Transplant International

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08:00–10:15

ABSTRACT PRESENTATIONS

01 LIVER TRANSPLANTATION IN HIV POSITIVE PATIENTS: A CASE CONTROL STUDY

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HIV positivity is no more a contraindication to liver transplantation (LT) due to efficacy of antiretroviral therapy. The aim of this study is to analyze LT in HIV+ patients compared with a matched HIV negative case–control group. From 2004 to 2008, 27 HIV+ patients submitted to LT were compared with 23 HIV- patients matched for age (45, range 39–58 vs. 50, range 37–57), gender, HCV (HCV+ 70% vs. 61%) and HCC (40% vs. 39%). Results (HIV+ vs. HIV): the median waiting list time was 3 months for both groups ($P = 0.83$). MELD was 17 (range 7–32) vs. 17 (range 8–29) ($P = 0.80$). Donor age was 46 (range 19–73) vs. 55 (range 17–75) ($P = 0.45$). No differences were found for cold ischemia time (457 ± 96 vs. 463 ± 95 $P = 0.83$), duration of transplantation (389 ± 84 vs. 392 ± 81 $P = 0.91$) and units of blood transfused (5, range 0–25 vs. 3, range 0–28, $P = 0.44$). The ICU and the total hospital stay did not differ between the HIV+ vs. negative group 5 ± 3 vs. 5 ± 2 ($P = 0.45$) and 18 ± 9 vs. 16 ± 7 days ($P = 0.64$). The median follow-up was 21 months (range 2–47) and 29 months (range 3–39) for HIV and non-HIV ($P = 0.93$). The estimated 1, 2 and 4 years patient's and graft's survival were respectively 90%, 82.5% and 82.5% for HIV+ vs. 100%, 94% and 79% for HIV–($P = 0.64$), and 95%, 87% and 87% for HIV+ vs. 95%, 89% and 82% for HIV–($P = 0.89$). HCV recurrence had a median grading and staging score respectively of 3 (range 2–6) vs. 3 (range 1–5), ($P = 0.20$) and 1 (range 0–4) vs. 1 (range 0–6), ($P = 0.51$) for HIV positive and negative cases. We suggest that LT in HIV+ patients, with a CD4 count>200 has similar medium term results than a matched HIV negative population.

02 LIVER TRANSPLANTATION FOR PRIMARY SCLEROSING CHOLANGITIS IN CHILDREN: A SINGLE CENTER EXPERIENCE

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Objective: The purpose of this study was to analyze the results of liver transplantation (LTx) for Primary Sclerosing Cholangitis (PSC) in paediatric recipients.
Methods: We reviewed our series of 356 isolated primary pediatric liver transplants performed between October 1997 and October 2008. RESULTS: PSC was the indication in 6 (1.7%) children (median age 5 years, 1–17). Three children were diagnosed in neonatal period; three patients were transplanted before the age of 2 years. The LTx was indicated in two patients for liver failure associated to portal hypertension and gastroesophageal bleeding, in one for a biliary stricture not treatable by a biliary stent placement, in two for progressive cholestasis with jaundice and intractable pruritus, in one for a progressive worsening of liver function up to a pediatric end-stage liver disease (PELD) score of 25. Median PELD score at the time of listing was 16 (10–25). In one case PSC was associated with histiocytosis X. Median waiting time between diagnosis and transplantation was 15.2 months (4.3–81.3). No patient had evidence of inflammatory bowel disease (IBD) before LTx. Four children received a left lateral segment split graft, two a whole graft. Median follow up was 457 days (20–291). All the patients received a tacrolimus-steroids based immunosuppression. Three children developed an acute rejection, one a mild histological chronic rejection. The 1, 3 and 5 year actuarial patient survival was 100%. A child developed a histological recurrence of PSC in his allograft and a mild IBD 8 months post LTx. All children at last follow up were alive and in good condition and their liver tests were in a normal range.
Conclusion: According our experience LTx provided good patient and graft survival rates in paediatric recipients, including infants with end-stage PSC.

03 MELD-BASED ORGAN ALLOCATION INCREASES TOTAL COSTS OF LIVER TRANSPLANTATION: A SINGLE-CENTRE EXPERIENCE.

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Introduction: In December 2006, MELD-based organ allocation replaced the CTP/waiting-time based system. The impact on costs of transplantation has not been evaluated yet.
Methods: Total costs for liver transplantations (LTx) before and after implementation of MELD-based organ allocation were identified (256 of total 283 cases, 01.01.05–08.12.07). 49 cases were excluded (re-transplantations, HU-listed recipients and patients with 30-day mortality). For the remaining 207 cases, total costs were compared with their corresponding MELD-Scores. Furthermore, 84 cases from the preMELD-era were compared with 123 cases of MELD-based organ allocation.
Results: Total costs for LTx correlate ($r^2 = 0.28$) to the recipients' lab MELD-Scores. No significant correlation could be identified for Child-Pugh Classification and total costs. MELD-Scores can be stratified in four groups (I: 6–10, II: 11–18, III: 19–24, IV: >24) representing a difference of 15.672 ± 2.233 € between each group ($P < 0.05$). Recipient lab MELD-Scores were significantly higher in the MELD-based allocation system by nine points and correlated to a median increase of costs by 11.650 €/case ($P < 0.05$). The indication for liver transplantation had no influence on total costs. For LTx of HU-listed patients, significantly more resources were needed.
Conclusion: MELD-based organ allocation has led to increased total costs of LTx. In accordance with other studies, sicker patients had higher healthcare costs.

04 REPERFUSION INJURY TO STEATOTIC RAT LIVERS AFTER TRANSPLANTATION CAN BE ATTENUATED WITH A MODIFIED HTK SOLUTION

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Background: Ischaemia/reperfusion injury (IRI) is still an obstacle especially in fatty livers. Most recently a modified histidine–tryptophan–ketoglutarate (HTK) solution, Custodiol-N, has been developed. This solution contains N-acetyl-histidine as buffer, the amino acids aspartate, glycine, alanine, and arginine to limit ischaemic injury and to improve reperfusion and the iron chelators deferoxamine and LK 614 to inhibit cold-induced cell injury. This study was designed to test the effects of Custodiol-N on IRI to fatty livers in a rat liver transplantation model.
Methods: Moderate steatosis was induced by a single dose of ethanol (8 g/kg BW) to female Sprague–Dawley (SD) donor rats 20h before organ harvest. Livers were harvested and cold stored at 4°C for 8 h with either HTK solution or Custodiol-N before transplantation. Serum transaminases and histology were compared at 1h, 8h and 24h after reperfusion ($n = 8$ animals per group). Survival was compared after 7 days.
Results: Custodiol-N significantly improved permanent survival from 12.5% in controls to 87.5% after 7 days. Further, Custodiol-N decreased the release of AST, ALT and LDH to up to 25% (e.g. AST after 24h 14456 ± 11493 vs. 4584 ± 2340) of controls ($P < 0.05$). These results were confirmed by histology.
Conclusions: These results clearly demonstrate that Custodiol-N is superior to the traditional HTK solution in experimental fatty liver transplantation.

05 THE NEW LIMAX-TEST ALLOWS IMMEDIATE DECISION MAKING TO RETRANSPLANTATION AFTER LIVER TRANSPLANTATION (LTX) BECAUSE OF PRIMARY NON FUNCTION

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Introduction: Primary non function (PNF) is a dangerous situation for the patients after LTX. However, diagnosis and decision to retransplantation is difficult since no valid liver function test is available until now which can provide clinical useful results. In this study we investigated the prognostic power of the LiMAx test for diagnosis of PNF.

Methods: A total of 99 Patient undergoing LTX were enrolled into this prospective observational study. Liver function capacity was determined by the LiMAx test. The test is based on intravenous bolus application of 2 mg/h/kg body weight 13C-labeled Methacetin. Emerging 13CO2 will be determined in breath online over 60 min by nondispersive isotope-selective infrared spectroscopy and a kinetic analysis was applied. Tests were performed at 6 h, day 1, 3, 5, 10, 14 and 28. Results were compared with laboratory values and the indocyanine green test.
Results: Patients with PNF, with complications during follow up and regular progression could be discriminated from each other by the LiMAx-test already 6 h after reperfusion ($P < 0.05$). Primary non function could accurately be diagnosed by the LiMAx test with high prognostic power at the first postoperative day. At this early time point other available diagnostic parameters were still indistinct. PNF could be diagnosed earlier than clinically realized.
Discussion: Individual actual maximal liver function capacity can be reliably determined by the LiMAx-test in every clinical situation including ventilated patients. The assessment of the initial graft function by the LiMAx test is highly predictive and allows reliable decisions independent from interfering recipient factors in the initial postoperative management after liver transplantation.

06 WHAT IS INITIAL POOR GRAFT FUNCTION AFTER LIVER TRANSPLANTATION? – NEW FUNCTIONAL DEFINITION FROM A PROSPECTIVE CLINICAL TRIAL

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Background: Initial poor function (IPF) is suspected to prolong posttransplant recovery and might decrease graft survival. No consensus on the definition of IPF has been reached yet. In this study, a new guideline for the classification of initial graft function is proposed, based on the LiMAx test.
Methods: A total of 99 Patient undergoing LTX were enrolled. Liver function capacity was determined by the LiMAx test. 13C-labeled methacetin was applied intravenously and emerging 13CO2 was determined in breath. Tests were performed at 6 h, day 1, 3, 5, 10, 14, 28 and1 year after LTX. A classification system for the results at 6 h and day 1 was developed. Patients were classified as nonfunction (PNF, LiMAx <60 μg/kg/h), poor function (IPF, LiMAx 60–120 μg/kg/h), and immediate function (IF, LiMAx >120 μg/kg/h). Patients with severe initial immunological and technical complications and recipients with rare indications were excluded from this analysis.
Results: At first postoperative day, 52 patients were classified as IF, 18 as IPF, and 3 patients as PNF, respectively. All three patients with PNF were retransplanted. IPF compared with IF resulted in a prolonged stay on the intensive care unit (11 vs. 6 days, $P = 0.003$) and higher total costs (45,142 vs. 27,400 Euro, $P = 0.008$). The mean serum bilirubin levels remained different until discharge. In contrast, the albumin level of IPF grafts resolved until postoperative day 28. The risk of graft failure within the first year was higher for patients with IPF (28%) compared with IF (8%) ($P = 0.028$).
Conclusion: Initial graft function plays an important role for the postoperative recovery and graft survival after LTX and can be accurately determined by the LiMAx test already at the first postoperative day.

07 SEGMENTAL LIVER TRANSPLANTATION IN CHILDREN USING NON-HEART-BEATING DONORS

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Purpose: Selected livers from controlled non-heart-beating-donors (NHBD) are now routinely accepted for orthotropic liver transplantation (OLT) in adults. Recent evidence has shown good medium term outcome. Purpose of this study was to report our experience of paediatric liver transplantation with whole and partial grafts from NHBD, analysing complications and outcome post OLT.
Methods: Retrospective review of all the recipients who underwent primary OLT between December 2005 and October 2008, using livers from NHBD. Demographics, post transplant complications and outcomes were analysed.
Results: Three children, (one male), mean age 7 years (0.2–15), mean weight 18 kg (3–38) underwent liver transplant using NHBD. Mean donor age was 15 years and mean warm ischaemia time (systolic BP < 50 mmHg to cold perfusion) was 13 min (10–15 min). Two children received reduced grafts (left lateral segments) and one a full graft. Mean cold ischemia time was 7.5 h, range (6–8.3 h). Liver function tests in these children were as summarized in the table. One child was treated for one episode of acute rejection. Post transplant complications included one case of mild ischaemic cholangiopathy, treated conservatively. Graft and patient survival was 100% with a mean follow up 14 months, (range 3–34 months)

Recipients	Diagnosis	Total bilirubin (μmol/l)		GGT (IU/l)		ALP(IU/l)	
		1 week	3 months	1 week	3 months	1 week	3 months
Patient 1 (F)	PFIC	60	7	449	274	194	817
Patient 2 (M)	Alfa-1 AT syndrome	11	9	77	16	155	647
Patient 3 (F)	ALF (giant cell hep.)	76	18	113	305	248	932

Conclusion: Short to medium term follow-up suggests that the best liver grafts from young NHBD with short warm and cold ischemia times can be safely utilized in paediatric transplantation

08* INTESTINAL MICROCIRCULATION IN CLINICAL INTESTINAL TRANSPLANTATION

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The intestine is particularly sensitive to ischaemia and low flow states, which may damage the mucosal barrier and promote bacterial translocation, immune activation and sepsis. Moreover, during acute rejection (AR) graft endothelium becomes a major target for recipient immune cells, with subsequent increased endothelial-leukocyte interactions. Experimental and clinical evidence indicated microvascular damage and altered microvascular perfusion during AR. Using laser-Doppler flowmetry (LDF) we studied the microvascular blood flow in the intestinal mucosa in nine patients receiving 10 intestinal grafts. Results were correlated with blood pressure, use of vasoactive drugs, pathology results and clinical course. Measurements ($n = 177$) were performed during the first month post transplantation, at follow-ups and readmissions, by introducing the flexible LDF probe through the ileostomy for 10–20 cm.
Results: Hundred out of the 177 measurements were performed within 24 h from endoscopic biopsy. In uncomplicated cases, mucosal perfusion increased throughout the first postoperative week and ultimately stabilized around patient-specific levels baseline). We found no significant correlations between microvascular perfusion, blood pressure or vasoactive medication (norepinephrine). In five patients we found a moderate/strong negative correlation between mucosal perfusion and Tacrolimus levels. Sudden and sustained decreases in mucosal perfusion by over 15–30% compared with the previous measurements were associated with sepsis, rejection, or both. Adenoviral enteritis did not impair mucosal perfusion.
Conclusions: Microvascular perfusion gradually increases after transplantation, mirroring the morphological repair after reperfusion injury. Autoregulation of intestinal mucosal perfusion is preserved after intestinal transplantation and mucosal perfusion is unaffected by clinically relevant doses of norepinephrine. However, increased Tacrolimus levels may impair intestinal microcirculation. LDF could detect perfusion changes associated with AR. The relatively low specificity of LDF is compensated by the fact that it is noninvasive, allowing frequent investigations. LDF may become an additional tool for routine monitoring of intestinal allograft.

09 POSITIVE FOLLOW-UP RESULTS ON LIVING LIVER DONORS

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Objectives: At our centre 4% of the liver transplantations have been performed with a living donor. The aim of the present study was to elucidate the current wellbeing of the donors in a cross-sectional study and their experiences being a donor.
Material and Method: Thirty-five healthy subjects donated a part of their liver between 1996 and 2007. Thirty-three of these accepted to participate in the study and filled in our questionnaire. A magnetic resonance imaging (MRI) of the liver and a physical examination was performed. Blood samples were drawn for analysis of blood haematology, liver function including α-fetoprotein and kidney function with electrolytes.
Results: Twenty-four subjects had donated the left lateral segment (of left lobe), and 11 the right lobe. The relation of donor to recipient was: father (18), mother (4), partner (3), sibling (3), grandmother (1), brother-in-law (1), aunt (1), cousin (1), cousin of father (1), workmate (1) and son (1). The hospital stay ranged from 5–19 days and the sick leave period from 8–12 weeks. Time for recovery was commonly 3–6 months. The most frequent long-lasting problems were heartburn, abdominal discomfort and hernia with pain from the abdominal scar. Twenty-five subjects experienced the donation as entirely positive and no one was regretful. MRI/CT (six left lobe, eight right lobes) showed recovery of total liver volume from median 1590 ml to 1426 ml. The transplantation results showed that 17/24 left lobe recipients and 7/11 right lobe recipients were alive today. Conclusion: Living liver donors recovered after approximately 3–6 months and perceived the donation as a positive experience with no regret. Durable side-effects were mainly heartburn and abdominal discomfort. The MRI data showed that 90% of the preoperative liver volume had regained and liver function tests were normal.

10 INTRA OPERATIVE HEPATIC BLOOD FLOW IN PEDIATRIC SPLIT LIVER TRANSPLANTATION, CORRELATION WITH THE OUTCOME

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Introduction: Little is known so far on the relationship between liver blood flow and graft function in the specific setting of pediatric liver transplantation

with cadaveric split grafts. We prospectively evaluated intra-operative variations of arterial and portal flow in pediatric recipients of left-lateral segment grafts from in situ split and impacts of the total flow on early graft function.

Methods: 30 children were studied. Portal vein (PV) and hepatic artery (HA) flows were measured in the native liver after dissection and after HA ligation, and in the graft after PV anastomosis, after HA anastomosis and at the end of the operation. Patient and graft weight were recorded, as well as INR after declamping. Postoperatively, US/Doppler and liver function tests (bilirubin, INR, AST, ALT, alkaline phosphatase and GGT) were recorded at days 1, 2, 3, 4, 5, 6, 7, 14 and 30. The correlation between flow/graft weight ratio (FGW) and graft function was analysed.

Results: The mean patient weight was 13.19 kg (SD9.39) and GR/WR was 3.19 (SD 1.58). The mean total liver flow was 516 ml/min (SD 304). The mean total flow/graft weight ratio was 175 ml/min/100g (SD 100). A Significant functional impairment of the graft was observed for low and high FGW, with cutoffs at 100 and 300 ml/min/100g respectively. These situations were correlated with significantly higher intra operative INR and post operative INR, AST ALT and GGT. Delayed graft function, vascular complication, and retransplantation rates were significantly higher in patients with high and low FGW. Particularly, delayed graft function was observed in all the three children with high FGW (420, 420 and 392ml/min/100gm respectively) we defined this situation as a 'small for flow syndrome'.

Conclusion: Low and High FGW seem to be independent determinants of post transplant delayed function and an effort should be done to maintain FGW between 100 and 300ml/min/100mg graft weight.

11 LIVER TRANSPLANTATION IN ISOLATED POLYCYSTIC LIVER DISEASE

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Introduction: Patients with end-stage isolated polycystic liver disease (PCLD) suffer from incapacitating symptoms due to huge liver volumes. Liver transplantation (LTx) is the only curative option. We aimed to assess its feasibility in PCLD.

Methods: We extracted demographics and outcome of patients listed in European Liver Transplant Registry (ELTR) database who underwent LTx 1985–2007 because of PCLD. Total of 534 patients underwent LTx; an initial screen excluded 232 patients because polycystic disease was not restricted to the liver (i.e. patients underwent combined kidney-liver transplantation) or was not the main indication for LTx. Additional data was collected using standardized questionnaires submitted to 75 European LTx centres.

Results: We received responses on 130 patients (37 centres) and isolated PCLD was confirmed in 38 patients (24 centres). Mean age of this cohort (6M, 32F) at time of diagnosis was 41.3 years (range 23–65years) and at time of LTx was 50.3 years (range 32–67years). Abdominal pain (63%), abdominal distension (63%) and dyspnoea (39%) were most commonly reported. Indications for LTx were mechanical difficulties (53%), invalidation (29%) and pain (24%). Mean operation time was 6.1 h (range 5–16 h). Explantation of the polycystic liver due to the grossly enlarged liver or adhesions was extremely difficult in 26%, and failed in one patient. Mean weight of the excised liver was 8.2 kg (range 2–25kg). Intra-operative complications occurred in 18% of patients including vascular complications (venous tears ($n = 2$), hepatic vein thrombosis ($n = 1$), revascularization issues ($n = 1$), bleeding ($n = 1$)). Postoperative complications (64%) included acute rejection ($n = 10$), infection ($n = 5$), or miscellaneous causes ($n = 15$). Two patients developed chronic renal insufficiency due to immunosuppressive treatment one requiring dialysis. In hospital mortality was 8%. 5-year patient and graft survival were 84% (follow-up 0–15.8 years). One patient died due to malignancy.

Conclusion: LTx is feasible in PCLD and leads to long-term survival. The mortality (approximately 16%) occurs mostly in the immediate postoperative period.

12 EARLY PREDICTION OF ACUTE OR CHRONIC ALLOGRAFT REJECTION IN FK506 TREATED RAT INTESTINE TRANSPLANT RECIPIENTS

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We monitored the expression of a novel marker for early prediction of allograft acceptance or rejection in a high responder rat model of ITx. DA-to-LEW ITx was performed under single dose FK506 (1, 3, or 5mg/kg; low/medium/high dose). Untreated recipients as well as nontransplanted/FK506 treated animals served as controls. Blood samples were collected on days 1, 3, 5 and 7 after ITx, grafts on day 7, 14 and 45 for H&E-staining and immunohistology (APAAP). Gene expression (real-time RT-PCR) of established rejection markers (CD3, perforin) was compared with the novel marker tolerance associated gene 1, TOAG-1. Survival was 50% in the medium and 100% in the high dose group after 45 days, while untreated recipients and animals with low dose FK506 died 8–10 days after ITx. The latter revealed severe acute rejection 7 days after ITx in contrast to minor changes in naive controls or recipients in the medium or high dose group (score day 7: low vs. medium/high dose; $P < 0.05$). Accordingly, significantly higher numbers of graft infiltrating dendritic cells, macrophages, CD4+ and CD8+ T-cells were detected. 45 days after ITx chronic structural changes had developed in medium dose animals (score day 45: medium dose vs. naive; $P < 0.001$) whereas animals in the 5 mg group showed less advanced chronic rejection. Gene expression of CD3 and perforin was irrespective of FK 506 dose. qPCR analysis of TOAG demonstrated significant differences between the groups at days 5 and 7. TOAG gene expression in PBMC was significantly higher in recipients treated with high dose FK506 compared with recipients receiving low dose or no treatment (day 5 as % of day 0: low vs. high; $P < 0.01$; medium vs. high dose; $P < 0.05$).

Conclusion: Acute rejection correlates with a significant early down regulation of the recently identified gene marker TOAG.

Saturday 21 March 2009
10:30–11:15

MY WORST CASES

13* VACUUM ASSISTED CLOSURE FOR MANAGEMENT OF COMPLICATED ABDOMINAL WOUNDS AFTER PAEDIATRIC LIVER TRANSPLANTATION

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Objective: We describe our experience using vacuum assisted closure (VAC) therapy system for the management of abdominal wound complications after liver transplantation (LTx) in children.

Methods: Between January and October 2008 five children (median age 2.7 years, 0.6–10.3) underwent VAC placement for complicated abdominal wound after LTx. We used polyvinyl alcohol foam dressing and application of negative, sub-atmospheric pressure, median 100 mmHg (100–150).

Results: Our cases included: 1 s retransplantation for a primary graft non function complicated by bowel perforations; one retransplantation for a delayed graft function complicated by a biliary leakage; one LTx for a unknown fulminant hepatitis complicated by a biliary stenosis, one LTx for biliary atresia complicated by bowel perforations; one LTx for biliary atresia associated to an hepatopulmonary syndrome complicated by portal vein and hepatic artery thrombosis and biliary leakage. Median Pediatric End-Stage Liver Disease score at LTx was 30 (−2, 38). All the children had a wound infection. The culture examinations included: *Escherichia coli* (3), multi-resistant *Pseudomonas aureginosa* (2), *Enterococcus faecalis* and coagulase-negative Staphylococcus (1). A child had a skin wound dehiscence; three children had a partial abdominal wall dehiscence; a child had an open abdomen with total exposition of the liver graft and bowel. Median time between transplantation and VAC placement was 23 days (12–61). Median time between surgery for LTx complication and VAC placement was 5 days (0–15). Median length of VAC use was 27 days (23–59). Wound closure occurred in three children. A treatment is in progress. One patient died for multiorgan failure. Any wound complications or enteric fistula occurred. Median follow up after wound closure was 168 days (132–188).

Conclusion: VAC can be safely and effectively used to manage complicated abdominal wound in paediatric liver transplantation.

14* MULTIMODAL TREATMENT OF THE RECURRENT HCC FOLLOWING LIVER TRANSPLANTATION

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Hepatocellular cancer (HCC) currently constitutes about 10% of the indications to liver transplantation (LTx) according to the Western registries (UNOS and ELTR). LTx is the most attractive option for the treatment of HCC, because it removes both detected and undetected nodules and simultaneously treats the underlying cirrhosis. The overall rate of recurrence of HCC after LTx is 11–18%. In patients, whose explant pathology is within accepted criteria the reccurence rate is 8%, in those outside – 50% (JP Roberts, Liver Transplantation, 2005). Case report: Female patient (JB, age 57) underwent LTx from cadaveric donor in April 2006 for HCC (4.5cm with small satellites) in six segments (# 455). The postoperative period was uneventful. HCC was diagnosed in August 2004 while patient's follow up for HCV + cirrhosis treated with IFN and ribavirine. Then, she underwent local resection with cryoablation of HCC in eight segments. 14 months after LTx the right lung and liver (segment 6) recurrence was diagnosed during routine follow up. The patient underwent lung and subsequent liver resection in June and August 2007. After next 12 months the new HCC recurrence was observed: again in the right lung and in the liver. The tumour in the lung was resected in August 2008 and three courses of TACE (August–September 2008) allowed to control the development of the liver tumour. Unfortunately after fourth course of TACE, the TIA occurred with subsequent brain stem stroke. The patient eventually died on 7 October 2008.

Conclusion: HCC recurrence after LTx requires aggressive surgical and interventional approach. A case-related multimodal therapy is advocated, with the use of surgery, RF ablation, cryoablation, TACE and other methods of tumour destruction, in order to control the tumour progression and prolong the patient survival.

15 LIVER TRANSPLANTATION FOR BILIARY ATRESIA AND SEVERE HEPATO-PULMONARY SYNDROME IN A 10 YEAR OLD GIRL WITH A PREVIOUS SPLENO-RENAL SHUNT

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Introduction: Hepatopulmonary syndrome (HPS) is a condition associated with end-stage liver disease. It is known that a porto-systemic shunt can worsen this syndrome. Case report: A 10 years old girl affected by biliary atresia and HPS was referred to us for liver transplantation. In her past medical history were relevant a Kasai portoenterostomy at the age of 2.5 months and a Warren procedure at the age of 7.5 years. After the porto-systemic shunt she developed a HPS (pO2/FiO2 200, pCO2 31.6 mmHg, Sat O2 73%, FEV1 60%) requiring continuous oxygen therapy. She underwent liver transplantation using a left lateral segment graft. During the operation the presumed Warren shunt was ligated. The postoperative course was complicated by: i) a prolonged hypoxemia not responding to the usual ventilatory support that required a prolonged intubation (30 days) and prolonged administration of Nitric oxide (39 days); ii) portal vein thrombosis on fourth postoperative day, treated by surgical exploration and thrombectomy with a Fogarty catheter; iii) a pancreatico-biliary fistula (that required several surgical revisions and radiological procedures to heal); iv) persistence of a portosystemic shunt that eventually was found to be a side-to-side spleno-renal shunt and was surgically closed. The prolonged hypoxemia could have played a role in delayed healing of the biliary fistula and abdominal wound. 2.5 months after transplantation a trans biliary drainage cholangiography showed a complete resolution of the anastomotic biliary fistula. The girls still require an oxygen supplementation. A large defect of the abdominal wall is still present and the wound is managed with a Vacuum assisted closure device.

16 SPONTANEOUS LIVER RUPTURE IN EHLERS–DANLOS SYNDROME TYPE IV

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Case History: A Pakistani woman aged 23 years experienced sudden chest pain and dyspnoea 5 days after caesarean section. Physical examination, chest radiography and arterial blood gas measurements showed nothing abnormal. She was anti-coagulated for risk of thromboembolic disease. Six hours later she reported right subscapular pain; her abdomen was now tense. Haemoglobin was 6.2 g/dl, platelets 119 x 10^9/l, bilirubin 45 μmol/l, alanine aminotransferase 102 IU/l, alkaline phosphatase 657 IU/l; prothrombin time was normal. An abdominal tap yielded frank blood and emergency laparotomy revealed a large subcapsular liver haematoma (no known antecedent trauma). Initial packing of the liver did not control the bleeding and she required a second laparotomy by a liver surgeon. On day two she was stable enough to allow transfer to our liver intensive care unit. Biphasic liver CT showed tightly packed liver with abnormal perfusion of the parenchyma and intrahepatic haematomas. Bilateral spontaneous pneumothoraces then developed, requiring chest drains. During further laparotomy there was uncontrolled bleeding from the liver, because of complete decapsulation. Abnormal fragility of the bowel and mesentery was noted. Thought was given to total hepatectomy with portocaval shunt and listing for transplantation, but the re was concern about her tissue, considered unsuitable for successful transplantation and further efforts were concentrated on achieving haemostasis. She became profoundly hypotensive and had an asystolic cardiac arrest. After cardiac massage, the suprahepatic inferior vena cava was found to have completely avulsed from her liver. Further resuscitation efforts were unsuccessful. A liver specimen taken at operation showed patchy fibrointimal hyperplasia of hepatic arterioles with smooth muscle and elastic-tissue hypertrophy, consistent with a connective tissue disorder. The patient's medical history was likewise suggestive. She had been born with bilateral club foot and contractures of her hand and had been registered handicapped with retarded motor delay at a young age. She had had several operations for hearing loss and had been seen by an ophthalmologist on account of her prominent globes and poor closure of her eyelids. There was no family history of note except for a brother with transposition of the great vessels, who had undergone heart transplantation at age 18; there was no evidence of collagen disorder in his case and he is currently well. The patient was a primigravida and her pregnancy had been unremarkable. During her caesarean section the fat was noted to be friable and the tissues exceptionally soft. The findings and the medical history led us to diagnose Ehlers–Danlos syndrome (EDS) type IV. Confirmation will require culture of fibroblasts, to detect abnormal collagen production, and mutation analysis.COMMENT: Spontaneous hepatic rupture, which is most often associated with a liver tumour together with coagulopathy is not a common feature of EDS. The abnormality in EDS type IV is a defect of the collagen most abundant in the skin, blood vessels and gastrointestinal tract—namely, type III. Affected patients who undergo surgery are at risk of postoperative arterial rupture, perhaps because surgical trauma increases collagenase activity. In childhood, complications are rare but a quarter of patients have their first complication by age 20 and more than three-quarters by age 40. The risk of lethal complications in EDS type IV seems to be augmented by pregnancy, and is especially high during labour and early postpartum. In the largest

survey of 'classic' EDS type IV, fatal pregnancy-related complications developed in 9–15% of women who became pregnant; therefore, the desirability of conception must be considered. Because the syndrome is inherited in autosomal dominant fashion genetic screening is important, and in the family discussed here all five of the patient's siblings are being tested. In the mother and sister, both of whom have a history of easy bruising, tests have already shown fibroblasts to be free from a collagen III defect. The child will need to be tested. This case illustrates the difficulties in early diagnosis of EDS type IV. Surgeons who encounter extreme tissue fragility at operation should think of connective tissue disorder. Although no specific therapies delay the onset of complications in these patients, awareness of the clinical signs and knowledge of the diagnosis may influence reproductive counselling, the management of pregnancy and surgical interventions.

17 LIVER TRANSPLANTATION WITH CAVAL THROMBECTOMY AND CAVOATRIAL SHUNT IN ACUTE BUDD–CHIARI SYNDROME

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A 38-year-old woman was admitted to her local hospital with acute-onset upper abdominal pain and vomiting. Examination revealed mild jaundice, ascites, smooth, tender hepatomegaly, and bilateral lower limb oedema. Liver function tests were abnormal, with increased serum bilirubin of 37 mol/l and aspartate transaminase of 515 IU/l. Abdominal ultrasound revealed a diffusely enlarged hypoechoic liver with thrombus in the inferior vena cava (IVC) extending to the hepatic veins, moderate ascites, and a patent portal vein. A procoagulant screen was normal, with the exception of lupus anticoagulant, which was increased at 1.46 (normal range 0.8–1.2). No anticoagulation therapy had been used. Abdominal computed tomographic scan confirmed the presence of luminal caval thrombus extending from the level of the bifurcation superiorly to the right atrium (RA). The patient was transferred to the liver intensive care unit for further management of acute Budd–Chiari syndrome. Her clinical condition deteriorated over several days, and she was listed for urgent liver transplantation. Intraoperative findings included moderate ascites, severe portal hypertension, and an enlarged, hard, congested liver. The IVC was thrombosed along its length from the iliac veins to the RA. Access for left axillary vein to portal vein venovenous bypass was prepared early. The femoral veins were not cannulated because of the presence of iliac thrombus. The supradiaphragmatic IVC was severely stenosed, with extensive hard caval thrombus. A midline sternotomy was performed, the RA cross-clamped just below the coronary sinus, and the stenotic IVC excised. The infrahepatic vena cava was thrombectomized with a Foley and a large Fogarty catheter, followed by retrograde infusion of 3 mg of recombinant tissue plasminogen activator. The liver was removed after clamping the infrahepatic vena cava. Because the donor heart had been retrieved leaving a very short suprahepatic cava, donor infrarenal IVC was used as an interpositional graft, with anastomosis to the RA. The graft was implanted by first suturing the suprahepatic vena cava to the caval interpositional graft. The infrahepatic vena cava was re-bled, and a further thrombectomy performed. Portal, arterial, and biliary anastomoses were completed in standard fashion. Postoperative recovery was complicated by renal failure and sepsis. The patient is currently well 1 year after transplantation and has patent cava and hepatic veins. Budd–Chiari syndrome is a heterogenous group of disorders characterized by obstruction of hepatic venous outflow.one Clinical presentation depends on the extent of hepatic venous outflow occlusion with fulminant, acute, subacute and chronic forms. The optimal mode of management is determined by the site and extent of venous occlusion. In fulminant Budd–Chiari syndrome, liver transplantation is the treatment of choice. Four Direct side-to-side portocaval shunt has been successfully used when performed early in the course of Budd–Chiari syndrome where occlusion is confined to the hepatic veins. Five In the presence of IVC thrombosis, the use of mesoatrial shunts have been associated with a high incidence of graft thrombosis and death in some series. Portal decompression combined with bypassing the obstructed IVC with side-to-side portocaval and cavoatrial shunts with synthetic graft has also resulted in long-term survival

POSTER PRESENTATIONS

18 GLYCINE AMELIORATES LIVER INJURY AFTER PARTIAL HEPATECTOMY IN THE RAT

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Some substances are beneficial for the graft and protecting the residual liver of the donor during the harvesting process by living donor liver transplantation. Pretreatment of the donor alpha-tocopherol (vitamin E), the flavonoid silibinin and the amino acid L-glycine alone or in combination might improve graft quality, and do not adversely affect the donor. The aim of our study was to analyse the effects of these pretreatments on the donor in a model of 90% partial hepatectomy in the rat.

Methods: Male Wistar rats received glycine 5%, vitamin E 100 mg/kg BW and/or Silibinin 100 mg/kg BW, afterwards 90% partial hepatectomy was performed. Rats were sacrificed after 0, 12, 24, 48, 72h and 4 weeks ($n = 6$) and samples were taken. AST, ALT, ALP, total bilirubin, prothrombin time (PTT) were assessed in serum samples, remnant liver was histological analysed.

Results: Glycine decreased the release of the transaminases (AST, 12 h: glycine 1292 ± 192 U/l vs. control 2311 ± 556 U/l, $P < 0.05$; ALT, 12 h: glycine 1013 ± 278 U/l vs. control 2038 ± 500 U/l, $P < 0.05$), activity of ALP and the total bilirubin level ($p < 0.05$). The PTT after 48h was significantly lower in the glycine group. Survival rate 48h: glycine 17/18 control 16/18, vitamin E 13/18, silibinin 15/18 and combination 14/18; 4 weeks: glycine 5/6, control 5/6, vitamin E 4/6, silibinin 5/6 and combination 4/6.

Discussion: If this advancing effect asserts in this model without namely ischaemia on the decreasing of microcirculatory failure or on impairment of mechanic injury components –like activation of Kupffer cell – is unclear. Pretreatment of donors before the operative procurement by living donation or patient undergoing major hepatectomy, e.g. tumour surgery might be worthwhile.

19 BILIARY INDOCYANINE GREEN EXCRETION – AN ADDITIONAL TOOL IN THE ASSESSMENT OF THE GRAFT FUNCTION AFTER ORTHOTOPIC LIVER TRANSPLANTATION – PRELIMINARY RESULTS

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Background: Indocyanine plasma disappearance rate (ICG-PDR) is a common tool for evaluation of graft function after orthotopic liver transplantation (OLT). The uptake of the dye (ICG) takes place at the hepatocyte's basolateral membrane and ICG will be excreted into the bile via the canalicular membrane. We hypothesize that the insult associated with ischemia reperfusion injury (IRI) after OLT differentially affects the two polar surfaces of the hepatocyte. We expect a better preserved transport from the sinusoid into the hepatocyte compared with biliary excretion of the dye depending on the degree of IRI.

Methods: We present the results of the 11 patients included so far. Twelve hours after OLT, we measured the ICG-PDR in standard practice and additionally quantified the excretion of the dye in the bile fluid. Spectrophotometric assessment of the concentration of ICG (wave length 800 nm) was read using a Nanodrop™ spectrophotometer (Nanodrop Technologies, Wilmington, USA). The graft function was evaluated using the criteria defined by Pokorny et al. (Transpl Int. 2000; 13 Suppl 1:S154–7).

Results: Using the aforementioned criteria, two patients had a good graft function, six had a fair one and three had a poor graft function whereby one needed a retransplantation. Biliary ICG excretion differed significantly between patients with fair and poor graft function (fair: 229.28 ng/μl ± 282.33; poor: 8.37 ng/μl ± 14.5; $P = 0.024$). There was no significant difference between patients with good and fair graft function ($P = 0.143$). ICG-PDR could not detect differences with regard to the graft function.

Conclusion: Our first results of that ongoing study are very encouraging. We assume that the analysis of the biliary ICG-excretion can be a helpful tool evaluating the graft function after OLT.

20 EARLY PROGNOSTIC SIGNIFICANCE OF PLASMATIC AMMONIUM, LACTATE AND CREATININE AFTER LIVER TRANPLANTATION (OLTX) IN CHILDREN

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Introduction: Mortality and morbidity after liver transplantation can be reduced by immediate identification of complications. There are currently no studies on the parameters to consider in the early postoperative period to help foresee the outcome the graft could have. Only daily liver ultrasound seems to be a useful strategy to better monitor vascular and parenchymal patterns. Design: Retrospective analysis of biochemical data collected within the first 36 h after OLTX in children.

Material and methods: We analysed 188 patients admitted to our PICU after OLTX between January 2002 and December 2007. We divided our population into two groups: group A, patients with an early recovery of liver function and–group B- patients giving signs of poor recovery who required a second (or more) liver transplantation or who died by one month after the first transplantation. For each group, we withdrew blood samples–plasmatic lactate, ammonium, creatinine level–every 12 h for the first 36 h of the postoperative period.

Results: A total of 169 (90%) children had a successful recovery of liver function after OLTX (group A); 19 (10%) developed end stage liver failure among them five died and 14 underwent a second (or more) liver transplantation (group B). The group B's records compared with group A's showed a rise of plasmatic lactate, ammonium and creatinine. Moreover, a multivariate regression analysis demonstrates that such increased values are a negative prognostic indicator of the graft's outcome.

Conclusion: We were able to early identify a poor recovery of the graft using blood samples analysis in addition to daily ultrasound. From the statistical results there emerges that the plasmatic level of lactate, ammonium and creatinine correlates with both graft's failure and patient's outcome.

21 LIVER TRANSPLANTATION IN ELDERLY RECIPIENTS (> 65 YEARS): INCREASED INCIDENCE OF POSTOPERATIVE MORTALITY DUE TO CARDIAC CAUSES

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Introduction: The advanced age of the recipient is considered a 'relative contraindication' to liver transplantation (LT). Here, we compared the outcome after LT in two different groups of recipients (young vs. elderly).

Methods: Between 01/2000 and 12/2006, 565 LT were performed in 502 recipients in our institution. Of these, 34 were performed in >65-years old recipients (elderly group). We focused our study comparing: donor age, ASA-score and co-morbidities, duration of operation, transfusions, and outcome.

Results: Elderly group: the mean donor age was 52.5 years (23–78 years) and the graft weight 1339 g (890–1880 g).Eighteen out of 34 recipients had HCC. Co-morbidities were recorded in 25 patients (73.5%): coronary artery disease (CAD) in 17 (50%), diabetes and chronic renal insufficiency in four (11.7%), chronic obstructive pulmonary disease in three (8.8%).Previously, liver or lung surgery in 2 and 1 case, respectively. Mean MELD score was 13.9 (range 10–29) and ASA score was two in 15 (44.1%); and three in 19 (55.8%) recipients. Mean operation time was 4 h 45 min, three patients received also combined kidney transplantation. Twenty-five (73.5%) recipients received blood transfusions (mean 3.2 PRBC).All deceased patients (elderly group) had ASA 3 and MELD 11, 14, 17, respectively. Morbidity was observed in 20 patients (58.8%).Overall patient survival was 80% (5-years follow- up), in particularly, at 30-days, 1-year, 3-year were 91%, 84%, 80%, respectively. The two groups were comparable regarding the preoperative assessment. Only two statistical differences ($P = 0.02$) were reported between the groups: the significant lower incidence of CAD and per-operative mortality due to cardiac causes in the younger group compared with those of elderly.

Conclusion: Our results suggest that the recipient age should not be considered an absolute contraindication for LT when the graft/recipient matching is optimal and when an adequate cardiac assessment is performed.

22 THE LONG-TIME OUTCOME OF PATIENTS TRANSPLANTED DUE TO ACUTE LIVER FAILURE WITH HEPATIC HHV-6 INFECTION

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Human herpesvirus-6 belongs to the beta herpesviruses. HHV-6 reactivation after transplantation is usually asymptomatic, but the virus may infect the liver transplant, cause an intragraft inflammatory reaction and graft dysfunction. Case reports show an association between hepatic HHV-6 infection and

indeterminate ALF, but establishing causality is challenging because of the ubiquitous nature of HHV-6. We have previously found HHV-6 antigens in the explanted livers of most patients (80%, $n = 32$) transplanted with indeterminate ALF, whereas the opposite was seen in patients with ALF of known cause. After transplantation, half of these patients with pretransplant HHV-6 infection (9/18) developed recurrence, whereas no posttransplant HHV-6 infection of the liver was seen in patients without pretransplant HHV-6. The aim of this study was to investigate the long-term course (6–11 years) of these patients. Two of the patients with a relapse of intrahepatic HHV-6 infection had also CMV hepatitis, whereas none of the other patients demonstrated intrahepatic CMV. During the follow-up of six years or more, one graft and 1–2 patients were lost in both groups (HHV-6 recurrence/HHV-6 negative patients). The reasons for graft loss were thrombosis of the hepatic artery and portal vein thrombosis. Two patients died in HHV-6 recurrence group, one because of a new arterial thrombosis (day 460) and one with functioning transplant (4.5 years after transplantation). In control group one patient deceased 1.5 years and one 10 years after LTx because of pneumonia. The association between HHV-6 and indeterminate ALF has been established. However, in our material HHV-6 relapse did not cause liver failure, and had no significant long-term effect on survivals. Clearly, more studies are needed to define the role of HHV-6 in liver transplantation and the pathogenesis of hepatic infection.

23 PRELIMINARY RESULTS OF CONTRAST ENHANCED ULTRASONOGRAPHY IN THE STUDY OF THE HEPATIC VASCULARIZATION AFTER LIVER TRANSPLANTATION

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Aim: To know if Contrast Enhanced Ultrasonography (CEUS) represents an improvement in the diagnosis of early and late arterial and portal complications after Liver Transplantation (LT).

Patients and methods: Since May 2008 in our Unit we began to use CEUS after LT as a part of the postoperative early follow up of arterial and portal patency. Every transplanted patient underwent CEUS and Doppler ultrasound in postoperative days 1, 7, 15 and 30 as a study protocol. Meanwhile we performed CEUS on historical patients (pts) in good health but with an established diagnosis of HAT. We recorded the CEUS finding or not of the hepatic artery (HA) and of the portal vein (PV), the time interval from the end of contrast injection to CEUS findings, the identification of the waveform of the HA and the value of the Resistive index (RI) at Doppler ultrasound. Data were examined comparing them with CT scan with vascular reconstructions and/or hepatic arteriogram.

Discussion and conclusion: According to our preliminary results CEUS after LT allowed us i) early detection of the absence of the image of the intrahepatic hepatic artery with a low-cost, bed-side diagnostic tool ii) to spatially locate the right hepatic artery thus improving its Doppler detection iii) to select pts with presence of arterial flow but a late comparison of it, thus identifying pts with a likely arterial hepatic insufficiency iv) to retrieve additional details concerning the arterial intrahepatic flow even in pts with a CT scan/ angiographic diagnosis of arterial thrombosis. These findings obviously need further studies to establish the real usefulness of CEUS after LT.

24 LUMINAL PRESERVATION SOLUTION INTESTINAL GRAFT QUALITY DURING COLD STORAGE OF RAT INTESTINE

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Background: Compromised intestinal graft quality limits the outcome of intestinal transplantation. Current standard for intestinal preservation is a vascular wash-out with University of Wisconsin solution (UW) followed by cold storage (CS) in UW with a closed lumen. This concept neglects the importance of the luminal compartment.

Aim: To compare intestinal graft quality after CS with or without luminal preservation in three different solutions.

Methods: After vascular flush with UW, rat intestine ($n = 4$) was stored at 4°C for 4 h and 19 h in UW, IGL or glutamine-enriched IGL (GIGL) with the intestinal lumen closed or open (luminal preservation). Intestinal graft quality, measured by structural damage (Park score) and functional integrity (transepithelial electric resistance, TEER) was assessed at T0, T4, T19. Results are expressed as mean ± SEM. Differences were considered significant when $P < 0.05$ (Mann–Whitney).

Results: At T4, UW with luminal preservation resulted in less morphological damage than UW without luminal preservation (Park score 2.75 ± 1.03 vs. 5.55 ± 0.2, $P = 0.027$). Furthermore, GIGL without luminal preservation exhibited superior morphology than UW without luminal preservation (Park score 2.0 ± 1.26 vs. 5.55 ± 0.2, $P = 0.035$). At T19, IGL either with or without luminal preservation demonstrated improved functional integrity compared with UW without luminal preservation (mean TEER IGL open 836 ± 66, IGL closed 818 ± 62 vs. UW closed 533 ± 48, $P = 0.02$, 0.04). TEER and Park scores correlated strongly (correlation coefficient -.62, $P = 0.01$, $n = 51$).

Conclusion: Luminal intestinal preservation in UW is superior to the current standard of CS with the lumen closed for short storage periods. For extended storage times, alternative solution (IGL) enhances functional integrity. TEER correlated strongly with Park scores, indicating that TEER is a valid, functional complementary parameter to assess intestinal graft quality. Luminal exposure to preservation solution or alternative intestinal preservation solution (concomitant to intravascular wash-out with UW) opens a window for improvement of intestinal graft quality.

25 TWENTY-FIVE YEARS ANNIVERSARY OF LIVER TRANSPLANTATION IN NORWAY

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Oslo University Hospital celebrates the 25 years anniversary of its liver transplantation program in February 2009. Since the first liver transplantation (LTX) in 1984 and until the end of 2008, a total number of 652 transplantations have been done. The annual number of LTX's was low during the first several years but has increased progressively during the later years and was the highest ever in 2008 with 79 LTX's. Milestones have been the introduction of veno-venous bypass (VVBP) in 1993 and the conversion to the Piggy-back technique in 2001. For the year of 2008 PSC (29%) was the most common cause of LTX, followed by PBC (10%), alcoholic cirrhosis (10%) and acute hepatic failure (7.2%). One year overall graft/patient survival for the following time periods, until the end of1989, 1990–1995, 1996–2000, 2001–2005 and 2006–2008 were as follows: 53%/53%, 65%/67%, 76%/83%, 83%/86%, 90%/96%. Five year overall graft/patient survival for the same time intervals until 2005 was: 42%/42%, 51%/58%, 62%/73%, 76%/83%. Three year graft/patient survival from 2005 to 2008 was 81%/89%. One and 5 years survival for children under 5 years from 2000 was 87% and 87%. One and 5 year graft/patient survival for patients over 60 years from 2000 was 89%/89% and 74%/74%.

Conclusions: Graft and patient survival has improved during each consecutive 5 years interval since 1984. Patient survival for children less than 5 years is superior to the results in adults. For patients over 60 years graft survival is comparable to total numbers for the same period, however patient survival is not as good as the best results in the latest time period but still acceptable.