Transplant International

ORAL PRESENTATIONS

ACUTE LIVER FAILURE — SESSION 2 — THURSDAY, FEBRUARY 10

Oral 01 IMPACT OF DONOR VARIABLES ON SURVIVAL AFTER ORTHOTOPIC LIVER TRANSPLANTATION (OLT) FOR ACUTE HEPATIC FAILURE – EVALUATION OF A NEWLY DEVELOPED NOMOGRAM

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Background/aim: The impact of donor risk factors for patient survival after liver transplantation for acute hepatic failure is still discussed controversially. A nomogram for donor extended criteria predicting 3- and 12 months patient survival after liver transplantation for end-stage liver disease has been newly developed. Aim of this study is to evaluate this nomogram in an acute hepatic failure (ACHF) cohort.
Materials/methods: A retrospective review of prospectively collected data on all patients transplanted at our center between 1998 and 2008 (n = 1204) was performed. Patients under age of 18 and split liver grafts were excluded (n = 65) leaving a total of 1141 patients for analysis. Patients transplanted for acute hepatic failure were identified (n = 69) and donor data at risk for survival according the nomogram (CIT, highest Na, highest gamma GT, cause of death, sex) were obtained. For acute hepatic failure patients estimated patient survival was correlated with actual patient survival.
Results: Of 1141 patients left for analysis, 69 were transplanted for ACHF, 768 for chronic liver disease and 304 for cancer. Patient Survival 3 months 12 months Acute 75% 71% Chronic 85% 78% Cancer 83% 67% Estimated survival as defined by the donor variable nomogram was correlated to actual survival in the acute hepatic failure cohort and did not show correlation (Pearson coefficient -0.171).
Conclusion: Three and 12 months patient survival after OLT for acute hepatic failure was comparable to published data from ELTR. In our single center cohort extended criteria donor grafts showed no correlation with actual survival. Therefore we conclude that in severely compromised recipients suffering from acute hepatic failure, quality of the graft is not of importance and post-transplant survival is triggered by recipient variables.

Oral 02 IMPORTANCE OF DIETARY COPPER FOR ONSET OF ACUTE LIVER FAILURE IN WILSON'S DISEASE

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Fulminant hepatitis in patients having Wilson's disease (WD) accounts for a significant portion of liver failure (ALF) worldwide. Lifetime dietary copper intake is implicated to be important for onset and course of disease. A LEC rat model of WD was used to study the impact of dietary high copper (hCu) for induction of ALF. hCu was administered directly after birth or at month 5 after having received a reduced copper (rCu) diet. LEC that received rCu throughout lifetime served as control. Serum markers, liver copper, liver histology, liver gene expression as well as survival were significantly affected in LEC receiving hCu. Animals (43/44) developed fulminant hepatitis and encountered ALF. However, onset of ALF with regard to start of hCu was more rapid in rats having received rCu for several months. Analysis of clinical and biochemical markers as well as gene expression data suggest that the molecular events of ALF are similar regardless of time point. Of note, Atp7b heterozygotes moderately responded to hCu but did not develop hepatitis. In contrast to hCu treatment, all LEC (22/22) that were housed on rCu throughout lifetime did not develop hepatitis and survived. Our data provide direct experimental evidence that reduced dietary copper intake significantly prevents disease but the risk to develop rapid onset of ALF persists throughout lifetime in ATP7B carriers. Our novel dietary model of WD has importance for understanding the molecular events of ALF, and for management of patients.

Oral 03 EFFECT OF REGIONAL CITRATE ANTICOAGULATION ON ELECTROLYTE BALANCE IN PATIENTS WITH LIVER FAILURE

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Objective: Regional citrate anticoagulation (RCA) has emerged as a promising method in critically ill patients at high risk of bleeding. However, in patients with liver failure, citrate accumulation may lead to electrolyte imbalances, notably of calcium. The aim of this study was to evaluate the feasibility and safety of RCA during liver support using a molecular adsorbent recirculating system (MARS) as well as its effects on electrolyte balance in patients with liver failure.
Design: Prospective observational study.
Patients: Twenty critically ill patients supported by MARS due to liver failure between January 2007 and May 2009.
Measurements and main results: The median duration of MARS treatment was 20 hours (IQR 18–22 hours). Two out of 77 MARS treatments (2%) were prematurely discontinued due to filter clotting and bleeding, respectively. The median citrate infusion rate, necessary to maintain the post-filter ionized calcium between 0.2–0.4 mmol/l, was 3.1 (IQR 2.3–4) mmol per liter blood flow. The median calcium chloride substitution rate was 0.9 (0.3–1.7) mmol/l dialysate. Total serum calcium remained stable during MARS treatments. There was a statistically significant increase of the ratio of total calcium to systemic ionized calcium (2.04 + 0.32 mmol/l to 2.17 + 0.35; P = .01), which reflected citrate accumulation due to liver failure. Under close monitoring, no clinically relevant electrolytes disorders were observed.
Conclusions: Our results suggest that RCA is a safe and feasible method to maintain adequate circuit lifespan without increasing the risk of hemorrhagic complications while maintaining a normal electrolyte balance in patients with liver failure supported by MARS.

ACUTE LIVER FAILURE — SESSION 3 — FRIDAY, FEBRUARY 11

Oral 04 GENDER INFLUENCES MACROPHAGE CLEARENCE IN A MURINE MODEL OF ACUTE LIVER INJURY

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Background: Hepatocyte-driven liver regeneration following acute injury is a highly orchestrated process in which remaining, healthy hepatocytes proliferate under the control of cellular, metabolic and hormonal networks. Immune response seems to have a pivotal role during this type of damage. Aim of this study was to evaluate the role of gender disparity and inflammatory microenvironment after acute liver damage.

Methods: Acute liver damage was induced in BALB/c mice aging 8 weeks by a single CCl4 administration (i.p. 0.75 ml/kg in olive oil). Animals were sacrificed at different time points after the injury. Livers were excised and then analyzed by immunohistochemistry, real time PCR, western blotting and FACS analysis.

Results: Immunohistochemical evaluation showed a different recovery after liver damage in male and female mice. Female livers after 8 days appeared almost normal in size and morphology, while male livers maintained an injured aspect. Immunohistochemistry shown a massive inflammatory infiltrated in both gender, but a predominant macrophage component in male tissue up to 12 days. Real-time PCR analysis shown a significant TNF-α and IL-6 mRNA up-regulation in treated mice, but we also found a significant up-regulation of IFN-γ, a typical Th1 cytokines, in female animals, while and increased expression of Th2 cytokines mRNA, such as IL-4 and IL-5 in male animals. Finally we found a significant up-regulation of androgen receptor in male mice compared to females.

Conclusions: It appears that male and female mice respond in a different manner following the same noxious stimuli. This could explain the different kinetics with which the liver is able to regenerate after an injury and probably emphasizes the role that hormonal component carries out in this repair process.

Oral 05 SUCCESSFUL LIVER TRANSPLANTATION UNDER EXTRACORPOREAL MEMBRANE OXYGENATION ECMO AND CONTINUOUS HEMODIALYSIS FOR FULMINANT MULTIORGAN FAILURE IN ACUTE WILSON'S DISEASE

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Wilson's disease is a genetic disorder resulting in acute fulminant liver failure (ALF) in 5% of cases. To date, liver transplantation (LTx) represents the only curative treatment option for ALF. ALF presents a special challenge and necessitates urgent decision making, due to acute mortality of 80–90%. Therefore it is critical to quickly and accurately identify those patients most likely to benefit from LTx with best short and longterm outcome. In this case study we report a successful LTx for fulminant liver failure due to Wilson's disease including multiorgan failure. Between the time of high urgency listing and LTx, renal and pulmonary failure developed due to toxic-liver-syndrome with the need of continuos Extracorporeal Membrane Oxygenation (ECMO) and Continuous Veno-Venous-Hemodialysis (CVVHD), both started at day two after admission. At day four, LTx in piggyback technique due to ECMO-katheter in the V. cava was performed. Notably, clamping of V. cava was not possible due to ECMO-katheter. ECMO and CVVHD treatment could be discontinued at days two (extubation on day 10) and 23 after LTx, respectively. The patient could be discharged from intensive care unit at day 24 and from surgical ward with normal liver, pulmonary, and renal function at day 52 after LTx. Since month 6 after LTx the patient is fully capable to work and enjoys highest quality of life. This successful outcome is based on the consequently interdisciplinary team work at our transplant center involving continuous longterm out-patient follow-up care and professional collaboration with general practioners/physicians. The presented case shows, that successful LTx under simultaneous ECMO and CVVHD in case of ALF complicated by pulmonary and renal failure is possible in selected cases allowing for good short- and long-term outcomes.

Oral 06 INDICATIONS FOR AND SURVIVAL AFTER LIVER RETRANSPLANTATION IN EUROPE: EVALUATION OF THE LAST 28 YEARS

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Introduction: Liver retransplantation (ReLT) remains the only treatment for patients with unsalvageable graft failure and is usually associated with increased morbidity and mortality compared to primary liver transplant (LT). Aim of this study was to evaluate trends in adult ReLT in Europe between 1980 and 2008.

Methods: Retrospective analysis was based on the prospective European Liver Transplant Registry (ELTR), including patients aged ≥16 years at LT. Patients and subsequent analyses were grouped according to three decades of retransplantation.

Results: Of 69010 adult LTs performed, 6397 (9.3%) patients required 7114 ReLT. Median recipient age at ReLT was 47.4 (range 16–74) years, 60% were male. 54% of ReLT were carried out three months after LT; 719 patients required multiple ReLT. Despite increasingly older donors ($P < 0.001$), overall 1-, 5- and 10-year actuarial survival increased from 36%, 28% and 26% in the 1980s to 56%, 45% and 37% in the 1990s, to 67% and 56% (10-year data not available yet) in the 2000s ($P < 0.001$). ReLT for acute/chronic rejection accounted for 36% of all ReLTs in the 1980's and decreased to 11% in the 2000's ($P < 0.001$). Conversely, hepatic artery thrombosis (23%) and HCV recurrence (8%) - one of the main ReLT indications in the 2000's –accounted for 4% and <1% in the 1980's ($p < 0.001$). Sepsis and disease recurrence were the main causes of death post ReLT.

Conclusion: Despite inferior long-term graft and patient survival following ReLT compared to primary LT, ReLT provides the only treatment for irreversible graft loss. Although the indications for ReLT have changed significantly from the 1980's to the 2000's - reflecting a general change for all transplants - advances in perioperative care and immunosuppressive regimes have significantly improved survival in the lastthreedecades.

ACUTE LIVER FAILURE — SESSION 4 — FRIDAY, FEBRUARY 11

Oral 07 EXTRACELLULAR BRAIN AMMONIA LEVELS IN ASSOCIATION WITH ARTERIAL AMMONIA, INTRACRANIAL PRESSURE AND THE USE OF ALBUMIN DIALYSIS DEVICES IN PIGS WITH ACUTE LIVER FAILURE

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Background: In acute liver failure (ALF) hyperammonemia plays a mayor role in the pathogenesis of hepatic encephalopathy (HE) but does not always correlate with the severity of mental deterioration and intracranial pressure (ICP). The aim of our study was to evaluate the association with extracellular brain ammonia, ICP and the therapeutical impact of two albumin dialysis devices.

Methods: Acute liver failure was induced by complete hepatectomy in 13 pigs. All pigs were monitored and treated under intensive care conditions until death. Arterial blood and cerebral microdialysis samples were collected and ICP data recorded. Additionally in 5 pigs, standard albumin dialysis and in 3 animals an albumin dialysis prototype was initiated as a tool.

Results: Arterial ammonia increased straight after hepatectomy, while extracellular brain ammonia remained on a moderate level 10 hours post ALF initiation. After 16 hours the brain ammonia reached arterial ammonia levels before plateauing at 1200 μM, though the arterial ammonia continued to rise. The ICP correlated with the brain ammonia levels. No impact of the different dialysis therapies on neither blood nor brain ammonia levels was observed.

Conclusions: In ALF the extracellular brain ammonia revealed a delayed increase compared to arterial ammonia. It correlated strongly with the ICP and could serve as a sensitive marker for HE development. Albumin dialysis did not affect blood or brain ammonia levels.

Oral 08 A NEW METHOD IN THE MONITORING OF DONOR LIVER GRAFT DRUG METABOLIZING CAPACITY USING PERIPHERAL BLOOD SAMPLE

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Drug-metabolizing capacity of liver or transplanted liver-graft primarily depends on levels and activities of cytochrome P450 enzymes (CYP). Significant portion of adverse drug reactions and therapeutic failures are caused by inter-individual differences in drug-metabolism. The most important reason of inter-individual variation is genetic polymorphism of CYP genes. Some CYP genes (CYP2C9, CYP2C19, CYP2D6) are highly polymorphic resulting in enzyme variants with reduced or even no activity. Validated analytical system with metabolomic and transcriptomic tools has been developed for estimation of drug-metabolizing capacity. This system is based on measurements of CYP enzyme expression at mRNA level in leucocytes with strong correlation of hepatic CYP activities. Phenotyping 100 (transplanted) liver donors in Hungary using peripheral blood sampling, the incidence of poor metabolizing liver grafts was up to 37% and in 80% from male donors. Screening the drug-metabolizing status of the transplanted (100) donor livers, the distribution of CYP gene expression measured from donor leucocytes is below: Poor Intermediate Extensive CYP3A4 37%, 50%, 13%, CYP2C9 37%, 46%, 17%, CYP2C19 13%, 75%, 12%, In the poor-metabolizer group (37 transplanted livers) poor metabolism was found for CYP3A4, CYP2C9 and CYP2C19 with an incidence of 81%, 70% and 10% respectively. The biopsy showed drug toxicity in 18 cases (48%) in the poor metabolizer group. In conclusion, graft survival depends on many factors, but prospective investigation of CYP status of donor livers, individual drug therapy can be benefitial, reducing drug side effects and drug failures after liver transplantation.

Oral 09 MONITORING OF CEREBRAL AUTOREGULATION USING PRESSURE REACTIVITY INDEX PRX IN ACUTE LIVER FAILURE DUE TO ACETAMINOPHEN-INTOXICATION IN A PORCINE MODEL

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Background: In acute liver failure (ALF) a raise of ICP in the context of cerebral edema is observed. The use of the pressure reactivity index (PRx) is described to be a sensitive parameter to monitor cerebrovascular pressure reactivity as the underlying mechanism of cerebral autoregulation. The usage of PRx and its correlation to ICP in the setting of an acetaminophen induced ALF is evaluated.

Materials and methods: Twenty-five German land race pigs were intoxicated with acetaminophen through a duodenal-catheter until acute liver failure. The pigs received full intensive care for the whole time. PRx and ICP were monitored continuously.

Results: The PRx oscillated between -0.10 and 0.10 during catheter placement. At time of intoxication it started to increase linear from 0.0 to 0.65 at 24 hours of intoxication which corresponds to 16 hours after ALF (in total 40 hours). Four hours after ALF the raise of ICP started from baseline levels of 20 mmHg (PRx already = 0.5) and terminated at levels above 40 mmHg at exitus. In sham animals no increase of ICP and PRx was observed. In 2 animals that recovered from ALF the raise of PRx started at the time of intoxication to levels of 0.3 but then returned to normal (0.0) during the intoxication period. No significant increase of ICP was recorded.

Conclusions: The persistent increase of PRx to pathological levels and thus the enduring loss of cerebrovascular autoregulatory capacity precedes the terminal increase of ICP by hours. The loss of cerebrovascular autoregulatory capacity is thus an important early factor. PRx monitoring is the ideal tool for early detection of candidates at risk for the development of raised ICP and a possibly lethal course of ALF.

VISCERAL TRANSPLANTATION — SESSION 5 — FRIDAY, FEBRUARY 11

Oral 10 SALVAGE THERAPY FOR REFRACTORY REJECTION AND PERSISTENCE OF DONOR-SPECIFIC ANTIBODIES AFTER INTESTINAL TRANSPLANTATION USING THE PROTEASOME-INHIBITOR BORTEZOMIB

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Antibody-mediated rejection (AMR) is a major challenge in intestinal transplantation (ITx) and poorly characterized. Persisting levels of donor-specific anti-HLA-antibodies (DSA) constitute a major risk, especially when appearing in the first year after transplantation, but data on therapeutic approaches and long-term follow up are rare. Additionally, AMR is less responsive to anti-rejection treatment, entailing chronic graft-manifestations and allograft losses. Plasmapheresis and rituximab reduce the concentration of DSA, but are ineffective against antibody-producing plasma cells. Bortezomib, a proteasome-inhibitor, was shown to deplete antibody-producing plasma cells and reduce DSA after kidney transplantation. We report the successful treatment with bortezomib in a patient with refractory rejection associated with persisting DSA levels after ITX. On POD 14, DSA-testing revealed high levels of anti-donor HLA DQ7 and DQ8 antibodies, entailing immediate plasmapheresis. On POD19, the patient experienced a mild ACR and received steroid pulse therapy (5 × 1000 mg) and rituximab (375 mg/m2), which decreased histological rejection signs. However, inspite of an anti-rejection therapy consisting of steroids and thymoglobuline, allograft biopsies continued to display persistent inflammatory signs, low grade fibrosis, cryptitis, and increased rate of apoptoses defined as indeterminate for rejection. C4d-staining revealed inconclusive results. Since 3 intervals of plasmapheresis, high-dose ivIG and 2 applications of rituximab failed to reduce DSA, bortezomib was applied as ultima ratio in standard labelled dosis (4 × 1.3 mg/m2), which was well tolerated. Within 4 weeks after bortezomib-application, DSA decreased significantly and histological signs of rejection disappeared completely (figure1). We applied bortezomib as a rescue therapy in a highly endangered patient with persistent DSA-levels and ongoing graft injury in the early phase after ITX. In this setting, the use of bortezomib as an adjunct agent to plasmapheresis, ivIG, and rituximab might be a new treatment option for AMR after ITX.

Oral 11 GOOD OUTCOME IN INTESTINAL TRANSPLANTATION AFTER SEVERE IMMUNOLOGICAL AND INFECTIOUS COMPLICATIONS:A CASE REPORT

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Objective: 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 thymoglobuline; 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. Mild signs of mucosal regeneration were noted on postoperative day 40, progressing to regeneration of normal epithelial after day 44. Azathioprine was added and temporarily discontinued due to a severe leucopenia. 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 postoperative 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.

Oral 12 TEN YEARS INTESTINAL AND MULTIVISCERAL TRANSPLANTATION: THE BERLIN EXPERIENCE

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Background: The intestinal and multivisceral transplant program at the Charité in Berlin, Germany, was established in 2000. We hereby present a single center experience with particular respect to immunosuppressive strategies and post-transplant outcome.

Methods: Twenty-nine patients (21 male, 8 female; median age 38.3 ± 11.4 years) of 80 patients referred to our center with irreversible and complicated intestinal failure due to ultra short bowel syndrome or motility disorder underwent isolated intestine (ITx; $n = 17$), combined liver/intestine (LITx; $n = 2$), or multivisceral transplantation (MVTx; $n = 10$). Data were collected prospectively.

Results: According to immunosuppressive strategies, two time periods were analyzed and compared: 2000–2005 (period I); 2006–2010 (period II). Period I comprised 15 patients (ITx: $n = 13$; MVTx: $n = 2$), period II 14 patients (ITx: $n = 4$; LITx: $n = 2$; MVTx: $n = 8$). Immunosuppression in period I consisted of daclizumab induction (tailored dose), ATG Fresenius single shot pre-reperfusion (8 mg/kg bw), tacrolimus (initial trough: 20–25 ng/ml), sirolimus, and steroids ($n = 10$), and campath induction (30 mg; POD 0/4), tacrolimus (trough: 20–25 ng/ml), delayed-onset sirolimus, and steroids ($n = 5$). In period II thymoglobuline induction (max. dose 7.5 mg/kg bw), single shot infliximab induction (5 mg/kg bw), tacrolimus (trough 10–15 ng/ml), steroids (tapered until month 3), and delayed onset sirolimus or MMF has been applied. 1-year and 5 year- patient and organ survival rates in period I were 66% and 60%, respectively, in period II 1-year and actuarial 3-year survival rates were 92% ($P < 0.05$). Mortalities were secondary to graft failure because of refractory rejection ($n = 4$), and NEC ($n = 1$) in period I as well as PTLD ($n = 1$) in period II. All long-term survivors are off parenteral nutrition.

Conclusion: ITx and MVTx have been established. Modifications in post-transplant management, particularly modifications in immunosuppressive strategies including infliximab induction have accounted for significant advances in post-transplant patient and graft outcome, currently reaching 93% at 1 and 3 years, respectively.

VISCERAL TRANSPLANTATION — SESSION 6 — FRIDAY, FEBRUARY 11

Oral 13 INTESTINAL TRANSPLANTATION (ITX) FOR CHILDREN WITH CHRONIC INTESTINAL PSEUDO-OBSTRUCTION (CIPO)

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Chronic idiopathic intestinal pseudo-obstruction (CIPO) is an uncommon intestinal motility disorder, with a reported high morbidity and mortality following ITx.

Aim: To review our experience of intestinal transplantation in children with CIPO. Subject and Methods. A retrospective review of 13 children with CIPO undergoing ITx from 1993 to 2009 was performed. Foregut dysmotility (evaluated with symptoms and contrast studies), complications and outcome were reviewed. Patients were categorized into 4 groups according to type of anastomosis between graft and native bowel.

Results: Children with satisfactory stomach emptying received a jejuno-jejunostomy (Group II, *n* = 2, D:R ratio 0.9 (0.6–3.2;Liver graft 4W) or gastro-jejunostomy (Group I, *n* = 4, D:R ratio 2.25 (1.4–2.9), Liver graft1W + 3R) in addition to jejunal-jejeunostomy. However, in initial experience, 1 child died of liver disease due to failure to establish feeds. Technique was further modified in subsequent transplants (Group III, N = 3, D:R ratio 1.2 (1.2–4.3);Liver Graft 2W + 1R; Group-IV,D:R ratio 1.6(1.3–2.2,liver graft 2W + 1R) with insertion of nasojejunal (NJ) tube at transplant to facilitate enteral feeding even in children with inclusion of stomach. Enteral feeds were successfully introduced in all 12/13 pateints (one patient died before establishing enteral feeds). The time to stop PN in Group 1, Group II, Group III, Group IV were 31 days, 55 days,18 days and 18 days respectively. The median follow-up (range)in Group 1, Group II, Group III, Group IV were 17 months (1.15–55.2), 4.7 months (1.1–5.86), 3.34 months (1.7–128.7), 25 months (6.6–47.3) *W = Whole; R = reduced.

Conclusion: Children with CIPO need careful evaluation of intestinal motility, but the majority benefit from having a multi-visceral graft with stomach resection and peri-operatuve placement of an NJ tube. This strategy achieves good drainage, effective establishment of enteral feeding and a five year survival of 60%, comparable to short bowel syndrome.

Oral 14 TECHNIQUE FOR IN-SITU LIVER SPLITTING ASSOCIATED WITH MODIFIED-MULTIVISCERAL GRAFT RECOVERY

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Introduction: Intestinal transplantation is a well established treatment in the management of intestinal failure. Some cases of intestinal motility disorders requires combined transplantation of the stomach and pancreaticoduodenal complex (modified multivisceral graft - MMV). The simultaneous performance of an in-situ split liver with recovery of a separate MMV graft poses challenges of vascular allocation in order that none of these organs are compromised.

Methods: The recovery was performed dividing the arteries as follows: the superior mesenteric (SMA) and celiac trunks were retrieved with a single aortic patch; the main hepatic artery was divided just above the GDA for the right liver graft and the left hepatic artery was divided close to its origin for the left lateral segment (LLS) graft. The recipients were a 12 years old male with intestinal motility disorder, a 6 month old male with biliary atresia and a 30 years female with acute intermittent porphyria. All the recipients are alive after a 12 months follow-up. The adult recipient presented a late arterial stenosis with intra-hepatic biliary stenosis and is actually waiting for retransplantation.

Discussion: We chose to maintain integrity of the gastroduodenal inflow for the MMV graft, but this attitude may potentially shorten or reduce the calibre of the vessel for liver transplantation. Compared to ex-situ liver splitting, the in-situ technique has theoretical advantages because it minimizes the cold ischemic time and allows excellent haemostasis on the cut surface.

Conclusion: We have demonstrated that in-situ liver recovery can be combined with safe recovery of an MMV graft. The hepatic artery can be transected just above the GDA providing a sufficient arterial length for the liver graft. The different grafts obtained were of good quality and implantation of these organs was performed without using complex vascular reconstruction.

Oral 15 REVIEW OF VARIOUS TECHNIQUES OF SMALL BOWEL TRANSPLANTATION IN PIGS

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Because of the anatomical and physiological similarities with human, porcine model is optimal to investigate and improve the surgical procedure of small intestine transplantation (SBTx). Different models of SBTx have been established to optimize the techniques as well as to improve the outcome. The aim of this work is to present a review of the current status of different surgical techniques of SBTx in the porcine model. An analysis of Medline-cited studies over different techniques of SBTx in porcine models was performed paying special attention to the surgical aspects. Concerning graft procurement and intestinal resection the reported techniques differ widely. Arterial reconstruction is mainly conducted through performing the anastomosis between the superior mesenteric artery (SMA) of donor and SMA or the infrarenal aorta of the recipient. Also an aortic graft of the donor is used which is anastomosed to the infrarenal aorta of the recipient. Venous anastomosis is frequently performed between the superior mesenteric vein (SMV) of the donor and SMV or the inferior vena cava of the recipient. The venous anastomosis between the portal vein of the donor and the recipient has also been reported. Bowel continuity is restored by end-to-end or end-to-side anastomoses. Meanwhile the improved techniques including Paul-Miculicz-Ileostomy with remarkable result as well as the prevalent Koop-type ileostomy and the Jejunostomy were introduced. Comparing the different techniques used in porcine SBTx models shows that applied techniques differ based on the aim of the proposed study. Therefore, according to the purpose of the study the most suitable technique should be carefully chosen.

CLINICAL CASES — SESSION 7 — SATURDAY, FEBRUARY 12

CC 01 EBV NEGATIVE PTLD AND GVHD – TO INCREASE OR DECREASE IMMUNOSUPPRESSION

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An 18 month old girl underwent modified- multivisceral-transplantation (MMVTx) and was discharged within 6 weeks. She developed papules on her hand and developed a florid skin rash suggestive of Graft-versus-Host-Disease (GVHD) 12 weeks after MMVTx. Her immunesuppression was increased, but rash continued to progress. She had extensive blistering of skin and was treated with high dose steroids without any response. She was recommenced on PN and she developed abnormal liver function tests (LFT's). She was then commenced on Basiliximab and Infliximab treatment after haematology consultation. Despite increasing her Tacrolimus(trough level of 12–15), her GVHD of skin and liver (maximum bilirubin of 500 micromol/l)progressed. At the same time she was noted to have abdominal lymphadenopathy on CT scan abdomen. Her EBV PCR was found to be negative and she underwent an abdominal lymphadenectomy. She was demonstrated to have polymorphic PTLD (CD20 negative) on histopathological examination. Her immunesuppression was decreased (trough levels of tacrolimus 6–8). We elected to ignore the EBV negative PTLD (after oncology consultation) and not to treat with Rituximab or any other form of chemotherapy to prevent the development of opportunistic infection. Her GVHD progressed and she received mesenchymal stem cells. She was maintained on a target trough levels of tacrolimus 6–8. Her GVHD improved but she developed immune mediated hemolytic anaemia and thrombocytopenia needing multiple blood and platelet transfusion. She did not respond to IV Immunoglobulins and was treated with Rituximab (4 courses) to which she eventually responded. Six months later, her GVHD has completely resolved, she does not have abdominal lymphadenopathy, she is no longer jaundiced and has no evidence of hemolytic anameia. She however still remains dependent on PN. This case demonstrates the importance of multidisciplinary team working and appropriate use of immunesuppression to manage a complex case with rare complications.

CC 02 FATAL SMALL FOR SIZE SYNDROME AFTER RIGHT LOBE DONATION

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A 39-year old man wanted to give a part of his liver for his father who suffered from terminal cirrhosis from unknown origin. He underwent the full pre donation work-up, including MRI with normal bile duct anatomy, CT evaluating the volume of the right lobe at 1050 ml and left lobe at 400 ml, and liver biopsy demonstrating a light (15%) macrovesicular steatosis. Both procurement and transplantation procedures were uncomplicated. Within 24 hours, the donor became jaundiced with reduction of liver function. A second-look laparotomy was performed on day 5 demonstrating a congestive liver remnant. 48 hours later, the patient developed peritonitis, and a colonic perforation at the hepatic flexure was surgically demonstrated and closed. Eight days later the patient developed recurrent colonic perforation at the same site, and an ileocolonic resection with terminal ileostomy was performed. The patient had to be re-operated during the night for continuous bleeding. One month later, while recovering in the ward, he developed ileal perforation secondary to volvulus, and a new ileostomy was constructed after bowel resection. He remained toxic and underwent exploratory laparotomy that excluded another septic source. He was improving when he developed acute cytolysis. CT showed a total necrotic liver remnant despite open portal vein, hepatic artery and hepatic veins. The patient was then listed for HU liver transplantation. After 48 hours the first offer was a steatotic liver that was accepted. The patient was then unstable, with diffuse bleeding. He had several cardiac arrest during the hepatectomy. He was supported by ECMO and hemofiltartion. The graft did not function related to the unstability of the recipient who was bleeding diffusely and finally died in the ICU when the ECMO was stopped due to impossibility to improve despite maximal ICU care.

ACUTE LIVER FAILURE — SESSION 8 — SATURDAY, FEBRUARY 12

Oral 16 LIVING DONOR LIVER TRANSPLANTATION FOR ACUTE LIVER FAILURE

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Background: Patients with acute liver failure (ALF) meeting transplant criteria require urgent liver transplantation which can be achieved only with living donor liver transplantation (LDLT) in the Asian continent due to scarcity of deceased donors. However, this presents several challenges including the need for rapid recipient and donor evaluation and ensuring adequate graft volume for the recipient. We present our experience in performing LDLT for ALF.

Methods: Data was collected on 568 LDLTs performed from October 2001–June 2010, (34 for ALF) from a prospectively maintained database.

Results: There was equal gender distribution with a mean age of 27 years. The causes of ALF were cryptogenic (15), hepatitis A (5), hepatitis E (4), drug induced (4), Wilson's disease (4) and hepatitis B (2). All patients were assessed with King's College criteria or Wilsons disease index for ALF. The mean MELD score was 38. The mean interval from listing to transplantation was 43 hours. The grafts included right lobe with middle hepatic vein (MHV) (20), right lobe without MHV (2), left lobe (11) and left lobe with caudate (1), with a graft to recipient weight ratio (GRWR) of 0.8–2.2 (mean 1.2). Postoperative complications included acute cellular rejection in 8 (23%), respiratory complications requiring prolonged ventilation (2), bile leak necessitating re-exploration (2). There were no vascular complications. Mean postoperative ICU and hospital stay were 9 days and 23 days. One patient required retransplantation due to primary graft non-function. Postoperative mortality was 3/34 (9%). The remaining 31 patients (91%) are well at a mean follow up of 28 months (range 0.5–76).

Conclusion: Living donor liver transplantation for ALF is logistically challenging but successful. Shorter listing to transplant and better graft quality may account for the excellent results.

Oral 17 LIVER TRANSPLANTATION FOR ISONIAZID INDUCED ACUTE LIVER FAILURE; SINGLE CENTRE EXPERIENCE IN THE UNITED KINGDOM

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Introduction: Anti-tuberculous treatment induced acute liver failure (ALF) caused by isoniazid (INAH) toxicity is a recognised complication reported in up to 0.08% cases. Liver transplantation (LT) is indicated in the majority; however there is paucity of data on clinical outcome of patients that have experienced INH-related hepatic failure.

Methods: Retrospective review of all cases referred between 1990–2010 with INAH-induced ALF. Clinical, laboratory and peri-operative outcomes were analysed in those undergoing LT. Results 25 patients [15(60%) female, median age 49(14–76) years] were referred during the study period. The majority ($n = 17$; 68%) were non-Europeans, 15(60%) were listed for LT fulfilling King's College criteria, of which 13(81%; 8 male) were transplanted with cadaveric full graft ($n = 11$) or split/reduced graft ($n = 2$). Two listed patients progressed to multiple organ failure (MOF) prior to LT. Further 5 patients with severe ALF and fulfilling criteria for LT were not considered fit enough for transplant and died of MOF. Spontaneous recovery was seen only in 5 patients. The table summarises data of patients that underwent LT. Peak pre-LT creatinine mmol/dl 97.5(45–325) Peak pre-LT bilirubin mmol/dl 406.5(139–704) Peak pre-LT INR (median, range) 3.75(1.9–14.4) CIT (median, range) 630 min (251–694) WIT (median, range) 45 min (43–55)) Post -LT ITU stay (median, range) 6(2–17) Post-LT hospital stay (median, range) 23(13–34) Apart from 2 patients all others received organ support before LT. One re-grafted for primary non-function. Peri-operative mortality was 4/13(30%) due to sepsis, MOF or brain death. 69% patients survived at one-year post-LT, and the median follow-up of the long term survivors was 106(29–198) months.

Conclusion: Liver transplantation is associated with increased survival in INAH induced ALF provided these patients are listed and transplanted before progression to MOF. Early referral to transplant centres may increase the survival chance.

Oral 18 PREDICTING THE DONOR LIVER LEFT LATERAL SEGMENT WEIGHT FROM ANTHROPOMETRIC VARIABLES

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Background: Most of pediatric liver transplantation grafts consists in a left lateral segment (LLS). Liver graft size matching is one of the major factors determining a successful outcome. It is then potentially important that evaluation of the segmental liver weight of deceased donors could be performed preoperatively.

Aim: The aim of our study is to develop a formula to evaluate the LLS graft weight using anthropometric parameters; helping transplant surgeons to avoid large-for size or small-for size syndromes.

Subjects and methods: One hundred and twenty-two donors from 2 European transplantation centres (United Kingdom and France) were retrospectively reviewed. There was 48 female and 74 male. Eighteen were living related donors and 104 deceased donors. The mean donor age was 28.2 years (range 15–63). The body weight and height were respectively 70.1 kg (range 45–111) and 172.7 cm (range 152–197). The body surface area (BSA) was 1.83 m2 (range 1.41–2.46).

Results: The whole liver weight (WLW, $n = 66$) was 1462 grams (range 921–2340) and the liver to body weight ratio (WLW/BW) was 2% (range 1.45–2.8%). The LLS graft weight was 313 grams (range: 183–537 g). The ratio between LLS and BW (LLS/BW) was 0.452% (range 0.27–0.74). The LLS represented 22.3% of the WLW with a large variability ranging from 15.4 to 31.3%. Our predictor variables were only moderately correlated with Pearson correlations between LLS and BSA of 0.458, LLS and BW of 0.446. Conveniently, the following formula can be used to approximate the LLS weight: LLS (grams) = 165 × BSA (m^2) + 10.

Conclusion: The present study shows that the LLS/BW ratio is 0.45% in European donors and LLS represent around 22% of the WLW. The weight of the LLS is highly variable and hardly predictable using simple anthropometric variables.