponectin levels before and after transplantation. Arterial stiffness was estimated by brachial-ankle pulse wave velocity (baPWV) and ankle-brachial blood pressure index (ABPI).
Results: Eleven (12.2%) patients were diagnosed with NODAT and 79 (87.8%) without (non-NODAT). The mean post-transplant serum adiponectin level in NODAT patients was significantly lower than that in non-NODAT patients (11.9 vs. 16.4μg/ml, p=0.01), whereas the mean PWV level in NODAT patients was significantly higher (1686 vs. 1468cm/s, p=0.016). In contrast, there was not a significant difference between the groups in regard to ABPI level. We found a significant inverse correlation between mean pre-transplant serum adiponectin and PWV level (r=-0.27, p=0.011). Furthermore, patients with lower serum pre-adiponectin levels ($<$20μg/ml) developed NODAT significantly more frequently than those with higher pre-adiponectin levels (p=0.038) and the mean PWV level in the former was also significantly higher (1520 vs. 1412cm/s, p=0.047).
Conclusion: Our results indicate that low serum adiponectin level is associated with arterial stiffness for the development of NODAT in patients who undergo renal transplantation.

P-281 VALIDATION OF THE SIMPLIFIED MEDICATION ADHERENCE QUESTIONNAIRE (SMAQ) IN RENAL TRANSPLANT PATIENTS ON TACROLIMUS

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Background: non-adherence to immunosuppressant medication associates to graft loss and death. Here, a version of the SMAQ instrument adapted for its use in transplant patients was validated in a sample of kidney graft receptors.
Methods/Materials: observational, longitudinal prospective study in 150 renal transplant patients on tacrolimus, over 18 years old, who had received graft at least a year before. Informed consent was required. At basal visit basic sociodemographic and clinical data were recorded; patients completed SMAQ twice (administered by doctor/nurse) and self-administered Morisky-Green scale. At three months' visit, actualized clinical data were recorded; patients completed self-administered SMAQ and Morisky-Green. Analysis database included 144 patients that met selection criteria and had provided required data (131 for second visit). Descriptive characteristics for all recorded parameters and psychometric characteristics of the questionnaire (reliability and validity) were studied.
Results: Mean age in the sample was 50.63 (1.44) years, 60.42% were men. At first visit 20.14% of patients presented sub-target tacrolimus levels ($<$5 ng/ml), for 13.48% unjustified variations in immunosuppressant levels were reported. Regarding SMAQ results 39.01%/41.84% of patients were non-adherent (doctor/nurse administration), 22.38% after Morisky-Green scale. Interobserver agreement kappa was 0.821 ($p<0.001$). Convergent validity Cramer's-V was 0.516 ($p<0.001$). SMAQ classification associated to unjustified variations in tacrolimus level. In the prediction of tacrolimus levels (target vs subtarget), SMAQ compared to Morisky-Green classified patients better, presented enhaced sensibility and reduced specifity. At second visit 23 patients had changed from twice-daily to once-daily tacrolimus. Wilcoxon test points to better adherence on once-daily tacrolimus.
Conclusion: the questionnaire presents good characteristics of validity and interobserver agreement. Sensitivity to change shows good tendency but should be tested in a larger sample. An enhanced sensitivity is of advantage to better detect non-adherent patients for a better follow-up.

P-282 THE DIFFERENCES IN THE POST-TRANSPLANT LYMPHOCELES IN DEPENDENCY ON THEIR ORIGIN

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Objective: Evaluation of the differences between renal (RL) and iliac lymphoceles (IL).
Material and methods: The group of the 33 lymphoceles was divided to the

two groups RL (renal lymph >50%) and IL (renal lymph ≤50%) according to the creatine activity (CK) in the content. In these groups CK activity, lymphocele size, time since transplantation, blood creatine, protein and albumin levels were evaluated and protein and albumin level in the content as well.
Results: RL was confirmed in 91% and IL in 9%. CK activity were 3.48μkat/l in IL, 0.99μkat/l in RL, proportions of renal lymph were 32% in IL and 74.7% in RL. Average lymphocele sizes were 70 mm in RL and 50mm in IL. The time periods between transplantation and lymphoceles finding were 6 weeks in RL and 10 weeks in IL. Blood creatine, protein and albumin levels in RL resp. IL were 219mmol/l, 57g/l and 35g/l, resp. 365mmol/l, 54g/l and 34g/l. Protein and albumin levels in lymphocele content in RL resp. IL were 16g/l and 9g/l, resp. 12g/l and 7g/l.
Conclusion: RLs are much more common, bigger in diameter and a diagnosis is made earlier. The clinical impact of the ILs is more important, because creatine level in time of diagnosis is significantly higher. The lymphocele origin seems to be important from the clinical point of view.

P-283 THE LONG-TERM RESULTS FOLLOWING THE TREATMENT OF THE POST-TRANSPLANT SYMPTOMATIC LYMPHOCELES

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Objective: The long-term results of the treatment of the symptomatic lymphocele is very important. Our interest was focused on the safety, the long-term renal function and surgical results.
Material and methods: Overall 34 patients with symptomatic lymphocele who underwent any kind of surgical treatment were evaluated. Patient age, sex, renal failure causes, lymphocele size, time period between transplantation and lymphocele formation were analyzed. Laboratory tests evaluated creatine, total protein and albumin levels were done as well.
Results: The lymphocele was found in 18 females (52.9%) and 16 men (47.1%). Causes of the renal failure were: interstitial nephritis in 12 cases, glomerulonephritis in 12 cases, polycystosis in 7 cases, nephrosclerosis in 1 case, diabetic nephropathy in 1 case and Alport syndrome in 1 case. The median lymphocele size was 66.5mm in diameter. Indication for active therapy were hydronephrosis in 16 cases, lymphocele size >30mm in 11, increased creatine level in 6 and infection in 3 cases. Median of the time between transplantation and lymphocele treatment was 8 weeks. Surgery was used in 14 cases, single aspiration in 11 cases and percutaneous drainage in 9 cases. Serum creatine, total protein and albumin levels were 184umol/l, 56g/l, 35g/l in time of therapy; 133umol/l, 68g/l, 42g/l in month 6; 135umol/l, 68g/l, 43g/l in the month 12 and 124umol/l, 69g/l a 42g/l at present. Graft failure in this group was observed in 2 patients due to chronic rejection and in 3 patients.
Conclusion: Any graft has not been failed due to the lymphocele presence or its therapy. Indicated adequate therapy promises good long-term results and is not risky for the patient and his transplanted kidney. Simple single percutaneous aspiration considered as an effective management modality even in 32.3% seems to be really optimistic.

P-284 HIGH LYMPHOCYTE COUNTS IN THE EARLY POST-TRANSPLANT COURSE OF KIDNEY ALLOGRAFT RECIPIENTS CARRYING IMPDH II 3757 T>C SNP

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Allele C in IMPHD II 3757T >C SNP (rs 11706052) is associated with increased IMPDH II activity. Data regarding association of IMPDH II gene SNPs with rejection are conflicting. Study aim was to evaluate the frequency of IMPHD II 3757T >CSNP among polish kidney recipients and its' association with post-transplant course.
Methods: In historical cohort study, 177 kidney recipients were genotyped for IMPHD II 3757T >C SNP, clinical data retrieved from medical files. Statistical analysis withWilcoxon and Fisher Exact Tests.
Results: F: requency of C allele IMPDH2 3757T >C was 15.2%, reported 9-12%. In early post-transplant period allelic variant of IMPDH II 3757C>T SNP associated with higher lymphocyte counts. In the polymorphic allele carriers there was tendency for higher lymphocyte counts in first and second post-transplant months 2.5 (0.2 - 5.3) *vs* 2.0 (0.2- 5.8) G/l; (p=0.06) and 2.3 (0.5 - 4.8) *vs* 1.9 (0.3- 4.2) G/l; (0.10). Lymphocyte counts below 1G/l were observed in 7/27 SNP carriers and 73/150 of non-carriers (p=0.052).
We found no association between allele C presence and acute rejection. Among common allele carriers acute rejection was diagnosed in 39/150, in C carriers 5/27 (p=0.62). Evaluation of early (within 3 month) and late (after 3 months) acute rejection remained similar: 31/150 vs 3/27 (p=0.13) and 14/150 vs 3/27 (p=0.72).
Conclusions: Lower lymphocyte counts in recipients with common IMPDH2 3757T >C variant stays in line with diminished enzyme activity reported by Sombogaard. It potentially predisposes for diminished alloreactivity. Our results incline towards conclusion that the risk of acute rejection may be increased in allelic variant carriers. Genotyping IMPDH2 3757T >C SNP may be of value in patient on MPA preparation and prior to calcineurin inhibitor diminution or withdrawal.

P-285 WEIGHT GAIN IN KIDNEY ALLOGRAFT RECIPIENTS CARRYING MDR2 2 4544G>A POLYMORPHISM

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Introduction and Aims: Multidrug resistance-associated protein 2 (MRP2) is an efflux pump responsible for excretion of xenobiotics and medications and potentially calcineurin inhibitors and mycophenolic acid. Post-transplant course may be associated with obesity and cachexia, both negatively influencing kidney recipient survival. In experimental studies MPA exposition results in diminished adipogenesis.
Study aim: To evaluate the impact of single nucleotide polymorphism 4544G>A (rs8187710) in the ABCC2 gene on post-transplant BMI gain in 97 kidney allograft recipients with primary immunosupression based on glucocoticoids, mycophenolate mofetil and either cyclosporine A or tacrolimus.
Methods: The ABCC2 4544A>G polymorphism was genotyped by specific PCR sequence amplification and restriction enzyme digestion (PCR-RFLP). Accuracy of the method was verified by direct amplicon sequencing using an ABI PRISM 377 DNA sequencer. General Linear Models were used to find interaction effect (GLM Procedure of SAS System).
Results: In patients on cyclosporine-based immunosuppressive regimen (n=63), carrying at least one allele A of ABCC2 4544G>A SNP was associated with significantly more pronounced time-dependent BMI gain. Body mass indexes were: 21.3±2.9 vs 22.7±3.1 at transplantation and 26.4±4.4 vs 24.5±3.5 at 24 months later (p=0.02 for interaction effect). In patients remaining on tacrolimus this time-dependent influence of allele A was not observed
Conclusions: Time-dependent effect of immunosuppressive treatment with mycophenolic acid and cyclosporine A on BMI derives from a complex interplay between drugs' metabolic effects, their elimination, gastrointestinal tolerance and the 4544G>A allelic variant of ABCC2 seem also to play a role here.

P-286 DOES PRE-OPERATIVE SPLIT RENAL FUNCTION TESTING PREDICT RESIDUAL POST-DONATION FUNCTION IN LIVING DONOR TRANSPLANTATION?

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Introduction: UK national guidelines for living donor assessment advise that split renal function testing is performed when there is significant disparity in kidney size so that if there is a significant difference in function the lesser functioning kidney should be removed. Our institutional guidelines include assessment of split kidney function in the routine work up for all live donors. This study aimed to see whether preoperative split function testing was predictive of post-donation function?
Methods: Records of 188 consecutive living donors were reviewed. Complete data was available for 174. CrEDTA GFR was measured to assess suitability for donation and a MAG3 renogram to assess split renal function. eGFR was assessed by the MDRD formula at the time of scan as well as postoperatively.
Results: The median follow up was 1 year (range 14-60 months)
The pre-donation mean eGFR was 74.5±8.50 $ml^{-1}.min^{-1}.1.73m^{2-1}$ compared to 46.5±4.46 immediately post op, 51.1±8.11 at 3 months, and 62.9±8.9 at 1 year.
There was no correlation between the theoretical remaining function and the actual change in function (r^2=0.13).
Patients with a split greater than 45%-55% (n=13) did not have a statistically significant difference in their remaining mean GFR when compared to the rest of the population (n=161) (mean 63.6±9.0 vs 62.5±8.4, p 0.55) at 1 year.
Conclusion: Preop knowledge of split function does not predict postop outcome.

In potential donors with equal or nearly equal sized kidneys it contributes little to the assessment.
Selected use of the test would result in a cost-saving of £270 (€ 314) per donor assessed. The mean GFR continues to improve following donation and rests at around 75-85% of the pre-donation GFR at 1 year.

P-287 CREATININE REDUCTION RATIO ON DAY 2: THE USEFUL MARKER FOR TRANSPLANT OUTCOME IN PATIENTS WITH LIVING DONOR TRANSPLANTATION

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Introduction: Delayed graft function (DGF) is a common complication after expanded criteria living renal transplantation (LRT). Although DGF is well defined, we introduced a criterion of creatinine reduction ratio between day 1 and 2 (CRR2) as a marker for graft survival in patients with LRT. Our first experiences are presented.
Methods: A retrospective study was performed in 120 LRT in the last 5 years.102 related and 18 unrelated donors are accepted. Daclizumab induction and triple drug (MMF, CyA and steroids) maintenance immunosuppression was used in all patients. According to the RR2 the patients were devided in group I (RR2 $>$ 30%) and group II (RR2 $<$ 30%). There were no difference between the groups in donor's age (61 vs 63), pretransplant GFR (80 vs 75 ml/min), recipient's age (40 vs 39), warm ischemia time (4 vs 3.7 min), cold ischemia time (225 vs 210 min) and HLA mismatch (2.4 vs 2.6). The serum creatinine (SCr) and creatinine clearance (CCL) were evaluated during the first week, 30th postoperative day and 24 months later.
Results: SCr on day 7th was 83$\pm$46 vs. 260$\pm$41, on day 30-th 98$\pm$20 vs 140$\pm$14 and 24 months later 121$\pm$8 vs 151 μmol/lit, in the groups I and II, respectively. The CCl was also superior on day 7th (77$\pm$13 vs 41$\pm$2) on day 30-th (78$\pm$14. vs 57$\pm$7) as well as 24 months later (60.3 vs 51.3 ml/min). No difference was observed in rejections (12% vs 14%) and graft lost (5 vs 6).
Conclusion: Our results confirmed that CRR2 correlates with renal function troughout the first two years after LRT. Defining DGF by CRR2 allows an objective diagnosis after transplantation and can help to modify the immunosuppression early after the surgery.

P-288 LARGE ANIMAL RENAL ALLOTRANSPLANTATION; A PORCINE RECOVERY MODEL TO ASSESS DELAYED GRAFT FUNCTION

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Aims: To test the impact of different organ preservation techniques on the primary function of DCD kidneys, in vivo. We studied differing flush, storage and recovery oxygenation methods; yet there is no limit to the permutations that might be applied to the model.
Methods: We used female cross-yorkshire landrace white pigs as donors (n=9) and litter matched females (n=18) as recipients. Donor kidneys were subjected to different treatments and recipients underwent bilateral native nephrectomy, allowing head-to-head comparison between animals.
ABO incompatibility was excluded.
Donor animals underwent laparotomy, cannulation of the aorta, and initial dissection before euthanasia by exsanguination. After 30minutes WIT, kidneys were retrieved and flushed at the back-bench, before 24-30hrs static storage.
Recipient renal implantation, by side-to-end vascular anastamoses to the infrarenal IVC and aorta. Ureteric reconstruction over a paediatric JJ stent by end-to-end anastamosis. A suprapubic catheter was inserted and tunnelled subcutaneously.
Animals were recovered for 6 days post-operatively. IV steroids, antibiotics, tacrolimus syrup bd and ranitidine syrup were administered daily. Daily blood sampling by central line. Post mortem conducted at day 6 after euthanasia of the recipients.
Results: Of 18 recipients;16 survived to day 6. 1 animal died suddenly at the start of day 6 following a brisk GI-bleed (following this H2-antagonists were administered post-operatively). 2 animals were euthanased on the evening of Day-5 when one subject developed severe ataxia and respiratory embarrassment with primary non-function of the allograft.
All animals displayed a degree of delayed graft function.
Conclusion: We present a simple model that serves as a pre-clinical assessment tool, with the aim, to expand the donor pool from DCD donors.
Warm ischaemic times can be adjusted to reproduce both "controlled" and "uncontrolled" Maastricht category donors. A shortened warm ischaemic time would undoubtedly reduce the degree of delayed graft function.

P-289 COMPARISON AMONG ACUTE REJECTION MEDITED BY CELLULAR AND ANTIBODY MECHANISMS IN PATIENTS SUBMITTED TO IDENTIFICATION OF C4d AND DSA IN RENAL BIOPSY

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Objective: To evaluate the incidence of antibody mediated rejection after the C4d and donor specific antibody detection was provided by Luminex in renal transplantation biopsies; to compare acute antibody-mediated rejection characteristics as related to acute cellular rejection.
Methods: 124 renal transplanted patients were evaluated through the detection of C4d in early biopsies of those presenting graft dysfunction and the detection of antibody against donor when C4d was positive. The acute antibody mediated rejection was treated by plasmapheresis and intravenous immunoglobulin.
Results: The incidence of acute rejection was 18.8%, being the acute cellular rejection 14.9% and acute antibody mediated rejection 6.6%. When both were compared, the main important different demographic data were presented in Table 1.

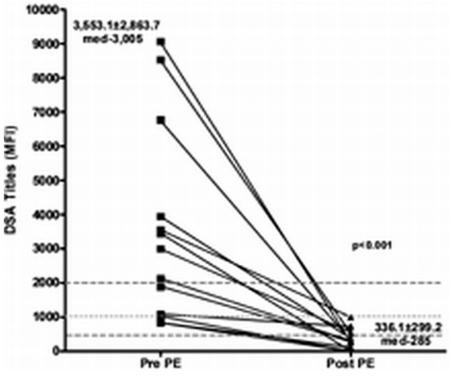
Table 1. Demographic data according type of AR

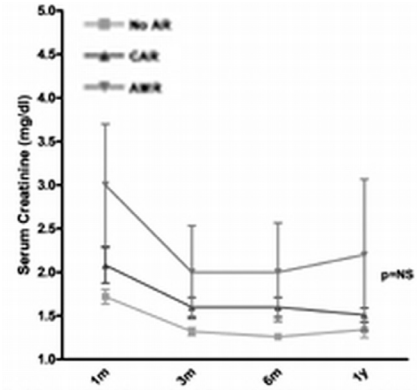
Variables	No AR	CAR	AMR	p
TIme in list (mo)	51.1	43.4	82.4	0.01
PRA	3.6	1.9	25.9	0.01
Re-transplant	2.3	6.7	30	0.002
Blood transfusion	1.9	2.0	4.2	0.05
HLA missmatch	2.9	3.5	2.7	0.06
Idade	44.2	40.8	51.2	0.04

Delayed graft function was more frequent in antibody mediated rejection (100% vs. 50%, p = 0.02). All patients with acute cellular rejection reversed graft function after treatment, with 100% graft survival after one year. Among patients with acute antibody mediated rejection, the treatment with plasmaferesis and immunoglobulin was efficient in reducing the titers of donor specific antibody (2605 vs. 202 mfi, p$<$0.001, figure 1, but 3/8 of patients evaluated with graft loss, making graft survival of 62.5% (p$<$0.001). Clinical and histological pictures in AMR patients were variable an is present in Table 2: more patients presented ATN with Cd4+.
Graft function was significantly worse in patients with AMR.

Table 2. Clinical and pathological pictures

Patient	Clinical Picture	OM	C4d	Control
1	DGF + Hemolysisi	TMA	+50%	TMA+C4d $>$50%
2	DGF	VR	30%	C4d neg
3	DGF	CCPT	neg	C4d neg
4	DGF	ATN	+50%	NR
5	DGF in AD	VR	30%	C4d neg
6	DGF in AD	ATN	+50%	C4d neg
7	DGF	ATN	+50%	NR
8	DGF	CCPT	+50%	C4d neg + CAR
9	DGF	CCPT	+50%	C4d neg
10	DGF + Hemolysisi	ATN	neg	C4d neg
11	DGF	ATN	+50%	NR





	1m	3m	6m	1y
No AR	1,7±1,0	1,3±0,5	1,2±0,3	1,3±1,0
CAR	2,0±1,1	1,6±0,6	1,6±0,6	1,5±0,4
AMR	3,0±2,1	2,0±1,6	2,0±1,6	2,2±2,3

Conclusions: The routine use of detecting C4d and donor specific antibody increased the incidence of acute rejection. Acute antibody mediated rejection presented clinical profile and therapeutic response different from acute cellular rejection identifying a worse prognosis as well as therapeutic success.

P-290 CARDIOVASCULAR RISK ASSESSMENT FOR RENAL TRANSPLANTATION. ARE PATIENTS BEING MANAGED APPROPRIATELY IN OUR HOSPITAL?

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Background: Cardiovascular (CV) disease remains a leading cause of post-renal transplantation morbidity and mortality. Currently, there is little consensus regarding both cardiovascular screening and management of coronary artery disease (CAD) prior to renal transplantation.
Purpose: To determine the effectiveness of current cardiovascular risk assessment, and ascertain whether attendance at a cardio-renal clinic before renal transplantation influences the incidence of Major Adverse Cardiac Events (MACE). Furthermore we sought to evaluate the impact of coronary artery revascularisation pre-transplantation on peri-transplant MACE.
Methods: A specialised cardio-renal clinic was established in 2003 at our hospital. Patients that received renal transplantation between January 2003-June 2010 and contact with the cardiology department were included in the study.
Results: A total of 116 patients (41% female, 59% male) underwent renal transplantation and had contact with the cardiology department; median age 51 years (range 24-71). Time between transplantation and data collection ~3.25 years.
Of the cohort, 41/116 (35%) had a cardiac problem and were seen in the cardio-renal clinic (24% low, 46% medium, 29% high CV risk). Of these, 28/41 (68%) attended the clinic pre-transplantation and 13/41 (32%) post-transplantation. Altogether, 4/41 (10%) experienced MACE; 3 had MI and 1 had cardiac arrest. Time between transplantation and MACE ~17 months. All patients reviewed in the cardio-renal clinic were free of peri-transplant MACE. A total of 20/41 (49%) underwent coronary angiography, of these 6/20 (30%) had no CAD (incidence MACE 0%) and 14/20 (70%) had CAD (incidence MACE 21%). Before transplantation, 6/41 (15%) underwent coronary artery revascularisation. None experienced MACE peri-transplantation. Percentage incidence of MACE increased with CV risk.
Low risk patients not seen in clinic (75/116, 65%) experienced no MACE post-transplantation.
Conclusion: Establishment of a specialised cardio-renal clinic at our hospital risk has contributed to effective and appropriate management of cardiac risk in renal transplant patients.

P-291 COMPARISON OF THE EFFICACY AND SAFETY OF CALCINEURIN INHIBITOR CONVERSION TO mTOR INHIBITOR AND CNI MINIMIZATION IN KIDNEY TRANSPLANTS WITH CHRONIC ALLOGRAFT NEPHROPATHY

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Background: CNI minimization or conversion to mammalian target of rapamycin inhibitor (mTORi) may be beneficial in the treatment of CAN.
Objective: The aim of this study was to compare the efficacy and safety between CNI conversion to mTORi and CNI minimization in the patients with CAN.
Methods: We performed a retrospective cohort study among 96 patients with biopsy-proven CAN between January 2001 and December 2008. We enrolled the patients who underwent kidney transplantation more than 3 months and had been on standard dosage of CNI, mycophenolate and steroid. The patients with prior rejection within 3 months before biopsy or concurrent evidence of rejection were excluded.
Results: Of 36 patients with biopsy-proven CAN, 21 patients were switched from CNI to mTORi whereas 15 patients had CNI minimization. In conversion group; mean GFR was improved at 6 month compared to baseline and remained stable at 12 and 24 months (p=0.002, 0.002 and 0.01, respectively). In CNI minimization group; mean GFR at 6 and 12 months were improved compared to baseline (p=0.02 and 0.05, respectively) but gradually decreased during the second year. In multivariable analysis, factors predicted graft failure after conversion were baseline GFR less than 21.3 mL/min and more than 60% IF/TA prior to conversion. There was no significant difference in proteinuria and side effects between two groups.
Conclusion: CNI conversion to mTORi in patients with CAN demonstrated improvement of renal function through 24 months, particularly in the subgroup with baseline GFR more than 21.3 mL/min and IF/TA less than 60%. CNI minimization strategy showed the benefit only in the first year. The prospective randomized controlled trials to compare the efficacy and cost effectiveness of these two regimens are needed.

P-292 PREDICTIVE REGRESSION MODELS IN A SINGLE-CENTER SERIES OF DOUBLE KIDNEY TRANSPLANTATION

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Background: Double kidney transplantation (DKT) may be a useful approach to reduce the number of discarded marginal kidneys. In this study, we retrospectively evaluated the potential predictors for patient and graft survival in a single-center series of 59 DKT procedures performed in the period 1999-2008.
Patients and Methods: The kidney recipients (mean age 63.27±5.17 years) included 16 women (27%) and 43 men (73%). The donors (mean age 69.54±7.48 years) included 32 women (54%) and 27 men (46%). The mean post-transplant dialysis time was 2.37±3.61 days. The mean hospitalization was 20.12±13.65 days. Serum creatinine (SCr) at discharge was 1.5±0.59 mg/dL. The proportional hazards assumption for each Cox regression model with $P < 0.05$ was tested by using correlation coefficients between transformed survival times and scaled Schoenfeld residuals.
Results: In Cox models for patient survival, the variables that reached statistical significance were donor SCr (P=0.007), donor creatinine clearance (P=0.023), and recipient age (P=0.047). By entering these variables into a multivariate model for patient survival, no further significance was observed. In the univariate Cox models performed for graft survival, statistical significance was noted for donor SCr (P=0.027), SCr 3 months post-DKT (P=0.043), and SCr 6 months post-DKT (P=0.017). A final multivariate model retained SCr at 6 months (P=0.042) and donor SCr (P=0.090).
Conclusions: SCr at 6 months seemed to emerge from both univariate and multivariate Cox models as a potential predictor of graft survival in DKT. Multicenter studies with larger double kidney recipient populations should be performed to confirm this finding.

P-293 THYMOGLOBULIN INDUCTION IN LIVING-DONOR RENAL TRANSPLANTATION

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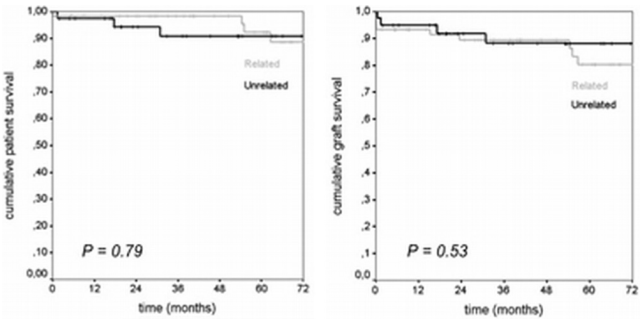
Background: The use of Thymoglobulin induction therapy in living-donor renal transplantation remains controversial. We aimed to evaluate outcomes in living-related donor (LRD) and living unrelated donor (LURD) renal transplants with Thymoglobulin induction.
Material and Methods: We retrospectively analysed the outcome of all Thymoglobulin induced living-donor renal transplants performed at our centre from 2002 to 2010.
Results: We reviewed 100 living-donor renal transplants (LRD = 60; LURD = 40) who received thymoglobulin induction (single dose, 1.5 mg/kg bodyweight) with a mean follow-up of 52.6±31.9 months. Although baseline characteristics of the LRD and LURD groups were similar, differences were noted for recipient age, gender, and HLA-matching. Overall, the estimated 5-year patient survival was 92% and graft survival, 83%. The 1- and 5-year patient survival rates were 97.4% and 90.7% for LRD and 98.3% and 92.2% for LURD (P =

0.79), respectively. Cumulative graft survival (LRD vs. LURD) rates were 93% vs. 95% after 1 year and 80% vs. 88% after 5 years (P = 0.53). Kidney graft function was comparable for both the groups. Acute rejection was observed in 17% LRD and 35% LURD patients (P = 0.035). Further, 10% of the patients experienced delayed graft function (LRD 11% vs. LURD 8%; P = NS). Rates of cytomegalovirus (CMV) infection (10%), polyomavirus infection (5%), malignancy (4%), and lymphoproliferative disorder (0%) were low, with no differences between the 2 groups.



Conclusion: Single-dose thymoglobulin induction in living-donor renal transplantation was associated with high patient and graft survival without increasing the risk of infections or malignancy and without significant differences between LRD and LURD patients.

P-294 EARLY DIAGNOSIS AND IMPACT OF TRANSPLANT RENAL ARTERY STENOSIS TREATED BY ANGIOPLASTY

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Background: Transplant Renal Artery Stenosis (TRAS) is a well reported, potentially curable complication with a prevalence of 1-23%.
Material & Method: We reviewed our renal transplants between April 2006 to December 2010. Magnetic resonance angiography (MRA) was used to investigate clinically underperforming transplants. Those appeared radiologically to have a significant TRAS underwent catheter angiography and proceeded to angioplasty if there was evidence of a significant stenosis or a demonstrable pressure gradient. Clinical outcomes were compared using the paired students t-test.
Results: Three hundred and seventy transplants were undertaken, of which 137 (37%) required an MRA as a result of an elevated serum creatinnine in the absence of hydronephrosis, rejection or pyelonephritis. Thirty five patients proceeded to angiography, of which 20 (57%) were deemed to have a significant lesion. Two of these were inaccessible, and 18 (3 live donor, 15 deceased donor including one peadiatric enbloc) underwent 29 angioplasties. Sixteen of these were within a year of transplantation. The re-treatment rate was six (33%). There was a significant improvement in estimated Glomerular Filtration Rate [Cockroft-Gault method] at three months (p=0.02). A modest improvement in hypertension was noted in four patients (22%) as defined by discontinuation of, or reduction in anti-hypertensive dosage. There was no significant weight reduction. Graft survival at a mean of 24 months follow-up was 16 (88%).
Discussion: MRA appears to be a reasonable non-invasive diagnostic tool for detecting TRAS which in this series is 5.4%. Angioplasty within this selected group resulted in only modest improvement in blood pressure in contrast to that seen in native RAS. In the transplant setting angioplasty alone is associated with a high retreatment rate. A multi-centre randomized trial comparing our current approach with the addition of stenting may be warranted

P-295 THE EFFECT OF COLD ISCHEMIA TIME ON THE DELAYED GRAFT FUNCTION AND ACUTE REJECTION IN KIDNEY TRANSPLANTATION

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Aim: To evaluate the relationship between cold ischemia time, delayed graft function and acute rejection episodes among the patients underwent deceased donor kidney transplantation.
Material: Medical records of 111 patients who underwent to kidney transplantation from deceased donors between Now,1994 and July, 2009 were retrospectively analyzed. To examine the impact of cold ischemia time on delayed graft function (DGF) and acute rejection (AR); 1,3 and 5 year level of serum creatinine, 1 and 5 year level of creatinine clearance, demographic parameters of donor and recipient were reviewed.
Findings: The mean cold ischemia time of the kidney was 14,6±5.5 hours. DGF was observed 54% of the patients and AR rate within first one year after transplantation was 9,9%. Incidence of DGF was higher among patients with longer cold ischemia time. (< p 0.05) The correlation between cold ischemia time and AR episodes weren't statisticaly significant. (p 0.43)
1, 3 and 5 year serum creatinine levels and hospitalisation time of patients with DGF were higher compared to patients without DGF.(< p 0.05) Altough there was a correlation between AR episodes and 1.3. and 5 year serum creatinine levels of the patients, it wasn't statistically significant. (p 0.76, p 0.74, p 0.56) Higher body weight of donor and recipient and older donor age were a significant risk factors for DGF. (< p 0.05)
Conclusion: Shortening cold ischemia time may help to decrease delayed graft function rates with the patients undergo deceased donor kidney transplantation. Thanks to decrease of delayed graft function rates, it may improve the graft function 1, 3 and 5 years after transplantation and diminish the hospital stay.

P-296 ALLOGRAFT OUTCOME OF SPOUSAL AND LIVING UNRELATED RENAL TRANSPLANTATION

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Background: Due to the inadequacy of the donor pool, spousal and living unrelated donors (LUD) can provide an additional source of kidney transplantation. In this study, we compared the outcomes of spousal transplantations with LUD allografts.
Methods: During five years we retrospectively analyzed the spousal and living unrelated renal transplant patients. Totally 378 patients were transplanted, among these; 25 corresponded to wife-to-husband (Gr 1), 15 were husband-to-wife (Gr 2) and 20 were LUD (Gr 3). The clinical characteristics and 1 and 3 years survival rates were compared.
Results: Of these patients 37 were male and 23 were female. The average recipient and donor age was 44±12,43±10 years, respectively. The number of human leukocyte antigen mismatches were 4.6, 3.3 and 3.9 in Gr 1, Gr 2 and Gr 3, respectively. Fifty - six (93.3%) of the patients received induction therapy with either anti-thymocyte globulin (n = 30) or anti-interleukin-2 receptor antibody (n = 26). Maintenance immunosuppression were tacrolimus+mycophenolate mofetil (MMF) in 37 (61.6%) and cyclosporine+MMF in 23 (38.4) with corticosteroids. Mean follow-up was 34±16 months. During this time, there were 4 graft loss (1 in Gr 1, 1 in Gr 2 and 2 in Gr 3) and 5 patient dead (2 in Gr 1 and 3 in Gr 3). According to the Kaplan Meier analysis, 3 year patient survival rates were 94, 100 and 88% in Gr 1, Gr 2 and Gr 3, respectively (p<0.05). Overall graft survival rates were 94, 100 and 77% in Gr 1, Gr 2 and Gr 3, respectively (p<0.05).
Conclusion: Utilization of living unrelated and spousal donors have yielded similar patient and graft survival rates compared to current practice; and must be encouraged both the patient and family.

P-297 SIGNIFICANT ASSOCIATION BETWEEN RESULT OF NOVEL CROSSMATCH TEST AND ANTIBODY-MEDIATED REJECTION AFTER RENAL TRANSPLANTATION

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Background: Antibody-mediated rejection (AMR) in renal transplantation has recently received focus against a background of decreasing acute cellular rejection. Several methods have been developed for detecting donor-specific HLA antibodies (DSA), though each presents a difficulty. Complement dependent cytotoxicity (CDC) and flow cytometry crossmatch (FCXM) have risks of false-positive results with a non-HLA antibody, and single-antigen bead test is too sensitive for clinical transplantation settings. Thus, we evaluated immunocomplex capture fluorescence analysis (ICFA); a novel crossmatch test to detect clinically significant DSA causing AMR.
Material and Methods: From 1997 to 2010, 326 patients underwent renal transplantation at 3 institutions, of whom 25 were positive for pre-transplant DSA and underwent a graft biopsy, and then were enrolled in this study. ICFA was performed according to the manufacturer's protocol using preserved sera, and the association between each result and AMR was reviewed. Briefly, donor lymphocytes reacting with patient serum were lysed and the lysates were incubated with beads coated with monoclonal antibodies specific for HLA

molecules. Beads that captured HLA immunocomplexes were analyzed with a Luminex100 system.
Results: Of the 25 patients positive for pre-transplant DSA, seven (28%) showed positive for ICFA class I. Five (71%) of 7 with positive ICFA results developed AMR, while only 1 (5.6%) of 18 with negative ICFA results developed AMR. There was a significant relationship between the ICFA result and AMR incidence (p=0.002). The value for molecules of equivalent soluble fluorochrome (MESF) of DSA was 24 414±5 123 (mean ± SE) in the ICFA class I positive group and 766±189 in the negative group ($p<0.0001$).
Conclusion: Our results showed that the present novel ICFA indicates clinically significant DSA causing AMR, promising this test would be useful for pre-transplant evaluation to determine appropriate immunosuppressive treatment.

P-298 OUTCOMES OF LIVE KIDNEY DONOR WORK-UP: A SINGLE CENTRE EXPERIENCE

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Background: Many potential donors are referred for live kidney donation (LKD), but only small percentage actually become donors. The aim aimed to assess the outcomes of LKD work up at our centre and to identify modifiable factors to increase the number of LKD.
Methods: A review of departmental database and case notes of all potential live kidney donors (PLKD) referred over 15 year period was carried out and outcomes of LKD work up was assessed.
Results: Of the 667 PLKDs evaluated, 152 (22.8%) proceeded to actual kidney donation. The reasons for non-donation are shown below.

Table 1

Donor-related reasons	291 (57%)
Recipient-related reasons	109 (21%)
ABO-incompatibility	72 (14%)
Positive cross-match	43 (8%)
Total	515

The donor-related reasons for non-donation were medical causes (n=96, 18.6%), donor withdrawal (n=55, 10.7%), renal vascular abnormalities (n=30, 5.8%), low glomerular filtration rate (n=22, 4.3%), urological abnormalities (n=21, 4%), and high body mass index (n=5, 1%). Although the PLKDs were suitable, donation was declined for recipient-related reasons such as existing cardiovascular co-morbidities (n= 44, 8.5%), a kidney transplant from a deceased donor (n=42, 8.1%), refusal by recipients (n=10, 2%), and patients transferred to other centres (n=6, 1.2%).
Discussion: Twenty-two percent (n=115) of the donor evaluated could not proceed to kidney donation from ABO incompatibility and positive cross match, which is a potential future source of donors to utilise. Increasing number of transplant centres, including our own centre, have recently adopted desensitisation and paired organ donation programmes. Importantly, thorough evaluation of the recipients is mandatory to exclude unsuitable recipients at a very early stage of live donor work-up. It is also important to remove recipients from the deceased donor transplant waiting list once the donor is fully worked up and theatre date scheduled in order to avoid disappointments.

P-299 ESTIMATED GLOMERULAR FILTRATION RATE AND LONG-TERM OUTCOMES FOLLOWING LIVE KIDNEY DONATION: A SINGLE CENTRE EXPERIENCE

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Background: Following kidney donation, a significant reduction in glomerular filtration rate (GFR) occurs, which may categorise them into stage 3 chronic kidney disease (CKD) as per K/DOQI NKF guidelines. The study aimed to examine the changes in the renal function (serum creatinine, eGFR and proteinuria) and long-term outcomes following kidney donation.
Methods: 164 live kidney donors were included in the study. The estimated glomerular filtration rate (eGFR) was calculated by using Modification of Diet in Renal Disease (MDRD) formula. Serum creatinine, eGFR, proteinuria, body mass index and blood pressure were measured before and after (3, 6, 12 and 36 months) kidney donation.
Results: The average age at donation was 43±11 years, with 50% being male. The mean pre-donation serum creatinine and eGFR were 76±14 μmol/L and 85±15 ml/min/1.73m^2, respectively. The serum creatinine increased to 108±24, 109±22, 109±21 and 106±21μmol/L and the eGFR decreased to 56±10, 51±18, 56±17 and 57±12 ml/min/1.73m^2 at 3, 6, 12 and 36 months, respectively. There was 34±9, 35±11, 33±9 and 35±18% fall in eGFR at 3, 6, 12 and 36 months, respectively, compared to the pre-donation level ($P<0.001$). At the end of 1 year 67% of the donors had a median eGFR of 50 ml/min/1.73m^2 (range, 35-59), thereby falling into the category of stage 3 CKD. However there was no significant proteinuria and hypertension post-donation.
Discussion: Although significant decline in renal function occurred after kidney donation, there was no significant proteinuria or hypertension in long-term follow-up. We conclude that reduction of eGFR after kidney donation should not raise any concern.

P-300 DOES CHRONIC ACTIVE ANTIBODY-MEDIATED REJECTION HAVE BETTER PROGNOSIS THAN CHRONIC T- CELL MEDIATED REJECTION?

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Chronic rejection is a main cause of renal allograft loss in long-term. Banff classification distinguishes between chronic T- cell mediated rejection (chronic TCMR) and chronic active antibody mediated rejection (late AMR).
The objective of this retrospective single centre study was to analyze documentation and biopsy material from 56 patients who underwent renal biopsy between 01/2003 and 01/2009 and developed chronic rejection. Diagnosis was based on the presence of chronic rejection in histological findings, C4d+ staining and detection of donor specific antibodies. Maintenance immunossuppresive therapy was based on tacrolimus, mycophenolate mophetil and corticosteroids. This treatment was administered in 20 out of 36 patients with diagnosis of late AMR and in 8 out of 20 patients with diagnosis of chronic TCMR. The patients were followed-up for 12 months from date of diagnosis.
There were no differences between donor age, PRA, HLA mismatches and the length of dialysis. The diagnosis of late AMR and chronic TCMR was determined at similar time after kidney transplantation (2.66±3.28 vs. 1.74±2.78 years, p= ns), predominantly in younger patients in case of late AMR (46.11±11.88 vs. 55.65±9.62 years, p= 0.002). The induction therapy with antithymocyte globulin or OKT3 was used more frequently in AMR patients compared to chronic TCMR patients. Renal function at biopsy was better in patients with diagnosis of late AMR compared to chronic TCMR (242.67±130.46 μmol/l vs. 320.06±163.85μmol/l, p= 0.033). There were no significant differences in proteinuria at 1-year after diagnosis (1.59±2.53 vs. 2.99±6.37 g/day), graft (72.22% vs. 70%) and patient survival (100% vs. 100%)
In this study, both chronic AMR and CMR share many similarities in their clinical presentation.

P-301 PROGNOSTIC ROLE OF PRE-TRANSPLANT DONOR KIDNEY BIOPSIES

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Background: Pre-transplant donor kidney biopsy ("0-biopsy") is a common practice in marginal donor. But "0-biopsy" can provide important information about kidneys from all donors. The aim of this study was to detect an impact of the initial state of a donor kidney on future renal graft function.
Materials and methodology: We analyzed 71 "0-biopsies" that were performed on a donor kidney (normally – right kidney) between 01.01.2004 and 31.12.2007. The study included patients who received a biopsied donor kidney (altogether 71 recipients). Patients were divided into three groups based on "0-biopsies" findings: group A – patients with 0-10% of nephrosclerosis on "0-biopsy"; group B – with 11-20% of nephrosclerosis on "0-biopsy"; group C – over 20% of nephrosclerosis on "0-biopsy". The patients have been observed for 3 years.
The groups were compared for the graft function and number of patients and graft loss during the follow up period.
Results: Histological examination revealed that 37 patients had 0-10% of nephrosclerosis on "0-biopsy" (group A), 21 patients had 11-20% of nephrosclerosis on "0-biopsy" (group B) and 7 patients had over 20% of nephrosclerosis on "0-biopsy" (group C). Six biopsy cases presented insufficient material for investigation. Comparison of the groups showed that in patients with more serious sclerotic changes more often develop delayed graft function ($p<0,05$), they have a worse graft function late after operation ($p<0,05$) and higher risk of acute rejection and graft loss ($p< 0,05$).
Conclusion: Pre-transplant donor kidney biopsy can help predict further kidney graft function and, thus, select an optimal treatment scheme after transplantation.

P-302 INFLUENCE OF POLYMORPHISMS GLUTATHIONE S-TRANSFERASE AND ANTI-GSTT1 ANTIBODY ON ALLOGRAFT OUTCOME IN RENAL TRANSPLANT RECIPIENTS

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The balance between oxidative stress and antioxidant defenses after kidney transplantation may be important to determine the development and progression to allograft dysfunction. Enzymes of the glutathione S-transferase (GST) are reduce the damaging effects of oxidative stress. On the other hand, when antibody response occurred in the receiver antibodies against glutathione-*S*-transferase T1 (GSTT1) expressed on the graft may lead to graft dysfunction. The aim of the study, polymorphisms of GST and anti-GSTT1 antibodies investigate the relationship between the development of acute/chronic rejection after transplantation.

The study included 122 patients/donors who underwent live donor primary transplant and 173 controls. Patients, 57 acute/chronic rejection episodes and 65 stabil graft function post tranplantation. The GSTT1 and GSTM1 polymorphisms were identified by polymerase chain reaction (PCR), GSTP1Ile105Val polymorphism was determined by PCR-RFLP. Anti-GSTT1 antibodies were studied by an ELISA.

When we evaluate the allele and genotype frequency of GSTT1, GSTM1, GSTP1 polymorphisms between recipient, donor and control group, there was no significant difference. We found that the rejection frequency is higher for the patients who were using cyclosiporine A comparing to patients who were using tacrolimus for the rejection group who with GSTM1 null genotype (p=0.029).

Anti-GSTT1 antibody was tested for 46 patients who with GSTT1 null genotype from whole patient group. Anti-GSTT1 antibody was positive for five of eight patients who have acute rejection attack and also it was positive for seven of thirty-eight patients who do not have acute rejection attack (p=0.01). When anti-GSTT1 antibody is evaluated in terms of calcineurin inhibitors, it is not statistically significant although patients who treated with cyclosporine A was higher compared to tacrolimus treated patients

P-303 TREATMENT OF VITAMIN D DEFICIENCY AND ITS IMPACT ON ALBUMIN EXCRETION IN KIDNEY TRANSPLANT RECIPIENTS: PRELIMINARY RESULTS OF A RANDOMIZED CONTROLLED TRIAL

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Background: The vitamin D system is considered to exert reno-protective effects. Indeed, the VITAL study recently proved that the active vitamin D analogue paricalcitol reduces residual albuminuria in patients with type 2 diabetic nephropathy who were treated with angiotensin-converting enzyme inhibitors or angiotensin receptor blockers (De Zeeuw, D. et al. Lancet 2010; 376: 1543-51). Whether treatment with the precursor, vitamin D3, influences albumin excretion in kidney transplant recipients, has not been studied today. Therefore, we aim to evaluate the effect of vitamin D3 therapy on albuminuria in vitamin D deficient kidney transplant recipients.

Methods/Materials: Within a randomized, controlled trial we are currently studying the immunomodulatory and reno-protective effects of high-dose vitamin D3 therapy in kidney transplant recipients showing 25-hydroxyvitamin D levels < 50 nmol/l at the time of transplantation. In total, 200 kidney transplant recipients will be randomized to receive either vitamin D3 at a dose of 6.800 International Units per day for one year or placebo. This interim report focuses on the effects of vitamin D3 on albuminuria at 6 months after treatment start. Albumin excretion is analyzed by means of the albumin/creatinine ratio in 24-hour urine samples.

Results: So far, we included 86 kidney transplant recipients. At 6 months after treatment start, median (minimum and maximum) albumin/creatinine ratio was 27 (3-99) mg/g in the vitamin D3-treated group (n=17) compared with 24 (6-143) mg/g in the placebo group (n=15). Albumin/creatinine ratio was elevated (> 30 mg/g) in 8 vitamin D3-treated participants (47%) compared with 6 placebo-treated participants (40%).

Conclusion: So far, our preliminary data suggest no difference in albumin excretion between the vitamin D3 and the placebo group.

P-304 RENAL FUNCTION MONITORING AFTER ORTHOTOPIC LIVER TRANSPLANTATION: ONE YEAR FOLLOW-UP

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Background: Kidney function in patients who are awaiting OLT is frequently compromised. Acute and chronic renal dysfunction (ARD and CRD) are common complications after orthotopic liver transplantation (OLT) and adversely affect patient survival.

Aim: Aim of our study was to assess the incidence of CRD after OLT and to evaluate the role of pre- and peri-OLT renal dysfunction.

Methods: Single centre study of 54 patients who underwent OLT 08/2008-01/2011. Pre-transplant, peri-operative and 1, 6 and 12 months post-transplant renal function was evaluated.

ARD was defined by RIFLE criteria, CRD was defined as a GFR $<$ 60 mL/min/1.73 m2 for more than 3 months (KDOQI).

Immunosuppressive therapy was based on a triple regimen with calcineurin inhibitors (CNI) in 86% of patients or mammalian target of rapamycin in 14% of patients. Introduction of CNI were delayed when renal function was compromised.

Results: Incidence of pre and post-OLT renal dysfunction is showed in the table.

Incidence of pre- and post-OLT renal dysfunction

	CRD pre-OLT	ARD	CRD 1 month post-OLT	CRD 6 months post-OLT	CRD 12 months post-OLT
No. of patients (%)	10/54 (18.5)	29/54 (53.7)	9/44 (20.5)	4/34 (11.8)	2/22 (9.1)

CRD: chronic renal dysfunction; ARD: acute renal dysfunction.

CRD 6 months post-OLT was associated with CRD pre-OLT (p=0.006) and 1 month post-OLT (p= 0.021). ARD was not associated with pre and post-OLT renal dysfunction. No association has been found between post-OLT renal function and CNI based immunosuppression.

Conclusions: Many different factors may contribute to the development of post-transplant CRD; in our series pre-OLT CRD seems to be the most important risk factor. We suggest that the evaluation of pre-OLT renal function should be always considered in the follow-up of liver transplant patients. CNI therapy may play a further role on already damaged kidney.

P-305 ACTIVATION OF MITOCHONDRIAL APOPTOTIC PATHWAY IN CADAVER KIDNEY TRANSPLANTATION LEADS TO THE SLOW GRAFT FUNCTION (SGF)

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Background: Slow kidney allograft (KAG) function is associated with decreased allograft survival, and is caused by interplay of ischemic and immunological factors. We aimed to study the apoptosis extent and mechanisms during ischemia-reperfusion injury (IRI) in cadaver kidney transplantation and gain an insight into those factors linking reperfusion to alloimmunity and development of SGF.

Methods/Materials: The study was conducted on the 75 recipients of cadaveric kidneys transplanted in our centre during 2005-2007. Biopsy was taken in 30 minutes after reperfusion and sections were stained with H&E and immunoperoxidase labeling with antibodies to leukocyte markers: CD45R0, CD68, and key regulators of mitochondrial apoptosis: bax and bcl-2. Apoptotic cells number per HPF were counted amongst tubular cells in H&E-stained sections. The number of T-lymphocytes and macrophages in interstitium per HPF, the percentage of bcl-2- and bax-positive cells amongst tubular cells were also scored.

Results: Immediate graft function (IGF) occurred in 55 patients, SGF - in 20 patients. In SGF-group the percentage of bax-positive tubular cells was higher than in IGF-group: 17,4% vs. 9,9% ($P<0,0001$). The percentage of bcl-2-positive tubular cells was less than in IGF-group: 27,9% vs. 42,1% ($P<0,0001$). As a result, the number of apoptotic cells was higher: 8 (3-10) vs. 5 (2-7), $P<0,05$. This stimulated higher graft infiltration by macrophages: 13 (8-26) vs. 5 (2-12) in IGF-group, $P<0,0001$, and T-lymphocytes 19 (3-36) vs. 8 (4-21) in IGF-group, $P<0,0001$.

Conclusion: Our data suggest that the renal tubular epithelial cells apoptosis during IRI mediated at least in part by activation of mitochondrial pathway. The higher apoptotic cells number may be predictive of cadaver graft immunogenicity and provoke mononuclear graft infiltration after reperfusion. Early inflammatory events after reperfusion may provoke SGF.

P-306 VENOUS DISPOSITION PROCEDURE (VDP) ON THE SHORT RENAL VEIN REMOVING BY LAPAROSCOPY: A SIMPLE PROCEDURE

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Background: The right renal vein (RRV) from living donor is usually short. A vein graft by saphene or genital vein is needful. We introduce a simple anastomosis technique by moving the right iliac vein (RIV) and prolonging the RRV, we call it the VDP.
Methods and Materials: This is a case study, in Cho Ray Hospital from 2004 to 2010. Patients (pts) were selected by its compatibility with donor, the graft is right kidney removed by retroperitoneal laparoscopy. Exclusion criteria: RRV $<$ 0.5cm; previous surgery on RIF.
The VDP concludes 2 steps:
(1) Dissect RIV ex situ in 4oC Euro-Collins solution, prolong the RIV and made a renal arterial disposition.
(2) A Gibson incision on the RIF of pts, dissect the RIV and move it to the right side of the external iliac artery which becomes nearer to RRV and a venous anastomosis was done.
Results: 60 pts undergoing the transplantation with right kidney. Mean age is 35.93$\pm$8.7 yo; 71.67% were males. The average following up time is 49.6$\pm$33.8 months, range [3, 144]. The VDP were successful for all of pts. There were not any arterial or venous complications.
Conclusion: Our VDP were successful on 60 cases. This procedure based on surgical anatomy. The technique is simple. A venous plastic surgery is needless.

P-307 THE EFFECT OF ANEMIA ON KIDNEY FUNCTION IN LIVING KIDNEY TRANSPLANTATION

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Background: Anemia is a risk factor of cardiovascular events and deteorientation of renal function in chronic kidney disease. However, there is no consensus about the optimal range of targeted hemoglobin (Hb) level in kidney transplantation. The aim of this study was to examine the influence of Hb level at 6 months on kidney function at 12 months.
Methods: 190 patients were retrospectively analyzed who received living kidney transplantation between 2006 and 2009 in single center, Nagoya Daini Red Cross Hospital, Japan. Anemia was defined as hemoglobin $<$11 g/dl. Kidney function was estimated by estimated glomerular filtration rate (eGFR) modified for Japanese, and low eGFR was defined as less than 50 ml/min/1.73m^2. Logistic regression analyses assessed the association of Hb levels at 6 months with eGFR at 12 months. Multivariable models were adjusted with age, sex, erythropoietin stimulating agents (ESA) use, iron supplementation, and angiotensin II receptor blockers (ARB) use.
Result: Mean Hb was 11.28$\pm$1.41 g/dl and 11.67$\pm$1.43 g/dl at 6 months and 12 months. The percentage of anemia was 47.8% and 30.2%, respectively. Mean eGFR was 44.01$\pm$12.03 ml/min/1.73m^2,and 43.41$\pm$12.16 ml/min/1.73m^2. In univariable analyses, patients with 1 g/dl higher Hb at 6 months had significantly associated with better kidney function at 12 months [Odds Ratio (95%CI): 0.693 (0.551-0.871), p value 0.002]. Multivariable adjustments did not attenuate its effect. [Odds Ratio: 0.630 (0.482-0.824), p value 0.001].

	Univariable model		Multivariable model	
	Odds Ratio(95%CI)	p value	Odds Ratio(95%CI)	p value
age (per 1 year)	1.024(1.000-1.049)	0.048	1.041(1.012-1.071)	0.005
sex (male, %)	1.985(1.044-3.775)	0.037	3.550(1.607-7.844)	0.005
ESA use (%)	10.48(1.380-79.58)	0.023	18.02(2.046-158.8)	0.009
iron supplement (%)	0.470(0.175-1.263)	0.134	0.396(0.107-1.465)	0.165
ARB use (%)	2.231(1.178-4.226)	0.014	1.661(0.813-3.391)	0.164
Hb level at 6months (per 1g/dl higher)	**0.693(0.551-0.871)**	**0.002**	**0.630(0.482-0.824)**	**0.001**

Conclusion: This study suggests that higher Hb levels at 6 months were associated with better kidney function at 12 months. Maintenance of high Hb levels could have an impact on better patient outcomes in kidney transplantation.

P-308 SUCCESSFUL ABO-INCOMPATIBLE KIDNEY TRANSPLANTATION IN PATIENT WITH CONGENIAL AFIBRINOGENEMIA: FIRST CASE REPORT

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Background: Congenital afibrinogenemia is a rare coagulation disorder with an estimated prevalence of 1 in 1 million. In normal wound repair, fibrinogen plays important roles in blood coagulation by mediating clot formation through its conversion to fibrin by the action of thrombin. Umbilical cord bleeding and bruising are major postnatal symptoms of afibrinogenemia, and fibrinogen replacement therapy (FRT) is the only available treatment for bleeding. Although prophylactic administration of fibrinogen has been performed for surgery preparation, perioperative serious bleeding tendency is a major complication in patients with afibrinogenemia. Herein, we report successful ABO-incompatible kidney transplantation in a patient with congenital afibrinogenemia.
Case report: A 33-year-old male with congenital afibrinogenemia was referred to our clinic for kidney transplantation. He had received FRT several times and became infected with hepatitis C from FRT. The patient began peritoneal dialysis at the age of 32 due to end-stage renal failure derived from chronic glomerulonephritis and underwent ABO-incompatible living-related kidney transplantation in January 2009 from his father. Pre-transplantation treatment consisted of 2 courses of double-filtration plasmapheresis and 2 injections of rituximab for AB0-antibody depletion, as well as 2 weeks of administrations of mycophenolate mofetil and methylpednisolone. The introduction immunosuppression agents were cyclosporine, mycophenolate mofetil, methylprednisolone and basiliximab. Supplementary fibrinogen was also given to maintain a fibrinogen level in serum of 100 mg/dl, while anti-coagulation therapy was done to avoid vascular thrombosis. The transplant surgery was successfully completed without abnormal bleeding or thrombosis. At the time of writing, graft function has been stable with a serum creatinine level of 1.7 mg/dl.
Conclusion: This is the first report of kidney transplantation in a patient with congenital afibrinogenemia. Our successful results can be attributed to fine control of balancing coagulation status with supplementary fibrinogen and anti-coagulation therapy.

P-309 HEMODIALYSIS ARTERIOVENOUS FISTULA IN KIDNEY TRANSPLANT RECIPIENTS: COMPLICATIONS AND SURGICAL INTERVENTIONS

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Background: The aim of this historical cohort study was to evaluate data on arteriovenous fistula (AVF) related problems and to analyze in detail the surgery performed on AVF after successful kidney transplantation.
Patients and methods: The study cohort included 59 recipients of a kidney transplant with symptomatic AVF complications between january 2006 and march 2011. For each patient data related to age, gender, location and side of AVF, type of the complication and follow-up therapy was evaluated.
Results: From the 59 recipients (mean age 50$\pm$10, range 14 to 73 years) 28 (47%) were males. Among all AVF, 42 (72%) AVF were located in the forearm (35 left, 7 right), 8 (13%) in the upper arm (4 left, 4 right) and 9 (15%) in the elbow (6 left, 3 right).
Complications associated with an AVF were painful thrombosis (29%, 17/59), thrombosis with thrombophlebitis (17%, 10/59), growing aneurysms (18.5%, 11/59), painful aneurysms (7%, 4/59), venous hypertension (7%, 4/59), steal syndrome (7%, 4/59), high output failure (5%, 3/59) and trauma (1.5%, 1/59). Three patients (5%, 3/59) experienced problems in the AVF area not related with AVF.
A total of 37 surgical interventions were performed in 35 patients (mean age 50$\pm$12, range 28 to 73 years). 16/35 (46%) of patients underwent AVF closure. Furthermore, extirpations of aneurysms were performed in 10/35 (28%) and an extirpation of thrombosed AVF in 1/35 (3%), simple trombectomies were performed in 5/35 (14%) and thrombectomies with reanastomosis in 2/35 (6%). All except two procedures were performed by interventional nephrologist.
Conclusion: Painful thrombosis, with or without thrombophlebitis, and aneurysms are the most frequent AVF related complications after a transplantation, often requiring vascular access surgery. Vascular access after a transplantation requires further study.

P-310 LIVE KIDNEY TRANSPLANTATION: DO TRAINEES MAKE THE GRADE?

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Background: Working time constraints upon Surgical Trainees operative exposure are well documented. Live kidney transplantation offers significant stressors regarding patient expectation causing reticence to allow Trainees to perform allograft implantation. However, Senior Trainees with Vascular competencies and cadaveric implant experience benefit from this training.
Methods: A retrospective analysis was performed of living donor allograft implantation over 76 months (01/2003 – 04/2010; 277 patients; M=168, F=109; mean age 36.1±1.01 (range 2-71)). Outcomes were compared between Consultant and Surgical Trainees (assessed by Consultants and with cadaveric implantation experience). There were no patient exclusions, including paediatrics. Primary endpoints were Surgical complications (vascular, urological and wound). Creatinine and Glomerular Filtration Rate (GFR) at 3 months were secondary endpoints.
Results: 147 patients (120 adults, 27 children; M=93, F=54; mean age 33.6±1.49, range 2-70) had transplants performed by Consultants whilst 130 were performed by Trainees (124 adults, 6 children; M=75, F=55; mean age 38.8±1.29, range 3-71, p=NS).There were a total of 3 vascular complications (1 arterial thrombosis - Consultant group; 2 haemorrhage requiring re-exploration - Trainees (p=0.49)) 5 patients had urological complications (stenosis) requiring intervention (2 Consultants, 3 Trainees, p=0.56.) There were 4 wound infections requiring antibiotics (1 Consultant, 3 Trainees, p=0.26) There were no differences between the 2 groups regarding mean Creatinine (135.5±7.6 and 128.5±5.1 respectively, p=0.46) or GFR (54.5±2.8 and 54.9±2.2 respectively; p=0.91)
Conclusions: The evolution of transplantation will place an increasing importance on live donation as a potential training opportunity. Emotional implications of graft failure coupled with perceived technical challenges have historically limited Trainee exposure to implantation. However, outcomes for Senior Surgical Trainees can replicate those of Consultants. Current challenges require a paradigm shift to enable capable Surgical Trainees are offered exposure to this procedure ensuring that they achieve the competencies to satisfactorily complete Surgical training.

P-311 ePTFE SUTURE ANASTOMOSIS: AN EFFECTIVE TOOL IN VASCULAR KIDNEY TRANSPLANTATION?

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Background: Suture plays an important role in any surgical procedure, and especially in kidney transplant. Expanded polytetrafluoroethylene (GORE-TEX® Suture – W.L. Gore & ass.) is a white non absorbable monofilament, with high tensile resistance force, and a microscopically proved 1:1 needle-filament ratio. We used ePTFE suture to perform vascular anastomoses during kidney transplantation and evaluated the time of bleeding and transfusion requirement.
Methods and Material: In the last 12 months, 43 patients underwent kidney transplantation (single n = 41). There were 33 males; mean age was 40±9 years (range, 32-70). In group A, vascular anastomoses were performed using ePTFE (n = 20), whereas in group B (n = 23), prolene was used. Groups were well-matched in terms of demographics and co-morbidities.
Results: Overall, major vascular or graft complications were not observed. Mean intraoperative blood loss was 150±75 mL in group A *vs.* 180±70 mL in group B ($p = 0.182$). We observed a statistical difference in total amount time of vascular anastomoses (35±3 min *vs.* 40±7 min, $p = 0.005$); no difference was noted in terms of additional stitches positioned. Major bleeding complication or perirenal hematoma were not observed; blood transfusion were needed in 3 (7.3%) patients only, all in group B ($p = 0.246$). Mean hospitalization was 20±5 *vs.* 19±5 days ($p = 0.516$).
Conclusion: In our preliminary experience, it contributed to reduce the time of vascular reconstruction; it confirmed the main characteristics of the filament and proved to be a potential alternative to other types of suture filament.

P-312 LATE SEVERE NON-INFECTIOUS DIARRHEA AFTER RENAL TRANSPLANTATION: HIGH RISK FACTORS, THERAPY AND PROGNOSIS

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Background: Late severe non-infectious diarrhea in renal transplantation can lead to malnutrition and graft loss in renal allograft receipts. This study tries to find the risk factors and summarize the therapy for these patients.
Methodology: Selected 541 receipts received kidney transplantation from Jan 2001 to June 2007 observed for more than 36 months. They received CNI combined with mycophenolate mofetil and were separated to four groups: CsA group (continuous CsA), pre conversion group and post conversion group (conversion from CsA to tacrolimus), tacrolimus group (continuous tacrolimus). The rate of late severe non-infectious diarrhea were compared in four groups, The high risk factors were analyzed between diarrhea and non diarrhea groups, The clinical characters and effect and safety were observed after the conversion of immunosuppressive protocol for late severe non-infectious diarrhea receipts.
Result: 28 receipts had late severe non-infectious diarrhea in 541 selected receipts. No one had chronic diarrhea in CsA group (n=145) and pre conversion group (n=95). The rate of diarrhea was 7.31% in post conversion group and 7.35% in tacrolimus group. Using multivariate Cox proportional hazards analysis, factors associated with increased risk of noninfectious diarrhea were CYP3A5 *3/*3 type, chronic renal allograft dysfunction and combination with Tripterygium Wilfordii Hook F. All dirrhea receipts experienced body weight loss, hypoalbuminia, and increasing serum creatinine. They were all received adjustment of immunosuppressive drugs and get remission totally. The renal allograft survival of diarrhea was worse than non-diarrhea receipts.
Conclusion: Tacrolimus with MMF can increase the risk of late severe non-infectious in renal transplant receipts contrast to CsA with MMF; CYP3A5 *3/*3 type, chronic renal allograft dysfunction and combination with Tripterygium Wilfordii Hook F. were high risks for late diarrhea. Prompt adjustment of immunosuppressive was an effective and feasible therapy for these patients.

P-313 HLA-DR OVEREXPRESS ON THE TUBULAR OF RENAL ALLOGRAFT IN EARLY ACUTE CELLULAR REJECTION AND LATE REJECTION IN RENAL TRANSPLANTATION

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Background: This study aims at disclosing which kind of injuries were related to the HLA-DR expression in acute rejection and late chronic injury of renal allograft.
Methodology: Total 92 receipts with 102 biopsy samples were selected in this study from Nov 2007 to Mar 2010. They were separated into early acute rejection group (early C4d negative acute rejection (n=13) and early C4d positive acute rejection group (n=7)), late monocyte infiltration group (late C4d negative acute rejection (n=12), late C4d positive acute rejection group (n=13) and BK Virus Nephropathy group (n=6)); late chronic injury groups ((IgA Nephropathy group (n=12), TA/IF group (n=7), BK Virus Nephropathy group (n=6) and chronic rejection group (n=12)). Ten acute cellular rejection receipts received repeated biopsy during the rejection time and protocol biopsy time. All the samples were stained with CD4,CD8,CD20,CD68 HLA-DR with immunochemistry, these markers were calculated with quantitative method and they were compared in subgroups in each group.
Results: The HLA-DR expression in early C4d negative acute rejection was higher than early C4d positive acute rejection. The HLA-DR expression in acute rejection was higher than in protocol biopsy in ten patients received repeated biopsy.The HLA-DR expression in late C4d negative and C4d positive acute rejection were higher that of BK Virus Nephropathy, which wasn't accordance with CD4,CD8,CD20,CD68 infiltration. In chronic tubular groups, the HLA-DR expression in chronic rejection was higher than IgA Nephropathy, BK Virus Nephropathy and TA/IF group, which also wasn't accordance with CD4,CD8,CD20,CD68 infiltration.
Conclusions: HLA-DR expression on renal tubular cells was associated with early acute cellular rejection and accordance with monocyte infiltration in renal allograft.
HLA-DR expression on renal tubular during the late period, especially in atrophy tubular was a marker of late rejection, wasn't accordance with monocyte infiltration in renal allograft.

P-314 WHAT HARM DO WE DO TO OUR ELDERLY PATIENTS? THE BRIDGE BETWEEN EVIDENCE BASED MEDICINE AND REAL LIFE IN TRANSPLANT MEDICINE

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Background: Elderly patients contribute increasingly to the kidney recipient patient pool and they show favourable outcomes concerning renal graft survival. It could be shown that graft survival itself, was not negatively influenced by evolving patient age and that older patients seem to derive a survival benefit from transplantation compared to those remaining on dialysis treatment. There are several reports in the literature dealing with quality of life assessment as well as functional ability of elderly patients on haemodialysis and peritoneal

dialysis. Little is known about functionality and social integration of old kidney transplant recipients so far.
Method: In a prospective single-center cohort analysis 121 renal kidney transplant reciepients (> 60 years) underwent comprehensive geriatric assessment (ADL, CCT, TUG, GDS-15, MNA, vigorimetry). Frailty index was then determined by the Cardiovascular Health Scale (CHS Frailty index).
Results: In total 70 men and 51 women were recruited. Mean duration from transplantation was 8.3±6.1 years (male 7.6±4.9/female 8.5±5.9). The overall prevalence of frailty was 9.9% (male 11,3, female 10.9). 21.9% were considered to be pre-frail (male 22.7/female 15.6). Frailty index war significantly correlated to numer of drugs prescribed (p=0,001) as well as number of chronic concimittant conditions (p=0,001). Personal well-being as indicated by GDS-15 was attributed to somatic and health associated functionality.
Conclusion: One fifth of the recipients tend to develop a functional decline. This observation positively correlates wit co-morbidities and number of drugs prescribed. Nephrologists have to bear in mind that improvement of prescription methods in elderly renal transplant recipients may not only have an impact not only on course of disease but also on functional properties of their patients.

P-315 PURE LAPAROSCOPIC LIVE DONOR NEPHRECTOMY RESULTS: A SINGLE INSTITUTION EXPERIENCE

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Introduction: Laparoscopic live donor nephrectomy (LLDN) is increasingly used by transplantation centers worldwide. The benefits of a minimally invasive approach to kidney donation, including improved cosmetics, less postoperative pain, and earlier return to work and regular activity.
Aim: of this study to report a single-institution results with pure LLDN performed using transperitoneal approach.
Patients and Methods: Nineteen female and four male subjects of mean age of 40,2±9 years were operated on during Jan 2008 – Mar 2011 at Gazi University Transplantation Center, Ankara. Data retrieved from patient charts, hospital files.
Results: The mean operative time for donor nephrectomy was 235±72 minutes (range 120–310), with a mean warm ischemia time of 3±0,8 minutes (range 1,3–5). Twenty two of the donor kidneys were left kidney, only 1 kidney was right kidney. The donors' mean hospital stay was 5±1,6 days (range 3–8). Only one donor (4,3%) operation was converted to open nephrectomy because of abnormal anatomy. There was no need for blood transfusions or reoperations in the donors. Average creatinine level at the discharge was 1.12±0.38 mg/dL. Only one minor surgical complication was registered (left inguinal hernia) among 23 donors. ATN was seen in only one recipient. It was resolved after 5 days ATG (2mg/kg-day) administration. There has seen 1 uretery leak after transplantation in pediatric recipient as uretery complication. This leak was resolved by conventional radiology by using retrograde nephrouretosistostomy and than DJ catheter insertion. One recipient died 6 months after transplantation due to H1N1 infection.
Conclusion: Today, LLDN became the standard approach for living kidney harvesting in many centers as well as in our institution. In this study and numerous trials have demonstrated that LLDN is feasible and safe for donor and recipient.

P-316 DONOR DNA LEVEL IN BLOOD OF KIDNEY ALLOGRAFT RECIPIENTS – CAN IT BE USED AS A DIAGNOSTIC FACTOR FOR REJECTION

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Background: Organ allograft releases a large amount of genetic material to the recipient circulation. The sources of donor DNA are the passenger cells and debris of damaged organ endothelial and parenchymal cells. Immunosuppression may cause additional release of genetic material due to its cytotoxic effects.
Aim: The question arises whether the level of released donor DNA may be helpful in assessment of the intensity of the rejection process. In our previous studies, we looked for the presence of donor-specific STR loci (phospholipase *A2-HUMPLA2A1(AAT)$_n$*, cytochrome P-450 *A2-HUMCYARO(AAAT)$_n$* and locus *D1S80*) in the recipient blood.
Material/Methods: In this study we have examined the plasma and blood mononuclear cells of recipients to assess the amount of *SRY* gene in sex-mismatched combinations and phospholipase A2-*HUMPLA2A1(AAT)$_n$* in the same sex recipients after kidney transplantation,
in relation to the patients probes before grafting by the use of the Real-time PCR method. Recipient's blood and donors spleen samples were collected before kidney transplantation and at different times after grafting. Genomic DNA was isolated from plasma and mononuclear cells. The amount of DNA in different samples after tx was calculated by using the comparative Ct method with *GAPDH* as internal control.
Results: We observed increase in donor DNA level in recipient's blood mononuclear cells already on day 1 after grafting. The relative amount of *SRY* gene was much higher in female's lymphocytes 21 days after transplantation than in plasma. The amount of *HUMPLA* gene was also higher in blood lymphocytes than in plasma 14 days after kidney transplantation.
Conclusions: Donor DNA is present either in "passenger cells" or recipient's phagocytes. An open question remains whether it may be incorporated into recipient cell genome.

P-317 IS IT POSSIBLE TO REDUCE THE RISK OF THROMBOSIS OF VEIN IN RIGHT KIDNEY ALLOGRAFT?HOW?

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introduction: For treatment of end stage renal disease Kidney transplantation is a best option from the economic and quality of life standpoint, but it has some complications in which the vessel complication is catastrophic because more time it leads to graft loss. Furthermore the right kidney allograft has more chances for the vessel complication than left kidney allograft because the difference in the vessel lengths. We introduce the method which may reduce the risk of the vessel complication with the right allograft kidney.
Method: In twenty kidney recipients (15 males five females) with age rang 55-65 in them right allograft kidney has been selected for placement in the right iliac fosse. First in the back table vein and artery of kidney carefully separated and some small connect vessel between artery and vein carefully liquated this careful dissection cause some increase length of vein. In recipient before clamping vessel heparin in dose of 30 units per kilogram are injected. Right kidney placed in iliac in up down (inversion) position and both the external iliac vessels (artery and vein) selected for anastomosis, and first the renal vein anastomosed to external iliac and then renal artery anastomsed to external iliac artery consequently.
Results: In all the recipients there was not any thrombosis for six months follow up.
Conclusion: it seems with care dissection in the back table and inversion position of right kidney at the right iliac fossa of recipient and selection external iliac artery for anastomosis and first anastomosis of renal vein and with heparin prophylaxis it may be possible to reduce the risk of right allograft kidney for thrombosis.

P-318 IS LEAVING EXPANSION PLACE FOR SUTURE IN ANASTOMOSIS OF VESSEL SAFE AND HELPFUL FOR PREVENTION OF STENOSIS?

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Introduction: The kidney transplantation is the most effective option for kidney replacement treatment, in which lifestyle (quality and quantity) is more similar to normal lifestyle. The vascular complication is one of the important side effects, which may be results in kidney allograft loss and sometimes not only kidney loss but also morbidity, which may result in death of kidney recipient, stenosis in site of anastomosis is one of them.
Method: In thirty kidney recipient patients (group1), after preparing hypogastric artery and external iliac vein and anastomosing to the allograft renal artery and renal vein with 6-7mm distance from artery and vein final tie made and after sometimes the expansion and hemostasis evaluated, in the other thirty cases with a nearly same condition with group 1 (group 2), the final tie made without distance from the vessel, and both groups followed with color Doppler sonography.
Results: In Group 1 there were bleeding in some cases who were controlled with very superficial suture and color Doppler control in all of them were normal. In group 2 a few cases had been bleeding in them just only with pressure by finger homeostasis performed, color Dopplers in three cases weren't normal (the velocity increased post anastomosis compared with velocity in iliac artery) which supposed stenosis at place of anastomosis.
Conclusion: Leave distance between vessel and tie for expansion of anastomosis is safe and may reduce chance of stenosis at the place of anastomosis.

P-319 REVASCULARIZATION OF TRANSPLANT RENAL ARTERY STENOSIS: DOPPLER ASSESSMENT

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Background: Transplant renal artery stenosis (TRAS) can be treated conservatively with antihypertensive medications or with invasive procedures (percutaneous transluminal renal angioplasty (PTRA) and surgery).
Methods: We compared changes in laboratory, clinical and Doppler ultrasound parameters such as creatinine, peak systolic velocity (PSV), end diastolic velocity (EDV), resistive index (RI), acceleration time (AT), both at the level of intrarenal arteries, before and one month after revascularization.
Results: In 14 patients, 4 female and 10 male, aged 52±18 (32-67) years, that received their first and cadaveric kidney graft (one patient received second graft), we diagnosed 16 TRAS by Doppler. 5 of them were confirmed by magnetic resonance angiography and 2 by computed tomography angiography before the revascularization. 8 stenosis were anastomotic, 7 at the main tree of renal artery and one stenosis was in external iliac artery. 13 stenosis were assessed as >70%, 3 as > 50%. 17 revascularization procedures were performed: 14 PTRAs, 6 with stent placement, 3 surgical corrections (performed 2 days, 13 days and 5 years after transplantation). One PTRA was unsuccessful and was resolved by surgery 5 years after transplantation. 2 restenosis occurred 4 and 6 months after first PTRA and were corrected by re-PTRA. Before revascularization, the average creatinine (μmol/l) was 239±157 (shortly after revascularization 123±28) (p=0.005). Before revascularization, the average PSV/EDV (m/s) was 2.85±0.7/1.0±0.5 (shortly after revascularization 1.65±0.6/0.5±0.3) (p<0.001/0.004). Before revascularization, the average RI was 0.59±0.1 (shortly after revascularization 0.7±0.1) (p=0.197). Before revascularization, the average AT (ms) was 172±35 (shortly after revascularization 62±39) (p<0.001).
Conclusion: Doppler is an ideal test for assessment of immediate and late revascularization results. Successful revascularization procedure is demonstrated by a decrease in PSV, increase in RI and shortening of AT.

Liver and intestine

P-320 RESULTS OF LIVER TRANSPLANTATION CRYPTOGENIC CIRRHOSIS: LONG-TERM FOLLOW-UP

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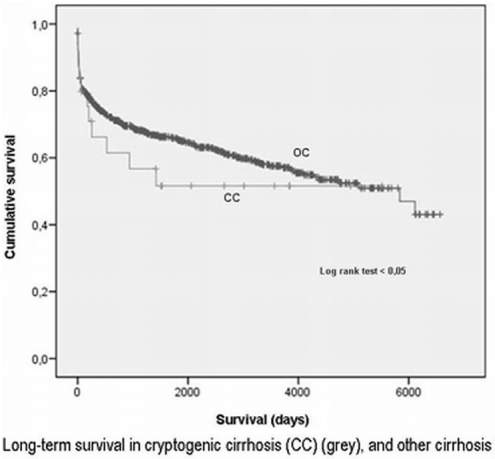
Background: Despite the great advances, there is a significant subgroup of patients with cryptogenic cirrhosis (CC), which remains a process without a specific etiology, most likely, actually represents a spectrum of disease (NASH, etc). Few studies have specifically analyzed the results of liver transplantation in CC.
Methods/Material: Retrospective analysis of 35 patients transplanted for cryptogenic cirrhosis among 784 patients in Virgen del Rocío Hospital (Seville, Spain), followed for 20 years. Similar distribution by sex (18 females and 17 males), mean age 47 years. Average MELD 16. 8% were transplanted for HCC.
Results: 28.6% of misdiagnosis: 3 autoimmune cirrhosis, 2 sarchoidosis, 2 negative-PBC, 1 sclerosing cholangitis, 1 congenital hepatic fibrosis and 1 Wilson's disease. No incidence of acute rejection, with a low incidence of complications: 4% hepatic artery thrombosis, 8% postoperative infection, renal dysfunction 16%, 8% biliary fistula. 20% postoperative mortality. 25% 4% chronic rejection or disease recurrence. Cumulative survival at 3, 5 and 10 years is less than in other indications (60%, 50%, 50%).
Median survival of 48 months.
Conclusions: 1. About one of three patients transplanted for CC have a specific etiologic diagnosis after histopathological examination of the explanted liver, 2. Although the incidence of acute rejection is nil in patients transplanted for CC, chronic rejection rate is higher than other etiologies, 3. The occurrence of vascular and biliary technical problems is similar to other transplant, although rates of surgical infection and renal dysfunction are lower, 4. Postoperative mortality is higher, and survival to 5, 10 and 15 years is lower than the rest of liver transplants.



Long-term survival in cryptogenic cirrhosis (CC) (grey), and other cirrhosis (OC) (black) (p<0,05)

P-321 RESULTS OF LIVER TRANSPLANT WITH DONORS OLDER THAN 70

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Background: shortage of organs has forced transplant centers performing liver grafts using expanded criteria. The aim of this study is to analyze the results of liver transplantation with grafts from donors older than 70 years.
Methods/Material: We retrospectively evaluated 72 patients who received liver grafts from cadaveric donors older than 70 years. We analyze the results compared with those obtained from patients who received grafts from donors younger than 70 years. Donors mean age 74.3 (range 70-82). Average weight of 74.3 kg (no court was not accepted steatosis)
Results: Mean follow up 4.8 years (range 1-15 years). There were no differences in biliary (18% older than 70 years vs 18.3%) or vascular complications (8.5% vs 9.4%), primary graft dysfunction 9, 7% vs 6.7%), renal dysfunction (57.7% vs 56.6%), acute rejection (21.7% vs 22.1%), ascites (15.5% vs 13.3%), neurological complications (16.5% vs 15.3%), postoperative bleeding (12.7% vs 13.8%) or retransplantation rate (8.3% vs 7.6%). Recipients required more blood transfusion (6.1 vs. 4.7) during the intervention (p <0.05), and had a higher incidence of postoperative infection (21.6% vs 17.7%) (p<0.05), postoperative mortality (16.6% vs 7.9%) (p <0,05), and a lower survival at 1, 5 and 10 years (65%, 58% and 45%) (p<0.05).
In univariate analysis, associated with increased incidence of primary dysfunction and mortality are, respectively, donor weight and MELD. In multivariate analysis, donor weight, ischemia time and MELD are the factors associated with more complications.
Conclusions: grafts older than 70 years have a higher incidence of postoperative infections and postoperative mortality. Survival at 1, 5 and 10 years is significantly lower. There should be a careful selection of the recipients of these grafts (lower MELD) and try to obtain a short ischemia time.

P-322 A HIGH MELD SCORE RELATES TO LOWER EMPLOYMENT RATES AFTER LIVER TRANSPLANTATION

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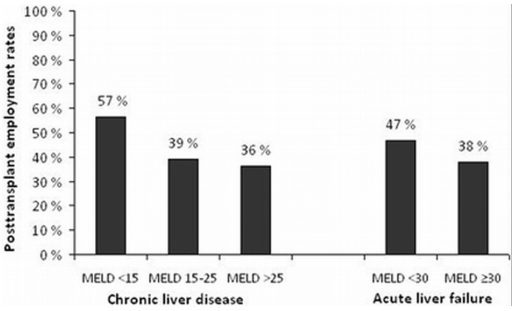
The influence of the MELD score upon working capacity after liver transplantation (LT) remains scantily studied. Among working-aged (20-65 years) patients undergoing first LT in Finland in 2000-2007, we calculated MELD scores at listing and assessed employment after LT by a questionnaire sent to the patients in 2007, on average at 4 years (SD 2) after LT. The response rate was 84% (n=178). Of 142 patients with chronic liver disease or liver tumor, 49% had been able to resume work after LT, compared with 42% of 36 patients with acute liver failure. In chronic liver disease patients, the MELD score was associated with lower posttransplant employment in logistic regression analysis (P=0.022). To determine the magnitude of this association, patients were di-



vided into subgroups based on clinically relevant MELD cut-offs (Figure). The largest drop in employment was seen with MELD scores above 15 (Figure). In acute liver failure, the association between the MELD score and employment was non-significant. In conclusion, our findings imply that postponing LT to very late stages of chronic liver disease impair patients' ability to resume work even after successful LT.

P-323 PREVENTION OF SMALL-FOR-SIZE GRAFT SYNDROME IN LIVING DONOR LIVER TRANSPLANTATION BY PORTOCAVAL SHUNT GRAFTING WITH A BIOABSORBABLE SYNTHETIC VESSEL

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Background: Adult to adult living donor liver transplantation (LDLT) is an wide spread application, but it requires some actions against the small-for-size graft syndrome (SFSGS) to improve the performance of the operation. Some authors reported that a port-caval shunt (PCS) is reconstructed when portal hypertension is confirmed after graft implantation. However the technique has possibility of disturbing appropriate graft regeneration because of lack of sufficient portal flow. In previous study, our group made a bioabsorbable synthetic vessel (BASV) as a substitute for regeneration of blood vessels. The BASV is able to be controlled about degrading time and patency on some level. This study focused on possibility of prevention of SFSGS by reconstruction of transient PCS with BASV.
Methods: The BASV was designed to degrade in about 8 weeks. In previous study, the BASV gradually became obstructed about 2-3 weeks if anti coagulant agent was not administered. Hybrid pigs (n=3) were laparotomized under general anesthesia. Bypass grafting was reconstructed between portal vein and inferior vena cava with BASV of 10mm diameter. And then left portal vein was ligated to make the state of portal hypertension. During the operation portal vein pressure (PVP) was continuously monitored. The animals were re-laparotomized at 12 weeks after implantation to be observe about the graft sites and estimate the portal pressure.
Results: PVP revealed 6.7±0.61, 9.8±0.23, 6.3±0.41 and 7.3±0.49 (mmHg) at the point of initial state, post left PV ligated, post PC shunt replacement, and re-laparotomy. At 12 weeks after the operation, BASV became scarred and occluded. Re-laparotomized intra-abdominal findings revealed a hypertrophic right lobe and an atrophic left lobe of the liver.
Conclusion: Transient PC shunt with BASV has potential for application as a novel prevention technique for SFSGS in LDLT.

P-324 LIVER DONATION AND TRANSPLANTATION IN SAUDI ARABIA

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Objective: The aim of the study is to evaluate and analyze the result of the liver donation and transplantation.
Methods: A retrospective study was done during the year 2004 and 2008 from the 402 living related (LR) and deceased donors (DD). Data includes donor's characteristics and acceptance rate for DD offered livers, recipients' status post transplant follow up period and patient survival.
Results: A total of 425 cases from DD were consented for liver donation and 278 (65.4%) cases were retrieved with 217 (78.1%) from them were able to transplant with donor mean age of 33.2 years. As to LR donors, mostly were son, mother and father related with a mean age of 26.6 years with male/female ratio of 3/1 for a total of 187 transplants. The mean follow up period was 745 days and the mean stay in hospital post transplant was 28.2 days with 11 cases having a primary non-functioning graft. At the end of the follow up period, there were 347 (86.3%) active patients and 51 (12.7%) died. 341 (98.3%) of the active patients are doing well at home and only 6 (1.7%) at the hospital. The patient survival at three and five years was 86.2% and 77.1% respectively.
Summary: The outcome of the liver transplantation in the kingdom is comparable to international levels, though the need to increase the acceptance rate and the use of procured liver requires more effort in the management of deceased donors. Both LR and DD transplant should be enhanced to meet the ever-increasing demand of organ transplantation.
Keywords: Deceased Donors, Living Related, Liver Transplantation, Saudi Arabia

P-325 CHANCE OF SALVAGE TRANSPLANTATION AFTER PRIMARY HEPATECTOMY FOR HEPATOCELLULAR CARCINOMA: A SPECIAL REFERENCE TO UP-TO-7 CRITERIA

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Background: We have reported that salvage liver transplantation (LT) could be the therapeutic option for patients with hepatocellular carcinoma (HCC) recurrence meeting Milan criteria (MC) of patients with HCC meeting MC within 1-year after post-hepatectomized first recurrence because cases with recurrence exceeding Milan criteria was observed from 1-year after primary recurrence (*Transplantation 2008*). Herein, we examined usefulness of Up-to-7 (UT7) criteria for salvage LT.
Patients and Methods: 142 patients, who underwent a curative hepatectomy for HCC, were included in this study. 99 patients meeting the UT7 criteria, while 43 patients exceeding the UT7 criteria. Long-term prognosis and detailed recurrence patterns were investigated.
Results: Overall survival rate in patients within the UT7 group was better than that of exceeding the criteria group (5y: 71.1% vs. 51.1%). There was no significant difference in recurrence-free survival rates between the two groups. HCC recurrence was observed in 72 patients (51%). Patients with HCC meeting the UT7 criteria (n=99), recurrences within the criteria was observed in 36 patients (Salvage group) and recurrence exceeding the criteria was observed in 8 patients. Tumor size ≤4cm and PIVKA-II ≤400mAU/ml were identified as the significant factors for having recurrence in Salvage group. Those with HCC exceeding UT7 criteria (n=43), recurrence within the criteria was observed in 12 patients (Down-stage group) and recurrence exceeding the criteria was observed in 16 patients. Only well differentiated type was identified as the significant factor for having recurrence as in Down-stage group. Cases with re-recurrence exceeding the UT7 criteria was observed early period, within 1-year, after first recurrence in both Salvage and Down-stage group.
Conclusion: Tumor size ≤4cm and PIVKA-II ≤400mAU/ml for salvage LT and well differentiated histology for down-stage LT are useful indicators to predict feasibility of LT after primary hepatectomy. However, UT7 is considered to be inferior to MC to assess chance of salvage and down-stage LT.

P-326 REVERSIBLE SEVERE IMMUNOLOGICAL AND INFECTIOUS COMPLICATIONS IN INTESTINE TRANSPLANT: A CASE REPORT

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Background: Clinical outcome after severe acute intestine graft rejection treated by maximized immunosuppression, followed by CMV graft enteritis and fungal pneumonia.
Methods: A 29 years old female patient with chronic intestinal pseoudoobstruction of unclear etiology underwent intestinal transplantation in December 2009. Basic immunosupression consisted of pulsed thymoglobuline induction, infliximab, tacrolimus and steroids. After good initial function with normal graft biopsy, a severe acute rejection with biopsy proven complete epithelial destruction occurred on postoperative day 26 following a preceeding one-time low tacrolimus level (9 ng/mL). After immediate high dosed antirejective treatment with totally 6.5 g methylprednisolone, thymoglobuline for 10 days and tacrolimus trough level about 20 ng/mL, no histological improvement was found until day 32. Mucosal regeneration was noted on day 40, progressing to regeneration of normal epithelial after day 44, allowing cautious taping of steroids doses. Azathioprine was added and temporarily discontinued due to a severe leucopenia, as was sirolimus for the same reason. On day 46, a CMV histologically proven graft enteritis was successfully treated by anti-CMV hyperimmunoglobuline + gancyclovir with cautiously reduced immunosuppression. A bilateral Aspergillus pneumonia occurred at month 6.
Results: Within a consequent systemic and topic therapy of liposomal Amphotericin B, followed by systemic Voriconazol and reduction of immunosuppression (obtained tacrolimus trough level 10 ng/mL) and low dosed prednisolone (10 mg), the pneumonia was regredient until month 9. At the end of the 1st year, the patient is in good general condition with a stable graft function (biopsy proven), sufficient oral alimentation, stable body weight, normal leucocyte count and reversible infections (cystitis, lid abscess, enoral herpes).
Conclusion: A stable graft function and quality of life was achieved after severe acute rejection, CMV-graft enteritis and pulmonary aspergillosis by cautiously adapting immunosuppression and a consequent antimicrobial treatment.

P-327 PATIENTS SURVIVING AT LEAST 10 YEARS POST LIVER TRANSPLANTATION: LONG TERM RESULTS

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Aims: to determine clinical and histological complications of patients surviving at least 10 years post-LT.
Methods: Of 323 patients transplanted between 1991-97, 161 (50%) were alive > 10 years post-LT.Clinical outcome measures included: immunosuppression (IS), metabolic (obesity, arterial hypertension-AH-, diabetes-DM-, dislypidemia), cardiovascular complications, renal insufficiency, de novo tumors and recurrent disease. Liver biopsies were performed.
Results: Median age at transplantation was 50 years, 67% male. Most common indication was postnecrotic cirrhosis (88%). Immunosuppression mostly consisted of cyclosporine (97.5%) with azathioprine (98%) and steroids (100%). At 10 years post-transplantation, AH was present in 72%, diabetes in 28%, dislypidemia in 39% and obesity in 31%. Most of these patients had already these complications at 1 year post-LT and very few developed it onward. Of 50 patients without AH at 1 year, 16% developed AH at 10 years. Of 112 non 1-year diabetics, 8% had DM at 10 years. Of 80 non 1-yr dislypidemic, 12% had dislypidemia at 10 years. Finally, only 14% of non-1yr obese patients were obese at 10 years. Cardiovascular events occurred in 10% of patients. De novo tumors (excluding skin cancer) developed in 30% (mostly solid tumors) at a median of 4.5 years post-transplantation. While renal insufficiency was present in 31% of patients at 10 years, only 4% required hemodialysis. Graft cirrhosis developed in 20% of cases, 96% related to HCV.
Conclusions: Metabolic complications are very common post-transplantation leading to cardiovascular events in a small percent of cases after 10 years of follow-up. A strong effort should be made to detect and treat these complications early after transplantation since it is uncommon for these to develop after the first year. Renal insufficiency is a common complication but rarely results in renal failure.

P-328 HEPATOPULMONARY SYNDROME IN CIRRHOTIC PATIENTS CANDIDATES TO A LIVER TRANSPLANTATION

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Objectives: To assess HPS prevalence in cirrhotic patients from enolic or viral etiology, and its relationship to etiology.
Patients and Methods: 77 patients with hepatic cirrhosis diagnose and candidates to a liver transplantation were studied. Patients were distributed in two groups: Group 1, patients with cirrhosis of enolic etiology (n=40). Group 2, patients with hepatic cirrhosis of viral etiology (n=37). Hepatic cirrhosis status was estimated by CHILD and MELD score. Presence of clinical ascites was estimated, as well as cardiac chambers and diastolic functions by two-dimension transthoracic echocardiography in M mode and Doppler. HPS was studied with agitated saline serum and intravenous contrast administration. HPS was considered as present when serum or contrast have passed to the left chamber before 5th cardiac cycle.
Results: Group 1 composed by 90% males (n=36) and 10% females (n=4) with an average age of 55.0±8.2 years. Ascites was detected in 42.5% of Group 1 patients with 24.7% of patients in Child-Pugh stage A, 61.7% in stage B and 13.6% in stage C. MELD score in Group 1 showed an average value of 15.0±4.0. Group 2 composed by 82.9% males (n=29) and 22.9% females (n=8). The average age was 55.5±8.0 years, being ascites detected in 47.5% of patients. Group 2 showed 28.6% patients in Child-Pugh stage A, 57.1% in stage B, and 14.3% in stage C, with an average MELD score of 13.0±4.0. There was no statistically significant differences among groups related to sex, age, cirrhosis status or ascites presence. HPS frequency was 35% in Group-patients and 64.7% in Group 2-patients, being such difference statistically significant (p= 0.01).
Conclusion: HPS frequency is related to cirrhotic etiology. Patients with cirrhosis from viral etiology showed a significant enhancement in HPS frequency compared to patients with cirrhosis of enolic etiology.

P-329 LIVER TRANSPLANT BILIARY MISMATCH: BILIARY TRANSPOSITION VS DUCTOPLASTY

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Background: Biliary complications remain a significant problem following liver transplantation. This is the first and largest series describing use of the recipient cystic duct for biliary reconstruction in cadaveric liver transplant recipients. We have named this drainage procedure "biliary transposition" (T). We compared biliary transposition (T) to recipient biliary ductoplasty (D) in cadaveric liver transplant.
Methods: We retrospectively reviewed a total of 22 reconstructions performed over 5 years (2006-2011). In the T group (n=12) five reconstructions were performed using an internal stent (8 Fr pediatric feeding tube), and seven were performed without. Of the ten ductoplasties, 2 were performed with a stent. Follow-up ranged from 2 months to 5 years. All patients were managed with standard immunosuppression and ursodiol.
Results: No patients in the T group required reoperation, one patient had an internal stent removed for recurrent unexplained leukocytosis, two patients required ERC and stent placement. There were no leaks or deaths in the T group. There were 2 anastomotic leaks and one death in the D group. Two patients required reoperation for biliary complications. All patients had improvement in biochemical markers of biliary flow post-transplant. There was no significant difference in biopsy proven episodes of acute cellular rejection, recurrent hepatitis C, graft or patient survival; there was a trend towards less intervention in the T group.
Conclusion: Our results indicate biliary reconstruction can be performed with either biliary transposition or ductoplasty. These techniques are particularly useful when a significant mismatch in diameter exists between the donor and recipient bile duct.

P-330 THE COMBINATION OF BOTH AICAR AND TMZ IN UW SOLUTION IS UNNECESSARY TO INCREASE SURVIVAL OF RECIPIENTS TRANSPLANTED WITH STEATOTIC LIVERS

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Background: Hepatic steatosis is a risk factor for transplantation. We evaluated the relevance of aminoimidazole-4-carboxamide ribonucleoside (AICAR) and trimetazidine (TMZ) (separately or in combination) as new additives in University of Wisconsin (UW) solution in steatotic liver transplantation. *Material and Methods.* Steatotic liver transplantation was induced in Zucker rats. The mechanisms potentially involved in the vulnerability of steatotic liver donors to ischemia-reperfusion injury and the survival of recipients transplanted with steatotic livers grafts were evaluated. *Results.* The addition of AICAR and TMZ (separately or in combination) to UW solution increased AMPK, NOS, nitrates and nitrites and protected against lipid peroxidation, nitrotyrosine formation and hepatic injury in steatotic liver grafts. Recipients transplanted with steatotic liver grafts preserved in UW solution showed 30% survival at 14 days, most of the deaths occurring within 2 days. The addition of TMZ and AICAR (separately or in combination) to UW solution reduced the lethality in recipients transplanted with steatotic grafts, and resulted in a 60% survival at 14 days. The activation of AMPK could explain the benefits of AICAR and TMZ in steatotic liver transplantations. When AMPK was inhibited, the benefits of AICAR and TMZ on NO, oxidative stress, hepatic injury and recipient survival with steatotic liver donor disappeared. *Conclusions.* TMZ and AICAR could be considered as new additives to UW preservation solution to improve the post-surgical outcomes in steatotic liver transplantation, whereas a combination of both seems unnecessary.
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* Elias-Miró and Jiménez-Castro contributed equally to this work.

P-331 EARLY AND EXTENDED THERAPY OF RECURRENT HEPATITIS C AFTER LIVER TRANSPLANTATION

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Background: End-stage cirrhosis due to Hepatitis C Virus (HCV) is one of the most common indications for liver transplantation (LT). Recurrence is universal and more aggressive than before LT. The aim of this study was to evaluate prospectively the efficacy and tolerability of antiviral therapy in recurrent HCV

after LT. Therapy was started even with mild fibrosis (F<2) and extended until 72 weeks, if it was possible.
Methods: Between November 2001 and December 2010, 279 LT were performed in 262 patients in our hospital; 81 (31%) for HCV-related cirrhosis. Nineteen patients were excluded because they died in their first 6 months. We analyzed the other 62 patients.
Results: 28 patients met the indication for antiviral therapy, 21 male (75%) and 7 female (25%), mean age 56 (range: 40-68). All the patients had histologically proven recurrent liver disease: F0-1 in nineteen patients (68%), F2 in four (14%) and F3-4 in five (18%). Mean time to recurrence: 23 months, range: 3-90. Adverse effects (leukopenia in 82% and anemia in 79%) were treated with GCSF and EPO and dose reduction of one or both agents. Four patients (14%) were withdrawn from the treatment due to adverse effects. Nineteen patients achieved EVR (68%), and the SVR was 54% (15 of 28 patients). Five patients died (18%): one developed endocarditis, 3 due to progression to HCV-related cirrhosis and one patient due to recurrent hepatocellular carcinoma.
Conclusions: Antiviral therapy is safe and effective in the treatment of recurrent HCV after LT. In our experience, this therapy should be started during an early stage of recurrent hepatitis C in the graft; and maybe, in extended therapy (72 weeks). Moreover, it's important to avoid dose reduction of antiviral drugs and treat side effects before dose reduction.

P-332 USEFULNESS OF C4d DEPOSITS IN DIFFERENTIAL DIAGNOSIS BETWEEN ACUTE LIVER REJECTION AND HEPATITIS C RECURRENCE

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Backgraund: Acute liver graft rejection is still a common complication after liver transplantations. The diagnostics of this process is based on histological findings, resembling the presentation of HCV infection. Also the clinical presentation of both processes demonstrate a number of similiarities. Correct differentiation between acute rejection and recurrent HCV hepatitis is very important because of differences in treatment - steroid pulses used in the treatment of acute rejection may cause severe fulminant hepatitis in patients with HCV reinfection. There are single reports concerning the role of C4d complement fragment in the diagnostics of acute rejection with humoral component in case of liver grafts. From the practical point of view C4d could be used in liver transplantology for differential diagnostics of acute graft rejection and recurrence of HCV infection. A few preliminary studies suggest usefulness of these marker in the diagnostics of AMR (antibody-mediated rejection) and differentiation between both liver pathologies.
Material/Methods: 83 liver biopsies including 57 with acute rejection and 23 with HCV reinfection were stained with antisera to C4d using an immunohistochemical method on formalin-fixed, paraffin-embedded tissue.
Results: C4d expression was detected in biopsies classified as acute rejection (58%) and recurrent hepatitis C infection (65%). In both liver pathologies C4d deposits were demonstrated along endothelial cells of portal arteries, capillaries and veins. No distinct distribution pattern of the C4d staing was apparent regarding vascular structures of the portal fields.
Conclusion: These results, which are different to recently published data show that C4d couldn't be used as a marker for differentiation between acute liver graft rejection and relapsed hepatitis C.

P-334 COMPARISON OF NORMAL SALINE AND LACTATED RINGER'S SOLUTION DURING LIVER TRANSPLANTATION

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Background: Normal saline (NS) is commonly used during liver transplantation (LT). Although lactated Ringer's solution (LR) is known for better acid-base and electrolyte balance than NS during major abdominal operation, the possibility of lactated accumulation in LT recipients is still anticipated. Therefore we compared the changes in latate, acid-base, and electrolyte balances between NS and LR in LT recipients.
Methods: Perioperative data of adult LT recipients were retrospectively collected from November 2008 to February 2011. Lactate, acid-base, and electrolyte balances between NS and LR groups were compared after induction (P-base), two hours after P-base (P-2H), after portal vein clamp (A-base), one hour after A-base (A-1H). Cases of transfusion administration except autotransfusion and preoperative hyponatremia (sodium <130) were excluded.
Results: Preoperative demographics and laboratory results at P-base were comparable between NS (n=24) and LR groups (n=22). Latate levels significantly higher in LR group than NS group at A-base (4.390±1.831 vs 3.133±1.478, p=0.01) and A-1H (6.412±2.246 vs 4.670±1.784, p=0.005). However, acid-base (pH, HCO_3^-, base deficit) and electrolyte balances (sodium, ionized calcium, chloride) were significantly better in LR group than NS group.
Conclusion: Although LR resulted in latate accumulation, the better outcome in acid-base and electrolyte balances in LR group than NS group suggest that LR may be a more appropriate choice in LT recipients

P-335 INFLUENCE OF CHOLESTASIS AND HEPATOCYTOLISIS ON LIVER STIFFNESS IN RECURRENT HEPATITIS C FOLLOWING LIVER TRANSPLANTATION

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Background: Transient elastography (FibroScan [TE]) is a novel non-invasive tool to assess liver fibrosis/cirrhosis also in HCV recipients after LT The following optimal TE cut-off values for HCV patients were used 4.7kPa for F≥1, 7.1kPa for F≥2, 10.9kPa for F≥3, and 17.3 kPa for F=4.
Methods: Fifteen HCV transplanted patients were prospectively included in the study between 1 January 2010 - 30 April 2010. Patients with histologically proven hepatitis C underwent TE and liver biopsies the same day after elastography evaluation; METAVIR score was used to assess the degree of inflammation and stage of fibrosis. Spearman's rank test correlation coefficient was used to measure the degree of association between two quantitative variables and k reliability test was used to measure the agreement between corresponding fibrosis stages evaluated by TE and liver biopsy.
Results: There were analyzed 15 patients (4 females and 11 males), with a mean age of 54.2±5.8 years. The median liver stiffness measurement (LSM) was 7.8kPa (range 3.9 - 25.6 kPa). There was a moderate agreement (k reliability=0.43) between fibrosis stages evaluated by liver biopsy and TE. There was a strong correlation between TE value and GGT (r=0.72, p=0.002) and alkaline phosphatase (r=0.68, p=0.004) values at the moment of evaluation and a moderate correlation between TE value and AST (r=0.58, p=0.02) and total bilirubin (r=0.54, p=0.03). There was no correlation between TE value and ALT, viral load or thrombocytopenia.
Conclusions: TE can be used for evaluating fibrosis stages in HCV transplanted patients, but accurate evaluation of fibrosis can be influenced by cholestasis and hepatocytolisis.

P-336 METABOLIC DERANGEMENTS FOLLOWING ORTHOTOPIC LIVER TRANSPLANTATION: THE PROBLEM INTO THE PROBLEM

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Background: Metabolic Syndrome is frequently observed in patients after liver transplantation (LT). Multiple causes may favour the development of this complication: restored liver function, genetic predispositions, weight gain, immunosuppressive therapy. This syndrome contributes to increase the cardiovascular risk in transplanted patients. Aim of this study was (1) to evaluate the prevalence and the incidence of Post-Transplant Metabolic Syndrome (PTMS); (2)To evaluate risk factors for PTMS; (3)To verify the influence of PTMS on patients' cardiovascular risk.
Patients and Methods: We enrolled 156 patients (mean age 58±9 years, 76% male) who underwent LT during the last ten years. Mean follow-up was 67±50 months (range 6-114 months).
Personal and clinical data were collected retrospectively for each patient; PTMS was diagnosed according to modified NCEP ATPIII criteria.Cardiovascular risk was calculated as suggested in www.iss.cuore.it
Results: Twelve patients (7%) had a diagnosis of metabolic syndrome before transplantation. PTMS was present in 28% of patients after LT.The majority of patients (>80%) had a diagnosis of PTMS within the first two years after surgery. All metabolic traits increased in prevalence from pre-LT to post-LT period (arterial hypertension form 13 to 52%, diabetes mellitus from 17 to 30%, hyperlipidemia from 8 to 58%).
The prevalence of overweight/obesity (BMI>28,8 Kg/m^2) did not change significantly (from 22 to 20%).
The presence of overweight/obesity and diabetes mellitus before transplant, first degree relative with diabetes and Tacrolimus regimen correlated with PTMS at univariate analysis (p<0,05).
Independent predictive factors for PTMS were pre-LT overweight/obesity ([OR]=8,2) and diabetes ([OR]=4,3), while Tacrolimus therapy seems to exert a protective role ([OR]=0,4). Twenty-one percent of patients with PTMS showed a cardiovascular risk ≥20%.
Conclusion: A close follow-up is mandatory to prevent the development of PTMS mainly in those patients overweight and diabetic before transplantation.

P-337 MICROVASCULAR RECONSTRUCTION OF HEPATIC ARTERY USING A NEW IMAGING DEVICE

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Background: Hepatic artery reconstruction is technically demanding, and thus challenging. In our hospital, all hepatic artery reconstructions are performed under surgical microscope by plastic surgeons. We have introduced surgical techniques and an imaging device from the field of plastic surgery into hepatic artery reconstruction. Here we report such cases of hepatic artery reconstruction.
Methods: Since 2009, we have performed 45 cases of microvascular hepatic artery reconstruction: 37 cases of Living-Donor Liver Transplantation, 4 cases of Deceased-Donor Liver Transplantation, and 4 cases of cancer resection at the hepatic hilum. Microvascular anastomosis was performed using 9-0 nylon and double-armed needle. Indocyanine Green infra-red camera system was used to confirm the patency after the microvascular anasomosis. If there are multiple hepatic arteries available for anastomosis, we try to reconstruct as many hepatic arteries as possible, even in cases where single artery reconstruction seems to be sufficient for perfusion of the whole liver. We reconstructed more than two arteries in 8 cases.
Results: Complications related to the procedure (arterial occlusion, postoperative bleeding, aneurism, etc.) were not seen. The multiple hepatic artery reconstruction provided two principal advantages which allowed safer transplantation: (1) peak systolic velocity was increased; (2) the direction of the arterial blood flow was changed to physiologic pattern.
Conclusion: New devices and techniques from the field of plastic surgery can contribute to safer microvasuclar reconstruction of the hepatic artery.

P-338 IMPACT OF LEFT LOBE GRAFT ON ADULT LIVING DONOR LIVER TRANSPLANTATION: SMALL-FOR-SIZE GRAFT IS NOT A RISK FACTOR FOR SHORT AND LONG OUTCOME

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Background/Aim: Operative mortality for a right lobe donor in adult-to-adult living donor liver transplantation (LDLT) is estimated to be high as 0.5-1%. To minimize donor's risk, left lobe (LL)-LDLT might be an ideal option in adult-to-adult LDLT. The aim of the study was to assess the feasibility of LL-LDLT in adult patients.
Patients: Between 2005 and 2010, eighteen consecutive LDLTs were performed at Tokushima University Hospital. Of the 18 adults, 15 patients underwent LDLT using LL-grafts with (n=12) or without (n=3) the caudate lobe. Four of 7 patients with HCC had HCC beyond the Milan criteria. Two cases with ABO-incompatible LDLT were included. Small-for-size graft (SFSG) was defined as graft volume-to-recipient standard liver volume (GV/SLV) $<$40% or graft-to recipient weight ratio (GRWR) $<$0.8. Patients were divided into two groups, SFSG (n=9) and non-SFSG (n=6); and outcomes were compared between the two groups.
Results: The mean graft weight of LL-grafts was 448g (340-520g), GV/SLV and GRWR were 39% (33-50%) and 0.78% (0.61-1.13). No difference was observed in the background variables such as diagnosis, age and genders. Postoperative complications were dissection of hepatic artery (n=1), sepsis (n=1), hemophagocytic syndrome (n=1), small-for-size syndrome (n=1), hemorrhage (n=3). No significant difference was observed in the incidence of postoperative complications between the two groups. The overall 1-, 3-, and 5-year patient survival rates in LL-LDLT were 100%, 93%, 93%, respectively. Only 1 patient who had HCCs beyond Milan criteria was lost. There was no significant difference in patient survival between the two groups.
Conclusion: Adult-to-adult LL-LDLT, even if SFSG was used, was found to be feasible without affecting patient survival. Further utilization of LL-grafts should be undertaken to keep the chance of donor morbidity and mortality minimal.

P-339 WHEY PROTEIN ISOLATE, MEIN®, CAN REDUCE LIVER DAMAGE EARLY AFTER LIVING DONOR LIVER TRANSPLANTATION

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Background: Whey protein isolate is known to protect drug-induced liver injury through anti-inflammatory function. We previously reported the beneficial effect of MEIN®, liquid diet including whey protein isolate, on hepatic ischemia/reperfusion injury in rats at Digestive Disease Week 2008. The aim of this study was to clarify the effect of MEIN® on etiology-unknown liver damage early after living donor liver transplantation (LDLT).
(Methods): Sixteen recipients, who underwent LDLT, were included in this study. No definite acute cellular rejection was observed. Eight patients had re-elevation of liver enzymes around 1 or 2 weeks after LDLT (MEIN® group), while the other 8 did not experienced re-elevation of ALT (Control group). In MEIN® group, MEIN® (200ml, 1kcal/ml) was administered orally once a day. Following parameters were compared between the two groups: postoperative liver function; asparatate aminotransferase (AST), ALT, total bilirubin (T-BIL) and C-reactive protein (CRP).
(Results): In MEIN® group, serum AST and ALT level 1 and 2 weeks after administration significantly decreased compared to before administration (AST; before: 113$\pm$66 U/l$\rightarrow$ 1w after: 54$\pm$35 U/l,2w after: 42$\pm$20 U/l,ALT; before: 248$\pm$118 U/l$\rightarrow$ 1w after: 148$\pm$110 U/l,2w after: 85$\pm$53 U/l). In addition, serum total bilirubin and C-reactive protein level 2 weeks after administration significantly decreased compared to before administration (T-BIL; before: 1.8$\pm$1.1 mg/dl$\rightarrow$ 2w after: 0.7$\pm$0.2 mg/dl and CRP; before: 1.5$\pm$0.3 mg/dl$\rightarrow$ 2w after: 0.7$\pm$0.3 mg/dl, each, $P<0.05$).
(Conclusion): These findings suggest that MEIN® could reduce liver damage early after LDLT, furthermore, that MEIN® might be useful to differentiate liver damage such as ischemic change from acute cellular rejection.

P-340 LATE ACUTE REJECTION MORE THAN 3 MONTHS AFTER LIVING AND DECEASED DONOR LIVER TRANSPLANTATION

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Background and Purpose: The aim of this study was to review our experience of late acute rejection more than 3 months after liver transplantation (LT) and analyze the long-term outcome.
Methods: We performed 140 living donor LTs and 2 deceased donor LTs from 1991 to 2010, and 127 recipients (89.4%) were survived more than 3 months. Twenty-three recipients had biopsy proven late acute rejection more than 3 months after LT. The long-term outcome of these 23 recipients was evaluated in relation to immunosuppresive therapy, complications, and quality of life.
Results: The average age at LT was 16.1 years old. Biliary atresia occupied 60% of the primary diseases. The mean follow-up period was 10.7 years. Two recipients died during the follow-up period, one was dead due to PSC recurrence and the other was due to HCV cirrhosis. Late acute rejection was diagnosed by biopsy at a mean of 2.5 years after LT (from 3 months to 9 years). Eight of the 21 recipients had late acute rejection later than 5 years after LT. All of those rejections were acute cellular rejections, the rejection activity index ranged from 3 to 5. At the time of rejection, 17 recipients had tacrolimus and 6 recipients had cyclosporine. Twenty-one of them improved with steroid pulse therapy. Two recipients had steroid resistant acute rejection and were administered deoxyspergualin after steroids. One recipient had refractory acute cellular rejections at the 1, 3, 6 and 8 years after LT. Chronic rejection was not observed in this series.
Conclusion: Around 18 percent of the recipients those who were survived more than 3 months had late acute cellular rejection. But all of them were safely cured by anti-rejection therapy without severe complications.

P-341 USEFULNESS OF THE PINCH-BURN-CUT (PBC) TECHNIQUE WITH MONOPOLAR FORCEPS DURING TOTAL HEPATECTOMY OF THE RECIPIENTS IN LIVER TRANSPLANTATION

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Objective: It is thought that intraoperative or postoperative bleeding complication in the recipients of liver transplantation is one of unfavorable factors worsening outcome of grafts and recipients. And this complication is strongly associated with surgical technique for recipient's operation. However, there are little published papers about surgical technique to reduce intraoperative bleeding or the incidence of postoperative bleeding. In this study, we evaluated the effect of PBC technique to reduce the bleeding complication of recipients during or after the liver transplantation.
Materials and Methods: Between July, 2007 and May, 2010, 93 recipients underwent liver transplantation in our institute. Among them, total hepatectomy of recipient's liver was performed using PBC technique in 46 recipients and conventional technique in 47 recipients. The amount of intraoperative transfusion, operation time, and the incidence of postoperative bleeding were analyzed and compared between two groups.
Result: The intraoperative transfusion of pRBCs was significantly reduced in recipients using PBC technique (13.32 12.241 vs. 7.48 10.766, p=0.001). And the operation time was significantly short in PBC group of recipients (717.9

176.3 min. vs. 654.9 143.3 min., p=0.012). However, the incidence of postoperative bleeding was lower in recipients using PBC technique than conventional technique, but had no statistical significance (14.9% vs. 8.7%, p=0.45).
Conclusions: Total hepatectomy of the recipient using PBC technique is effective to reduce intraoperative bleeding and operation time.

P-342 LIVING DONOR LIVER TRANSPLANTATION: IMPACT ON DONOR'S HEALTH-RELATED QUALITY OF LIFE

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Aim: To evaluate the health-related quality of life of living liver donors after living donor liver transplantation (LDLT).
Methods: Health-related quality of life (HRQOL) in fifty-five living liver donors operated on at our center between 2002 and 2009 was assessed using the German Version of the 36-Item Health Survey (SF-36).
Results: Donors after full-right lobe hepatectomy (n=18) scored similarly and without statistical significance to the German reference population, whereas donors after left lateral segmentectomy (n=37) revealed statistically significant higher average score values ($p < 0.005$) in the categories of physical functioning, bodily pain and general health compared to the German reference population. In the analysis between donors after full-right lobe hepatectomy and donors after left lateral segmentectomy there was no statistically significant difference observed in any of the SF-36 categories. Postoperative complications of the donors and postoperative recipient mortality were particularly revealing regarding HRQOL. Donors who developed postoperative complications presented a lower HRQOL especially in the categories of role physical, bodily pain and social functioning where a statistically significant difference ($p < 0.005$) was observed. Similarly, postoperative recipient mortality was correlated to lower mean score values in all SF-36 categories but a statistically signidicant difference ($p < 0.005$) was reached only in the categories of role emotional and mental health.
Conclusions: Donors did not regret their decision to donate as health-related quality of life was not affected by the operative procedure of the donor hepatectomy. Living liver donors scored as well as or even better than the German reference population but it was clearly shown that the development of postoperative donor complications and the postoperative recipient mortality had a negative effect on HRQOL of the donors.

P-343 PERIOPERATIVE ANTIMICROBIAL PROPHYLAXIS IN LIVER TRANSPLANT RECIPIENTS

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Introduction: Perioperative infections in liver transplant recipients remain an important problem reducing graft and recipient survival. Pretransplant recipients' condition and the severe operative stress demand antibacterial and antifungal prophylaxis.
Aim of the study: was the evaluation of the effectiveness of standard antimicrobial prophylaxis after orthotopic liver transplantation (OLTx) with piperacillin with tazobactam (Pip) and fluconazole.
Material and methods: Group of 84 recipients after 87 OLTx performed in 2005-2010 was analyzed. 5 recipients were excluded from that group because of early (3 days after OLTx) death or reOLTx. Mean age of the recipients was 48,8±11,2 and liver failure in MELD score was 17,0±7,6. All patients received the same immunosuppression – tacrolimus and corticosteroids. Prolonged standard antimicrobial prophylaxis was provided: Pip 3x4,5 and fluconazole 100mg/24h. High risk recipients with asymptomatic urinary tract and ascites fluid infections received meropenem 2x1,0 or vancomycin 2x1,0. Effectiveness of prophylaxis was assessed according to blood, urine and bronchoalveolar lavage (BAL) culture up to the 14th postoperative day (pd).
Results: Standard antimicrobial prophylaxis was administrated in 72 cases. In that group one patient (1,4%) had positive blood culture, 6 patients (8,3%) had positive urine culture and 4 (5,6%) – positive BAL culture during 14 pd. Pre-OLTx asymptomatically infected recipients were blood culture negative, one (11,1%) urine and 5 (55,6%) – BAL culture positive. D-group streptococci dominated in urine positive cultures and staphylococci – in BAL positive cultures. Fever and high C-reactive protein as clinical markers of infection was not observed in culture-positive patients. There was no infection-related death during 30 pd.
Conclusions: The analysis of the early posttransplantation period confirmed the effectiveness of standard antimicrobial prophylaxis based on piperacillin with tazobactam and fluconazole. Routine culture controls are crucial in posttransplantation patients monitoring.

P-344 INTRAOPERATIVE HEPATIC ARTERY BLOOD FLOW PREDICTS EARLY HEPATIC ARTERY THOMBOSIS AFTER LIVER TRANSPLANTATION

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Background: Graft complications after orthotopic liver transplantation are associated with a high graft loss and mortality rate. The aim of this study was to assess the relation between hepatic blood flow on revascularization and early hepatic artery thrombosis (HAT).
Methods: Retrospectively, we reviewed perioperative variables from 110 consecutive liver transplants carried out at the University Hospital "Virgen del Rocío" from Seville (Spain) during 2007-2010. We evaluated the following preoperative (donor and recipient) and intraoperative variables: donor and recipient age, CMV-serology, ABO-compatibility, anatomical variations of the donor hepatic artery, number of arterial anastomosis, portal and hepatic artery flow before closure, cold ischemia time, blood transfusion. These variables were included in a univariable analysis.
Results: Of the 110 patients included in the study, 85 (77.7%) were male subjects. The median age was 52 years. ABO blood groups were identical between donor and recipient in all patients. Crude mortality with/without HAT was 22% vs 2% (p=0,001), respectively. Crude graft loss rate with/without HAT was 27% vs 4% (p=0,003), respectively. Early HAT was shown to be primarily associated with intraoperative hepatic artery blood flow (93,3 ml/min recipients with HAT vs 187,7 ml/mint recipients without HAT, $p<0,0001$).
Conclusion: In our experience, intraoperative hepatic artery blood flow predicts early hepatic artery thrombosis following liver transplantation.

P-345 LONGTERM RENAL DYSFUNCTION IN LIVER TRANSPLANT RECIPIENTS

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The immunosuppressive medications are frequent associated with posttransplant renal dysfunction. Progressive decline in renal function is predicted by a decline in renal function over the first 3-12 months after transplant.
The aim of this study was to identify the evolution of chronic renal dysfunction (CRD) after liver transplantation treated with immunossupressiv standard protocols.
Material and methods: We evaluated 110 liver transplant recipients. None of the 110 patients presented kidney affection before transplantation. Standard immunosuppression protocols were used (46,1% received tacrolimus, 53,9% ciclosporin) We evaluated the risk of developing chronic renal dysfunction in the absence of pre-existing renal conditions. We also evaluated the relationship between renal failure and posttransplantation dyslipidemia (hypertriglyceridemia >150 mg/dL, high-density lipoprotein cholesterol <40 mg/dL in men or <50 mg/dL in women). Kidney affection was considered in case of: proteinuria >3 gr/24 hours and/or hematuria > 2000/min (Addis-Hamburger probe), the presence of cilinders in urine spot or a creatinine clearance of < 90 mL/min calculated using the MDRD formula (Modification of Diet in Renal Disease).
Results: After 3 years follow up the proteinuria > 3 gr/24 hours and hematuria (>2000/min) were present in 4,5% of transplanted patients. II-nd degree chronic kidney failure developed in 45.71% of cases and III-rd degree chronic kidney failure in 31% of all transplants. Renal dialysis was necessary only in a case who developed nephrotic syndrome and chronic renal failure IV-th degree. 46% cases developed dyslipidemia, but no relationship was found between dyslipidemia and renal failure postliver transplantation.
Conclusions: Renal failure occurs frequently after liver transplantation (76.71%). Tacrolimus, as well as Ciclosporin, may be considered as risk factors for kidney affection postliver transplantation.

P-346 AMYLOID POLYNEUROPATHY RELAPSED 7 YEARS AFTER DOMINO TRANSPLANTATION WITH THE LIVER OF A 62-YEAR-OLD FAP DONOR

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Background: Familial amyloid polyneuropathy (FAP) is one of the progressive diseases which are in adaptation of adult liver transplantation. Graft liver taken from the recipient with FAP can be implanted as a temporary graft for other patient with end-stage liver failure, because the deposition of amyloid to the organs including heart, kidney, gastrointestinal trunk and nerves is completed

in at least over 20 years and the liver function is preserved excluding production of transthyretin. It is called as domino transplantation which has been generally performed in the world-wide. We experienced a rare case of amyloid polyneuropathy relapsed only 7 years after domino transplantation.
Case: The patient was a 37-year-old man who had decompensated liver function due to Wilson's disease. He received domino transplantation with the graft liver from 62-year-old FAP patient. He experienced appetite loss, decreased grip strength and reduced sensory perception 7 years after transplantation. His nerve conduction velocity showed dissociated sensory loss leading to selective impairment of autonomic nerve such as pain or temperature which was recognized as the typical pattern in early stage of amyloid polyneuropathy.
Conclusion: The symptoms of amyloidosis are expected to appear at least over 20 years after domino transplantation. Therefore, the patients could acquire the improvement of their quality of life during long term period after transplantation although some of them needed to undergo retransplantation in the future. In this case, amyloid polyneuropathy was relapsed only 7 years after domino transplantation. Donor age with above 60 years old might affect to the rapid progression of the disease. This case might indicate that we need to put these rapid recurrences of FAP in mind in case of domino transplantation.

P-347 PRE-TRANSPLANT PREDICTORS OF HEMODYNAMIC INSTABILITY AND NEED OF VENO-VENOUS BYPASS DURING LIVER TRANSPLANTATION

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Aim: The role of veno-venous by-pass (VVBP) during liver transplantation (OLT) is still a matter of debate. The aim of the study is to identify potential preoperative factors predicting hemodynamic instability and the need for a VVBP during OLT.
Methods: All 171 adult recipients of conventional liver transplantation (with supra- and infra-hepatic anastomoses and excluding live donors) performed in Geneva between 2005 and 2010 were included in the study. An intra-operative algorithm based on the level of SVO2 was used in order to decide which patient had to undergo a VVBP. The studied variables included: model of end-stage liver disease (MELD) score, Child, porto-systemic gradient, presence of comorbidity (cardio-pulmonary, prior surgery), kidney function, emergency transplant, retransplant.
Results: Mean age was 49±11 years, with a female/male ratio of 50/121 (29%/71%). The main indications for transplantation were hepatocellular carcinoma (34%), hepatitis C (13.5%), alcohol (10%) and hepatitis B (6%). During the study period, VVBP was used in 33/171 (19.5%) liver transplantations with a stable incidence over time. Only the American Society of Anesthesiology score (p=0.089) and the presence of kidney failure (p=0.06) tended to predicted the need for VVBP. Of note, MELD score was not a significant predictor as both very sick patients and those with mild disease and no portal hypertension required VVBP. Following the intra-operative algorithm, only one patient failed without VVBP (1/133, 0.75%) and required an unexpected splenectomy for a spleen rupture during venous clamping.
Discussion and conclusion: Overall, none of the studied variable predicted the need for VVBP, but the used intra-operative algorithm was accurate and sure. Despite the advances in anesthesia and surgery, VVBP remains a valuable choice in some selected patients and should be available in all transplantation centers.

P-348 CAVERNO-PORTAL ANASTOMOSIS TO RESTORE PORTAL FOW IN PATIENTS WITH PORTAL VEIN THROMBOSIS AND HEPATOPETAL CAVERNOMA UNDERGOING LIVER TRANSPLANTATION

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Introduction: Portal vein thrombosis is no longer a contraindication for liver transplantation since techniques such as jump graft anastomosis, left reno-portal anastomosis, arterialisation of the portal vein, cavo-portal hemi transposition or combined liver-small bowel transplantation can generally circumvent this problem. For some patients, however, the above mentioned solutions are not optimal.
Method: We present an alternative surgical procedure that re-establishes the physiological, hepatopetal flow of an existing cavernoma: a caverno-portal anastomosis (CPA) that recovers all important hepatopetal varices in a large afferent mouth that is anastomosed to the graft's portal vein.
Between 2008 and 2010, 3 patients with a hepatopetal portal cavernoma underwent liver transplantation in our department. The preoperative CT scan did not show spontaneous spleno-renal shunts or other porto-systemic shunts, so that a reconstruction by reno-portal anastomosis was considered at high risk of failure. In all 3 cases, a CPA was performed using 3 to 6 varices as the recipient's portal anastomotic mouth that were anastomosed to the graft's portal vein.
Results: One patient was reoperated on post-operative day 1 because of absent portal flow on routine Doppler ultrasound. Normal flow (velocity 22 cm/sec) recovered as soon as a VAC device was removed and the abdomen closed. Subsequent postoperative course in this patient and in the remaining 2 patients was uneventful, with a mean hospital stay of 28 days (21-38) and with normal portal flow on repeat Doppler ultrasound and contrast-enhanced CT-scan examination.
Conclusion: CPA is a challenging surgical technique, but is more physiological or less morbid than other alternatives in patients with hepatopetal cavernoma undergoing liver transplantation.

P-349 THE POSSIBILITY OF ADIPOSE-DERIVED REGENERATIVE CELLS FOR AN ALTERNATIVE THERAPY FOR LIVER FAILURE

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Background: Adipose tissue represents an abundant source of adult stem cells, termed "adipose-derived regenerative cells (ADRC)", with the ability to differentiate along multiple lineage pathways. Recent studies have shown the ADRC have the ability to attenuate to repair and regenerate some damaged organs. In this study, we demonstrate ADRC have the ability to differentiate into hepatocytes and to protect them *in vitro* and *in vivo*.
Methods: We obtained the ADRC by the Celution system® (Cytori Therapeutics), which allows the isolation of ADRC fractions from human adipose tissue. We co-cultured mouse hepatocytes (1.0×10^5 cells/well) with ADRC (1.0×10^5 cells/well) in a state of no cell-contacts, and examine the viability of hepatocytes over time. In addition, we investigated whether ADRC decrease liver damage in vivo.
Results: The viability of hepatocytes in ADRC + hepatocytes co-culture groups was better than only hepatocytes culture groups (21.5±4.3% v.s. 6.9±1.3% in day5, 16.6±2.1% v.s. 1.1±0.2% in day7). The injection of ADRC in combination with heparin (0.2U/kg) into the caudal tail vein in 70% hepatectomized nude mice significantly decreased the serum the ALT, AST and LDH level within 24hrs after operation. We also demonstrated the injected Xenolight DiR® labeled ADRC were accumulated into regenerative liver using IVIS® imaging system.
Conclusions: These results suggest that ADRC can protect hepatocytes through homing to damaged liver and certain trophic effects. Therefore, ADRC-based therapy might have the potential of an alternative therapy for liver failure.

P-350 LIVER TRANSPLANTATION FROM DCD DONORS – THE ROYAL FREE EXPERIENCE

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Background: Liver transplantation from DCD donors, whilst increasing the number of organs available, has been shown to have inferior results to transplantation from DBD donors.
Methods/Materials: We reviewed the results of our DCD donor transplantation programme, all data having been stored on a computerised database.
Results: 27 transplants were performed over a 5-year period. Primary non-function (PNF) occured in 4/27 (14.8%), ischaemic cholangiopathy in 5/27 (18.5%) and hepatic artery thrombosis in 3/27 (11.1%) patients. PNF only occurred in organs with cold ischaemia times greater than 9 hours. 2-year graft and patient survival were 65.2% and 88.8% respectively.
Conclusion: Liver transplantation from DCD donors has a higher incidence of arterial and biliary complications and PNF compared to DBD donors, but careful donor selection, and minimising cold ischaemia time can improve outcomes.

P-351 HEMOLYTIC ANEMIA DUE TO PASSENGER LYMPHOCYTE SYNDROME AFTER LIVER TRANSPLANTATION

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Introduction: Passenger lymphocyte syndrome is due to the production of antibodies by donor B lymphocytes against the recipient's red blood cell antigens (usually against the ABO and Rh system). It usually is a self-limited process that occurs in 1–3 weeks posttransplant. PLS can develop abruptly and can vary from mild to severe.
Clinical Case: Male 59 yo with alcoholic cirrhosis and HCC transplantated with a 75 yo compatible but not identical ABO cadaveric donor (the recipient is AB and the donor was B). Early postoperative was uneventful with progressive normalization of liver tests. At the 10th postoperative day, abruptly the patient worsened with elevation of the liver tests (AST 1341 and ALT 542), severe anemia (Hb 3), jaundice (total bilirrubin 18), disnea and renal failure. Doppler US and abdominal CT normal. Hematological tests showed elevated LDH (3220), haptoglobin 5.8, direct combs positive (IgG+++, C3d+++, IgA++ and IgM–), serological anti-A in the recipient (produced by donors lymphocytes), indirect Coombs negative and anti-A over the red cells. All theses finds are compatible with hemolytic anemia due to passenger lymphocytes. We treated the patient with transfusion of 16 units of RBC (B), fluid reposition, renal replacement, steroids and change of immunosuppression from tacrolimus to everolimus because renal failure, with progressively improving of red cells count, renal function and liver tests. The patient was discharged at 31 postoperative day with Hb 10.9, liver tests normal, LDH 176 and Cr 1.9.
Conclussions: The passenger lymphocyte syndrome is due to the production of antibodies by the donor B lymphocytes against the recipient's red blood cell antigens. It courses abruptly usually with alteration of hepatic tests and hemolytic anemia and is self limited. Treatment is transfusion and sometimes steroids.

P-352 GRAFT VERSUS HOST DISEASE AFTER LIVER TRANSPLANTATION, A RARE BUT SEVERE INMUNOLOGICAL COMPLICATION

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Introduction: GVHD after LT has an incidence <1% and can involve gastrointestinal tract, skin and bone marrow. There are a lot of treatment options: from increase immunosuppression to withdrawing immunosuppression to restore immunological competence; but the results are very poor with high mortality rate. Clinical case. Male 68 yo with alcoholic cirrhosis transplanted with a 42 yo identical ABO cadaveric donor. Postoperative course was right being discharged at 17th day with triple therapy immunosuppression: tacrolimus, MMF and prednisone. Six days after he was readmitted due to diarrhea (6-10 liquid stools every day), renal failure and trunk and arms desquamative rash and 37,7°C. Laboratory tests were normal except renal failure, blood cultures and viral serology negative and repeated stool specimens were negative for *Clostridium Difficile.* Gastroscopy and colonoscopy: mucosa ulcerations, irregular,nodular and friable mucosal surface in duodenum, ileum and colon. Mucosal biopsy: ulcerations with loss of superficial epithelium, crypt destruction and apoptotic cells without viral inclusions. Skin biopsy: vacuolar degeneration at the basal plane with dyskeratotic cells, apoptotic cells and lymphocyte infiltration.With the diagnosis of GVHD grade III we treated the patient with steroids boluses of 1000 mg during 3 days with initial good response improving the diarrhea and the rash but when we decrease the steroids dosage the patient worsened, so we withdrawal baseline immunosuppression and added basiliximab (x2). Broad-spectrum antibiotic, antiviral and antifungal therapy were added too. More than 90 days after the LT the patient died due to a systemic CMV infection.
Conclusions: GVHD is a rare but severe complication with high mortality rate. It involve usually skin and gastrointestinal tract. There is no consensus about the treatment: increase or withdrawing immunosuppression; associated with intensive care and antibiotics and antifungal to avoid infections complications.

P-353 LIVER TRANSPLANTATION AFTER RADIOEMBOLIZATION WITH YTTRIUM-90 MICROSPHERES

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Background: Liver transplantation remains the only curative treatment option for patients with unresectable hepatocellular carcinoma (HCC). However, the limited availability of donor organs prolongs the waiting time and increases the risk of tumor progression. Several bridging treatment options have been developed and are currently in use. Radioembolization is mostly employed in the control of large HCCs when other treatment modalities such as chemoembolization or radiofrequency ablation are not indicated.
Methods: Between December 2006 and December 2010, 12 patients underwent liver transplantation (LT) after bridging treatment with radioembolization in our transplant center. We followed the postoperative course and histopathological examination of the explanted livers was performed.
Results: Patients underwent LT 37 [8-359] days after radioembolization. In the explanted liver viable tumor cells were found in four patients, in six patients partial necrosis was seen and in two patients complete necrosis of tumor cells were noted. 191 [0-1439] days after LT 10 patients are alive. One patient died during transplant surgery due to cardiac shock and one patient died due to septic shock on POD 10. In two patients, osseous metastases developed 6 and 13 months after LT.
Conclusion: In certain cases radioembolization is a valuable treatment option for bridging to LT. Histopathological assessment demonstrates at least partial necrosis. The optimal timing for LT after radioembolization still needs to be defined.

P-354 BUDD-CHIARI SYNDROME AS A INDICATION FOR LIVER TRANSPLANTATION

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Introduction and Aim: Presentation of the results of adult liver transplant recipients transplanted for Budd-Chiari syndrome (BCS) in the single centre.
Material: In the period 1989 – 03.2011, 904 orthotopic liver transplantations (oltx) were performed, including 47 retransplantations.
The Budd-Chiari syndrome in 28 cases was primary indication to oltx.
Patients age: 17 – 56 years (avg=34, sd=12), gender F/M: 17/11
Cold ischemia time: 270-725 minutes (avg=522 minutes, sd=125)
MELD status: 12-20 (avg=16 minutes, sd=3)
UNOS status before re-oltx: UNOS 1 – 5, UNOS 2a – 13, UNOS 2b – 9, UNOS 3 - 1
In all patients the classical orthotopic liver transplantation with veno-venous bypass was performed.
Results: Operative mortality: 1 patient
No major complications were observed in postoperative period
Survival: alive – 22 (78.6%), died – 6 (21.4%), 0-10.41 years (avg=4.62, sd=3.24)
1-year survival in Budd-Chiari group was 78.6% and accordingly in the whole oltx group 85.2%
6-year survival accordingly 78.6% and 75.5%, p=0.86
Retransplantation was necessary in 2 cases (acute rejection, arterial thrombosis)
Conclusion: There is no significant difference in survival time between Budd-Chiari group and whole oltx group
Mortality in BCS group was highly correlated with the UNOS status just before OLTx.
In our experience orthotopic liver transplantation is relatively safe and an efficient procedure in Budd-Chiari syndrome treatment.

P-355 ASSOCIATED FACTORS WITH THE TRANSFUSIONS NEEDS IN LIVER TRANSPLANTATION

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The need of blood products is high in liver transplantation (OLT). In recent

years the intraoperative transfusions have decreased because of the improvement of surgical and anesthetic techniques.
Objective: To analyze retrospectively the factors associated with greater transfusion requirements in OLT to design strategies to minimize those needs.
Material and Methods: We studied 131 OLT in 123 patients OLT made since January 2007 until December 2010. We reviewed age, gender, re-OLT, OLT-indication, transfusion requirements (RBC, plasma, platelets), BMI, previous surgery, diabetes, hypertension, and death in the next 3 months. Patients were classified in three groups: a)transfusion of 5 or less RBC b) 5 to 10 CH c)10 to 20 RBC d) more than 20 RBC.
Results: 28 patients were women and 97 men. 8 were re-OLT. The indication for OLT was alcoholic cirrhosis in 34 patients (27.6%), hepatocellular carcinoma in 51 (41.5), viral hepatitis (HBV, HCV or both) in 24 (19.5%), fulminant liver failure, 4 (3.25%), CBP 7 (5.7%) and other in 3 patients (2.4%). 29 patients (23.6%) had previous surgery and overall mortality in the third month was 22 patients (7.6%). 50 (45.8%) patients received <5 UCH (a group), 31 (23.6%) between 6 and 10, 34 (25.9%) between 11 and 20 and 16 (12.2%) over 20 CH. The mortality associated with each group was 14, 6.45, 11.7 and 56% respectively, showing significant differences between group receiving more than 20 CH. Likewise, the prevalence of previous surgery was significantly higher in the group d (34.25% versus 22%). The average of transfusion decreased significantly in 2010 compared to earlier.
Conclusions: The support with blood products during OLT is critical. Re-OLT and prior surgery are two key factors that determine the increase in blood transfusion. Transfusion of more than 20 CH RBC in our series was associated with significantly higher early mortality.

P-356 COAGULATION BETWEEN DONOR AND RECIPIENT IN THE EARLY PERIOD AFTER LIVING DONOR LIVER TRANSPLANTATION

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In this study we investigated about differences of peri-operative blood coagulation and fibrinolytic system between donor and recipient following adult living donor liver transplantation (LDLT).
Patients and Methods: Both eight recipients and donors who underwent LDLT were investigated about the changes of soluble fibrinogen (SF), TAT, PC, FDP, D-dimer, PIC, α2-PI, Plt, and PAI-1 on the day 1, 3, 7, and 11 following LDLT aided by Mitsubishi Tanabe Pharma Corporation. Donor were three females and five men. Recipients were 4 males and 4 females. 2 fuluminant hepatitis, 4 type C liver cirrhosis, and one Wilson disease, and one primary biliary cirrhosis.
Results: The coagulation system of donor analyzed by TAT, SF, PT, and Plt suppressed by the day 3 to 7 and recovered after the day 7 after LDLT. Conversely, the fibrinolytic system of donor analyzed by FDP-P, D-dimer, and PIC activated from the day 3 to 7 after LDLT. SF of recipients was tended to recover after transplantation. The fibrinolytic system of recipient was same to donor except PAI-1. PAI-1 remarkably increased on the day1 after transplantation in the recipients.
Discussion: The understandings of BCF system between donor and recipient is thought to be very important for the management after LDLT. In the consideration with both data of donor and recipient, the recipient is thought to be DIC state in the early period after LDLT and SF might be useful marker for the improvement of BCF system. The elevation of PAI-1 of recipients on the day 1 after transplantation might become a marker of injury by shear stress of excessive portal hypertension after LDLT.

P-357 POST LIVER TRANSPLANT EVEROLIMUS BASED IMMUNOSUPPRESSION THERAPY: A MONO-CENTRIC EXPERIENCE

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Introduction: The main therapeutic challenge after orthotopic liver transplantation is the reduction of anti-rejection therapy (ART) toxicity and prevention of the recurrence of the native liver disease (viral or cancer). Everolimus has so far shown lower nephrotoxicity and antitumoral activity.
Materials: Since January 2010, 12 pts transplanted for HCC ("Milano out": 6) and 11 pts transplanted for Viral Cirrhosis with Renal Impairment (RI) due to CNI (Calcineurin Inhibitors) have been selected to receive ART with Everolimus. 13 patients were at time treated with Cyclosporine and 10 with Tacrolimus. The protocol to introduce Everolimus claims proteinuria $<$1gr/die and GFR$>$ 40 ml/min. On Day 1 Everolimus is introduced at a dose of 1.5 mg x 2 and CNI reduction of 50%. On day 7, if the Everolemia is greater than 3 ng/ml, the CNI is interrupted. On day 14 the the dose of everolimus should serve to maintain the Everolemia between 6-12 ng/ml.
Results: 10 patients are currently on Everolimus-based ART monotherapy: 4 patients with previous CNI-related RI, 5 with transplanted for HCC (3 "Milano out") and no recurrence and 1 transplanted for HCC ("Milano out") with lung cancer recurrence.
The remaining patients continue a combinated regimen with Everolimus and CNI. None of the 23 patients experienced rejection. In these patients, the evaluation of the renal function has shown a better performance compared with standard CNI-based therapy.
Conclusions: The conversion of the post-OLT ART from a CNI alone to Everolimus monotherapy or combined reduced dose CNI-Everolimus is feasible and able to reduce the post OLT nephrotoxicity. The antiproliferative effects of Everolimus to prevents HCC recurrence after OLT, despite encouraging results, need further prospective studies.

P-358 ASSOCIATION BETWEEN PATENT FORAMEN OVALE & ACUTE SUPERIOR MESENTERIC ARTERY OCCLUSION: IMPLICATIONS FOR INTESTINAL TRANSPLANTATION

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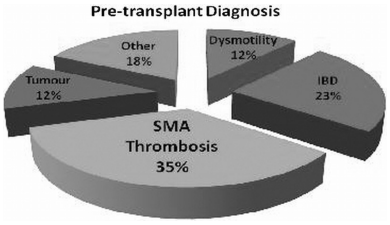
Background: Acute vascular catastrophe of the mid gut resulting in intestinal failure is a common diagnosis in adult patients presenting for intestinal transplantation. Acute occlusion of the superior mesenteric artery (SMA) is associated with arterial embolic events secondary to atrial fibrillation, valvular defects and thrombophilia. Patent Foramen Ovale (PFO) may present with acute embolic events i.e. cryptogenic stroke. Association of PFO with acute SMA occlusion has not been previously reported.
Methods: From 06/2008-11/2010, 17 patients were listed for intestinal transplantation at the Oxford Transplant Centre. All patients underwent cardiac investigation including transthoracic echocardiography and myocardial perfusion scintigraphy. Patients listed due to acute SMA occlusion also underwent a thrombophilia screen and bubble contrast echocardiography. Any PFOs detected were closed with transcutaneous transluminal prostheses.
Results: Of 17 potential recipients, 35% (n=6) had suffered acute SMA occlusion.



Within the SMA occlusion cohort, 50% (n=3) had a PFO. 33% (n=2) demonstrated thrombophilia. 75% (n=3) of patients with SMA occlusion without thrombophilia, had a PFO. No patient had valvular pathology or AF. There was no difference in inducible myocardial ischaemia or left ventricular function between the SMA occlusion group and patients with other pre-transplant disease.
Conclusion: There is an association between PFO and acute SMA occlusion in potential intestinal transplant recipients. 75% of those with acute SMA occlusion and no other embolic aetiology had a PFO, compared to probe patency incidences of 15-35% reported in the general population. Although numbers in this cohort are small, the findings are important as they identify treatable pathology which could result in further embolic events post-transplantation. During preoperative assessment of such patients, we recommend investigating for PFO, with a view to closing defects pre-transplantation.

P-359 EFFECTS OF CALCINEURIN INHIBITOR-BASED IMMUNOSUPPRESSION ON PRE-EXISTING RENAL IMPAIRMENT FOLLOWING ORTHOTOPIC LIVER TRANSPLANTATION

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Background: Approximately twenty-five percent of patients undergoing orthotopic liver transplantation (OLTx) have been shown to have pre-existing renal dysfunction. Such dysfunction confers a significant decrease in both graft and patient survival, and has been shown to be an independent predictor of permanent renal dysfunction post transplantation. Post transplantation renal function also has a significant correlation with the use of Calcineurin Inhibitor (CNI)-

based immunosuppression, such as Tacrolimus. Our aim was to investigate the effect of Tacrolimus based immunosuppression on post-transplant renal function, in OLTx patients already identified as having pre-existing renal impairment.
Methods: A retrospective case note review was carried out for all patients undergoing OLTx in a single UK transplant centre in one year, 2008. Data was collected on pre-transplantation renal function by calculating creatinine clearance for each patient, with pre-existing renal impairment defined as a creatinine clearance of less than 60mls/hr. Further data on demographics, post-operative immunosuppression regime and monthly post-operative creatinine levels was then collected.
Results: A total of 39 OLTx were performed in 2008. Of these, 13 were identified as having pre-existing renal impairment. One patient died intra-operatively; therefore data on post-operative renal function was collected on 12 patients. At the end of the first 6 month post-operative period, 9 patients had a lower serum creatinine level, compared to pre-operatively. Although monthly creatinine levels varied, requiring a subsequent adjustment in Tacrolimus dosage, no patients needed to discontinue Tacrolimus immunosuppression due to renal dysfunction during the first 6 months post-transplantation.
Conclusion: A large number of factors may affect post-operative renal function in OLTx, but this small retrospective case review suggests there is no need for alteration in our centres' current Tacrolimus-based immunosuppression therapy protocol, and Tacrolimus continues to be used in those patients with pre-existing renal impairment.

P-362 SVR TO ANTIVIRAL TREATMENT FOR POST-OLT RECURRENT HCV HEPATITIS CAN BE IMPROVED BY THE USE OF GROWTH FACTORS

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Background: The antiviral treatment of established HCV recurrence after liver transplantation is the only strategy to prevent the progression of the disease and severe liver damage*:* however SVR is achieved in a minority of cases and the discontinuation of therapy is frequent as a result of adverse events. The use of growth factors (GF) in the transplant setting, might contribute in lowering the rate of drug discontinuation or reduction, thus contributing to improve the outcome of treatment.
Aim: Evaluate the impact of GF on SVR in OLT recipients undergoing antiviral therapy.
Patients and Methods: A retrospective analysis was conducted on data collected from a multicenter database of 464 patients from 12 Italian Centres treated for histologically proven HCV recurrence after liver transplantation from 1992 to 2008: a combination treatment with interferon (80 patients-17,2%-with standard IFN and 384 -82,8%- with Peg-IFN) and Ribavirin. 73,9% were genotype1.148 patients (31,9%) received GF during antiviral therapy (20,2% G-CSF; 58,9% Eritropoietin; 20,9% epo plus G-CSF. Mean supporting treatment duration was 8 months for Epo, 8,7 months for G-CSF.
Results: Overall SVR was 34,1% (158 patients):SVR was 34,8% in the GF group compared with 25,3% in non GF-support patients (p=0,03). EOT was statistically different (p=0,02) between the two group (GF 66,2% vs Non GF 55%). A significant correlation between patients treated with >80% of ribavirin dose (a factor related to SVR in our analysis) and use of epo (61,7%) emerged from the analysis.For genotype 1 patients, EOT is significantly correlated to GF use (62,5% of patients:p=0,001). At the multivariate analysis, mean duration of G-CSF treatment (12,8 vs 6,9 months) was a significant factor associated with SVR (p=0,01).
Conclusions: The use and the mean duration of GF in transplanted patients was related to EOT and SVR respectively

P-363 THE PRESENCE OF DIABETES REDUCES SVR AFTER ANTIVIRAL THERAPY FOR POST-TRANSPLANT HCV RECCURRENCE

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Background: The antiviral treatment of HCV recurrence is the only available strategy in the attempt to prevent progression of the disease and graft failure after liver transplantation: the achievement of SVR (sustained virological response) appears to improve both histological picture and patient survival. Diabetes and insulin-resistance are well known negative prognostic factors for antiviral treatment in the non-transplant setting. Few data are available in the transplant setting.
Aim: to evaluate the impact of diabetes on SVR in liver transplant recipients undergoing an antiviral treatment for HCV recurrence
Patients and methods: data from a multicenter database of 464 patients transplanted for HCV-related ESLD in 12 Italian Centers from 1992 to 2008 were retrospectively collected. All patients underwent a treatment with interferon and Ribavirin for histologically proven HCV recurrence. Mean age at LT was 53,5 yrs, 73,9% were genotype 1, 151 patients (32,5%) were diabetics.
Results: Overall SVR in our population was 34,1%: 25,3% in diabetic patients compared with 40,6% in non diabetics (p = 0,04). Among diabetics, the use of insulin (71% of the diabetics) was associated with a lower rate of end of treatment response (EOT): 49% vs 67,4% in non-insulin dependent diabetics (p=0,04).
The pre treatment viremia is the only factor that significantly differs between the two group (diabetics vs non diabetics: p=0,01); whereas no differences in term of donor and recipient characteristics, genotype, duration of antiviral therapy, distance from olt, interval olt-recurrence, pre treatment fibrosis, emerged at the analysis.
At multivariate analysis the presence of diabetes was confirmed as independent negative predictor of SVR (p=0,05).
Conclusions: The presence of diabetes and the need for insulin emerge as negative prognostic factors for the response (SVR and EOT) to antiviral treatment for HCV recurrence post-liver transplantation.

P-364 MULTIVISCERAL TRANSPLANTATION FOR MASSIVE ABDOMINAL TRAUMA

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Background:
Intestinal transplantation is worldwide considered an effective surgical therapy for intestinal failure, even if, when possible, intestinal rescue is preferable, avoiding long term immunosuppression effects.
Methods: An 18 years old young man was victim of a devastating abdominal trauma and a total evisceration (stomach, duodenum, pancreas, spleen, small bowel and colon) was needed.
Results: After a first attempt to transplant the patient, which failed because of his septic conditions, the young man was finally transplanted with a multivisceral graft, including the liver because of his impendig liver failure. The vascular venous drenaige was performed with the piggy back technique while the inflow was ensured by an anastomosis between the aortic conduit of the multivisceral graft and the left iliac common artery. A gastro-gastric anastomosis was performed for the reconstruction of the upper digestive tract and a ileo-colic anastomosis was performed for the inferior tract. Finally an ileostomy was performed. Because of the impossibility to close the abdomen, due to the loss of domain of the intestine in the abdominal cavity, a recti fascia was harvested in the donor and was transplanted, but subsequently removed for severe infection. A VAC therapy was applied, resulting in the resolution of the abdominal infection and finally a skin graft from the thigh was performed.
Conclusions:
After 2 months from transplant the patient was discharged and he is alive after 5 months. The abdomen is well closed with the graft skin; he is completely off total parenteral nutrition and the multivisceral graft is well functioning.

Lung

P-365 AN UNUSUAL CASE OF LUNG TRANSPLANTS AND BREAST IMPLANTS

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We report on a 28 year-old lady undergoing bilateral lung transplantation for idiopathic pulmonary hypertension. During transplantation she became haemodynamically unstable and veno-arterial extracorporeal membrane oxygenation (ECMO) was started.
Post-operative ventilation was difficult and a computer tomogram (CT) of the chest showed herniation of the heart outside the pericardial sac with compression of the pulmonary veins. On day three, she underwent re-exploration, with return of the heart to the pericardial sac.
On day seven she required urgent re-exploration due to cardiac tamponade. Infarction of the left lung led to a left pneumonectomy and removal of ECMO on day nine. The left thoracic cavity was filled with three breast implants to prevent mediastinal shift and allow for future re-transplantation.
A persistent air leak was noted from the left bronchial stump with an unsuccessful attempt at closure made with an endobronchial injection of fibrin. In view of the risk of infection posed by the implants in the left thoracic cavity, she received constant irrigation with taurolidine via intercostal drains.
Despite her ongoing ITU stay seeing renal, liver and bowel function return to normal, she remained ventilator-dependent with no signs of active infection. It was felt that rehabilitation with a single lung allograft would not be possible. Therefore, after four months she underwent removal of thoracic cavity implants with left lobar transplantation. She was discharged from hospital two months later and is now well with good functional status.
Taurolidine irrigation can be an effective method of managing airway infection secondary to persistent air leaks. Prevention and treatment of air leaks can be difficult and unfortunately endobronchial fibrin injections were unsuccessful on this occasion. Breast implants can be used to permit future re-transplantation if rehabilitation with a remaining single lung allograft is unsuccessful.

Pancreas

P-367 BEWARE THE PANCREAS TRANSPLANT RECIPIENT WITH ELEVATED FIBRINOGEN AND HYPOTENSION

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Introduction: Thrombotic complications remain a significant challenge in pancreas transplantation, and with treatment of established thrombosis notoriously difficult, early detection is paramount. Noting that patients with complications in our series had elevated fibrinogen levels, we reviewed our series to determine whether there was a genuine association.
Methods: We retrospectively reviewed the case records of consecutive patients receiving whole-organ pancreas transplants in our centre from 2005 to 2009, noting serum fibrinogen levels on routine coagulation screens, whether there were episodes of hypotension, and whether a thrombotic complication arose in the graft.
Results: There were 10 patients with thrombotic complications (9 pancreatic, 1 renal), all of whom had full data in their records. There were 45 other patients without thrombosis, of whom 14 had missing blood pressure data, leaving 31 to be included in the study. Patients with fibrinogen levels $>$7g/dl and hypotension were significantly more likely to experience a thrombotic complication (odds ratio 16.7, p=0.001, Fisher exact test), but fibrinogen levels alone were not an independent predictor of thrombosis.
Conclusions: The combination of hyperfibrinogenaemia and hypotension appears to be a harbinger of thrombosis in pancreas transplantation. Fibrinogen, as an acute phase protein, may simply be a marker of underlying event predisposing to thrombosis, but as a coagulation protein it may also be an independent causative agent, especially in the context of low flow states associated with hypotension.
Discussion: Further studies are needed to establish whether fibrinogen has a causal role, as there may then be a therapeutic option of fibrinogen removal by plasmapheresis or immunoadsorption.

P-368 "TIMING THE IMPLANT": OUTCOMES IN PANCREAS TRANSPLANTATION

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Aim: To evaluate if performing pancreatic transplants within out of hour time represent an intrinsic risk toward the patient and the organ, thus trying to establish whether the pancreatic transplant should be performed as soon as possible, aiming to reduce the CIT, or it should rather be rescheduled to day time, offering a better result and a safer surgery to the patient.
Methods: A retrospective analysis of 201 patients received was pancreatic transplantation in our unit between 2001 and 2010 was carried out, Complete data was available on 175 patients (SPK 133, PAK 30, PTA 12). This cohort was subdivided and contrasted according to the time of surgery was initiated. 101 patients operated between 8am-4pm, with a median age of 43 years, (81 SPK, 15 PAK, 5 PTA) and a median CIT of 803 minutes. The group II were 56 patient, with median age of 42 years, (41 SPK, 11 PAK, 4 PTA), and a median CIT of 924 min. Group III was of 18 patients, with a median age of 44years, (11 SPK, 4 PAK, 3 PTA) and a median CIT of 915 min. There were no significant differences in terms of donor or recipient demographics across the groups. The primary endpoint utilised was patient mortality at 30 days and one year, with secondary endpoints of graft failure and surgical complications analysed.
Results:

Time started	No.	CIT	30d graft failure	30d mortality	1yr mortality
I: 08:00–16:00	101	821m	22 (22%)	2 (2%)	4 (4%)
II: 16:00–22:00	56	929m	10 (18%)	2 (3.5%)	5 (9%)
III: 22:00–8:00	18	898m	3 (17%), p=0.63	0 (0%), p=0.55	1 (5.5%), p=0.65

Major surgical complications	Group I	Group II	Group III	p value
Graft thrombosis	16 (16%)	6 (11%)	4 (22%)	NS (0.51)
Bleed/Haematoma	12 (12%)	6 (11%)	2 (11%)	NS (0.93)
Wound infection	18 (18%)	7 (13%)	2 (11%)	NS (0.49)
Radiological collection drainage	10 (10%)	7 (13%)	0 (0%)	NS (0.17)
Major intestinal fistula	11 (11%)	2 (4%)	0 (0%)	NS (0.14)
Peritonitis / Abdominal Abscess	18 (18%)	12 (21%)	3 (17%)	NS (0.91)

Conclusion: Based on ours experience pancreatic transplant during out of hours per se doesn't seem to represent a risk factor for the life of the patient nor for the success of the operation. The main factors for a successful transplant are the careful selection of donor and recipient in terms of age, BMI, PMH and more importantly the CIT.

P-369 HHV-8 ASSOCIATED LYMPHADENOPATHIC KAPOSI'S SARCOMA MIMICKING PTLD AFTER PANCREAS TRANSPLANT

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Background: Kaposi's sarcoma currently comprises more than 5% of all *de novo* neoplasms in this group. The average time to development of Kaposi sarcoma following transplantation is 15-30 months. Human herpesvirus 8 (HHV-8) genomic sequences have been identified by polymerase chain reaction in more than 90% Kaposi sarcomas.
Materials: From 2003 to 2010, Kaposi's sarcoma was identified for study from 65 patients with 69 pancreas transplants performed at Taipei Veterans General Hospital. Literature review was also done.
Results: Only one case of Kaposi's sarcoma was identified, with an incidence of 1.5%. The patient suffered from varicellar zoster Infection (chicken pox) 11 months after pancreas transplant alone (PTA). Four months later (15 months after PTA), lymphadenopathy with enlargement of multiple lymph nodes in neck, around celiac trunk, along the superior mesenteric artery and abdominal aorta, which mimicked posttransplant lymphoproliferative disorder (PTLD). The biopsy for pathology turned out to be Kaposi's sarcoma. HHV-8 viral gene is detected by the molecular (PCR) assay. The lymphadenopathic Kaposi's sarcoma disappeared 3 months after treatment by adding sirolimus, reducing the dose of tacrolumus and discontinuing mycophenolate mofetil. There has been no evidence of tumor recurrence for more than 2 years, and he has been enjoying an insulin-free life with euglycemia for more than 3 years.
Conclusion: This is an unusual HHV-8 associated Kaposi's sarcoma mimicking PTLD presenting as lymphadenopathic form, instead of usual cutaneous form. Sirolimus is recommended for the treatment of Kaposi's sarcoma, in addition to reduction, cessation or modification of immunosuppressive regimen.

Pediatric transplantation

P-370 PEDIATRIC LIVER-KIDNEY TRANSPLANTATION: A SINGLE CENTER EXPERIENCE

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Introduction: Combined liver-kidney transplantation (CLKT) is a viable option for a select group of patients with severe liver and kidney disease. While CLKT has become more common in adults, it remains an infrequent procedure in children.
Methods: From October 1997 to December 2010 we performed a CLKT in 10 children (median age 9 years, median weight 24 kg). Indication for CLKT were primary hyperoxaluria (3), congenital hepatic fibrosis (3), methylmalonic acidemia (1), progressive familial intrahepatic cholestasis with chronic kidney disease of unknown origin (1), cranioectodermal dysplasia with incomplete biliary cirrhosis (1), biliary atresia with chronic kidney failure (1). 3 whole liver and 7 left lateral segment grafts from an in situ split were used. Immunosuppression was based on basiliximab, tacrolimus and steroids.
Results: No rejection of the kidney was observed. One patient 1 year after CLKT developed an hepatitis B and was put on lamivudine. One patient 8 years after CLKT developed a Non Hodgkin lymphoma and was treated with chemotherapy and rituximab. In another patient 1 year after CLKT Mofetil Mycophenolate was added to tacrolimus due to an early chronic rejection of the liver. One patient, 4 months after CLKT, developed a septic shock due to cholangitis and underwent a re-transplantation of the liver and eventually died during the operation. The patient who underwent CLKT for methylmalonic acidemia died 18 months later for a metabolic crisis. Both patient and graft survival is 90% and 79% at 1 and 5 years. One patient 8 years after CLKT showed an initial alteration of the renal function.
Conclusions: In children indications for CLKT are very heterogeneous and due mainly to rare diseases. Recipients of a CLKT are usually older than those of liver alone. Patient and graft survival are satisfactory even in the long term.

P-371 PEDIATRIC KIDNEY TRANSPLANTATION: A SINGLE CENTER EXPERIENCE

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Background: Kidney transplantation has become the routine treatment for the pediatric population suffering from end stage renal disease (ESRD). The aim of this study was to investigate the case characteristics and the long-term outcomes in this patient group.
Methods: In our Center, the program for pediatric transplant began on January 1987, once a satisfactory experience had been acquired in adults. Up until January 2010, 1392 transplants had been accomplished; 341 of these (315 from cadaveric donors and 26 from living – related donors) were performed in recipients being under 21 years of age (mean age 13.6$\pm$5.5 yrs).
Results: The patient survival rates at 1 year, 5 and 10 years were 98.5%, 97.2%, 94.1%, respectively. At the same time points, the graft survival rates were 94.9%, 89.8%, and 80.6%, respectively. A double-drug regimen was used before 1990; this was replaced by a triple–drug regimen including a calcineurin inhibitor in 1991. Eighty-seven (26%) grafts were lost, 54% as a result of immunological and the rest as a result of non–immunological causes; 18 recipients (5%) died during the follow-up period. Bacterial infections were the main cause of patient loss; surgical complications, immunological reasons and recurrent disease were for graft loss.
Conclusions: Long–term survival in children was better than reports in adult renal transplant recipients. This finding suggests that pediatric kidney transplantation may offer favorable graft outcomes.

P-372 ABDOMINAL COMPARTMENT SYNDROME IN PEDIATRIC KIDNEY TRANSPLANTATION

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Background: Transplantation of large kidney in small children can lead to many complications. One of these, often underrated, is abdominal compartment syndrome (ACS). An early diagnosis of ACS is recommended to prevent multi-organ failure.
Patient and Methods: From June 1985 to June 2007 we have performed 314 kidney transplants (KT) in pediatric patients (male/female: 167/147). Deceased donors were used in 289 procedures, while 25 KT were carried out from living related donors. In this cohort, the weight of 83 kidney recipients was less than 20 Kg. Of these patients, 16 received a large kidney.
Results: ACS occurred in 7 kidney recipients (hemodialysis/peritoneal dialysis: 5/2). All patients weighted less than 15 Kg. The kidney was procured from adult donors. The ACS signs included firm tense abdomen, hypotension, reduction in ventilation, decrease in lung compliance, increase in airways pressure (increase peak inspiratory pressure), impaired gas exchange with possible hypercarbia and acidosis. In one case a patient underwent abdominal decompression by re-exploration and closure with a PTFE mesh in the immediate post-operative period. From 2005 we measured during transplantation the possible intra-abdominal hypertension via urinary bladder pressure.
Conclusions: In pediatric kidney recipients, especially for the condition "large kidney in small children", the continuous measurement of urinary bladder pressure may be a simple, non invasive and inexpensive approach to provide an early detection of ACS.

P-373 LIVER RETRANSPLANTATION IN THE LONG TERM IN CHILDREN

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Aims: description of processes leading to late retransplantation (ReLT).
Methods: In 1998-2009 15 children underwent late ReLT ($>$1 yr after LT), 12 survived $>$1 yr. Review of 11 survivors to assess recovery of systemic damage. One had 2 late ReLT. Diagnosis (explant pathology n=12): 6 chronic rejection (CR), 4 biliary disease (BD), 1 CR+BD and 1 ischemic necrosis (IN). PostReLT follow-up:1-12 yrs.
Results: a) Median (m) age at 1st LT: 2 yrs. Biliary atresia (6), BSEP (2), OTC (1), Alagille (1), cryptogenic (1).
b) Graft disease lasted 6-48 months (m: 30), overt symptoms 2-48 months (m: 8). ReLT was performed 1.1 -15 years (m: 4.7) after LT.
c) Antecedents: 1 repaired portal vein thrombosis (CR+BD), 1 immunosuppression (IS) withdrawn for PTLD (CR), 3 Hypogammaglobulinemia (2BD, 1CR), 1 de-novo AIH (CR), 2 multiple cholangitis (2BD).
d) Clinical and biopsies data led to preReLT diagnosis: BD (2), CR (7), non conclusive-BD vs CR (2), unknown (1). Explant was discrepant in 3.
e) Treatment: 10 increased IS: steroids, TAC, MMF (5), antiIL2R (2), rapamycin (4).
f) Before ReLT: glomerular filtration (GFR) worsened to 28-60 ml/min in 8. Left ventricle hypertrophy (LVH) in 9. Five (3CR, 1IN, 1BD) developed GFR deterioration plus schistocytes (thrombocytopenia in 4) 1-16 months (m: 1) before ReLT; the condition resembled microangiopathy and resolved with cyclosporine (2), low/withdrawn TAC (2) or ReLT (1).
g) Before ReLT all were jaundiced, 4 showed ascites/bleeding. Laboratory: bilirrubin m: 16.4 mg/dL, ALT m: 270 U/L, hypercholesterolemia 11, hypoalbuminemia 7.
h) Explant pathology: ductopenia (2), ductopenia + obliterative arteriopathy (3), ductopenia + acute &c hronic duct inflammation (1), ductopenia + sinusoidal dilatation centrilobular congestion (1), centrilobular necrosis (1), biliary fibrosis+ductal proliferation (2), and acute + chronic cholangitis (2).
i) After ReLT: One (no LVH, normal GFR) died at 4th yr, 10 patients are alive. LVH is mild, 3 obstructive LVH subsided (on cyclosporine). GFR is $>$70 ml/min in 8. Graft complications developed in 2 (PVT, BuddChiari).
Conclusions: Graft diseases leading to late ReLT associated LVH and GFR deterioration. Microangiopathy complicated 5 of 12 processes. Cardiac and renal damage improved after ReLT in most survivors.

P-374 FIRST EXPERIENCE WITH EVEROLIMUS IN PEDIATRIC LIVER TRANSPLANT RECIPIENTS

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Background: The role of m-TOR inhibitors, such as everolimus (EVL), has not been established for pediatric liver transplant recipients up to now, although data from adult solid organ graft transplantation are very promising. Major complications post pediatric liver transplantation in the long-term course includes chronic graft rejection and CNI associated nephrotoxicity. The purpose

of our current study was to report first results using EVL as a rescue therapy in pediatric liver transplant recipients.
Methods: We used EVL based immunosuppression prospectively in children for the following indications: Chronic graft dysfunction n=12, suspected CNI toxicity n=3, Hepatoblastoma post Ltx n=2, and recurrence of primary sclerosing cholangitis post Ltx n=1.
Results: Four patients with chronic graft dysfunction developed completely normal liver function tests using EVL, six patients showed partial improvement, and two patients did not respond at all. One patient with CNI induced nephropathy showed a slightly improved GFR. Both patients with hepatoblastoma did not develop any metastasis post Ltx.
Conclusions: First experience with EVL in pediatric liver transplant recipients show promising results in patients with chronic graft failure when standard immunosuppression has failed. The future role of EVL in immunosuppressive protocols for children post Ltx has to be proved by controlled clinical trials.

P-375 ULTRASONOGRAPHY OF THE CAROTID WALL THICKNESS IN PEDIATRIC LIVER TRANSPLANT PATIENTS. OUR FINDINGS

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Cardiovascular risks and metabolic disturbance must be determine in pediatrics patients after liver transplantation.
Aim: Determine carotid wall thickness for cardiovascular risk in pediatric OLT patients studied by ultrasonography.
Population: From July 2008 up to May 2009, pediatric liver transplant (OLT) patients performed in our hospital were studied.
Results: 83 pediatric OLTpatients, 37 male, were evaluated for cardiovascular and metabolics risks after OLT. Mean age at study 12.8±4.4 (SD) years, mean age at transplant 5.2±4.2 (SD)years. Mean time after transplant 7.7±3.6 (SD) years. Most common abnormality was hypertriglyceridemia in 28%, 7% had hypercholesterolemia, 4.5% had hypertension. Neck ultrasound was done to measure the thickness of the intima-media carotid wall thickness (CIMT). Values were averaged in each patient. Data analysis from pediatric healthy population was used. Mean CIMT in the second decade of life ranging from 0.38 to 0.54 mm reaching a value of 0.6 mm in most of the studies by adding 2 standard deviations. Liver transplant patients studied had mean values of CIMT of 0.56 mm ±0.19 and 75 percentile (Plo) had a value of 0.7 mm. This variable was analyzed as a dichotomous outcome variable using as cut-off percentile 75. 15 patients were over 75 Plo. 27% had impaired glucose metabolism. When assessing variable results, intima-media thickness greater than 75° Plo and glucose impaired metabolism proved to have a P: 0.05 and 4.76 odds ratio.
Conclusions: Patients with more cardiovascular risk factors had thicker carotid intima-media which is predicting increased risk of premature cardiovascular disease. This shows the need to reduce avoidable risk factors. No association was found between the different immunosuppressive regimens and cardiovascular risk factors, alterations in glucose metabolism and the vascular wall thickness.

P-376 QUALITY OF LIFE RELATED TO HEALTH: EXPERIENCE IN PEDIATRIC PATIENTS WITH CHRONIC DISEASES IN A PUBLIC HOSPITAL IN ARGENTINA

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During the first year of this project was locally validate PedsQL 4.0 instrument. The validation results showed that the instrument is understandable and feasible to be used by our patients, and has good psychometric properties in most subgroups studied (age and follow-up program), except for children 5 to 7 years (difficulty already found in other validations). The results of the validation process were submitted for evaluation and approved by the Institute of regulation of quality of life instruments Mapi and the author of the instrument, J. Varni, so that the instrument became available for use in our population.In addition to common goals with the other protocols, this was intended to assess HRQoL in children receiving a transplant.In neither case could be made pre-transplant evaluation and reassessment few 2nd stipulated.
Population: Pediatric patiens who received a liver transplantation in our hospital.
Results: 46 pediatrics liver transplant (OLT) patiens were evaluated, 42% male, Mean age 8±2-18 years, mean age at transplantation 41±4-216 months, mean time after transplantation 44 (3-144) months, 35% due to acute liver failure, inappropriate schooling 22%, without health coverage 61%, socioeconomic status poor-indigent 60%. All parents and children could complete the questionnaire except 2 children with delayed maturation, 2 teenagers who refused to participate.
Conclusions: In relation to the PedsQL 4.0 instrument: feasibility reliability validity could be proven.Scores of children were systematically worse than those reported by their parents, a fact that contrasts with the classically referred in the literature. Most patiens were tested or had presented any chronic health condition where the physical disability was the most important fact.In relation to the introduction of HRQL indicator:The practical experience of validation and introduction of a measuring instrument seems to have served as a guideline for the introduction, spread and start using the indicator.

P-377 LIVING DONOR LIVER TRANSPLANTATION FOR ACUTE LIVER FAILURE IN CHILDREN

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Introduction: Living Donor Liver Transplantation (LDLT) for patients with Acute Liver Failure (ALF) is controversial but may be an effective alternative for obtaining grafts in a timely fashion particularly in small children.
Aim: The aim of this study was to analyze the outcome of pediatric patients with acute liver failure who were transplanted with living donor grafts.
Material and Methods: 43 liver transplantations in children with acute liver failure were performed between 1997 and 2010 in our institution. 14 (32%) children aged from one month to 15 years (mean 5,6 years) were transplanted the graft from living donor. The body mass ranged from 3,1 to 46,7 kg (mean 20,1 kg). The causes of acute liver failure were: mushroom poisoning -2, paracetamol toxicity -1,Wilson's disease -2, HBV hepatitis -1, neonatal hemochromatosis -1, acute AIH -1, toxins -1, iron poisoning -1, unknown -2. The time from qualification to transplantation, postoperative complications, long-term results was analyzed.
Results: The time from listing to transplantation ranged from 11 to 105 hours (mean 39 hours). Two children (14%) died on the third day after transplantation due to multiorgan failure (1 patient) or neurological complications (1 patient). One patient required retransplantation 3 months after first transplantation due to vascular complication. In one child central nervous system complications occurred. Follow-up period range from 7 to 122 months (mean 69 months). 12 (86%) patients are alive with good liver function. No serious complication occurred in any living donor.
Conclusions: Living donor liver transplantation is a good option for pediatric patients with acute liver failure. With limited resource of cadaveric graft, transplantation from living donor may be performed within short period of time with satisfactory results in recipients and low risk in donors.

P-378 ESTABLISHMENT OF A PAEDIATRIC RENAL TRANSPLANT SERVICE IN TUNISIA

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Purpose: The development of a new Paediatric Transplant program in Sousse, Tunisia as a result of a collaboration with International Society of Nephrology (ISN) Sister program.
Method: Retrospective review of 5 paediatric living related renal transplant recipients over a successive 5 day period in June 2010. Medical and surgical complications were noted.
Results: 5 dialysis dependent paediatric patients aged 8-14.3years (median 9yrs) and body mass of 20-22kg. (median 20kg) were transplanted. Waiting times were 0.7-8.3years (median 3.2yrs). Causes of renal failure included nephronopthisis, renal cystic disease, glomerulosclerosis, dysplasia and reflux (2). The donor operations were open; the recipients had intraperitoneal placement of the grafts on the right common iliac artery with venous drainage into the inferior vena cava.
Immunosuppression included Basiliximab, Tacrolimus, Mycophenolate Mofetil and Steroids.
Medical complications included diarrhoea, lymphocoele/fluid collection, and haemolytic uraemic syndrome, requiring conversion to Ciclosporin.
One patient developed post operative renal dysfunction due to a large subcapsular hematoma requiring emergency surgical evacuation with resultant normal renal function. No donor complications were encountered.
At 6 months post transplant, all patients have local follow-up with normal renal function.

Conclusion: New paediatric transplantation programs are possible with the combined support of International Renal programs (ISN Sister program) using experienced transplant surgeons and paediatric nephrologists, working together with units where successful adult renal transplant programs already exist. Extensive local team work in Sousse, Tunisia including adult and paediatric staff make establishment of such a program possible with favourable results. This initiative has catalysed the establishment of an important new centre of paediatric renal transplantation in North Africa which will offer opportunities of transplantation to a large paediatric population in Southern Tunisia. A second joint ISN sponsored series of transplants is planned in 2011.

P-379 SURGICAL COMPLICATIONS OF PEDIATRIC KIDNEY TRANSPLANTATION: A SINGLE CENTER EXPERIENCE

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Purpose: The complex nature of pediatric kidney transplantation create the potential for a number of complications. To decrease surgical complications we have performed kidney transplantation via the extraperitoneal approach even in children who weigh less than 20 kg. In this study, we evaluated the surgical complications and their consequences after kidney transplantation in children.
Material and methods: From February 1983 to November 2010, A total of 302 pediatric and adolescent kidney transplants were performed at our institute. Of these patients, there were 172 boys and 130 girls with a mean age of 11.9±4.9 yr (range 1-20 yr). Mean weight was 29.6 kg. at transplantation, and 89 and 213 patients weighed less than 20 and 20 or more kg, respectively. The extraperitoneal technique was performed in all recipients, even in low weight children. The aorta and inferior vena cava, common iliac artery and vein or hypogastric artery and external vein were used for vascular anastomosis depending on recipient size. The ureter was anastomosed to the bladder via a modification of Paquin's method or an extravesical technique.
Results: During observation 14 surgical complications (4.9%) were noted, including ureteral stricture, ureteral necrosis, renal artery stenosis, lymphocele, subcapsular hematoma significant vesicoureteral reflux to the graft and wound infection in 1 patient each. Urinary leakage was seen in 4 cases (1.4%). Hemorrage of vascular anastomosis was seen in 2 cases (0.7%). There were no gastrointestinal complications. Five patients required surgical repair, and 1 underwent laparoscopic fenestration of a lymphocele. Overall only 1 graft (0.4%) was lost to a surgical complication (renal artery stenosis).
Conclusion: The incidence of surgical complications of the extraperitoneal technique in pediatric kidney transplant patients was low (4.9%) and seems to be acceptable. The extraperitoneal technique did not cause any gastrointestinal complications, which seems to be its greatest advantage.

P-380 THE EFFECT OF ANTI CD-25 AB INDUCTION TREATMENT ON GRAFT FUNCTION IN THE ADOLESCENT KIDNEY TRANSPLANTATION FROM LIVE DONORS

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Backround: After anti CD 25 Ab has been introduced for kidney transplantation, many reports has been reviewed that better graft function and survival rates with anti CD 25 Ab. The aim of this study is to evaluate the effect of anti CD 25 Ab on graft function in the adolescent kidney transplantation from live donor.
Material-Method: A retrospective analysis on 19 adolescent renal transplants (at age 13-17 year) performed at our center since 1995 was analyzed. Patients not first time transplantation and treated without CNI immunsupression protocol were excluded.
Results: Mean recipient and donor age were 15.8, 40.8 year, respectively. The mean CIT was 83 min. 53% of patients were under hemodialysis and the others under peritoneal dialysis treatment. Mean dialysis time was 20 month. The ratio of patients with over 3 HLA mismatch was 19.7%. Max BMI and minimum BMI were 21.2 kg/m^2, 16.1 kg/m^2, respectively. None of the patients had delayed graft function. Anti CD-25 Ab introduced 42% of the patients. Median GFR rate for posttransplant 3. year was 69±15 ml/min. There was a correlation betweeen 1.year serum creatine level and recipient age and 3 year serum creatinine level with groupe B HLA mismatch number($p<0,05$). There was no difference for kidney graft function in first and third year between the patients treated with or without anti CD 25 Ab ($p> 0,05$)
Conclusion: Although there are many studies about the effects of induction treatment with antiCD 25 Ab on kidney graft function in children, to review these effects on graft function for adolescent groupe, we need more comprehensive studies.

Tissue injury / preservation

P-381 INNATE IMMUNE RESPONSES IN CORONARY ARTERY BYPASSES BY A NEW P38 MAPK-INHIBITOR

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Introduction: Vein graft failure following bypass surgery is an important clinical problem. Endothelial damage, inflammation, and signaling through mitogen activated protein kinases (MAPKs) are one of the pivotal mechanisms. CBS 3830, a new high selective inhibitor of p38MAPKs, may ameliorate intimal hyperplasia (IH) and inflammation in arterialized vein grafts.
Methods: 80 SPF SD male rats were randomly divided into four groups. Control group with reversed right jugular vein to common carotid artery interposition graft was compared with sham-operated, single- and double-dosed animals. Blood samples were taken at 0h, 24h, 48h, 4d, 1w, 2w. TNF-α, IL-1β and IL-6 were determined. Vein grafts (1w, 2w, 4w) were analyzed for intimal/medial morphometric examination and expression of proliferating cell nuclear antigen (PCNA). Expression of p38 MAPK was evaluated.
Results: CBS3830 significantly reduced TNF-α, IL-1β and PCNA for the single- and double-dose group compared to sham-operated and control group. Single-dose group compared to double-dose group showed no difference. Single and double dose group intimal, medial thickening was significantly lower than the control group at each time point.
Conclusion: CBS3830 significantly decreases inflammation and intimal hyperplasia. These results may have strong implications for the development of strategies aimed at blocking or reducing IH and inflammation in bypass grafts. Furthermore, these results confirm the idea if innate immune responses could be inhibited at an early stage, there is no need for maintenance medication.

P-382 A NOVEL PERFUSION FLUID FOR DCD DONOR KIDNEYS; BETTER AS A FLUSH OR A STORAGE MEDIUM?

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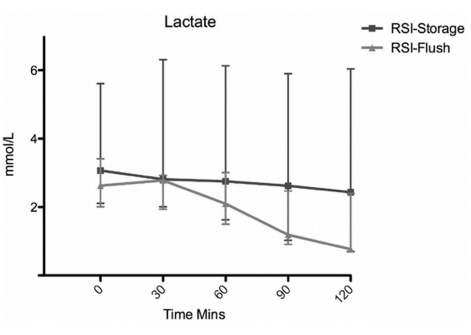
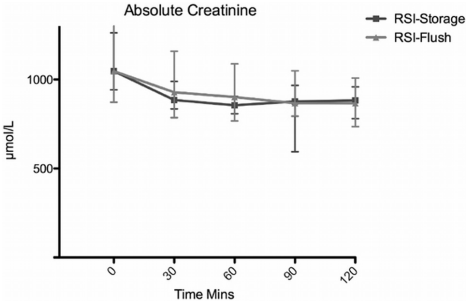
Aims: Aqix® RS-I is an innovative non-phosphate pH buffered solution with proven benefit in tissue preservation. Its role in renal organ perfusion and preservation in the context of donation after cardiac death (DCD) transplantation is unclear. In particular whether it confers better protection of the organ as a flush or storage medium is to be determined.
Methods:
- Kidneys were procured from cross-Yorkshire landrace pigs after schedule-1 euthanasia and subjected to 30minutes of primary warm ischaemia.
- Both groups were then administered thrombolysis as per Newcastle protocol.
- All organs were flushed with 250mls of ambient room temperature (18-23°C) Aqix® RS-I solution followed by 250ml cold (4-8°C) Aqix® RS-I solution.
- Kidneys were then subjected to static cold storage for 24hours in either RS-I solution (n=6) "RS-I Storage group" or UW solution (n=5) "RS-I Flush group"
- Organs were then reperfused on an ex-vivo sanguineous oxygenation circuit (Model 30, Functional Circulation®) to simulate transplantation and reanimation.

Results:
- Comparative viability testing of the organs on an extra-corporeal circuit revealed similar performance between the groups



- Mean lactate at 2hours reperfusion was 2.6±0.79 mmol/L in the RSI-Storage Group vs 1.08±0.33 (SE) RSI Flush group.
- Mean serum creatinine fell by 160±20 μmol/L in RSI Storage vs 210±20 μmol/L in RSI Flush group.
- Renal vascular resistance was higher in the RSI flush group finishing at a mean of 1.19±0.24 mmHg/ml/min in the RSI storage group vs 1.29±0.1 in the RSI flush group.



In all cases the trends were compared using repeated measures ANOVA and were not found to be statistically different.
Conclusion: Whether storage in RS-I confers an additional protection from the deleterious effects of cold storage and ischaemia-reperfusion injury requires further investigation, ideally in the form of a transplant model.

P-383 INFLUENCES OF THE DONOR TYPE ON ORGAN ENERGY STATUS: LIVING VERSUS BRAIN DEAD VERSUS NON-HEART BEATING DONOR

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Organs from living donors seem to have a better graft function after transplantation compared to organs from brain dead and non-heart beating organ donors. We hypothesized that brain death might impair the energy status of organs and therefore systematically evaluated high energy phosphate content in organs from living, brain dead and from non-heart-beating donors in a pig model.
In 6 pigs brain death was induced under general anaesthesia by inflating a balloon in the epidural space. 10 hours after confirmation of brain death organs were retrieved. In 6 animals cardiac arrest was induced using 9 V direct current and mechanical and medical reanimation was performed after 10 min of ventricular fibrillation without cardiac output for 30 min. In 6 pigs organs were explanted without induction of brain death. Tissue was harvested before perfusion, after perfusion and after cold ischemia. Xanthine, hypoxanthine, adenosine-monophosphate, adenosine-diphosphate and adenosine-triphosphate were measured using high-performance liquid chromatographie. Energy charge and ATP/ADP ratio were calculated.
Overall, after ischemia no difference in energy status of organs was observed between the different donor types. In all organs an increase in hypoxanthine levels and a decrease of high energy phosphate content was observed during perfusion and ischemia, irrespective of the donor type.
In conclusion our hypothesis that brain death or cardiac arrest significantly impairs the energy status of donor organs did not hold true. Therefore the negative impact of brain death or cardiac arrest on graft function can not be attributed to changes in energy status.