Transplant International

POSTER PRESENTATIONS _

ACUTE LIVER FAILURE



A WELL REPRODUCIBLE PORCINE MODEL OF ACETAMINOPHEN INDUCED ACUTE LIVER FAILURE OFFERS DEFINED SURVIVAL TIMES

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Background and aims: Severe intoxication following acetaminophen overdose is the most common cause of acute liver failure in many western European and North American countries. A reproducible large animal model of acetaminophen intoxication has not been successfully evaluated previously.

Methods: Eight male pigs underwent an acetaminophen intoxication receiving an initial enteric bolus of 250 mg/kg body weight acetaminophen followed by acetaminophen plasma level (300–450 mg/L) adapted enteric maintenance dose of 1000–3000 mg/h to the onset of acute liver failure (prothrombin time value <30%). Vital and ventilation parameters were continuously recorded until death. Saline, hydroxyethylstarch, fresh frozen plasma and erythrocytes units were used for volume substitution, norepinephrine to prevent severe hypotension

Results: All animals developed acute liver failure after a median of 24 (20-30) hours, which was confirmed by laboratory values, clinical course and histologic examinations. All animals died due to acute liver failure after further 21 (16-32) hours, precipitated by cerebral oedema.

Conclusions: Using an initial enteric acetaminophen bolus, followed by body weight adapted acetaminophen plasma level intoxication it was possible to establish a reproducible, clinically relevant porcine model which may be used for the investigation of novel therapeutic approaches in this life threatening condition



EFFECTS OF LARGE PORE HEMOFILTRATION IN A SWINE MODEL OF FULMINANT HEPATIC FAILURE

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Introduction: Systemic inflammatory response might be involved in pathogenesis of brain oedema and intracranial hypertension complicating fulminant hepatic failure (FHF), by inducing an increase in cerebral blood flow and brain water content. We recently demonstrated in endotoxic shock models in the pig, that large-pore membrane hemofiltration (LPHF) with a 80 kDa cutoff may induce a significant IL-6 and IL-10 clearance and an improvement of hemodynamic stability and survival. In this study, we used the validated ischemic FHF model in the pig, to evaluate the effects of this 80 kDa LPHF on intracranial pressure (ICP) and cerebral blood flow (CBF) and on hemodynamic parameters, in relation with the clearance of proinflammatory cytokines and the blood liver tests.

Methods: Fifteen pigs were randomised in three groups: sham, FHF, and FHF + LPHF. FHF was performed by porto-caval anastomosis and hepatic artery and bile duct ligation. All pigs were monitored over the following 6 hours. In the FHF + LPHF group, LPHF was instituted for 4 hours, from Time 2–6 hours. Hemodynamics, CBF and ICP were continuously recorded. AST, aromatic amino acids, total bilirubin, glucose, lactate, IL-6, IL-10, TNFα, were collected before liver devascularisation (T0), and after two (T2) and 6 (T6) hours.

Results: The FHF groups developed blood characteristics of liver failure, without difference between FHF, and FHF + LPHF, two groups that developed intracranial hypertension. Despite a cytokine clearance, there was no significant difference in CBF and ICP between FHF and FHF + LPHF.

Conclusions: In this ischemic FHF pig model, LPHF with a 80 kDa cutoff did not improve liver tests, nor CBF or ICP.



LIVER TRANSPLANTATION FOR ACUTE HEPATIC FAILURE DUE TO CHEMOTHERAPY-INDUCED HEPATITIS B VIRUS REACTIVATION IN LYMPHOMA PATIENTS

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Hepatitis B (HBV) reactivation induced by chemotherapy is a recent problem encountered in the management of malignant diseases. Chemotherapy-induced HBV reactivation may ultimately lead to terminal acute liver failure. Liver transplantation (LT) remains currently the only definitive treatment option for such cases, but is generally denied to patients suffering from malignancy. Herein, the authors describe two cases of cancer-free and HBV graft

re-infection free survivals after LT performed for terminal liver failure due to HBV reactivation induced by chemotherapy for advanced stage lymphoma. These two cases, and some other reports in the literature, may suggest that patients suffering from hematologic malignancies and terminal liver disease should be considered for LT, if the prognosis of their hematologic malignancy is good.



ACUTE LIVER FAILURE BY AMANITIN INTOXICATION: LIVER TRANSPLANTATION OR WAIT FOR SPONTANEOUS REGENERATION? EVALUATION OF PROGNOSTIC INDICATORS IN A PORCINE MODEL

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Background: Acute liver failure caused by drug ingestion, viral hepatitis or poisoning is still associated with an extremely high mortality rate. Liver transplantation remains the life-saving therapy for all effected individuals, but shortage of donor organs remains the limiting factor. Aim of this study was to simulate the clinical course of α -amanitin intoxication in a pig model. Prognostic indicators for spontaneous liver regeneration were evaluated.

Methods: Seven male German landrace pigs received 5 mg (0.15 mg/kg body weight) (n=4) α -amanitin intravenously or 10 mg (0.35 mg/kg body weight) (n=3) intraportally. Pigs remained under deep general anesthesia until conclusion of the study protocol. Ventilation and vital parameters were recorded continuously, laboratory values including TNF- α as a potential regeneration marker were analysed every 8 hours, liver biopsies were taken every 24 hours.

Results: All pigs 100% (8/8) developed acute liver failure, which was defined by a prothrombin time below 30% within 40 ± 8 hours. All pigs receiving 10 mg amanitin died due to multi-organ failure. Pigs which received 5 mg amanitin survived poisoning. They recovered spontaneously after 50 ± 14 hours in acute liver failure and were euthanized after 112 hours, when prothrombin time returned to levels above 50%. Clinical, biochemical and histological signs of liver regeneration were recorded. Laboratory values started to recover 96 ± 7 hours after intoxication paralleled by clinical stabilisation. TNF- α levels in the regenerating animals were significantly higher starting from 48 hours after intoxication. First histological appearance for regeneration could be detected by Ki67 immunostaining 72 hours after intoxication in liver biopsies.

Conclusions: TNF-levels and liver biopsies were identified as the first indicators for spontaneous liver regeneration 48–72 hours after intoxication even long time before liver function biochemically and clinically impairs.



MOLECULAR ADSORBENTS RECIRCULATING SYSTEM IN PATIENTS WITH LIVER FAILURE — EXPERIENCE OF A SINGLE ROMANIAN CENTRE

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This is a retrospective, observational study regarding the experience of a single center in the application of the Molecular Adsorbents Recirculating System (MARS) albumin dialysis in patients with liver failure. From January 2002 until October 2010, we performed 58 MARS sessions, in 32 patients, with mean age 38.7 ± 19.1 years. The etiology of liver failure was: acute liver failure (ALF) in 10 patients, acute-on-chronic liver failure (AoCLF) in 12 patients, post — liver transplantation (LTx) in 8 patients, and post-hepatectomy in 2 patients. Before starting MARS, 10 patients presented multiorgan dysfunction, 6 patients required mechanical ventilation, 10 patients presented sepsis, 10 patients had renal impairment. In ALF group we noticed an improvement in bilirubin, creatinine and an increase in mean arterial pressure (P < 0.05). Of the 10 patients with ALF, 5 patients survived due to their own liver recovery. In AoCLF group, we obtain a significant decrease in bilirubin, creatinine, an increase of sodium and improvement of the MELD score (P < 0.05). Two patients survived, two patients were transplanted, and for the remaining patients the mean survival was 26.0 ± 33.3 days. In the post-LTx group, we noticed a significant improvement in bilirubin, creatinine, lactate, and sodium (P < 0.05). In this group, one patient was retransplanted, one patient is allive and the mean survival of the other 6 patients was 28.5 ± 39.8 days. MARS therapy was well tolerated and efficiently removed toxins. MARS seems to be a promising therapy for ALF, allowing the patient's own liver to recover or to gain time until transplantation. The timing of treatment initiation and proper patient selection is very important for clinical success. The unfavorable prognostic factors were multiple organ dysfunction and sepsis.



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

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



AUXILIARY TRANSPLANTATION IN 2 CHILDREN WITH ACUTE LIVER FAILURE

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Introduction: Acute liver failure (ALF) is a rare illness in children with a high mortality unless liver transplantation is performed. In some cases ALF resolves without need for transplantation and liver function normalizes with complete restitution of liver parenchyma. Therefore auxiliary partial orthotopic liver transplantation (APOLT) can be a good option for patients necessitating liver transplantation to bridge the acute situation and allow native liver to regenerate giving the opportunity to withdraw immunosuppressive therapy.

Methods: We report on two children (2.25 and 9.5 years; 1 female, 1 male) who presented with fulminant ALF necessitating rapid liver transplantation. The cause of ALF was Non-A-to-E-Hepatitis in one case and a simultaneous infection with rotavirus and herpes virus type 6 in the other case. Both children received APOLT by a left lateral lobe of a deceased donor. The graft was placed in the position of the left lateral lobe after resection of the recipients liver segments I, II and III. Graft size was small enough to allow primary closure of the abdominal wall. In both cases standard immunosuppression with Basiliximab, Prednisolone and Cyclosporine was initiated. Graft function was monitored by laboratory testing, graft perfusion via Doppler ultrasound. Excretory liver function was screened by repeated HIDA scans.

Results: Both children survived and are doing well. In both cases graft function was good and rapidly stabilized the clinical situation, liver function tests gradually normalized. In the 3 year old patient the native liver regenerated completely and immunosuppression could be withdrawn. In the older patient the native liver did not regenerate, graft function is good. This patient remains on immunosuppression.

Conclusion: These two cases emphasize that APOLT is a good option for patients with ALF necessitating transplantation. It gives the opportunity to withdraw immunosuppression if native liver regenerates.



WHICH ARTIFICIAL LIVER SUPPORT IN CHILDREN WITH **FULMINANT HEPATIC FAILURE?**

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Objective: To investigate the feasibility of the use of continuous veno-venous hemodiafiltration (CVVH) in children with severe hepatic encephalopathy. Background: Fulminant hepatic failure (FHF) is characterized by the development of encephalopathy and impaired synthetic liver capacity. Orthotopic liver transplantation (OLTx) seems to be the only therapy proven to improve patient survival in most cases. The role of artificial liver support is controversial and encompasses toxin removal and the reversal of the inflammatory process. Different depurative techniques such as molecular adsorbent recycling system, plasmapheresis, Extracorporeal Liver Assist Device and CVVH have been used in this aim.

Design: Single center retrospective analysis in children affected by FHF who underwent depurative liver support technique.

Setting: PICU in a pediatric liver transplant center.

Patients: Nine children with FHF were referred for OLTx and admitted to our PICU.50% were female and mean age was 57 months ± 9.5. Most common cause of FHF was autoimmune (50%) followed by drugs and toxins induced (40%). The mean Pediatric End-Stage Liver Disease (PELD) score was 33 ± 9 and the electroencephalography recording showed severe signs of encephalopaty in all the patients.

Methods: All patients underwent CVVH, arbitrarily chosen among the depurative procedures. Delay beetween diagnosis of FHF and beginning of the depuration therapy ranged from few hours to 3 days.

Results: All children showed both clinical and electroencephalographic neurological improvement after 24 hours treatment with no complication that could be related to the procedure. 5/9 patients underwent successful OLTx, the 4 remaining had a spontaneous recover and were removed from the list. All patients were discharged with a good neurological status.

Conclusions: We conclude that the application of a depurative support system does not increase the mortality risk and may be safely used in children with FHF awaiting liver transplantation.



P09 ACUTE LIVER FAILURE - OUR EXPERIENCE

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Acute liver failure (ALF) typically presents in the absence of any previously known liver disease with clinical and laboratory evidence of significant liver injury that leads to impaired hepatic function. In the past 5 years in our hospital 8 patients with ALF were treated, 2/8 (25%) women, and 6/8 men, mean age 32.4 years. Predominant cause of ALF were viral hepatitis: hepatitis B in 3/8 (37.5%) of patients and hepatitis A in 2/8 (25%) patients. In two cases (25%) Wilson disease was diagnosed, and in one case cause of the ALF was toxic hepatitis. Mean time of the onset of hepatic encephalopathy was 5.5 days. Mean range of INR and total bilirubin was 4.32 and 230 nmol/l, rectospectivly. Even we proced standard protocol of ALF therapy, all 8 (100%) of patients died, in 2 days after the presentation of hepatic encephalopathy. 17-years old boy, with Wilson disease was prepared for liver transplantation, but he died on the way to transplant centre in Italy. These data suggests that we need much more knowledge and experience about the treatment of ALF to maximize the chance of recovery and/or extend the window of opportunity for liver trans-



EXTENDED RIGHT SPLIT LIVER GRAFT FOR PRIMARY TRANSPLANTATION IN ADULTS: A MATCHED PAIR ANALYSIS

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Objective: Scepticism remains about the use of extended right (ER) split graft or adult liver transplantation (LT). We compared the outcome after transplantation of the ER liver lobe with whole liver transplantation (WLT) using a matched pair analysis.

Methods: Between November 1996 and December 2009, 44 ER LT were matched with 44 WLT. Matching criteria were: 1) indication for transplantation, 2) United Network for Organ Sharing (UNOS) status, 3) recipient Model for End Stage Liver Disease (MELD), 4) recipient age, 5) donor age, 6) cold ischemic time and 7) year of transplantation. All splitting procedure were performed in situ and in all cases celiac axis stayed on the left. The outcome was analyzed retrospectively.

Results: Median follow up was 72 months (range: 1-156). Actuarial 1 and 5 years patient and graft survival after ER LT were 89%/84% and 84%/81% versus 93%/90% after WLT. ER LT is not associated with an increased risk of vascular complications (P = 0.5, HR = 1.5, IC 95%: 0.43–5.00). Number of vascular complications (P = 0.3, H = 1.3, H = 1.3, H = 1.3). In some complications were significantly higher if an interposition graft was used (P = 0.05). In spite of ER graft seems to be a risk factor for biliary complications (P = 0.04; HR 3.00, IC 95%: 1.9–8.63), the higher incidence of these between split liver grafts, 30% vs. 11% in WLT, didn't reach statistically significance (P = 0.06). We did not observe significant differences between the groups in term of short term and long term morbidity.

Conclusion: ER LT provides a safe and efficient procedure in adult patients. In attempt to decrease the incidence of hepatic artery thrombosis an increasing collaboration among transplant teams about where to maintain celiac trunk, is advisable.



DELTA MELD PREDICTS THE FIRST YEAR SURVIVAL RATE AFTER LIVER TRANSPLANTATION

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Aim: The Model for End-stage Liver Disease (MELD) score has been established as a useful tool to rank patients awaiting liver transplantation depending on disease severity. Currently the actual MELD serves as predictor for patient survival on the waiting list. Still the impact of dynamic changes of the MELD score (δ-MELD) and its impact on 1-year survival are discussed controversially. Aim of the study was to evaluate the impact of δ -MELD on 1-year post transplant survival.

Methods: Five hundred and twenty-one adult patients were analyzed who were listed for liver transplantation between 1997 and 2008 for end stage liver disease without malignancy. The MELD scores at time of listing (MELD ON) and transplantation (MELD TX) were gathered. Delta-MELD was calculated MELD ON-MELD TX. Transplanted patients had a minimal follow-up of 366 days.

Results: MELD ON and MELD TX did not show a significant difference between 1-year survivors and non-survivors after transplantation (P = 0.08). In contrast, patients who died within the 1st year after transplantation showed a significant increase in the MELD score (mean δ -MELD +2.03) during waiting time (P < 0.01). Patients with δ -MELD <-3, representing the 10th percentile of our study population, showed significantly better 1-year survival than patients with δ -MELD >4, representing the 90th percentile of our study population (91,7% vs. 69,7%; P < 0.01).

Conclusion: Patients with a substantial increase of the MELD score (>4) during waiting time had a significant poorer 1-year post-transplant survival. In contrast, the absolute MELD score at time of listing or transplantation had no impact on the post-transplant survival rate.

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TRANSIENT ACUTE LIVER FAILURE FOLLOWING LIVER RESECTION BRIDGED BY MULTIPLE PROMETHEUS-TREATMENTS

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Objective: To report a case of succesful liver function bridging using to the PROMETHEUS in a patient following liver resection.

Methods: Retrospective chart review.

Results — Case report: A 62 years old patient underwent extended right hemihepatectomy for metachronous liver metastases and a solitary pulmonary metastasis two years after diagnosis of rectal cancer treated with neoadjuvant radiochemotherapy and a lower anterior rectum resection. Following tumor recurrence (tumor Ki-RAS wild type positive), a polychemotherapy (FOLFIRI + cetuximab) had been administered. On postoperative day (POD) one, mass blood transfusions and a relaparotomy were necessary for acute bleeding from the resection plane, resulting in multi-organ dysfunction with liver, renal and pulmonary failure. Postoperative bilirubin levels reached 44 mg/dl on POD 7. The patient was reintubated, renal function was supported by hemodialysis and a total of nine PROMETHEUS dialyses were performed until POD 21. Using this approach, hepatic function ameliorated slowly. On POD 23, bilirubin decreased without further PROMETHEUS treatments, and the patient was admitted to a normal ward on POD 28 with a bilirubin of 15 mg/dl. Liver function levels completely normalized until postoperative month 3. Renal

function remained impaired without need for regular hemodialysis after postoperative month 2. Five months after the liver resection, the pulmonary metastasis was removed by thoracoscopic wedge resection. Pathology revealed R0 resection in liver and lung, and the patient is free from tumor recurrence 6 months after hepatic resection.

Conclusion: Extensive liver resection after multiple poly-chemotherapies is critical due to limited residual liver parenchymal reserve. In this case, an additional complication (bleeding with mass transfusion requirement) further decreased liver function and resulted in acute liver failure. However, temporary PROMETHEUS support helped to stabilize the patient long enough to facilitate liver regeneration.

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OUR EXPERIENCE ON PATIENTS WITH ACUTE LIVER FAILURE (ALF) UNDERWENT ORTHOTOPIC LIVER TRANSPLANTATION (OLTX)

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Introduction: ALF is one of the most serious causes of liver transplantation. It counts for about 15–18% of all liver transplantation. The one year survival rate is 50-60%. We present our little experience with patients undergone OLTx due to ALF.

Methods and patients: We performed 32 OLTx in 3-year time, in our new liver transplant unit. Four patients underwent OLTx due to ALF: 1) 56-year-old male, presented with jaundice and small multiple liver lesions, increasing rapidly his bilirubin up to 66 mg/dl and renal impairment. Final diagnosis was of epithelioid haemangioendothelioma. 2) 43-year-old male, presented with jaundice and renal failure. Admitted to the ITU and intubated soon after his admission. He had high fever for 2–3 days before his admission and had some anti-inflammatory drugs. Two months later he had simultaneous liver and kidney transplantation. 3) 33-year-old male, presented with ALF –due to chronic use of paracetamol for headaches- on chronic liver cirrhosis due to hepatitis B (HBV). 4) 27-year-old female, presented with fulminant ALF due to acute HBV infection. She received a liver graft from a 73-year old female. Results: Three out of four patients are well and alive, for 1.5–2 years after OLTx. The first one, extubated the 9th post-operative day, returned to the ward –still on haemodialysis- and the two days later presented with respiratory failure, intubated and 12-hour later died due to heart attack.

Conclusion: ALF remains a challenge for all OLTx centers. However, in centers with small OLTx numbers and low rate of donation, ALF is always an extremely difficult case. Although even number of our cases is small, we managed to have a 75% survival rate in these difficult cases, in our small unit.

ELTR-STUDIES

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SURGICAL COMPLICATIONS IN SPLIT LIVER TRANSPLANTATION; A 12 YEARS EXPERIENCE

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Background: Split liver transplantation (SpLT) was developed in order to overcome the organ donor shortage for pediatric liver recipients. It remains a technically demanding procedure and is considered to be associated with a higher incidence of complications.

Aim: The aim of this study was to analyze a single-center experience of pediatric SpLT performed between 1998 and 2010.

Subjects and methods: One hundred and thirty-six children receiving SpLT were retrospectively reviewed. The recipient age and weight at transplantation were respectively 20.5 months (14 days –15.2 years) and 10 kg (2.6–66.6 kg). Main indications for transplantation were extrahepatic biliary atresia (n=56, 41%), metabolic diseases (n=27, 20%) and acute liver failure (n=12, 9%). Donor age was 25 years (10–59 years) and donor to recipient weight ratio was 6 (0.75–24.6). A left lateral segment was used in 114 (84%), a left lobe in 13 (10%) and an extended right lobe in 3 (2%). The graft was reduced to a monosegment in 6 SpLT (4%). The median cold ischemic time was 10.1 hours (6.2–17.5).

Results: The ICU and hospital stay was respectively 2 days and 23 days. 71 reoperations were necessary in 43 recipients (31.6%). Vascular complications occurred in 25 cases (18.4%), related to hepatic artery in 6 cases (4.4%), portal vein in 13 (9.6%) and venous outflow in 6 (4.4%). Biliary complications were encountered in 26 patients (19%) with 16 biliary leaks and 12 anastomotic strictures. Acute and chronic rejection developed respectively in 49% and 6% of recipients. The 1-, 5- and 10- year patient and graft survival were respectively 97%, 92%, 89% and 93%, 86%, 82% with a median followup of 60 months.

Conclusion: Pediatric SpLT is a safe procedure in experienced centres with excellent long term results. Biliary complications remain a difficult issue in SpLT.

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ABO-INCOMPATIBLE LIVER TRANSPLANTATION IN SMALL

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Background: Liver transplantation (LT) for very small recipients is challenging but in experienced centres, good results can be achieved. Despite the risk of antibody-mediated acute rejection, some studies have demonstrated the safety of ABO incompatible liver transplantation (ILT) in children and particularly in infants. The aim of our study was to describe the outcome of liver transplantation in infants <5 kg and the safety of using ILT in this group.

Methods: All LT performed between 1991 and 2010 in children <5 kg were reviewed. 29 patients were included, five of whom had an ILT. Acute liver failure was encountered in 20 cases. The recipient age and weight at transplantation were respectively 63 days (range: 14–268 days) and 4 kg (range: 2.4–5 kg). The graft-to recipient ratio was 6.1% (range 2.3%–9%). An aortic conduit and delayed abdominal closure were used respectively in 76% and 81% of the procedures.

Results: The 1- and 5-year patient and graft survival were respectively 62%, 62% and 62%, 57.9% with a median follow-up of 95 months. Vascular complications occurred in 6 cases (21.4%) and biliary complications were encountered in 5 patients (17%). Acute and chronic rejection developed respectively in 37% and 26% of the recipients. The 5 patients undergoing ILT are all alive without graft lost after a median follow-up of 34 months (range 7–55 months). When compared with the ABO-compatible LT group, no significant differences were found regarding patient or graft survival, vascular or biliary complications and rejection rates.

Conclusion: In our experience, ILT in small infants has short and long term outcomes comparable to ABO-compatible grafts and excellent results can be achieved with a standard immunosuppressive protocol. To avoid mortality on the waiting list for neonatal recipients, ABO-incompatible liver grafts can be used safely.



ARE THERE NEW DEFINITIONS OF EXTENDED LIVER DONOR CRITERIA AT THE BEGINNING OF THE 3RD MILLENNIUM? EXPERIENCES FROM 6133 DONORS

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Introduction: The disparity between organ demand and available grafts has increased over the past years due to improved outcome data after liver transplantation. Therefore donor criteria for liver grafts have been expanded to increase the donor pool. No exact definitions for extended donor grafts have been established yet. The aim of this study was to analyze the impact of several donor related parameters on the first year survival.

Methods: Six thousand one hundred and thirty-three deceased whole liver donors of the Eurotransplant (ET) area were analyzed due to their impact on 1-year survival. The dataset was established in collaboration with Eurotransplant (Leiden, Netherlands) and European Liver Transplant Register (Paris, France), including donors from 2000 to 2005.

Results: Trauma as cause of donor death showed a significant better 3 and 12 months survival after transplantation compared to cardiovascular related death or other causes of death (3 month: P < 0.01, 12 month: P = 0.04). In the single variant analysis age, CIT, creatinine, gamma-GT, and highest sodium were significant factors for 3 and 12 month survival. In the multi variant analysis CIT, highest sodium, cause of donor death, gamma-GT and donor sex (female) were statistically significant for the 3 month survival. For the 12 months survival only CIT and cause of donor death remained as statistically significant factor. Based on all significant predictive values a nomogram was established to predict early survival (Figure 1).

Conclusion: A nomogram allows to define several survival related donor factors in liver transplantation, nevertheless the final decision will still be based on medical urgency and surgical experience.

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AUXILIARY TRANSPLANTATION IN A CHILD WITH CRIGLER-NAJJAR SYNDROME TYPE I

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Introduction: Crigler-Najjar-Syndrome type I (CNS I) is a rare inherited disease caused by complete deficiency of bilirubin glucuronyltranferase activity. The disease presents with pronounced jaundice during the neonatal period and thereafter. The enzyme deficiency leads to permanent high values of unconjugated bilirubin with risk of neurologic complications. Acute treatment relies on daily phototherapy for multiple hours. Up to date the only effective longterm treatment is liver transplantation. Yet, someday genetic engineering may be a viable treatment. Therefore auxiliary partial orthotopic liver transplantation (APOLT) should be considered as a bridging option.

Methods: We report on a 4 year old girl who was transplanted because of CNS I. It was decided to perform APOLT because of above mentioned reasons. APOLT was performed by a left lateral lobe of a deceased donor. The graft was placed in position of the left lateral lobe after resection of the recipients liver segments I, II and III. Gaft size was small enough to allow primary closure of the abdominal wall. Standard immunosuppression (Basiliximab, Prednisolone, Cyclosporine) was initiated. Graft function was monitored by laboratory testing, graft perfusion via Doppler ultrasound. Excretory liver function was screened by repeated HIDA scans.

Results: Immediately after transplantation bilirubin levels decreased to low normal values demonstrating good graft function. The remaining native liver demonstrated good perfusion at all times. Yet, portal venous perfusion of the graft was repeatedly compromised necessitating recurrent operations. In the end portal venous flow to the graft was stabilized by subtotal narrowing of the portal vein to native liver.

Conclusion: APOLT is a good option for correcting metabolic diseases mainly localized in the liver. Surgically it can be a challenging procedure. By this technique recipients later have the option of genetic engineering and withdrawal of immunosuppression.

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OUTCOME OF LIVER TRANSPLANTATION USING SUPERAGED (\ge 80-YEAR) GRAFTS. A EUROPEAN LIVER TRANSPLANT REGISTRY STUDY

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From Jan. 1988 to Dec. 2008, 69185 first LT have been performed in Europe. First, ELTR data of ≥ 80 years donors (n=464) were compared to those <80 years. Thereafter, ≥ 80 years donors' data were analyzed in order to identify risk factors of recipients' death or graft loss. Whereas ≥ 80 years aged donors represented overall 0.7% of LT, this rate has increased to 2.2% in 2008. By comparison with <80 years, there was more females (58 vs. 40%, P=0.007). Grafts of ≥ 80 years donors were more frequently used in ≥ 60 years aged recipients (33 vs. 17%), in HBsAg+ (18 vs. 12%), AntiHCV+ (34 vs. 26%), in malignancies (27 vs. 14%), Alcoholic (37 vs. 33%) or viral (45 vs. 38%) cirrhosis (mainly HCV), elective LT (93 vs. 88%), ABO isogroup (96 vs. 92%), full size LT (99.8 vs. 87%), with isohemic time <12 hours (96 vs. 83%), Celsior preservation solution (30 vs. 7%), and LT with vena cava preservation (41 vs. 33%) (all P<0.01). Graft and patient 5-year survival were decreased with ≥ 80 years grafts, 52% vs. 66% and 55% vs. 71%, respectively (P<0.001). Regarding the cause of death or graft failure after LT, recipients with ≥ 80 years grafts had more non-tumor disease recurrence (18 vs. 9%, P<0.001), and less cardiovascular failure (1.6 vs. 6%, P<0.05). Survival of recipients with ≥ 80 years grafts was impaired in: HBsAg-, AntiHCV+, urgent LT, UNOS status <3 and ischemic time ≥ 12 hours (P<0.05). Only UNOS < 3

(RR = 2.2) and AntiHCV+ (RR=1.7) were identified as independent risk factors. In conclusion, aged donors are increasingly used in LT affording a 55% 5-year patient survival. However HCV+ and pre-transplant recipient hospitalization represented independent risk factors. Avoidance of urgent LT and long ischemic time may further improve the results.

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LIVER TRANSPLANTATION FOR RECIPIENTS ≥70 YEARS. IS IT WORTHWILE?

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Sixty-five years represents the upper age limit of recipients for liver transplantation (LT). An increased number of patients exceeding this age limit are presently transplanted. We evaluated the long-term outcome of ≥ 70 years LT recipients in the European Liver Transplant Registry. From January 1988 to December 2008, 74334 patients have been transplanted in Europe. The data of ≥ 70 years aged recipients (n=302) were compared to those <70 years. Moreover, data of ≥ 70 years aged recipients were analyzed by uni- and multivariate analysis to identify risk factors of death or graft loss. Compared to <70 years, ≥ 70 years recipients were more frequently transplanted with ≥ 60 aged donors (31 vs. 16%, P < 0.001) and, differed for the following characteristics: HBsAg+ (5 vs. 12%), AntiHCV+ (33 vs. 26%), malignancies (26 vs. 14%), Alcoholic (12 vs. 33%), HCV cirrhosis (83 vs. 62%), elective LT (94 vs. 88%), ABO isogroup (94 vs. 92%), (≥ 70 years vs. <70 years, all P < 0.01). Graft and patient 5-year survival were 61% and 65%, compared to 62% and 71%, respectively for <70 years (P=0.06). Regarding the cause of death or graft failure, aged recipients had significantly less technical complications (5 vs. 12%, P < 0.05), and more cardiovascular failure (12 vs. 6%, P < 0.05). Survival of ≥ 70 yrs recipients was statistically impaired in case of: male recipient, donor age ≥ 55 years, combined transplantation (all P < 0.05). Living donor (RR=4.2), UNOS status<4 (RR = 2.1) and donor age ≥ 55 (RR = 1.7), were identified as independent risk factors of death or graft loss. In conclusion, although still scarce in Europe, LT of aged recipients leads however to almost 65% patient 5-year survival. This survival is obtained despite the high level of malignancies or

HCV among those patients and the higher use of aged donor grafts in this population.

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EVOLUTION OF COMPLICATIONS AND MORTALITY OF LIVING LIVER DONATION IN EUROPE

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Because donor hepatectomy-related complications or mortality are critical issues of living donor liver transplantation, we performed an analysis of European Liver Transplant Registry data to provide information from a large multicenter cohort of living donation. From October 1991 to December 2008, 3115 LDLT were performed in 76 European centers. We compared from 2 chronological periods (1991–2000 and 2001–2008) the evolution of the incidence of two-month post-hepatectomy donor mortality and complications according to the Clavien grading system (Grade I-II: complication requiring either no treatment or symptomatic; Grade III-IV: complication requiring interventional treatment; Grade V: death of donor). The type of graft (RLV: right liver, LLV: left liver) was also considered in the analysis. Overall, donor mortality has declined after 2000 (0.1 vs. 1%, P < 0.03). Six of the 7 donors' deaths have occurred after a RLV donation. No donor mortality was reported for a LLV donation after 2000. Early complications have similarly declined after 2000 (12 vs. 19%, P < 0.001). This decline was highly significant in RLV (15 vs. 29%, P < 0.001), mainly for biliary complications (5 vs. 11%, P < 0.002). The same decline was observed for LLV (7 vs. 14%, P < 0.002) but not for biliary complications. According to the Clavien grading system, the incidence of Grade III-IV complications has not changed after 2000, neither in RLV, nor in LLV donors. However, the incidence of Grade I-II complications has dramatically decreased for RLV (11 vs. 23%, P < 0.001) and for LLV (5 vs. 12%, P < 0.001). In conclusion, donor mortality have significantly decreased from 2000 to only 0.1% overall, and none for the LLV. This improvement could be attributed partially to a better management of surgical complications, including reoperation and transplantation as the last solution. More improvements are still necessary to further reduce complications in RLV.

INTESTINAL TRANSPLANTATION



MUCORMYCOSIS: A RARE CAUSE OF GASTROINTESTINAL NECROSIS AFTER MULTIVISCERAL TRANSPLANTATION

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Background: Mucormycosis (Zygomycosis) is an emerging fungal infection in immunocompromised patients. The ubiquitous spores are inhaled or ingested, germinate and fungi develop very quickly with vascular invasion and thrombosis, leading to tissue necrosis. The most common locations are central nervous system, nasopharynx, lungs, skin and gastrointestinal tract. Prognosis is often fatal.

Case report: Four year-old girl presenting with Chronic Intestinal Pseudo Obstruction, dependency on total parenteral nutrition, recurrent central venous line infections, recurrent jaundice and moderate liver fibrosis, megacystis. She underwent a modified multivisceral transplantation, including half stomach, duodeno-pancreas, small bowel and right colon. On post-operative day 5,

digestive content appeared in the wall dressing. The child was apyrexial with normal inflammatory markers. Surgical exploration revealed a small necrotic area on the native stomach, which was externally drained. On following day, a massive gastric bleeding occurred, with haemodynamic instability and haemoglobin falling to 4 g/dl. Emergency laparotomy found two haemorragic ulcers on the transplanted stomach. Both were resected, as well as the perforated area in the native stomach, and a new gastro-gastric anastomosis was performed. Histological analysis and mycological culture showed mucormycosis (Lichtheimia corymbifera). High dose liposomal Amphotericin B IV was immediately started, associated with intragastric amphotericin. No extension was found on total body CT and nasofibroscopy. The child recovered after this episode and work-up after 6 weeks therapy showed no evidence of residual disease. She is alive and well, off parenteral nutrition, 1 year after transplantation.

Conclusion: Mucormycosis is a life threatening invasive fungal infection in the immunocompromised patient. Due to vascular thrombosis and tissue necrosis, it may lead to surgical complications, especially in the gastro-intestinal tract. Urgent therapy includes resection (if possible) of the invaded areas and high dose anti-fungal agents.



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EXTRACORPOREAL MEMBRANE OXYGENATION FOR SEVERE HEPATOPULMONARY SYNDROME AFTER PAEDIATRIC LIVER TRANSPLANTATION

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We report on the use of ECMO for refractory hypoxemia after paediatric liver transplantation for severe hepatopulmonary syndrome (HPS).

Case report: A boy presented with biliary atresia, polysplenia, and partial atrioventricular canal. He underwent Kasai operation (day 70), and complete repair of the heart defect (7 and 15 months). His heart was thereafter assessed as functionally normal. Secondary failure of the Kasai operation occurred with biliary cirrhosis, jaundice, portal hypertension, and cyanosis secondary to massive intrapulmonary shunts (proven by heart catheterism), requiring pre-operative continuous oxygenotherapy. He underwent urgent LT (age 17 months, weight 10 kg) with a split graft. Intra-operative course was uneventful. In the immediate post-operative course, he developed severe hypoxemia, unresponsive to intensive conventional mechanical ventilation, Trendelenburg position, nitric oxide, high frequency oscillator ventilation, and leading to multiple organ failure. Liver graft function and neurological assessment were satisfactory. Because of the cardiac dysfunction, an arterio-venous ECMO was placed in the ICU bed between the right jugular vein and right carotid artery, with minimal heparinotherapy. Blood oxygenation, and hemodynamic parameters immediately improved, multiple organ failure recovered. He remained on ECMO for 9 days and he was extubated 9 days after decanulation. On day 21, he had an episode of pulmonary oedema, due to mitral regurgitation secondary to post-ischemic valve dysfunction. Nine months after LT, the child is alive and well, with normal blood oxygenation on air, as well as normal liver function tests, renal function, neurological examination and cognitive development. He still has a moderate mitral regurgitation requiring medical therapy.

Conclusion: ECMO can be used after LT in children with life-threatening hypoxemia secondary to HPS, as a bridge to reversal of the shunts. It might better be considered before the occurrence of irreversible complications of severe hypoxemia.



FATAL OUTCOME OF LIVER TRANSPLANTATION AND RETRANSPLANTATION FOR ACUTE CCL4-INTOXICATION

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Objective: Report of a case of acute liver failure after CCI4 intoxication. Methods: Retrospective chart review.

Case Report: A 23 years old patient with acute liver failure 48 hours after ingestion of 10 ml of CCl4 underwent liver transplantation from a cadaveric donor. Immunosuppresion consisted of OKT 3, cyclosporine and steroids. On postoperative day (POD) 2, anuric renal insufficiency developed, together with tachyarrhythmia, rhabdomyolysis and neurological impairment. Postoperative liver biopsy revealed extensive cell damage. All these symptoms were thought to be related to persisting CCl4, and serial plasmaphereses were carried out. Screening cultures grew enterococci and pseudomonas in the lungs and enterococci and staphylococcus aureus in the bile, and were treated according to susceptibility testing. On POD 12, liver and pulmonary function improved, followed by restarting urine production on POD 14. Ambulation and enteral feeding were possible starting from POD 24. On POD 30, liver function again rapidly decreased, which was interpreted as acute rejection and treated with pulsed steroid boli. However, the patient's hepatic, renal and neurological situation deteriorated, followed again by rhabdomyolysis, cardiac instability and decreasing pulmonary function requiring reintubation. On POD 32, the patient was listed for high urgent liver re- and kidney transplantation, carried out on POD 31. Two days post retransplantation, microbiological cultures grew aspergillus fumigatus, and amphotericin B was started. However, the patient's condition deteriorated and he deceased 3 days after the retransplantation. Post-mortem pathology revealed disseminated aspergillosis as the reason of death.

Conclusion: Chlorinated hydrocarbons are highly toxic to the liver and other organs. Due to their lipophilic nature, they persist in the body fat for a long time. In the case presented, the massive efforts to control the intoxication facilitated development of an invasive muccosis.



P24 | WILSON'S DISEASE

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Wilson's disease is a hereditary, auto - recessive disorder of copper metabolism, characterized by the reduction of copper excretion, resulting in copper accumulation in toxic concentrations in the liver, brain, kidneys, corneas and other organs, from which results a diverse clinical feature with the prevalence of hepatic or neurological deficits.

Case report: Female patient, 34 years old, was hospitalized with the clinical feature of acute cholecystitis- vomiting, fever, abdominal pain, jaundice, while the CT scan of the abdomen arouses suspicion of the infiltration in the region of porta hepatis. Until the current disease completely healthy. Laboratory test results taken on the admission to hospital indicate chronic liver lesion, and with the additional diagnostic procedures liver cirrhosis was diagnosed in the area of Wilson disease. With the detailed family history, the fact that her sister died in the early 20 s with the clinical feature of fulminating hepatis within Wilson's disease was obtained, but the family members had not done any further tests. During hospitalization, the patient's condition deteriorated in terms of development of liver decompensation, in the treatment D penicillamine was applied along with substitution therapy, to which the patient's condition is improved, so she was sent home after 60 days stay in hospital, in good general condition. The patient was put on the waiting list for liver transplantation, MELD Score 15, CP Score 6 (A). Three weeks latter, despite the regular intake of the recommended therapy, the patient was rehospitalized with manifestations of decompensated liver cirrhosis. Despite the undertaken substitutional and diuretic therapy the patient died after 7 days. The above case points at two burning medical issues in our country: the lack of health culture of the population and the problem of organ availability to vitally vulnerable patients.



LIVER TRANSPLANTATION USING A LLS FROM AN INJURED LIVER, RESCUED BY LIVER RETRANSPLANTATION WITH A LLS FROM AN OLDER DONOR

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A 6 months old boy (weight 7 kg, height 65 cm) underwent liver transplantation for biliary atresia. A left lateral segment (LLS) graft was procured by an in situ split, with removal of segment IV, from a 22 year old woman (165 cm, 65 kg) who suffered a street accident with a major liver trauma that required a right hepatectomy in emergency (graft weight 375 gr, GRWR 5.4). The child was re-operated on the 2nd post operative day for a complete portal vein thrombosis. A redo of the portal anastomosis was performed using an interposition vascular graft. On post-operative day 4 a portal vein thrombosis reoccurred and patient was listed for a re-transplantation. During the following days the clinical condition and neurological status of the child deteriorated (Ascites 900 ml/day, AST 794 U/L, ALT 955 U/L, Ammonia 138 U/L, INR 3,6) and hepatic artery thrombosis was discovered. A continous venous venous hemo diafiltration (CVVHDF) was started because of hepatic encephalopathy and metabolic acidosis. Eventually on post-operative 11th a LLS graft (graft weight 260 gr, GRWR 3.7) from a 65 year old female donor was offered for retransplantation. At re-transplantation the presence of portal vein and hepatic artery thrombosis was confirmed. After re-transplantation the clinical conditions continue to improve and the child was discharged 23 days after retransplantation. Patient is alive and well 3.5 years after transplantation. In conclusion, due to a long waiting time before a donor was available for a urgent re-transplantation (9 days), use of CVVHDF help to bridge the patient with a PVT and HAT to re-transplantation in acceptable conditions. Use of a LLS graft from an older donor is safe even in emergency conditions



ACUTE LIVER FAILURE IN A PATIENT WITH SUSPECTED FAMILIAL LIVER DISEASE: INVESTIGATING UNCOMMON

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Acute liver failure accounted for approximately 4.6% of liver transplant cases in the United States in 2009; of those, 16.9% of cases had no identifiable etiology. This study investigates a patient with acute liver failure, with special attention to genetic and metabolic causes. A previously healthy 47 year old Caucasian male presented with a three day history of jaundice, dark urine and light colored stools following a one month history of nausea and fatigue. History and laboratory testing were negative for drugs/hepatotoxins, viral hepatitis and autoimmune serologies. Laboratory values were as follows: AST 1,269 U/L, ALT 2,059 U/L, total bilirubin 12.7 mg/dL, direct bilirubin 6.6 mg/dL, GGT 341 U/L, total protein 4.4 g/dL, albumin 3.5 g/dL, and INR 2.7. Alphaantitrypsin was 101 mg/dL, ceruloplasmin 18.7 mg/dL, 24 hour urine copper 69 mcg, serum copper 77 mcg/dL. His total MELD was 28, and Child-Pugh score 12 (class C). The patient underwent urgent liver transplantation. During evaluation it was discovered the patient's sister suffered liver failure at a similar age (52 years) and also underwent transplantation, which was later discovered to be attributed to alcoholic cirrhosis. However, initial suspicion for genetic/metabolic etiologies were investigated. Histopathology demonstrated extensive bridging necrosis and early fibrosis, ductular proliferation, and cholestasis. Among the differential diagnoses, Wilson disease and progressive familial intrahepatic cholestasis 3 (PFIC3) were investigated. Genetic testing for Wilson's disease and PFIC3 were negative, and tissue copper was 13 mcg/g dry weight (normal range). The underlying etiology remains undetermined. The patient remains healthy 6 months post-transplant. Thorough history and laboratory testing are essential in the workup of acute liver failure.

Cases of suspected familial liver failure require investigation of uncommon etiologies in addition to more common causes.



INTRAOPERATIVE DEATH DUE TO HEART FAILURE FROM FAT EMBOLIA DURING LIVER TRANSPLANTATION

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Introduction: Liver Transplantation (LTX) became widely used for end stage liver disease. We describe a case of fatal intraoperative cardiopulmonary resuscitation due to fat embolia.

Case presentation: In January 2008, a 60 years old male was admitted to liver transplantation. The indication was alcoholic liver cirrhosis (MELD 14) with a HCC inside the Milan criteria. A transarterial chemoembolization was done prior to the operation. The Donor was 70 years old male, 180 cm height, 105 Kg weight, blood type A positive, CMV IgG Positive. No health problem was known. The donor showed a micorvesicular fatty degeneration of 30% as well as a macrovesicular fatty degeneration of 20%. The operation was done in piggy-back technique. Warm ischemia time was 45 minutes and the cold ischemia time was 8 hours and 50 minutes. After the anastomosis was completed, the reperfusion phase followed. The Reperfusion flow was low, initial function of the liver was reduced and the color of the liver after reperfusion was marbled. The consistency of the liver was tensed. 30 min after the reperfusion, the saturation deteriorated, bradycardia observed and the blood pressure dropped. Resuscitation began immediately. After 60 minutes of resuscitation the patient died without a chance of establishing cardiac function. The cause of the patients death was unclear during the operation. The autopsy performed afterwards showed fat embolii in the hepatic veins, the inferior vena cava and the pulmonary arteries of unknown origin.

Conclusion: Fatty embolism is a rare cause of death during liver transplantation. We therefore would like to present the data and pictures of the case in the worst case session.



BILIARY COMPLICATIONS AFTER SPLIT LIVER TRANSPLANTATION: MY WORST NIGHTMARE

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A 63 year old female underwent split liver (1, 4-8) transplantation because of HCV cirrhosis, MELD 18, and hepatocellular carcinoma. The biliary anastomosis was a T-T duct to duct splinted by a T-tube. 10 days after liver transplantation an anastomotic biliary leakage was diagnosed by trans-kehr colangiography and treated with stent positioning by ERCP. 1 month after she underwent surgery because of extra hepatic biliary necrosis in the absence of arterial stenosis or thrombosis and a hepaticojejunostomy was performed on

the intrahepatic right bile duct over an external stent. The bile leak recurred 15 days after surgery and emergency surgery for a biliary reconstruction was performed with evidence of complete dehiscence of the hepaticojejunostomy that was successfully redo using a new Roux en Y loop; due to multiple previous surgery and infection related to the bile leak, direct abdominal wall closure was not possible and a biological prostesis was positioned; it was removed few days after because of infection despite antibiotics. Vacuum therapy was started in order to restore the huge defect of the abdominal wall, however, spontaneous perforation of distal portion of Roux en Y occurred with high amount percutaneous bile leak, despite several efforts to suture the perforation. Finally, we tempted to close the abdominal wall defect by skin transposition creating an enterostomy over the percutaneous bile leak. Unfortunately, few days after this attempt the patient developed sepsis due to Pseudomonas Aeruginosa and died despite prompt and aggressive antimicrobial therapy.



GRAFT LOSS FOR REJECTION AFTER LIVING RELATED SMALL BOWEL TRANSPLANTATION BETWEEN HLA-IDENTICAL BROTHERS?

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Introduction: Intestinal Transplantation became a useful tool for end stage intestinal failure and short bowel syndrome. Nevertheless graft loss due to rejection remains a challenge in the early and late postoperative course.

Case report: A 48 year old male presented with short bowel syndrome (less than 50 cm) following intestinal resection due to graft versus host disease (GvHD) after allogenic bone marrow transplantation for myelodysplastic syndrome. The patient's brother who already donated bone marrow leading to HLA identical chimerism agreed to living related small bowel transplantation. 150 cm distal small bowel were transplanted. The donor procedure and course were uneventful. An intensified immunosuppressive therapy was not necessary, the patient received 500 mg of MMF once per day anyway. After good initial graft function the patient underwent relaparotomy for anastomotic insufficiency at the proximal intestinal anastomosis on POD 8, 11 and 12. On 22nd, on 26th and on 34th POD relaparotomy was necessary due to recurrent intraabdominal bleeding. On 40th POD another fulminant bleeding due to a graft necrosis with arrosion of the aorta and venous anastomosis finally led to the resection of the graft. The histological examination of the resected graft could not differentiate between necrosis due to acute rejection and recurrent GvHD. The further clinical course of the patient showed severe gastric CMV infection requiring ongoing ganciclovir therapy. The resected graft was reevaluated for CMV but showed no evidence of CMV infection. Finally the patient could be discharged and is in restitution now. Another full-size intestinal graft from an cadaveric donor is discussed now.

Conclusion: Even under the perfect condition of HLA chimeric brothers, living related small bowel transplantation has a wide spectrum of complications leading to graft loss in this case.