Invited Lectures

A01 EVOLUTION OF LIVER TRANSPLANTATION IN EUROPE

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Following the first successful orthotopic liver allograft in Europe in 1968, the next few years saw the slow and often disappointing development of this therapy. Learning by mistakes and disasters, a whole new patient management strategy had to be devised under the headings: (1) Patient selection and preparation. (2) Donor selection and preparation, initially at a time when heart beating cadaveric donation was not permitted. (3) The three parts of the operation, donor removal and preservation. Removal of the diseased liver and transplantation of the new liver. An error at any stage usually led to disaster. (4) Intensive aftercare of the same quality as the anaesthetic care in the operating theatre. (5) Management and prevention of bleeding. (6) Immunosuppression. (7) Recognition of recurrent disease and efforts to prevent and treat recurrent disease. Now nearly 40 years on the procedure of liver transplantation is routine and excellent results are to be expected. Success has increased demand for the operation and shortage of cadaveric donors has resulted in an ever increasing pressure for live donation, which has raised new and worrying ethical dilemmas that so far we have not been able to resolve.

A02 KILI LIVER LIVE TOLERANCE OF LIVER TRANSPLANT PATIENTS TO STRENUOUS PHYSICAL ACTIVITY IN HIGH ALTITUDE

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Physical functioning is improved after liver transplantation but studies comparing liver transplant recipients to normal healthy people are lacking. How liver (and other organ transplant recipients) tolerate strenuous physical activities is unknown. There are no data on the tolerance of transplant patients to high-altitude. Six liver transplant subjects were selected to participate to a trek up Mount Kilimanjaro 5895 m, Tanzania. Physical performance and susceptibility to acute-mountain-sickness were prospectively compared with fifteen control subjects with similar profile and matched for age and body-mass-index. The Borg-scale (a rating of perceived exertion) and cardiopulmonary parameters at rest were prospectively compared with six control subjects also matched for gender and VO2max. Immunosuppression in transplant subjects was based on tacrolimus. No difference was seen in physical performance, Borg-scales and acute-mountain-sickness scores between transplant and control subjects. 83.3 per cent of transplant subjects and 84.6 per cent of control subjects reached the summit ($p = 0.7$). Oxygen saturation decreased whereas arterial blood pressure and heart rate increased with altitude in both groups. The only difference was the development of arterial hypertension in transplant subjects at 3950 m ($p = 0{\cdot}036$). Selected and well-prepared liver transplant recipients can perform strenuous physical activities and tolerate exposure to high-altitude similarly to normal healthy people.

A03 CURRENT INSIGHTS IN THE PATHOGENESIS OF INTRAHEPATIC BILIARY STRICTURES AFTER TRANSPLANTATION

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Biliary complications continue to be a major source of morbidity, graft loss and even mortality after liver transplantation. The most troublesome types of biliary complications are the so called ischemic type biliary lesions (ITBL), with an incidence varying between 5–15%. ITBL is a radiological diagnosis, characterized by strictures and dilatations of the intrahepatic bile ducts on imaging studies of the biliary tree in the presence of a patent hepatic artery. Several risk factors of ITBL have been identified, strongly suggesting a multifactorial origin. Risk factors for ITBL can be grouped into three categories: (i) preservation or ischemia-related, (ii) immune-mediated and (iii) induced by bile salt toxicity. Ischemia-related risk factors for ITBL include prolonged ischemic times and disturbances in blood flow through the peribiliary plexus. Immunological injury has been assumed as an underlying mechanism based on the relationship between ITBL and ABO incompatibility, polymorphism in genes encoding for chemokines, and pre-existing immune-mediated diseases, such as primary sclerosing cholangitis and autoimmune hepatitis. Evidence for a pivotal role of bile salt-mediated toxicity in the pathogenesis of bile duct injury after liver transplantation has gradually emerged during the last decade. Endogenous bile salts contribute to the pathogenesis of bile duct injury by acting synergistically with ischemia-induced injury. Apart from the various mechanisms of bile duct injury leading to ITBL, recent studies have shown that the biliary strictures may have a different pathogenesis depending on the time interval after transplantation when they first occur. Biliary strictures presenting early (≤1 year) after transplantation are strongly associated with preservation-related risk factors and most frequently located in the central bile ducts. Biliary strictures presenting late (>1 year) after transplantation has been found more frequently in the periphery of the liver and are associated with immunological risk factors. In conclusion, intrahepatic biliary strictures, or ITBL, after liver transplantation in the presence of a patent hepatic artery are not a single disease. Several risk factors have been identified and both ischemia-related and immunological factors seem to be involved in the pathogenesis. In addition, endogenous bile salts play a critical role in the development of bile duct injury. Better understanding of the pathogenesis of intrahepatic bile duct strictures contributes to the development of more effective preventive methods and techniques.

A04 TREATMENT OF BILIARY STRICTURES AFTER WHOLE LIVER TRANSPLANTATION

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Biliary complications are one of the most common postoperative problems after liver transplantation (LT) comprising bile leaks, biliary strictures and choledocholithiasis. They occur in 5–34% of LT patients despite standardization of techniques of biliary reconstruction (1–5). Biliary complications may proceed to be a significant cause of morbidity and mortality in patients following LT. Biliary strictures can be differentiated between non-anastomotic (NAS) or anastomotic strictures (AS). The clinical outcome of both entities are markedly different. NAS occur with a reported frequency of 2–20% and are associated with graft loss and substantial patient morbidity and mortality. They are often related to predisposing factors, in particular to hepatic artery problems, prolonged cold or warm ischemic time, reperfusion injury, pre-transplant diagnosis of primary sclerosing cholangitis and ABO incompatibility. Among the etiologic factors for the AS, which occur most frequently within the first few months post-LT with an incidence of 5–20%, technical issues are the most important, such as improper surgical technique, small caliber of bile ducts and inappropriate suture material. Surgical repair has traditionally been the primary approach to manage these complications. Endoscopic transpapillary and interventional radiological procedures, however, have recently replaced surgery especially for AS. Surgical revision is reserved for patients who have failed the proceeding therapies, but reLT is still the final therapeutic option. Several reports have demonstrated the efficacy of endoscopic treatment by means of biliary balloon dilatation and/or stent placement (1–4). In our own prospective study, which is the largest series to date addressing the outcome of patients with biliary strictures after LT, endoscopic modality provided an effective and safe therapy in almost 80% of patients with AS achieving successful long-term resolution (5). In seven patients endoscopic treatment failed, but complete resolution could be achieved either by a PTC (n=4) or surgical approach (n = 3). In contrast to AS, no complete resolution could be achieved in any of the patients with NAS, multiple intrahepatic strictures. In addition, these patients required more often balloon dilatation and endoscopic stenting compared to patients with AS, which is consistent with previous reports (6). However, almost 65% of our NAS patients showed partial response to endoscopic treatment and improved clinically. A complete resolution of clinical symptoms with normal cholestatic parameters and no significant bile flow impairment on ERC could be achieved in 21% of patients. Subsequent percutaneous and surgical approaches did not confer additional benefit. Nevertheless, graft survival was significantly lower in the NAS group; 21% required reLT. Moreover, three NAS patients of our series died on the waiting list for reLT because of infectious complications arising from the biliary tract. The complication rate of the endoscopic procedures was very low. Severe complication necessitating hospitalization of the patient occurred in five patients (1.2%) because of biliary leakage (2) and cholangitis (3). Unfortunately one patient died (mortality rate 0.2%) because of fulminant cholangitis leading to sepsis despite prophylactic antibiotic treatment. Percutaneous transhepatic therapies showed success rates ranging from 40–85% (7); however, this approach carries the risk of causing hemorrhage, bile leakage and infections. In addition, with the percutaneous approach, the transhepatic tube has to be left in place for several days, which adds to the risks mentioned above. Endoscopic procedures should be the primary approach for patients with biliary strictures after LT. Several studies have shown that endoscopic therapies are highly efficacious in the treatment of biliary strictures. Moreover, the long-term outcome for those patients is excellent, especially for patients with AS. Development of NAS, however, reduces graft but not patient survival after endoscopic therapy. Surgical revisions are reserved for patients who failed to respond to endoscopic or radiologic transhepatic treatments. Retransplantation is the ultimate therapeutic option, especially for patients with complicated intrahepatic biliary strictures.

A05 CHOLESTASIS AFTER LIVER TRANSPLANTATION, DIAGNOSIS AND MANAGEMENT:

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Cholestasis (loosely defined as failure of the liver to clear bile from the blood) is seen commonly following liver transplantation and is usually because of intrinsic liver damage, in our experience occurring in 55% of patients at some point post-transplant. There are many causes of post-transplant cholestasis as shown below: within the first week after transplant, ischemia and reperfusion injury are the commonest cause of new or increasing cholestasis although other common causes include acute cellular rejection, sepsis (usually bacterial). In the first-post-operative month, cholestasis may also be associated with the small for size syndrome, drug toxicity (rare) and infection with CMV. Cholestasis is also associated with problems with biliary drainage: anastomotic strictures can occur both early (when often associated with oedema) and late, when associated with scarring. Non-anastomotic strictures are associated with re-perfusion injury, rejection, ABO incompatibility, rejection. Later causes of cholestasis include rejection (both late acute cellular rejection and the late manifestations of the increasingly rare ductopaenic rejection), sepsis and infection (especially viral infections with CMV where the timing and consequence will depend on the use of pre-emptive or prophylactic treatment, and recurrent HCV or HBV associated with cholestatic hepatitis), drug toxicity, malignancy (especially post-transplant lymphoproliferative disease where cholestasis may be present in the absence of liver infiltration). Cholestasis associated with recurrent cholestatic diseases, such as primary biliary cirrhosis and primary sclerosing cholangitis) occurs late; cholestasis may be associated with a return to alcohol or other drug use. The cause for the cholestasis is rarely made on liver function tests as these are non-specific. A full clinical history, sound clinical judgement, imaging and sometimes histology are usually required to make or confirm the diagnosis. Treatment will depend on the underlying cause.

A06 CHRONIC INTESTINAL FAILURE

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Intestinal failure is defined as a reduction in the functioning gut mass below the minimum amount necessary for adequate digestion and absorption of nutrients to achieve and maintain normal nutritional status. Home parenteral nutrition (HPN) is the 'artificial gut' for the medical treatment of irreversible chronic intestinal failure (CIF). Survival rates on HPN at 1 and 5 years have been reported to be 91–97% and 62–68% in adults, and 97% and 89% in children. Deaths related to HPN complications were 3–20% of the total deaths in adults and 23–42% in children. Intestinal transplantation (ITx) is a surgical option for irreversible CIF. Data from the International Transplant Registry show that both patient and graft survival steadily improved over time since 1985. For transplants completed after 1998, the 1-year graft/patient survival rates were 65%/77% for intestinal grafts, 59%/60% for small bowel and liver grafts, and 61%/66% for multivisceral grafts. The overall 5 year graft survival was lower than 50%. Almost all the deaths after ITx were related to the treatment (sepsis 46.0%, graft rejection 11.2%, post-transplant lymphomas 6.2%, technical reasons 6.2%, graft-thrombosis 3.2%). On the basis of data on safety and efficacy, HPN is considered the primary treatment for CIF. The USA Center for Medicare and Medicaid Services has approved the payment for ITx when life-threatening complications related to HPN occur (HPN failure). The American Society of Transplantation position paper on paediatric ITx also considers patients with high risk of death or with very poor quality of life (QoL) related to the underlying intestinal failure as candidates for ITx. Selecting patients for ITx is a challenge. Patient referral for ITx may come too late, and this may increase mortality rates among those on the waiting list or following ITx. Epidemiology of candidacy for intestinal transplantation and timing for referral for ITx are unknown. In January 2004, a multicenter survey in Europe evaluated the prevalence of candidacy for ITx on the basis of the Medicare and of the American Society of Transplantation indication criteria. The physician attitudes toward ITx was evaluated by asking doctors taking care of the HPN patients to judge the candidacy for ITx as immediate or potential. Forty-one centres from nine countries enrolled 688 adults (>18 years) and 166 paediatrics. One hundred and sixty-five patients were candidates, because they had an indication and non-contraindication for ITx. Candidacy for ITx was 15.7% in adults and 34.3% in paediatrics (HPN failure, 62.1 and 28.1%; high risk underlying disease, 25.9% and 59.6%; very poor QoL on HPN, 12.0% and 12.3%, respectively). Immediate candidacy was required for 14.8% of adult and 15.8% of paediatric candidates. Of the remaining patients, 271 had a contraindication for ITx according to the guidelines for referral and management of patients eligible for solid organ transplantation and 418 were non-candidates because they had no indication and no contraindication for ITx. A two-year prospective follow-up was carried out to compare the survival rate of the 165 patients' candidates and of the 418 patients' non-candidates for ITx. The 2 years probability of survival was 96%, 88% and 71% for non-candidates, candidates who did not receive ITx and candidates who received ITx, respectively. In candidates non-ITx and in non-candidates, cause of death was HPN-failure in 60% and 14%, underlying disease in 29% and 43%, other in 11% and 43% of total deaths, respectively. No death occurred in candidates non-ITx having a poor QoL as an indication for ITx. In candidates non-ITx, a clinical judgement of immediate candidacy was associated with a statistically significant increased risk of death on HPN in comparison with a clinical judgement of potential candidacy. This result further underlines the key question of the timing for referral of candidate patients.

A07 UK EXPERIENCE OF SMALL BOWEL TRANSPLANTATION IN CHILDREN

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Around 20%-40% of children on parenteral nutrition (PN) develop life threatening complications related to PN including: recurrent line infections, thrombosis of major vessels and intestinal failure associated liver disease (IFALD). Intestinal transplantation is a life saving option in these selected children with small bowel failure. The indications for intestinal transplantation include: irreversible intestinal failure and one or more of the following: impaired venous access (reduced to two suitable veins for placement of feeding catheter), progressive liver disease with coagulopathy, ascites and encephalopathy or life threatening catheter sepsis.

Between 1993 and 2006, a total of 239 patients have been assessed and 107 advised transplantation, with 6 patients improving and 33 waiting list deaths. A total of 46 (median age 1.25 years, range 6 months to 16yrs) intestine transplants (44 primary grafts, 2 retransplantations; liver and bowel n=37–whole liver/bowel 14, reduced liver/bowel 23, isolated bowel n=9) have been carried out for the following conditions: atresia (5), gastroschisis (33); intestinal aganglionosis (9); microvillus inclusion disease (6); necrotising enterocolitis (11); pseudo-obstruction (14); mid gut volvulus (2); others (11) (Intestinal lymphangiectasia; congenital short gut, meconium ileus and volvulus). A further 17 were underwent isolated liver transplantation (ILTx) for IFALD, 2 as a bridge for later intestinal transplant (ITx) and 15 for short bowel with the expectation of eventual full adaptation.

Results: Overall 33 are alive. Thirty-one are on full enteral feeds with two immediately post transplant. Actuarial survival with up to 8 year follow-up is 58% for ILTx, and 53% for intestinal transplants. However, survival for ISBTX and CSBTX performed in the last 3 years is 80% (13/16). The current immunosuppression regime since 2002 comprises steroids, an anti IL2 mab - basiliximab, tacrolimus and mycophenolate mofetil. Due to the shortage of size matched donor organs, a majority of recipients receive a reduced size en bloc graft. Achieving primary abdominal closure is infrequent with most children requiring staged closure. Additional surgical complications include bowel perforations and compartment syndrome. Early acute rejection is less of a problem now compared to the early years of the programme, however there remain significant challenges related to late rejection (both acute and chronic), and the development of EBV related PTLD, as most of these recipients (usually EBV negative) receive grafts from EBV positive donors. Waiting list mortality remains high, particularly in smaller reciepients (weight < 10 kg), a group with inferior post transplant outcome. Changes in UK organ allocation has improved availability of grafts for these children, but is yet to have any impact on waiting list mortality in recipients < 10 kg, which is currently in excess of 50%.

In conclusion, we have seen a modest increase in small bowel transplant activity with improved outcomes. The results in terms of waiting list mortality and patient survival are inferior in children < 10 kg compared to older children. Most children receive reduced size en bloc liver bowel grafts. The main obstacle to wider application remains the severe shortage of suitable cadaveric donor organs. EBV related PTLD and late rejection are significant complications that impact on long term outcome.

Orals

O01 OUTCOME AFTER LIVER TRANSPLANTATION FOR BUDD–CHIARI SYNDROME – REPORT ABOUT 42 PATIENTS

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Aim: Advanced forms of thrombotic occlusion of post-sinusoidal venous outflow with severe liver dysfunction or failure can be effectively treated by liver transplantation. Aim of this study was the analysis of outcome and specific complications when compared with other indication groups.
Methods: Between 1988 and 2006 we performed 2007 OLT in our institution. Frequency of OLT for Budd–Chiari syndrome (BCS) was 2.1% (n=42) with 14 cases of acute BCS and 28 cases seen with a chronic form. The mean follow up period was 78.4 (1–195) months. Patients were classified as Child B in 57.1% of the cases, followed by Child C with 31.0% and Child A with 11.9%. 25 patients had a preoperative diagnosis of hematologic disease.
Results: The actuarial 5-year survival for the BCS subpopulation (n=39) is 89.4% in comparison to 80.7% for other indications (n = 1742). Analyzing graft survival rates after 5 years, favourable results with 78.1% in BCS patients compared with 72.1% in other patients can be observed. The differences are not significant in statistical analysis. Concerning the preoperative occlusion type, liver veins (92.9%) were followed by portal vein (23.8%) and vena cava (16.7%). Retransplantation was necessary in three patients (7.1%. While the number of reoperations for bleeding was lower in the BCS-group, incidence of post-operative thrombosis was significantly higher. Thrombosis of portal vein occurred in 4.8% vs 0.8% of the patients, while liver veins were affected in 2.4% vs 0.2%. Bile duct stenosis was observed in eight patients (19.1%), ischemic type biliary lesions in another four cases (9.5%).
Conclusions: Our data shows that BCS with acute liver failure or chronic progressive forms can be successfully treated by OLT. Despite higher rates of vascular complications, patients and graft survival are similar or even better when compared with other indication groups.

O02 OUTCOME OF PATIENTS TRANSPLANTED FOR PRIMARY SCLEROSING CHOLANGITIS – ANALYSIS OF THE EUROPEAN LIVER TRANSPLANT REGISTRY

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Aims: The aim of our study was to compare the outcome of patients transplanted for primary sclerosing cholangitis (PSC) with patients transplanted for primary biliary cirrhosis (PBC) as well as alcoholic liver cirrhosis as a non-immunological liver disease.
Methods: Out of 10942 patients declared to the European liver transplant registry and transplanted between the years 1998 and 2004 for autoimmune liver disease or alcoholic cirrhosis, 1215 patients with PSC, 1365 with PBC and 5305 with alcoholic cirrhosis with a single diagnosis at transplantation were included. Statistical analysis was performed applying Kaplan Meier estimates, log rank tests, Cox proportional hazard models and Holms procedure. The results are presented in terms of 5-year survival estimates and relative risks accompanied by their respective 95% CI.
Results: 5-year patient survival after liver transplantation for PSC [0.84 (0.81–0.87] was similar to that for PBC [0.85 (0.82–0.87)] and significantly better than for patients transplanted for alcoholic cirrhosis [0.77 (0.75–0.78)]. However, 5-year graft survival for PSC [0.75 (0.71–0.78)] tended to be worse than for PBC [0.81 (0.78–0.83)] and similar to that for alcoholic cirrhosis [0.73 (0.71–0.75)]. Accordingly, the risk of retransplantation for patients with PSC was significantly higher than for PBC [RR 1.93 (1.45–2.57)] as well as for alcoholic cirrhosis. The reason for this may be a higher rate of vascular and biliary complications. In PSC, but not in PBC or alcoholic cirrhosis, recipients age had a significant impact on patient and graft survival. However, the risk of cardiovascular complications as cause of death was significantly lower in PSC as compared with PBC or alcoholic cirrhosis [RR 0.36 (0.14-0.9)]. Within 5 years of transplantation for PSC, tumor development or recurrent disease did not seem to have a relevant impact on patient or graft survival. In PSC, the choice of immunosuppressive regimen did not significantly alter patient or graft survival.
Conclusions: Liver transplantation for PSC demonstrates an excellent 5-year patient survival but the risk of retransplantation is higher as compared with PBC or alcoholic cirrhosis.

O03 200 CONSECUTIVE PRIMARY LIVER TRANSPLANTATIONS WITH LEFT LATERAL SEGMENT (LLS) SPLIT GRAFTS

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Introduction: Use of split liver grafts for pediatric orthotopic liver transplantation (OLTx) have reduced mortality on the waiting list to near 0%.
Methods: We analyzed 200 consecutive children (median age 0.97 years, range 0.08–14.55; median weight 8 kg, range 2.3–3.5) who received a LLS graft as a primary isolated OLTx at our Center (188 in situ split, 10 reduced size, two ex situ split). Indications were biliary atresia in 128 (64%) children, Alagille syndrome in 17 (8.5%), Byler's disease in 8 (4%), cancer in 9 (4.5%), cryptogeneic cirrhosis in 6 (3%), fulminant or acute liver failure in 12 (6%), metabolic diseases in 7 (3.5%) and others in 13 (6.5%) cases. Among the recipients 15 (7.5%) children were UNOS status 1, 14 (7%) status 2A, 71 (35.5%) UNOS status 2B and 100 (50%) status 3.
Results: Apart from UNOS status 1, no child died on the waiting list. Overall patient/graft survival at 3 months, 1 year and 5 years was 93%/88%, 90%/85% and 88%/82% respectively. Considering separately the periods of the years 1997–2003 and 2004–2006, 1 year patient/graft survival were 88%/83% and 96%/91% respectively. Incidence of hepatic artery thrombosis was 4.5% (9 cases). Re-OLTx was performed in eight children and was successful in six. Incidence of biliary complications was 30% (anastomotic stenosis 16.5%, anastomotic fistula 5.5%, leakage from the cut surface 4.5%, bile collection 3.5%). A surgical re-intervention was required in 15 (7.5%) patients.
Conclusion: Use of LLS from split liver grafts revealed to be the technique of choice for pediatric OLTx. Also at a high volume split liver procedures center a continuous learning curve and technical improvements allowed for these short and long term results. Biliary complication remains the ''Achilles' heel'' of the split liver grafts but they don't seem to have a negative impact on patients and grafts survival.

O04 IS IT WORTH PERFORMING LIVER TRANSPLANTION WITH MARGINAL DONOR ORGANS IN HIGH-RISK (MUC II) PATIENTS?

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Introduction: Increasing waiting time for liver transplantation leads to extension of the donor criteria. Aim of this retrospective analysis was to evaluate the outcome of high-risk MUC II recipients receiving a marginal organ concerning outcome.
Methods: 13 patients in MUC II status were transplanted between 08/2004 and 11/2005 with a mean follow up of 266 (±141) days. Mean donor age was 70 (±6) years with varying grades of steatosis up to 40%. Indications for transplantation were viral cirrhosis in five patients, hereditary metabolic diseases in two patients, and alcoholic cirrhosis in six cases. Cold ischaemia time was 653 min (±102 min.). Prophylactic immunosuppression consisted of CNI/MMF and a rapid steroid taper. The laboratory values AST, ALT, GGT, bilirubin and PT were evaluated.
Results: Liver grafts showed a good initial function. One patient underwent relaparotomy for bleeding. No other surgical, mayor infectious or immunological complications were observed. Patients were discharged after an average of 22 (±9) days. That patient and graft survival was 100% over the observation time. Liver enzymes and the bilirubin levels, measured at pod 1, 7, at discharge from hospital and at the last outpatient visit. Are as follows: AST 1476 U/l (±838), 48 U/l (±23), 28 U/l (±12), 37 U/l (±34); ALT 884 U/l (±265), 335 U/l (±512), 51 U/l (±33), 43 U/l (±48); GGT 123 U/l (±68), 315 U/l (±196), 204 U/l (±182), 158 U/l (±182); Total bilirubin 7.8 mg/dl (±6.3), 4.2 mg/dl (±3.8), 1.9 mg/dl (±0.8); 1.2 mg/dl (±0.9) PT 68% (±19), 92% (±16), 93% (±14), 105% (±9). The elevation of the GGT persisted over the whole observation period.
Conclusions: Despite the increased risk profile for MUC II patients liver transplantation even with marginal organ quality achieves good results. The clinical relevance of persisting elevation of the GGT is unclear. We speculate that this finding may reflect chronic biliary ischemia and/or damage.

O05 DISASTROUS OUTCOME AFTER LIVER RETRANSPLANTATION IN A YOUNG WOMAN WITH DYSFUNCTION OF THE PRIMARY GRAFT

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Introduction: Graft dysfunction (or small for size syndrome) after liver transplantation is a poorly defined entity of multifactorial origin. Depending on the

regenerative capacity of the graft, symptoms can vary from short-lived cholestasis to irreversible liver damage with septic complications and death, unless retransplantation is accomplished. The decision to perform a retransplantation and timing of the procedure can be a difficult clinical challenge.

Case report: A 20-year-old female was transplanted because of autoimmune hepatitis. Two weeks post-transplant portal occlusion occurred. The portal vein was successfully recannulated and the patient was discharged from hospital 4 weeks after the transplantation. One week later she was readmitted because of liver dysfunction, sepsis and respiratory distress. Following 3 weeks of massive antibacterial, antifungal and antiviral (CMV) treatment we decided to retransplant the patient. The operation was uneventful and the liver functioned perfectly since. Unfortunately, her respiratory insufficiency persisted and *Aspergillus* was found in trachea. She was treated with caspofungin, vorikonazol and amphoterecin B and after months of treatment the microorganism seemed to be eradicated. The patient appeared clinically healthy (except for the ventilator!) and she was mentally intact. However, restitution of her respiratory system was discouraging. CT scans! revealed signs of bronchiectasia and emphysematic bullae. She developed multiple bronchial stenosis, which progressed to a dynamic collapse of the respiratory tree as seen in tracheo-malacia. All treatment options including lung transplantation and bronchial stents were considered but abandoned because of repeated episodes of respiratory infections. The ventilator was finally demoted and the patient expired peacefully, 6 months following the primary transplantation.

Discussion: Numerous factors are decisive for redo in liver transplantation. Makeing the right decision at the right time can be very difficult and has critical consequences for the patient, for organ supply, for the staff and for budgets.

O06 PTLD – A RARE COMPLICATION AFTER LIVER TRANSPLANTATION

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Post-transplant lymphoproliferative disease (PTLD) is a unique, serious, life-threatening complication following solid organ transplantation with a high mortality. Often is caused by a primary or reactivated Epstein-Barr virus (EBV) infection. The incidence of PTLD varies from 1–10% depending on the organ transplanted and the immunosuppressive regimens used. The aim of the study is to present and discuss the case of 36-years-old woman, who underwent liver transplantation for the primary biliary cirrhosis. PTLD has developed 3 years after transplantation with fatal outcome.

Case report: D. L., 34-years-old woman, chronically treated with encorton i azathiopr ine for the rheumatoid arthritis, was admitted to the department in March 2002 with the diagnosis of PBC, established in 1998 on the basis of liver biopsy and high titre of ANA, AMA, SMA antibodies. In 2002 clinical symptoms of liver function decompensation appeared as jaundice, ascites, encephalopathy and bleeding from esophageal varices. Patient's MELD was 23, and UNOS – 2B. On 27th October 2002 the piggy-back liver transplantation from cadaveric donor has been successfully performed. Post-operative course was uncomplicated, patient received double drug immunosuppression: encorton and tacrolimus. For 3 years general patient's condition in outpatient observation was very good. In November 2005 the patient was admitted to our hospital for the epigastric pain, nausea and subfebrile body temperature and symptoms of subileus. Colonoscopy revealed four tumor lesions – in coecum, transverse and descending colon. Ultrasound and CTscan diagnosed also infiltrative focal lesions in the liver, kidneys and epigastric lymph nodes. Patient underwent operation. Diagnosis was intraoperatively confirmed and right extended hemicolectomy was performed. Histopathological examination confirmed PTLD – lymphoma (centroblastic B-cell plasmocytoma IVa, according to Ann Arbor classification). Post-operative course was complicated by renal failure requiring hemodialysis. Rapamune was introduced to immunosuppressive treatment. Chemotherapy according to CHOP + Mabthera protocol was introduced. After four courses chemotherapy the regression of the infiltrative lesions in kidneys and lymph nodes was observed, as well as almost complete regression of liver lesions. After the 6th course of chemotherapy the rapid deterioration of patient's general condition occurred with coagulopathy, upper airways infection and subsequent multiorgan failure, which resulted in patient death on April 7th, 2006.

Conclusion: PTLD is a major complication after liver transplantation, usually with high mortality ratio. Early diagnosis and combined treatment can contribute to the improvement of the long-term survival; however these methods are not free of fatal complications.

O07 LIVER TRANSPLANTATION FOR A PSC WITH A MARGINAL GRAFT: NOT RADICALLY RESECTED INCIDENTALOMA AND DELAYED CHOLESTATIC GRAFT FAILURE

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A 37-year old patient with a history of PSC/Colitis ulcerosa, first diagnosis 08/2004, underwent orthotopic liver transplantation with a marginal graft. A cholangiocellular carcinoma pT3, pN1 (5/7), L1, M0, G2 (R1-resection at the common bile duct) was detected in the explanted liver. Initial immunosuppression consisted of CyA/steroids. Primary organ function was good, no surgical, nore infectious and immunological complications were observed. Within 2 months bilirubin raised continuously to levels of 25 mg/dl, biopsy showed several cholestasis and a mild rejection. After a steroid bolus therapy and converting the basal immunosuppression to tacrolimus and rapamycin cholestasis persisted with continuous graft detoriation. Questions: No treatment? Chemotherapy? Pancreas head resection and lymphadenectomy? Pancreas head resection and lymphadenectomy and retransplantation?

O08 LONG-TERM PLACEMENT OF SUBCUTANEOUS RUSCH-TYPE STENTS FOR DOUBLE BILIARY STENOSIS IN A LIVING-DONOR LIVER TRANSPLANT RECIPIENT

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We report on a case of a 54-year-old Caucasian male affected by HCV and HCC who underwent right lobe living donor liver transplantation. The graft was revascularized trough an end to side anastomosis between the right hepatic vein of the graft and the recipient vena cava; the inflow was re-established by an anastomosis between the right portal vein of the graft and the common portal vein of the recipient, the right hepatic artery of the graft was anastomosed with the right hepatic artery of the recipient. Rx cholangiography performed during donor surgery showed a 3 mm diameter accessory biliary duct, draining segments 6 and 7, coming from the common bile duct. Biliary reconstruction was achieved trough an end-to-end anastomosis of the right hepatic duct of the graft with the common hepatic duct and of the accessory duct with the cystic duct of the recipient. Five days after transplantation, the patient underwent laparotomy for biliary leakage from the principal biliary duct, which has been treated by T-tube positioning. The immediate post-operative period was characterized by hyperbilirubineima (maximal value 39 mg/dl). A Doppler ultrasound, performed after surgery and Rx-cholangiography performed through the T-tube showed persistent dilatation of the intrahepatic biliary tree because of anastomotic stenosis of the right hepatic duct on the common hepatic duct, and dilatation of the accessory duct because of stenosis of anastomosis with the cystic duct. After ERCP failure, we decided to use a percutaneous approach by PTC, with removing of the T-tube, and positioning of a subcutaneous internal–internal Rusch-type stent, and the patient was discharged from the hospital with bilirubin to 5 mg/dl. However episodes of cholangites with increase of bilirubin relapsed. A follow-up Doppler ultrasound of the liver showed dilatation of the accessory biliary duct draining segment 6 and 7 of the graft. A second PTC with puncture of the dilated accessory biliary duct and positioning of an internal–internal stent Rusch through the anastomotic stenosis was performed without complications. After this procedure bilirubin levels normalized and the patient was discharged home; at 1-year follow-up no more dilatation of the biliary tree was evident at ultrasound and the patient is alive and well at home without episodes of cholangites.

O09 IMMUNOLOGY OUT OF CONTROL: GRAFT-VERSUS-HOST DISEASE AFTER ORTHOTOPIC LIVER TRANSPLANTATION

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Graft-versus-host disease (GvHD) after liver transplantation is an infrequent but devastating immunological complication caused by donor derived immunocompetent T cells. Initial clinical symptoms display skin rash, fever, pancytopenia or diarrhea. Treatment with either reduction or intensified immunosuppression has often proved to be ineffective with a mortality greater than 90%. We here describe a case of GvHD after liver transplantation with respect to diagnosis, clinical course and treatment options. A 63-year-old male patient with cirrhosis of the liver (MELD score 21) received an orthotopic liver graft from a 53-year-old male donor. The patient recovered completely within 2 weeks post-transplantation and had normal liver function tests but was not able to be discharged because of ongoing impaired renal function. Twenty-eight days after transplantation rash, fever, leukopenia and thrombocytopenia was noted. Immunological diagnostics comprised HLA retyping, DNA finger printing using short tandem repeats and chimerism-tests, which were highly suspicious for GvHD. Skin lesions showed high expression of HLA-DR associated with dense lymphocytic infiltrates. There was no macroscopic gastrointestinal involvement upon first clinical skin symptoms as detected by endoscopy and mucosal biopsies of the stomach and small bowel. Two therapeutical strategies were decided: Immunosuppression was intensified using steroids. Additionally leukapheresis was carried out for ex vivo separation and in vitro expansion of recipient derived T cells (*1*). Upon HLA-typing of the leukapheresis product GvHD was again confirmed. Due to rapid progression of the skin lesions Campath-1H was administered followed by a drop in total lymphocyte count and slight amelioration of cutaneous symptoms. At that time antimicrobial treatment comprised voriconazole, meropeneme, metronidazole, erythromycins and hyper immunoglobulin infusions. Six weeks

after diagnosis of GvHD the patient deteriorated and developed dissaminated zygomycosis infection and died of multiorgan failure before infusion of recipient expanded and activated T cells could be applied.

O10 ADVANTAGES OF ANTITHYMOCYTE GLOBULIN INDUCTION IN ORTHOTOPIC LIVER TRANSPLANTATION

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Aim: For years there has been a discussion about the initial immunosuppression after orthotopic liver transplantation (OLT). Aim of this study was to analyze the effects of antithymocyte globuline (ATG) induction therapy on rejection rates, renal function, infection rate, patient and graft survival.
Methods: In a retrospective study we analyzed 391 patients after OLT. 129 patients received calcineurininhibitors immediately after OLT, 262 patients received a 3-day ATG induction with delayed start of calcineurininhibitors on post-operative day 3.
Results: One-year acute rejection rate was 14.5% vs 31.8% in favor for the 3-day ATG group. ($p = 0.0008$), chronic rejection was not influenced. Also the rate of acute rejection in need of treatment was significantly lower in the 3-day ATG group (7.3% vs 23.3%; $p = 0.001$). Serum creatinine at transplantation was similar in both groups (1.14 mg/dl vs1.18 mg/dl; $p>0.05$). Post-operative haemofiltration was less frequently seen after induction therapy ($p>0.05$). A decreased renal function at 1 year was generally observed but serum creatinine (1.26 mg/dl vs 1.37 mg/dl; $p = 0.015$) and eGFR (81 ml/min vs 75 ml/min; $p = 0.02$) were better in the 3-day ATG group. There was no significant difference in infection rate and post-operative death because of infection. 5 year overall survival (70.1% vs 74.3%; $p>0.05$) and 5-year graft survival (68.0% vs 71.8%; $p>0.05$) were similar.
Conclusion: Short-term ATG induction therapy with delayed use of calcineurin-inhibitors can offer improved acute rejection rates with less need for treatment. Even more it has significant positive effects on renal function immediately after OLT and later on without risk of a higher rate of negative side effects.

O11 BILIARY AND VASCULAR COMPLICATIONS USING EXTENDED RIGHT SPLIT LIVER GRAFTS

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Introduction: There is reluctancy about the use of the extended right split liver graft (ERG segments I, IV–VIII) because of concerns for a higher complications rate. We reviewed the incidence of vascular and biliary complications among the adult and pediatric recipients of an ERG.
Methods: In 42 patients (29 adults and 13 children) an ERG was used. 37 cases received a primary liver transplant (LTx) (34 liver, 2 liver + kidney, 1 liver + double lung), four cases received an ERG as a first re-transplant (3 liver, 1 liver + kidney, 2 urgent re-LTx and 2 elective Re-LTx), one case received an ERG as a second urgent re-transplant. All the splitting procedures were performed in situ. In 17% of cases an interposition graft was used for arterial reconstruction. Biliary reconstruction was by a duct to duct anastomosis in 64% of cases and with an Roux en Y hepatico-jejunostomy in 36%.
Results: Hepatic artery thrombosis occurred in three cases (7%).Re-LTx was performed in all cases and was successful in two. In two cases a stenosis of the suprahepatic caval anastomosis were successfully treated by pneumatic dilatation. Overall biliary complications were 26% (anastomotic fistula 7%, cut surface leakage 5%, anastomotic stenosis 14%). A conservatively treatment was used in 16% of the biliary complications. Among the recipients of an ERG as a primary LTx, 1 and 5 year patient and graft survival is 97%/94% and 94%/90% respectively. Overall patient and graft survival after re-LTx with ERG is 40% and 20% respectively.
Conclusion: The incidence of HAT using an ERG, in our experience, is comparable to that reported in the literature. A slightly higher incidence of biliary complications with ERG does not have a negative impact on patient and graft survival.

O12 PEDIATRIC LIVER RETRANSPLANTATION: A SINGLE CENTER EXPERIENCE

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Introduction: Liver re-transplantation (re-OLTx) is the treatment of choice for patients who develop irreversible graft failure after OLTx.
Methods: We performed 329 OLTx in 291 children. 256 children received a primary OLTx, 1 child who was previously transplanted elsewhere, underwent to re-OLTx at our Center. 35 children underwent a re-OLTx and in three of them a second re-OLTx was required. We analyzed several factors that could have an impact on patient survival.
Results: 1, 3 and 5 years patient survival after primary OLTx was 92%, 90% and 88% whereas after re-OLTx was 59%, 59% and 53% ($p = 0.001$). No statistically significant differences were found in term of patient survival between the groups of age > or <1 year, weight > or < 6 kg, bilirubin > or <13 mg/dl, INR > or <1.8 and ischemia > or <7 h. Survival using a whole graft was 83% at 1, 3 and 5 years, whereas with a split graft was 49%, 49% and 42% ($p = ns$). With creatinine <1.3 mg/dl patient survival was 66% at 1 and 3 years and 57% at 5 years; with creatinine >1.3 mg/dl survival was 38% at 1, 3 and 5 years ($p = ns$). With an interval between OLTx and re-OLTx <7 days survival was 42% at 1, 3 and 5 years; with an interval of 8–30 days 1, 3 and 5 years survival was 73%, 73% and 49%; with an interval >30 days survival was 66% at 1, 3 and 5 years ($p = ns$).
Conclusion: Survival after pediatric re-OLTx is worse compared with survival after primary OLTx. None between the analyzed factors was found to be a strong predictor of survival after pediatric re-OLTx. We advise a multicenter study to have a larger sample size to verify these results.

O13 SIGNIFICANT REDUCTION OF PROINFLAMMATORY CYTOKINES BY TREATMENT OF THE HUMAN BRAIN DEAD DONOR. A PROSPECTIVE RANDOMIZED TRIAL

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Aim: Experimentally it was proven that the brain death of the donor has a significant impact on graft quality. It is unknown, whether the upregulation of proinflammatory cytokines can be reduced by donor treatment and therefore the donor organ quality optimized before transplantation.
Methods: We investigated the expression pattern of cytokines comparing serum (n=102) in human brain dead donors. In a prospective randomized trial 49 donors were treated with steroids before organ harvesting (250 mg initial, afterwards 100 mg/h until laparotomy). The outcome after liver transplantation was compared between treated and untreated donor organs. Serum samples were gathered after declaration of brain death and before laparotomy. The assessment of serum cytokines was performed by CBA-kits (IL-6, IL-8, IL-4, IL-2, IL-10, LPB, CD3, TGFb, TNFa, HO-1, Mip1a). Additionally steroid levels, FT3 and FT4 were determined. After transplantation the ischemia/reperfusion injury liver function was assessed (AST, ALT, GLDH, bilirubin)
Results: The transcription of pro-inflammatory cytokines is increased significantly in untreated brain dead donor livers compared with donor grafts after steroid application ($p<0.005$). Donor treatment with steroids lead to significantly decreased serum expression of proinflammatory cytokines ($p<0.005$) and revealed comparable levels to living donors. The reduction of proinflammatory cytokines correlated with reduced transaminases after liver transplantation. Serum protein levels of proinflammatory cytokines are a valuable and easy accessible marker for defining the immunological graft quality.
Conclusions: Our study suggests a beneficial effect of anti-inflammatory donor treatment in brain dead organ donors. Standardized donor treatment regimens should be established.

O14 COMPUTER-SIMULATION OF THE MIDDLE HEPATIC VEIN'S BRANCHING PATTERNS BEFORE RIGHT LIVING-DONOR HEPATECTOMY MAY BE HELPFUL TO ASSESS ITS DRAINAGE TERRITORIES

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Aims: One of the major problems after transplantation of a full right hepatic split graft for adult-to-adult living donor liver transplantation (LDLT) is venous drainage of segments 5 and 8. Thus, this study was designed to provide information on venous drainage of right liver lobes for operation-planning.
Methods: Fifty-six CT data sets from routine clinical imaging were evaluated retrospectively using a liver operation-planning system. We defined and analyzed venous drainage segments and the impact of anatomic variations of the middle hepatic vein (MHV) on venous outflow from segments 5 and 8.
Results: MHV variations led to significant shifts of segment 5 drainage between the middle and right hepatic vein. In cases with the most frequent MHV branching pattern (n=33), a virtual hepatectomy closely right to the MHV intersected drainage vessels that provided drainage for 30% of the potential graft, not taking into account potential veno–venous shunts. In individuals with inferior MHV branches that extend far into segments 5 and 6 (n=10), the overall graft volume at risk of impaired venous drainage increased by 5% ($p<0.05$).
Conclusion: If this is confirmed in clinical trials and correlated with intraoperative findings, the use of liver operation-planning systems would be beneficial to improve overall outcome after right lobe LDLT.

O15 SIGNS OF REPERFUSION INJURY FOLLOWING CO_2 PNEUMOPERITONEUM FOR LAPAROSCOPIC LIVING DONOR HEPATECTOMY: AN *IN VIVO* MICROSCOPY STUDY

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Aims: Recently laparoscopic living donor hepatectomy has been performed for transplantation. During laparoscopic surgery, pneumoperitoneum is generally established by carbon dioxide (CO_2) insufflation which may disturb hepatic microperfusion. The desufflation at the end of the procedure is suggested to create a model of reperfusion in a previously ischemic liver thus predisposing it to reperfusion injury. Thus, this study was designed to assess its effect on graft injury and microperfusion prior to transplantation.

Methods: Sprague-Dawley rats underwent pneumoperitoneum with an intra-abdominal pressure of 8 or 12 mm Hg for 90 min. Subsequently, in vivo microscopy was performed to assess intrahepatic microcirculation and transaminases were measured to index liver injury.

Results: CO_2 pneumoperitoneum of 8 mmHg did not change serum transaminases; however, further increase of intraperitoneal pressure to 12 mmHg significantly increased AST, ALT, and LDH measured after desufflation almost 1.5 times as much as control values of 49±5 U/L, 31±3 U/L, and 114±12 U/L. In parallel, in all subacinar zones, the permanent adherence of both leukocytes and platelets to the endothelium increased by about 6- and 3-fold, respectively. Further, latex bead-labeled Kupffer cells as an index for their activation were significantly increased compared with controls.

Conclusion: This *in vivo* observation demonstrated reperfusion injury in liver induced by the insufflation and desufflation of CO_2 pneumoperitoneum. The clinical relevance of this finding as well as the issue of using hepatoprotective substances to prevent this injury should be further investigated.

O16 INDIVIDUAL DRUG THERAPY ADJUSTED TO DRUG-METABOLIZING CAPACITY AFTER LIVER TRANSPLANTATION

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Drug-metabolizing capacity of liver 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 of transplanted liver. This system is based on measurements of CYP enzyme activities and expression at mRNA level. We also made an attempt to determine the phenotype of donor liver from leucocytes. Phenotyping 29 (21 transplanted) liver donors in Hungary, strong correlation between CYP activities and mRNA levels in liver tissues was found in the case of CYP2C9, CYP2C19 and CYP3A4. CYP mRNA levels in leucocytes also reflected CYP activities of the liver. It means that transcriptomic analyses of donor leucocytes provide information on drug-metabolizing capacity of transplanted liver. This tool allows predicting potential 'poor or extensive metabolizer' phenotypes of donors. Testing drug-metabolizing status of the transplanted (21) donor livers, the distribution of CYP gene expression measured from donor leucocytes are below:

	Poor	Intermediate	Extensive
CYP3A4	48%	24%	28%
CYP2C9	14%	53%	33%
CYP2C19	29%	43%	28%

In CYP3A4 poor-metabolizer group, cyclosporin doses were lower and blood levels were significantly higher compared with intermediate-, or the extensive-metabolizer group. The biopsy proved drug toxicity in four cases in the poor metabolizer group. Reduced cyclosporine dose improved the outcome. In conclusion, graft survival depends on many factors, but prospective investigation of CYP status of donor livers can be beneficial, reducing drug side effects and drug failures after liver transplantation.

O17 REGENERATIVE SIGNALS OF THE LIVER AFTER TRANSPLANTATION

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The role of the regenerative factors like hepatocyte growth factor (HGF), transforming growth factor alpha (TGFα) and vascular endothelial growth factor (VEGF) were described in the context of hypertrophy and regeneration after liver resection. No data are known after transplantation. In 63 consecutive liver transplantations with a graft survival >2 weeks the factors HGF, TGFα and VEGF were determined postoperatively (day 1, 3, 5, 7, 10, 14) and correlated to graft survival (Kaplan–Maier). The median levels of HGF were constant during the observation period (day 1: 2591 pg/ml, day 7: 2434 pg/ml, day 14: 2490 pg/ml). An increase to levels above 4000 pg/ml in the middle of the observation period correlated to a worst one-year graft survival (54% vs 85%). Similar was the course of TGFα. An increase from the median concentration of 39 pg/ml to levels above 80 pg/ml was observed in the context of a decreased primary function. Regarding VEGF an almost linear increase of the concentration from 60 pg/ml via 177 pg/ml to 424 pg/ml (day 1, 7 and 14) was observed. Here it became obvious, that an extensive increase of the VEGF concentration correlated to a good transplant function. It can be concluded that vascular regeneration induced by VEGF substantially contributes to graft survival, whereas a temporal increase of HGF and TGFα rather has to be interpreted as an indicator of an injured graft with a decreased functional prognosis.

O18 TRANSPLANTATION AND INTESTINAL INSUFFICIENCY IN PAEDIATRICS: THE INITIAL EXPERIENCE OF AN ITALIAN CENTRE

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Aim of the study: To review outcomes after liver and intestinal transplantation in children on home parenteral nutrition (HPN) for chronic intestinal falilure (CIF).

Methods: Retrospective analysis of clinical charts.

Results: 46 patients (29 males) were on HPN for short bowel syndrome (43%), intractable diarrhoea (39%) and primary motility disorders (17%) for 52.2 months (DS 68.2) on average; mortality rate was 24% (11 cases) , for end-stage liver disease (ESLD) in six, underlying diseases in three and transplantation in two cases. In our centre 7 CIF patients have been evaluated for transplant: two for liver, seven for intestine (1), multivisceral (2) and combined liver-intestine (1) transplants; one child did not meet the criteria of irreversible intestinal failure. Out of these cases, we reported one death after 8 months on waiting list for a multivisceral transplant, in a 2-year-old girl affected by ESLD in dismotility disorder. Transplantation has been performed in five cases (10.8%): one isolated intestine, one multivisceral, one liver-intestine, and 2 orthotopic liver transplants (OLTx), in a child affected by Alagille syndrome and SBS, and in an 18-month girl, for ESLD in SBS. The latter patient is still on HPN and CIF adaptation is likely. Two patients (Alagille syndrome and liver-intestine recipients) died after surgery, for complication related to liver transplant; multivisceral (age 18 months, 4.9 kg) and intestine (7 years, 22 kg) transplanted patients are off PN after 4.5 follow-up months on average.

Conclusions: CIF patients referred for transplantation often present severe clinical courses for ESLD in short bowel syndrome or dismotility disorders. These are poor growing babies, who need complex procedures (intestine and liver) with low probability to find size-matched donors, long-time on waiting list and high mortality risk. Adequate surgery at birth, good management of PN and early referall to transplant unit, now possible also in Italy, are mandatory.

O19 VENO-VENOUS BYPASS: STILL NEEDED DURING LIVER TRANSPLANTATION?

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Aim: Before the introduction of cava-sparing techniques of orthotopic liver transplantation (OLT) the use of temporary passive femoral-to-jugular veno-venous bypass system (VVB) during liver transplantation reduced the mortality rates during the anhepatic phase. However the use of VVB is time consuming, cost intensive and high iatrogenic complication rates have been reported. Nowadays the rapid development of cava-sparing surgical techniques and better anesthetic management question the routine use of VVB. Aim of this study was to analyze the benefit and risk of selective VVB use.

Methods: Prospectively collected data from cadaveric orthotopic liver transplantations between January 1996 and December 2005 were analyzed. Eighteen patients operated between 1996 and 2001 with standard technique and VVB (group 1) were compared with eighteen patients operated after 2001 with modified piggy-back technique without VVB (group 2) selected by matched pair analysis. Variables included indication for OLT and urgency. Outcome was focused on operating time, transfusions, graft survival, patients' survival, ICU stay, duration of ventilation, complications and post-transplant laboratory findings.

Results: Indication and urgency of LTx were similar in both groups. The operating time was significantly longer and while the need for intraoperative PRBC and FFP was similar, TC use was significantly higher in patients of group 1. ICU stay and ventilation support as well as hospital stay were significantly longer in group 1 while complication rates and post-operative laboratory findings were similar in both groups. The median graft and patients' survival were similar in both groups.

Conclusion: In an era where more and more compromised livers are implanted because of shortage of donors the cavo-caval implantation technique with avoidance of VVB and shorter warm ischemia times is of importance. As cavo-caval OLT without VVB is safe from nephrologic,

neurologic and gastrointestinal point of view the application of VVB should be reserved for much selected patients.

O20 SERUM CREATININE AT TIME OF SWITCH TO SIROLIMUS IS PREDICTABLE FOR SUCCESSFUL RESCUE THERAPY IN LIVER TRANSPLANT PATIENTS WITH DETERIORATING KIDNEY FUNCTION

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Aims: Immunosuppression with calcineurin inhibitors (CNI) following liver transplantation is associated with nephrotoxicity. The aim of this study was to analyze whether late conversion to a sirolimus (SRL) based and CNI free immunosuppressive protocol would have a beneficial effect on deteriorating renal function in patients after orthotopic liver transplantation.

Methods: Seventy-eight patients after orthotopic liver transplantation (OLT) between 2001 and 2005 were switched to SRL from their former CNI based immunosuppression. Indication for switch was serum creatinine (SCr) elevation above 1.2 mg/dl. SCr levels were measured at 3, 6, 12, 24 and 36 months after liver transplantation.

Results: Median time between date of liver transplantation and switch was 37.01 (12.91; 85.62 q1; q3) months. Median follow up was 12 (3.92; 24.45 q1; q3) months. Primary analysis showed mean SCr at time of switch of 2.20 (r = 1.20−4.79) mg/dl, 1.93 mg/dl at 3 months ($p = 0.01$), 1.79 mg/dl at 6 months ($p = 0.009$), 1.79 mg/dl at 12 months ($p = 0.02$), 2.28 mg/dl at 24 months ($p = 0.4$) and 3.00 mg/dl at 36 months ($p = 0.24$) respectively. In a subgroup analyses we compared two groups:

Group A n = 35 Patients with a mean SCr at time of switch of 1.77 (r = 1.5−2.0) mg/dl revealed significant improvement in renal function with a mean SCr of 1.45 mg/dl at 3 months ($p<0.000$), 1.42 mg/dl at 6 months ($p<0.000$), 1.42 mg/dl at 12 months ($p<0.000$), 1.37 mg/dl at 24 months ($p = 0.007$), and 1.36 mg/dl at ($p = 0.09$) respectively.

Group B n=26 Patients with a mean SCr at time of switch of 3.00 (r = 2.01−4.79) mg/dl. Further mean SCr was 2.67 mg/dl at 3 months ($p = 0.167$), 2.46 mg/dl at 6 months ($p = 0.09$), 2.57 mg/dl at 12 months ($p = 0.516$), 3.47 mg/dl at 24 months ($p = 0.10$), and 4.09 mg/dl at 36 months ($p = 0.139$) respectively.

Conclusions: Primary analysis showed short-term beneficial effect of conversion to SRL that could not be seen in long-term follow-up. Subgroup analysis showed that patients with a SCr beween 1.5 and 2.0 mg/dl had significant benefit from conversion to SRL. SCr at time of switch is predictive for the benefit of a late SRL conversion as rescue therapy in OLT patients with deteriorating kidney function.

Posters

P01 RECURRENCE OF HEPATITS C AND BILIARY COMPLICATIONS AFTER LIVER TRANSPLANTATION: RESULTS FROM A SINGLE CENTER

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Background: HCV-recurrence and biliary complications (BC) are two major causes of morbidity and mortality following liver transplantation (LT). This study evaluates HCV-recurrence, BC and survival in transplant recipients.
Methods: All adults transplanted between January 1999 and February 2005 were evaluated. HCV-recurrence was confirmed on protocol liver biopsies performed at 6 months and yearly after LT, BC were defined when biliary anastomotic and non-anastomotic stenosis, leak or stones were seen on cholangiogram, MRCP, ERCP, TC, US in all but patients who were retransplanted or died within 1 month after surgery. The influence on patient survival of recipient age, HCC, HBsAg+ and alcohol etiology, extended donor criteria (EDC), acute rejection were assessed by multivariate analysis. Kaplan–Meier and Cox proportional hazards were used.
Results: Among 380 patients 361 were enrolled, 155 (42.9%) HCV+ and 206 (57.1%) HCV-, 251 (69.9%) male and 110 (30.5%) female, mean age 50 years, mean follow-up 4 years. On 622 liver biopsies performed fibrosis because of the HCV-recurrence was reported in 38% and 57% at 1 and at 5 years from LT respectively ($p = 0.049$). The progression to severe hepatitis or cirrhosis was assessed in 25.8% of liver biopsies at 5 years after LT. BC occurred in 46/155 (29.7%) HCV+ and 43/206 (20.9%) HCV- patients ($p = 0.06$). The overall patient survival was 86% at 5 years, lower in HCV+ compared with HCV- patients ($p<0.05$), whereas there was no difference when patients were grouped as HCV+/BC+, HCV+/BC-, HCV-/BC+, HCV-/BC-. EDC was the only significant predictor of overall mortality ($p = 0.035$).
Conclusions: The fibrosis because of HCV-recurrence increases after LT affecting more than half of patients at 5 years. The long-term survival is significantly lower in HCV+ compared with HCV- recipients and the use of EDC further impairs the survival. The BC does not influence the survival either in HCV+ and HCV- recipients.

P02 SEXUAL DYSFUNCTION IN FEMALE PATIENTS WITH LIVER CIRRHOSIS: THE ROLE OF DEPRESSION AND HORMONAL STATUS

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Background: Sexual dysfunction has been scarcely investigated in patients with chronic liver disease. The aim of this study was to investigate the association between liver function, sexual hormones, depression and sexual function in female patients with liver cirrhosis.
Methods: A cohort of 18 females with liver cirrhosis evaluated for liver transplantation at a single center were enrolled in the study (mean age±SE 52.2±3.8 years); eight patients had alcohol related, 10 non-alcohol related liver cirrhosis. CPT, MELD, sexual hormones (estradiol, PRL, thyroid hormones, testosterone total and free, DEAS, SHBG, 17-OH progesteron) were assessed in all patients who also ful-filled 2 validated questionnaires [Female Sexual Function Index (FSFI for pain, arousal, lubrification, orgasm, satisfaction); Beck Depression Inventory (BDI)]. Statistical analysis was performed by means of the Student's t test.
Results: Eight out of 18 (44.4%) patients had severe sexual dysfunction (SSD), with significantly worse BDI score compared to patients with mild or no sexual dysfunction (MNSD) (mean BDI±SE SSD 12.1±3.9 vs MNSD 6.4 ± 2.1, $p < 0.05$). In the 6/18 (33.3%) patients found to have mild depression, a significantly worse FSFI compared to patients with no depression was seen (mean FSFI ± SE 9.9 ± 4.5 vs 21 ± 6 $p < 0.05$). CPT and MELD scores, etiology of liver disease, sexual hormones did not correlate with sexual dysfunction.
Conclusions: Female patients with liver cirrhosis waiting for liver transplantation experience high prevalence of sexual dysfunction associated with depression but not with sexual hormone levels. Moreover, either cause of liver disease or liver function apparently do not play a role on sexual dysfunction. Studies to investigate the effect of liver transplantation in improving the sexual dysfunction are ongoing.

P03 EVIDENCE OF DECREASED FIBRONOLYSIS AND BLOOD TRANSFUSION REQUIREMENTS IN CHOLESTATIC LIVER DISEASE PATIENTS DURING LIVER TRANSPLANTATION (OLT)

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Introduction: A proportion of patients with cholestatic liver disease have been reported to have decreased bleeding tendency during OLT compared with those with cirrhosis of other etiology. A previous study with thromboelastography (TEG) demonstrated hypercoagulability in 32% of cholestatic patients.
Aim: To compare coagulation during liver transplantation in patients with PBC/PSC and cirrhosis of other etiology by TEG. To investigate its correlation with blood and blood product transfusion requirements.
Materials and methods: 20 consecutive patients with cholestatic liver disease (Group 1) and 20 cirrhosis of other etiology (Group 2) were enrolled. Patients with acute liver failure were excluded. TEG (with and without heparinase), total thrombin generation and lysis shown by TEG, haemodynamic variables and blood products were recorded for every stage of the OLT (baseline, dissection, anhepatic, reperfusion, end operation). TEG parameters, kinetic of the clot and blood/blood product transfusion requirement were compared between the two groups.
Results: Prior to incision group 1 showed significantly better standard coagulation parameters compared with group 2 (INR 1.7 vs 1.2 $p = 0.001$; PLT 81 vs 200 $x10^9$/L, $p = 0.001$). Group 1 also demonstrated a less hyperdynamic circulation (cardiax index 5.7 vs 4.2, $p = 0.002$; systemic vascular resistance 503 vs 716, $p = 0.06$). TEG analysis of the clot kinetics showed a greater amount of thrombin generation (total thrombin generation 5006 vs 4088 mm*100) and significantly less fibrinolysis (–79.9 vs –534.1, $p = 0.008$) in group 1 compared with group 2. The difference in fibrinolysis was seen throughout the operation. Group 1 showed significantly decreased blood (4.2 vs 8, $p = 0.008$), fresh frozen plasma (4 vs 9.1, $p = 0.001$), platelet (0.6 vs 2, $p = 0.001$) and cryoprecipitate (0.7 vs 2.9, $p = 0.004$) requirements, particularly during dissection and reperfusion phases.
Conclusions: Our study has demonstrated increased thrombin generation and less fibrinolysis in patients with cholestatic liver disease compared to cirrhotics with other etiology. This may contribute to the decreased need for transfusion in these patients during liver transplantation.

P04 ELDERLY DONOR IN HCV VS NON-HCV RECIPIENTS – PATIENT SURVIVAL FOLLOWING LIVER TRANSPLANTATION

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Introduction: Chronic liver failure because of HCV-related cirrhosis is the leading indication for liver transplantation in literature. Inferior long-term results have been reported for liver transplantation in HCV patients, especially when marginal donor livers are utilized.
Aim: The aim of this study was to retrospectively analyze the outcome of liver transplantation from elderly donors in HCV vs non-HCV recipients.
Methods: Among 330 livers transplantation (OLT) performed from January 1994 to December 2006 we analyzed 244 OLT. Acute hepatic failure, children and retransplants were excluded. The Kaplan–Meier actuarial survival was used to compare donors over 50 years and below 50 years. We studied 14 variables among donors using descriptive statistical test.
Results: We observed 210 (86%) donors over 50 years and 34 (14%) donors bellow 50 years. The number of marginal donors according to Cordoba score was 0%. They were 164 (67.2%) men and 80 (33.0%) women. We have reported 7.0% alcoholism; 23.0% virous infection; 8.2% cardiac arrest; 24.2% arterial hypotension and 20.9% mild/moderate steatosis. When we compared HCV or non-HCV recipients we observed higher mortality on HCV recipients from old donors (1-year survival rate for positive HCV was 23% and 45% for old donors and bellow 50 years, respectively; and for non-HCV donors was 67% and 75% for old donors and bellow 50 years, respectively).
Conclusion: Advancing donor age had an adverse influence on patient survival for HCV recipients.

P05 ISCHEMIA – REPERFUSION INJURY: A POTENTIAL BENEFIT BY INOS-INHIBITION?

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Aims: It is well recognized that nitric oxide (NO) plays a pivotal part in acute rejection by means of inflammatory response and apoptosis. The role of aminoguanidine hydrochloride (AGH), a potent inhibitor of the inducible nitric oxide synthetasis (iNOS), as an immunosuppressive agent is discussed

controversially at present. The aim of this study was to identify the effect of AGH on NO_2/NO_3-levels as well as on ischemia-reperfusion injury and survival following orthotopic liver transplantation.

Methods: AGH was administered orally (1% in tap water) in fully allogeneic rat liver transplantation from the 5th pre-operative day on throughout the post-operative period. Syngeneic transplanted untreated rats as well as allogeneic FK506 treated rats served as controls. NO_2/NO_3-levels were quantified by means of HPLC; HE-staining and immunohistochemistry was performed at various time points.

Results: Allogeneic untreated as well as allogeneic AGH-treated rats succumbed to acute rejection on day 11.3 ± 1.7 whereas syngeneic as well as allogeneic FK506-treated rats presented long-term survival >30 days. NO_2/NO_3 remained at 71.1±1.9 mM postoperatively in FK-treated allogeneic rats similar to the syngeneic group (88.1±4.1mM) in contrast to untreated allogeneic rats (681.8±1.9 mM). In AGH-treated rats NO_2/NO_3 was 30.4±3.7 mM on day 5 and increased up to 266.7±1.9mM on day 10 post-OP. Graft histology exhibited minimal signs of rejection in AGH-treated rats prior to death.

Conclusion: The results of this study suggest that inhibition of inducible nitric oxide synthase has a beneficial effect on ischemia-reperfusion but does not extend graft survival in rat orthotopic liver transplantation.

P06 EVALUATION OF DONOR-RECIPIENT MATCH IN PATIENTS UNDERGOING LIVER TRANSPLANTATION (LT)

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Background: Prioritization of patients in the WL for LT is still a critical issue and numerous models have been developed to estimate the risk of death without LT also including donor variables.

Aim: The aim of the study was to prospectively evaluate: severity of liver disease and mortality in WL in patients with liver cirrhosis with and without HCC undergoing LT; patient survival after LT according to donor and recipient variables.

Materials and methods: A mathematical algorithm based on seven patient measures -MELD, CTP, UNOS, HCC, BMI, waiting time, age- was created by a software to prioritize patients in WL. Donor variables -sex, age >60 years, anti-HBc+, cold ischemia time, cause of death, HCV+, sodium >150 mEq/L, steatosis, ABO compatibility, partial/split graft- were evaluated. Fisher's, Mann–Whitney, Kaplan–Meier tests were used for statistical analysis.

Results: 118 patients (75 M/43 F, mean age 55 years) who underwent LT from July'04 to June'06 were evaluated. The mean CTP and MELD at listing were 8.44 and 13 respectively. Mortality in the waiting list was 13% in 24 months, significantly higher in patients with MELD>25 compare with MELD 0–15 ($p = 0.0001$) and MELD 16–25 ($p = 0.0007$) at listing. Overall, the mean MELD at transplant was 15 (range 7–36) significantly lower in patients with HCC compared to patients without HCC (mean HCC-MELD 12 vs non-HCC-MELD 16; $p = 0.0003$). 600-day survival was significantly lower in patients with MELD>25 (57%) compared with MELD<25 (MELD: 0–15=87%, 16–25=92%, $p = 0.017$) at LT, whereas no different survival was observed in patients with and without HCC (81%). Donor variables did not influence patient survival.

Conclusions: Sickest patients are characterized by high mortality in WL and after LT. HCC patients are transplanted in a better condition and have the same survival compared with non HCC patients. Suboptimal donors can be used prior donor–recipient mismatch evaluation.

P07 INNOVATIVE USE OF BEVACIZUMAB (AVASTIN) IN HEREDITARY HAEMORRHAGIC TELANGIECTASIA REVERSING THE NEED FOR LIVER TRANSPLANTATION

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Aims: Hereditary haemorrhagic telangiectasia (HHT) can affect the liver and may lead to liver failure, portal hypertension, bile duct necrosis and high output cardiac failure (HOCF). Treatment of hepatic HHT with HOCF is currently via liver transplantation. Bevacizumab (Avastin) is a human/mouse hybrid antibody to vascular endothelial growth factor, used in oncology.

Methods: A 46-year-old woman with hepatic HHT was assessed for liver transplantation. Indications were HOCF, portal hypertension with resistant ascitis and malnutrition. The patient had no other visceral manifestations of HHT. She was considered a poor candidate because of her nutritional status and cardiac failure. The rationale for this first use of Bevacizumab in HHT was to improve her HOCF through reversal of intrahepatic neovascularization before considering transplantation. Bevacizumab was given at a moderate dose of 5 mg/kg (250 mg) once monthly for 6 months.

Results: The patient had a dramatic clinical improvement (from bed-bound in hospital to returning to work). Liver function tests were mildly deranged by the treatment, settling in the 2 weeks after each infusion. Ascitis resolved a two times reduction in liver volume and normalization of cardiac output were observed within 6 months.

Start time of Avastin	MRI liver volume (ml)	MRI cardiac output (l/min)
0 months 0 course	4807	10.2
3 months 3 courses	3151	6.3
6 months 6 courses	2269	5.1

Conclusions: Avastin has induced a strong biological response in this case of HHT with HOCF. All indications for liver transplantation resolved, including HOCF, ascitis and malnutrition. Ongoing assessment and further collaborative studies are indicated.

P08 NEUROMONITORING IN ACUTE LIVER FAILURE – A LARGE ANIMAL MODEL

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In order to investigate the complex intracerebral and systemic pathophysiologic changes after acute liver failure (ALF), we applied different methods of neuromonitoring after total hepatectomy in a pig model. Seventeen female pigs (German Landrace), weighing 35±4 kg were included for intracerebral examinations. ALF was induced by total hepatectomy with end-to-side portocaval anastomosis. Anhepatic pigs were monitored under general anaesthesia and standard intensive care until death occurred. Licox Clarke-type oxygen probes (n=13) and Camino fiberoptic pressure transducers (n=17) were inserted in the frontoparietal white matter. Intracranial pressure (ICP), brain tissue oxygenation ($p_{ti}O_2$) and mean arterial pressure (MABP) were measured continuously. Ammonia (NH_3) was examined periodically. Five brains were removed and fixed for histological examination. Mean survival time after hepatectomy was 46.7 ± 24.1 h. Mean baseline values were: ICP 16.6 ± 2.2 mmHg, ptiO2 5.9 ± 5.2 mmHg, CPP 53.9 ± 8.1 mmHg, NH_3 88.5±24.2 μM. High ICP baseline values resulted from the unphysiological supine position of the surgical procedure. The animals remained in this position after surgery. The ICP values increased to 41.9 ± 10.1 mmHg before death occurred. The parameters of ICP neuromonitoring revealed different trends: early increase was followed by high level values or late increase occurred after predominant normal values at the upper limit. $P_{ti}O_2$ values improved 12 h after hepatectomy to 31.5 ± 18.2 mmHg followed by a new decline to 3.8 ± 6.0 mmHg. Rapid and extensive alterations of the oxygen saturation were detected for the complete period of the experiment (Fig. 4). Within this time, the arterial blood oxygen saturation was >95%. CPP values were calculated as difference from MABP and ICP. As MABP values were therapeutically stabilized, the decrease of CPP was primarily because of the rise of ICP. NH_3 concentration rose to 1878.6 ± 1681.7 μM at exitus. However, most of the animals showed only moderate, sometimes decreasing NH_3 values in the anhepatic stage. The finding of high ICP, decreasing CPP and fluctuating $p_{ti}O_2$ demonstrates the leading role of cerebral alterations as a major cause of death in ALF. Despite the significant increase of NH_3 at exitus, a direct correlation between increasing ICP values and NH_3 concentration could not be shown in this setting. This model is well reproducible, and is therefore suitable for the assessment of bio-artificial liver devices. It emphasises the necessity of additional online neuromonitoring. The early recognition of trends is crucial. Especially $p_{ti}O_2$ values are directly responsive to physiological and pathophysiological variations. The early detection of ischemic periods facilitates interventions in order to avoid consequential cerebral dysfunction.

P09 LONG-TIME INTENSIVE CARE THERAPY IN ANHEPATIC PIGS

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Introduction: Establishment of intensive care therapy in anhepatic animal model to realize long-time survival studies of liver failure.

Methods: Hepatectomy was performed in 15 female pigs (30–41 kg) by reconstructing the vena cava and portal vein through a three-way vascular prosthesis. Post-operatively animals stayed under deep narcosis and pressure controlled ventilation. The following parameters were recorded continuously: electrocardiogram, mean arterial pressure, SO2 oximetry, core body temperature, intracranial pressure, urinary output. Serum electrolytes, acid–base balance, blood gases, blood glucose levels and haemoglobin were hourly monitored and immediately corrected as required. Pigs received sodium chloride 0.9%, hydroxyethylstrach 6% and fresh-frozen-plasma units. Red blood cells were given to cover blood loss. All pigs received furosemid to keep on dieresis as long as possible, when renal failure occurred they were treated by dialysis.

Results: After hepatectomy a continuous worsening of other organ systems appeared. To maintain adequate mean arterial pressure Noradrenalin was given in heightening dosage up to 30 μg/min. Blood lactate concentration stayed stable during sufficient circulation and raised when decompensation occurred. Pulmonal function impaired progressively and therefore it was necessary to increase PEEP and airway pressure to maintain sufficient ventilation and oxygenation. All animals suffered from renal failure, which was treated by dialyses. Though this regime blood concentration of ammonia could

be kept constantly stabile (500 μg/dl) for a long-time. Maximum survival time was 88.5 h (mean survival time 52 h).
Conclusion: We were able to establish a standardized intensive care therapy treatment which can be used for long-time survival studies and artificial liver support.

P10 A NEW SURGICAL MODEL OF HEPATECTOMY IN PIGS

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Introduction: The aim was to establish a surgical method for hepatectomy in pigs without a temporary extracorporal bypass and total clamping of the inferior vena cava. The study was to evaluate a new model of loss.
Methods: En-bloc hepatectomy including retrohepatic vena cava was performed in twenty female pigs (30–41 kg). Using end-to-side anastomosis between the vena cava above the right renal vein, the portal vein above the confluence, and the intrathoracic vena cava with a three-way vascular prosthesis, blood flow was maintained stable during hepatectomy by performing only partial clamping of the vessels. After completion and release of the bypass hepatectomy was performed.
Results: Using this new surgical technique makes it possible to avoid a total clamping of the mayor veins, so that maximal intra-and post-operative hemodynamic stability can be reached. Hemodynamic parameters like heart rate, mean arterial pressure, central venous pressure and oxygen saturation were extremely stable. Post-operative survival was 100% after 12 h, 95% after 24 h. Maximum survival time was 88.5 h; mean survival time was 50 h. All animals died due to multiple organ failure.
Conclusion: This new surgical technique permits total hepatectomy with minimal blood loss and stabile circulation without using an extracorporal bypass within overall survival time compared with other more complex models of hepatectomies.