Posters

HEPATOCELLULAR CARCINOMA

P01 TUMOR RECURRENCE AFTER LIVER TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA: RECURRENCE PATHWAY AND PROGNOSTIC FACTORS

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Introduction: Liver transplantation (OLT) has been advocated as a good management option for patients with carcinoma hepatocellular (HCC). More recurrences are extrahepatic due to many pathological factors.

Patients and Methods: From April 1986 to December 2003, we performed 95 OLTs for HCC including 73% men of mean age of 54.7 years and 25.3% not filling Mazzaferro's criteria.

Results: The recurrence incidence was 15.8% ($n = 15$), including only extrahepatic lesions in 11 (mainly lung recurrence, seven) and hepatic plus extrahepatic in four. Main late mortality was due to tumor recurrence (33.3%). No differences were observed among sex, preoperative chemoembolization, age, Child, Okuda, etiology, or satellite nodules. A greater incidence of tumor recurrence was observed with a preoperative biopsy ($P = 0.0001$); and alpha fetoprotein (AFP) >200 ng/ml (37.5% vs. 13.3%); known HCC ($P = 0.008$); vascular invasion ($P = 0.001$); >5 cm single nodule ($P = 0.004$); more than three nodules (50% vs. 13.9%); moderately to poorly differentiated tumors (37.5% vs. 12.7%); pTNM IV ($P = 0.0001$); and not meeting Milan criteria ($P = 0.001$). These are the same factors for extrahepatic recurrence. For hepatic recurrence the prognostic factors were: vascular invasion ($P = 0.008$), more than three nodules ($P = 0.004$), moderately to poorly differentiated tumors ($P = 0.003$), pTNM IV ($P = 0.006$), and not meeting Milan criteria (13.6% vs. 1.5%).

Conclusions: Recurrence incidence with Milan criteria was less than 10%, mainly extrahepatic (lung). Prognostic factors for tumor recurrence were pathological features, namely vascular invasion, more than three nodules, size larger than 5 cm, moderately to poorly differentiated tumors, pTNM IV stage. The use of preoperative chemoembolization did not decrease the recurrence rate. A preoperative biopsy increased the incidence of extrahepatic recurrence.

P02 RESULTS OF RESECTION AND TRANSPLANTATION FOR HCC IN CIRRHOSIS AND NON-CIRRHOSIS HEPATOCELLULAR CARCINOMA

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Background: Hepatocellular carcinoma (HCC) is one of the most common cancer worldwide. Both resection and transplantation are surgical treatment options depending on the size of tumours and the presence of cirrhosis. Liver cirrhosis is the main reason for the high early postoperative mortality after resection. Even in the Child A stage, extensive resections are not recommended.

Objectives: This study presents the results of the surgical treatment (LR or LT) for HCC in cirrhotic- and non cirrhotic livers.

Patients and Methods: We analysed the data of 76 patients who underwent LR or LT for HCC from January 2001 to December 2006.

Results: In non cirrhotic livers the following resections were performed: 30 right and extended right hemihepatectomies (54,5%), 11 left hemihepatectomies (20%) and 14 mono- or bisegmentectomies (25,5%). In cirrhotic livers were performed in Child A stage 1 right hemihepatectomy, one extended right hemihepatectomy, one extended left hemihepatectomy and 4 mono- or bisegmentectomies and in Child B stage 3 mono- or bisegmentectomies. In 11 patients who underwent transplantation were two patients with tumors exceeding the Milan criteria and five patients of them (5/11) were treated with TACE before the transplantation.

Conclusions: Liver resection for HCC in cirrhosis should be performed with caution (no long-term survival in our data). Our study confirms that transplantation shows good long- term survival in early HCC stages. However, this may also be true for stages above the Milan criteria. For HCC in non-cirrhotic livers resection remains the treatment of choice, justifying an extensive surgical approach. This achieves favourable long term survival as demonstrated in the study presented.

P03 MOLECULAR STAGING OF HCC PATIENTS BEFORE ELEGIBILITY FOR RADICAL THERAPIES

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Objective: To explore the potential prognostic role of a combined use of preoperative vascular endothelial growth factor (VEGF) and blood AFP mRNA in a cohort of patients with hepatocellular carcinoma (HCC) eligible for potentially radical therapies.

Background: VEGF and AFP mRNA determinations in the blood have shown promising results when used as single prognostic factors for HCC patients.

Methods: One hundred twenty four patients with a diagnosis of HCC were prospectively enrolled in the study. Inclusion criteria were: (a) Histological diagnosis of HCC and assessment of tumor grade (percutaneous biopsy or histology of surgical specimens); (b) Determination of AFP mRNA status and VEGF levels in the blood; (c) Patient's eligibility for potentially radical therapies.

Results At preoperative evaluation, 40% of the study group had AFP mRNA in the blood, 35% had VEGF >23 pg/ml. Surgery (resection, liver transplantation, and laparoscopic ablation) was performed in 64 patients, 48 had percutaneous ablation procedures, while 12 had trans arterial chemo-embolization (TACE). AFP mRNA in the blood and VEGF>23 pg/ml were both significantly correlated to vascular invasion, tumor grade, nodule size, AFP levels, TNM and BCLC staging, PST and presence of cirrhosis. After a median follow-up of 19 months (range, 1–60), 1, 3, and 5-year survival rates were respectively 71%, 46% and 41%. Multivariate survival study selected only surgical therapy, encephalopathy, child B-C, AFP mRNA and VEGF as independent survival variables. The contemporary use of the two biomarkers showed a significant stratification ability in identifying four main prognostic stages.

Conclusion: The preoperative determination of AFP mRNA status and VEGF may potentially refine the prognostic evaluation of HCC patients and improve the selection process for radical therapies.

P04 INTERPRETING

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Findings of "No significant difference" or *P*-value >0.05 are often interpreted as indicating clinical or practical equivalence. An alternative, indistinguishable explanation is type II error: incorrectly rejecting a true hypothesis, often on the basis of a study with insufficient subject numbers. The success of the Milan criteria for hepatocellular carcinoma in expanding the indications for liver transplantation has spawned a debate as to whether even more 'liberal' criteria might produce acceptable results. The UCSF criteria have been demonstrated to show a statistically significant improved 3 to 5 year patient survival, as compared to tumors exceeding the criteria. We performed an extensive literature search for studies in which direct comparisons could be made for 3 to 5 year patient survival between patients meeting the Milan criteria and patients exceeding it but meeting the UCSF criteria. On these we performed a meta-analysis, which revealed that adding subjects, did not alter the odds ratio (0.75), which, as expected, slightly in favor of Milan criteria. The strongest evidence for an assertion of clinical equivalence between these groups would be $P < 0.05$ but with an odds ratio near 1.0–statistically but not clinically significant. However, the number of subjects needed to achieve this rises exponentially as the odds ratio approaches 1.0. Almost as compelling is a consistent pattern of studies, as evidenced by the stability of the odds ratio between studies and the *P* value smaller in the combined studies than in each individual. Of note, whenever possible, we used explant pathology as the basis for criteria inclusion. The problem of pre-transplant, or clinical, under-staging is a serious, but distinct, problem. We conclude that there is good evidence suggesting equivalent patient survival between patients meeting the Milan criteria and the somewhat more expansive UCSF criteria.

HEPATITIS C

P05 THE CHOICE OF CALCINEURIN INHIBITOR DOES NOT AFFECT POSTTRANSPLANTATION OUTCOMES IN TERMS OF HCV RECURRENCE: A RANDOMIZED PROSPECTIVE STUDY

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Introduction: Recurrence of hepatitis C (HCV) after liver transplant in HCV positive recipients is a relevant problem of liver transplantation programmes
Objective: To compare the incidence and time of reactivation of HCV. Group A: Cyclosporin with C2 monitoring, steroids wand mycophenolate mofetil. Group B: Tacrolimus and steroids
Material and Methods: 151 receivers were included. Exclusion criteria are the following ones: non heart beating donors type I/II, combined transplants, HIV recipients, acute liver failure and paediatrics recipients. After the transplant, all the patients were evaluated of specifically, in the following days (1, 5, 7, 14, 21, 28) and months (3, 6, 12) of the postoperative course.
Results: A total of 74 patients belonged to group A. There was no postoperative mortality. The percentage of lost grafts was 10.6%. There were no differences neither in the actual survival of the graft to 1, 3 and 5 years, nor in the rate of crude survival between both groups (group A: 90.5% versus group B: 88.3%). At the end of the study, 87.3% HCV recipients have histological recurrence over the graft. After data analyses, we not find significant differences in the hepatitis incidence (group B: 94.3% versus group A: 78.6%), but recurrence is earlier with tacrolimus (group B: 8.88±3.06 months versus group A: 11.50 ± 3.16; $P = 0.003$).
Conclusions: The use of mycophenolate mofetil in combination with cyclosporin, seems to delay the reactivation of the HCV over the graft, although this fact does not have impact neither in the survival of the graft nor in the percentage of patients with HCV recurrence.

P07 RESULTS OF INTESTINAL AND MULTIVISCERAL TRANSPLANTATION IN ADULT PATIENTS: SPANISH EXPERIENCE

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Background: Short-bowel transplantation has experienced a substantial growth worldwide following improved results from the late 1990s on, and its coverage by Medicare.
Objective: To know our results regarding patient and graft survival from the first Spanish series of intestinal transplants in adult recipients.
Material and methods: We present our experience in the assessment of 22 potential candidates to short-bowel transplantation between June 2004 and September 2007, 14 of whom were rejected and eight were transplanted, which makes up the sample of our study. Of these, seven were isolated short-bowell transplant and one multivisceral, which represents the first multivisceral adult transplant performed in Spain.
Results: To this date eight transplants have been carried out in seven patients. Indications for transplantation were desmoids tumours due to Gardner syndrome ($n = 4$), retransplants ($n = 2$), short bowel syndrome after excision as a result of mesenteric ischemia ($n = 1$) and as result of Crohn disease ($n = 1$). Upon study completion and after a mean follow-up 30 months (range 21–39 months) five recipients are alive (71%), and all grafts of alive patients are fully operational (62%), with complete digestive autonomy. All patients received induction with alemtuzumab except one, who received thymoglobulin; in all induction was initiated with no steroids. In five cases rejection episodes were diagnosed. These were grade-II rejections in four patients (effectively treated with OKT3 10 ml/IV/24 h for 10 days), and a grade-III event in one patient, which was refractory to OKT3 and alemtuzumab, and led to intestinal graft excision.
Conclusions: Intestinal and multivisceral transplantation represents a therapeutic option that is applicable in our setting and valid for recipients with an indication who have no other feasible alternative to keep their intestinal failure under control.

SMALL BOWEL TRANSPLANTATION

P06 THE IMPACT OF BASILIXIMAB ON RENAL FUNCTION AFTER PAEDIATRIC INTESTINAL TRANSPLANTATION

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Introduction: Intestinal transplantation (IT) programme began in 1993 and 40 transplants have been done till December 2005 with Tacrolimus based immunosuppression. Primary induction with Basiliximab was introduced in 2002 with a reduction in target Tacrolimus levels. We aimed to evaluate the pattern of renal dysfunction in long-term survivors and to study the impact of Basiliximab use on long-term renal function.
Methods: We did a retrospective review of 16 children who survived for more than 24 months following IT between 1993-2005. Six patients received Basiliximab induction. The following clinical characteristics were recorded: age, weight z-score, underlying diagnosis, type of transplant, number of rejection episodes and follow up. Renal function deterioration was defined as worsening of calculated glomerular filtration rate (c-GFR) expressed in ml/min/1.73 m^2 using the modified Counahan-Barrat formula from the pre-transplant status and was documented by serial measurements until the last follow-up appointment. The median Tacrolimus levels were identified from the medical records. Statistical analysis was performed by using SPSS software.
Results: All 16 children showed a deterioration in renal function after IT suggesting that peri-transplant levels of Tacrolimus are a key factor in determining renal deterioration. There was a highly significant relationship between high Tacrolimus levels and reduced c-GFR in the first 6 months ($P = 0.002$). In the whole group, c-GFR decreased within the first 6 months post-transplant and then gradually improved and stabilized on long-term follow up. In the post-Basiliximab era there was no significant difference in Tacrolimus levels but there was a decrease in the number of episodes of rejection, a significant slower decline in c-GFR and recovery to pre transplant baseline c-GFR at 24–36 months.
Conclusion: Deterioration in renal function is commonly seen following IT. Basiliximab use may have a role in recovering long-term renal function after small bowel transplantation.

P08 INCIDENCE OF HISTOPATHOLOGICAL DEMONSTRATED REJECTION IN OUR SERIES OF ADULTS UNDERWENT SMALL BOWEL TRANSPLANTATION

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Introduction: The small bowel transplantation require the contribution of pathology service in the diagnoses of acute cellular rejection (ACR) and morbidity caused of human intestinal allograft. The recipients have to experiment one or more acute rejection, generally into 2 months post transplant. Any clinic changes usually must have control by biopsies. Data clinic course and observed endoscopy macroscopic changes may be too late for the treatment exit of ACR.
Aim: To show the incidence of ACR in our series of adult small bowel transplantation
Material and Methods: We perform eight human intestinal transplants, seven adult patients receive small bowel transplantation, 1 patient receive multiviceral transplantation during the 18 month period (median follow-up 5 months, range 2/16 months). Our clinical protocol of survillance endoscopy utilized was: 2nd day, two per week the 1st month, one per week 2 and 3 month, then one every 2 weeks 4 and 5 month, and one per month at the end first year posttransplantation. Moreover we indicated the control biopsy if we detect increased of stomal output, fever abdominal pain or other symptoms. The immuno-suppression was alentuzumab 30 mg. only doses and calcineurinics agents.
Results: We diagnose 10 episodes of ACR in 25 biopsies with relation, wich appear in eight patients (grading criteria Mild ACR 9, Moderate ACR 12 and severe ACR 4). Three of them who presented severe ACR finished with lost of grafts despite the treatment. Anyone presented severe ACR in 3 month following transplantation. Only one of them had a moderate ACR initially. The ACR are showed in five grafts with relation in four recipients.
Conclusion: The severe ACR present a high risk of graft lost. In our series, all of them occurs after 3 month postransplant. In this period Alentuzumab improve the rates of ACR.

P09 CHRONIC REJECTION AFTER COMBINED LIVER AND SMALL BOWEL TRANSPLANTATION IN A CHILD WITH CHRONIC INTESTINAL PSEUDO-OBSTRUCTION

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An 11-year-old boy with irreversible intestinal failure secondary to chronic intestinal pseudo-obstruction and intestinal failure associated liver disease (IFALD) underwent a combined en-bloc reduced liver and small bowel transplantation. He was discharged home after 9 weeks on full oral intake without requiring intravenous nutritional or fluid supplementation. The first episode of mild acute rejection occurred 18 months after the transplant and it was successfully treated with steroids. An episode of severe Rotavirus gastroenteritis led to severe exfoliative rejection of the bowel graft which was resistant to steroid and Infliximab treatment, but responded to OKT3. There was associated EBV viremia with no evidence of PTLD. Another episode of moderate to severe acute liver rejection occurred 5 months later. At the same time multiple biliary strictures were diagnosed and treated. Persistent clinical symptoms (abdominal pain and increased stomal output) and atrophy of the ileum mucosa on several biopsies, suggested the possibility of chronic rejection (CR). A second combined whole liver and small bowel transplant was performed and the diagnosis of CR was confirmed on the histology of the explanted graft. The postoperative course was severely complicated and 71 days after the re-transplantation, the boy died because of respiratory failure and multi-organ failure. In summary, intestinal transplantation (IT) can be performed in children with CIPO and it gives them the opportunity to be free from total parenteral nutrition (TPN). As survival following IT continues to improve, the problem of CR has become increasingly important and the only treatment available is re-transplant which is associated with poor outcome.

ELTR STUDIES

P10 DOMINO DONOR RISK TRANSPLANTATION. IS TECHNIQUE A FACTOR?

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Background: Domino Liver Transplantation (DOLT) is a frequent procedure since 1995 first procedure by Prof Furtado, relates to the incidence of FAP, mostly Met30 varient patients we transplant. Obviously no major series is published by other one center, but as Piggy-Back (PB) hepathectomy spreads, the question arises how to safely perfom the donor operation.
Methods: Since April 1996 and December 2006 we performed 242 FAP patients OLT. Since the inception of the DOLT program 126 patients were donors. All of DOLT patients had a classic hepathectomy, and implants were under mesenteric vein-axilar vein by-pass. We compared results at 6 months, as this period relates mostly to operative complications, as far as morbidity and mortality, for total FAP and DOLT patients, comparing the 2 techniques.
Results: The majority (89%) of non-donors had a PB technic (104 of 116). Overall FAP OLT/DOLT survival was 86/90%, 86/88% and 80/81% at 6 months, 1 and 5 years (ns). Cold and warm ischemia times were comparable (average 407/49 min).Classic hepathectomy was perfomed in 138 patients, with a 6 months mortality of 12% comparable to the Piggy-Back OLT in 104 patients with a mortality of 13% for the same period.
Conclusion: In our experience type of total hepathectomy makes no difference in the context of Domino OLT.

WORST CASES

P11 GRAFT VESSEL WALL PATHOLOGY IN A CASE OF HEPATIC ARTERY PSEUDO-ANEURYSM IN A LIVER TRANSPLANT RECIPIENT

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A 59-year-old male suffering from HCC, and alcoholic cirrhosis underwent OLT in October 2006. Donor liver biopsy revealed only a 20% macrosteatosis. The graft was revascularized trough a piggy-back technique. The patient was discharged from hospital on post-operative day 17. ERCP for sphincterotomy, internal stent positioning, and Kehr removal was scheduled 3 months after transplantation. 3 days later, acute intestinal bleeding was identified. An abdominal CT revealed a HA-Pseudoaneurysm with no evidence of any intra-abdominal collections. X-ray angiography confirmed the HA-Pseudoaneurysm, with a fissure into the duodenum. It proved impossible to insert a covered stent-graft. The patient underwent emergency open surgery: after closing the HA, an aorto-hepatic bypass was fashioned using an iliac vessel graft obtained from the organ donor to restore graft flow. The anastomosis between aorta and iliac channel was completed without difficulty, but the one between the HA, close to the bifurcation, and the iliac vessel proved impossible due to a progressive dissection of the graft artery wall. The patient underwent retransplantation the next day, but died 25 days later due to sepsis. The HA of the explanted liver revealed an edematous muscle component with an irregular trend and disruption of the elastic fibers and myofibrous cells associated with intimal fibrous deposits on the inside of the internal elastic lamina coinciding with a focus of wall dissection. Weigert's reaction showed irregularities and discontinuities of the internal and external elastic lamina, especially up against the dissezione, with delamination and fibrous reorganization of the internal lamina, with numerous fragmented and uneven fibers. There was no evidence of any bacterial or fungal infection involving the HA wall, and there was no significant lymphocytic component to support an inflammatory pathogenesis of the damage.

P12 3 CONSECUTIVE LIVER TRANSPLANTATIONS IN A PATIENT WITH REPEATED ACUTE GRAFT NECROSIS

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Introduction: Liver retransplantation is challenged by vascular and biliary difficulties and critically ill patients. We report the case of patient who necessitated three consecutive liver transplantations within one hospital stay.
Case Report: A 46-year-old male patient diagnosed with HCC underwent left hemihepatectomy. He developed intrahepatic recurrence 10 months later and was listed for transplantation. The liver from a 47 year old heart-beating donor was transplanted in piggy-back technique. The patient recovered quickly and was due to be discharged from hospital on day 10. The night before dismission he developed sepsis and required reoperation. Infected necrosis of multiple liver segments as well as the donor bile ducts was encountered. High urgent retransplantation became necessary due to acute liver failure. A 62 year old heart-beating donor organ was allocated. Back table preparation revealed an aberrant right hepatic artery ascending from the superior mesenteric artery and a lesion of the left hepatic artery. Arterial anastomosis had to be revised three times intraoperatively. Again the patient developed extensive necrosis of the bile duct and left liver segments followed by peritonitis and multiple re-operations. Intraoperative findings showed occlusion of the hepatic artery. The patient had to be listed for second retransplantation. The organ of a 64 year old donor was transplanted successfully. An infrarenal aorto-hepatic allograft bypass augmented from iliac and supraaortic allografts provided sufficient arterial revascularisation. After a prolonged, but uneventful recovery the patient was discharged 6 weeks later. Today, 18 months later, the patient is fit and free of recurrence.
Conclusions: Vascular reconstruction in liver retransplantation is crucial and can be challenging. Failure of sufficient revascularisation commonly causes graft loss due to parenchymal and biliary necrosis. When options for vascular reconstruction are poor, insertion of an aorto-hepatic bypass should be considered early without compromises.

BASIC SCIENCE

P13 DOSAGE DEPENDENT ACETAMINOPHEN-INDUCED ACUTE LIVER FAILURE IN PIGS

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Objective: A reproducible pig model of acute liver failure due to intoxication for evaluation of therapeutic strategies and devices, omitting the variability induced by multiple non-liver injury sites (e.g. anaemia, cardiac failure), is urgently needed.
Methods: Twelve pigs underwent an intoxication with a single enteric acetaminophen bolus of 1500 mg/kg b.w.($n = 3$), 1250 mg/kg b.w ($n = 3$),1000 mg/kg b.w ($n = 6$). Seven pigs received a bolus of 500 mg/kg b.w.($n = 3$) or 250 mg/kg b.w. ($n = 4$) and afterwards blood levels of 300–400 mg/l acetaminophen were maintained by continuous enteric administration until acute liver failure occurred (decline of liver depended clotting factors and albumin). Pigs remained under deep narcosis with pressure controlled ventilation until death. Sodium chloride 0.9%, hydroxyethylstarch 6% were used for volume substitution and noradrenalin for hemodynamic stability. Parameters like heart rate, mean arterial pressure, pulse oximetry were continuously monitored, blood gas analysis was performed hourly and corrected as required. Acetaminophen blood levels, albumin, AST, ALT and liver depending clotting factors were measured every 8 h after intoxication.

Results: All animals receiving 1500 mg/kg b.w. or 1250 mg/kg b.w. died within 11 ± 10 or 13 ± 7 h caused by cardiocirculatory failure. Three of the pigs receiving 1000 mg/kg b.w. died due to acute liver failure within 30 ± 8 h, but three animals recovered after severe liver damage and were killed after 48 h. Animals with 500 mg/kg b.w. bolus and blood levels of 300–400 mg/l died after 21 ± 9 h due to cardiac arrest. Pigs with 250 mg/kg b.w. bolus and blood levels of 300–400 mg/l survived minimum 27 and maximum 45 h (mean 37 ± 7) and died due to acute liver failure.

MISCELLANEA

P14 COMBINED TREATMENT WITH SCLEROTHERAPY AND BANDING FOR VARICEAL BLEEDING IN CANDIDATES FOR LIVER TRANSPLANTATION: PRELIMINARY RESULTS

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Objective: According to the literature, endoscopic banding is as effective as sclerotherapy to stop variceal bleeding in emergency. Banding gives less complications, but, in presence of severe bleeding the kit on the endoscope tip decreases the lumen visibility. Aim of the present study was to evaluate the efficacy and safety of a combined therapy with one session of sclerotherapy to stop the bleeding and thereafter banding for variceal eradication. With this combined treatment we add the good bleeding control of sclerotherapy and the low risk of complications of banding.
Patients and methods: From 2000 to 2007 in the Liver Transplantation Unit of Padova we treated for variceal bleeding in emergency 65 patients. In all was performed a first session with sclerotherapy, thereafter in 38 patients variceal eradication was completed with sclerotherapy, in 27 with banding.
Results: The number of sessions required to achieve variceal eradication was significantly lower in the patients treated with combined sclerotherapy + banding versus sclerotherapy alone (respectively 4,4 ± 1,9 vs. 5,9 ± 2,2, $P < 0.01$). After a mean follow-up of 20 months, no significant difference was found when comparing rebleeding (24% sclerotherapy vs. 15% combined), variceal recurrence (29% sclerotherapy vs. 15% combined), mortality (11% sclerotherapy vs. 15% combined) and complications (11%sclerotherapy vs. 7% combined).
Conclusion: Combined treatment with sclerotherapy followed by banding for variceal bleeding is an effective and safe method. It requires less sessions to obtain variceal eradication when compared with the sole sclerotherapy. Randomized prospective studies should be performed to confirm if this method is preferable to sclerotherapy.

P15 INDIVIDUAL DRUG THERAPY IN LIVER TRANSPLANTATION

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A well-designed therapeutic strategy may contribute to the patient/graft survival and success of liver transplantation. The vision of IMMUNOCYP project is to develop a global approach by combining immunological and drug-metabolizing factors for establishment of individual drug therapy for transplanted patients. Drug-metabolizing capacity of liver depends primarily on the levels and activities of the cytochrome P450 enzymes (CYP). The early detection of poor-metabolizer status of the graft and of adverse immunological reactions facilitates rationalization of medication. A validated analytical system with genomic, transcriptomic and metabolomic tools has been developed for estimation of the drug-metabolizing capacity of transplanted liver, which allows the prediction of potential poor-metabolizer phenotypes of donors and reflects drug-related hepatic injury. CYP genotyping is able to estimate permanent poor-metabolism derived from inactivating mutations. CYP phenotyping detects the lack of functional activity of CYP enzymes. Strong correlations were found between CYP activities of the donor liver and mRNA levels of the donor leukocytes ($r > 0.9$). It means that CYP mRNA levels in leukocytes reflects CYP activities of the liver. Of the 42 liver donors in Hungary, frequency of functional poor-metabolizers was found to be 14%, 29% and 48% for CYP2C9, CYP2C19 and CYP3A4, respectively. The recipients transplanted with CYP3A4 poor-metabolizer liver required reduction of cyclosporin doses, in case of other CYP enzyme defect mediaction was tailored as well.. Some patients transplanted with CYP3A4 extensive-metabolizer graft produced high concentrations of toxic cyclosporin metabolites and needed alternative immunosuppressive therapy. As verified by 42 recipients, the optimization of drug choice and/or dose for more effective therapy leads to avoid adverse effects and drug failures.

P16 HEPATIC VENOUS HEMOGLOBIN OXYGEN SATURATION AS AN EARLY PREDICTOR OF LIVER FUNCTION IN ORTHOTOPIC LIVER TRANSPLANTATION

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Specific objective: In this study we measured hepatic venous oxygen saturation (ShVO2) in liver transplantations in order to evaluate its usefulness as a predictor of early postoperative graft function after orthotopic liver transplantation.
Method: We study 35 adult patients who underwent cadaveric liver transplantation. All the patients were at Child-Pugh class C, with end-stage cirrhosis. They underwent the same anaesthetic and surgical technique. They were divided in two groups: group A ($n = 28$) patients with satisfactory function of liver graft and group B ($n = 7$) patients with primary non- function or primary dysfunction during the first postoperative month. During the operation, whole blood was taken from recipient's hepatic vein in the following phases of transplantation: (i) 10 min after reperfusion of portal vein (PV) (pv1) (ii) 20 min after reperfusion of PV(pv2) (iii) 10 min after reperfusion of hepatic artery HA (ha1) (iv) 20 min after reperfusion of HA (ha2) and (v) at the end of the operation (ha3). Postoperatively, the function of the graft was evaluated from coagulation tests, alanine aminotransferase, aspartate aminotransferase, bilirubin, serum glucose and lactic acid.
Results: We found out that ShVO2 of grafts with good function was over 60% after reperfusion and the mean value was 71.68 (95% CI 67.2–74.8%). ShVO2 of the grafts with poor function never increased over 60% after reperfusion and the mean value was 53.8% (95% CI 35.1–69.1%). Especially, there were statistically significant difference among the two groups in each phase of liver transplantation.
Conclusion: Monitoring of ShVO2 is a useful method to evaluate early grafts function during liver transplantation, even though immediately after reperfusion.

P17 OUTCOME OF HEPATICOJEJUNOSTOMY FOR BILIARY TRACT OBSTRUCTION FOLLOWING LIVER TRANSPLANTATION

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Background: Biliary strictures and concrements are common complications following liver transplantation. Endoscopic treatment might not lead to a definitive cure in all patients, especially in strictures involving the biliary bifurcation. The aim of this study was to determine the efficacy and the long-term outcome of hepatico-jejunostomy for post-transplant biliary tract obstruction.
Material and Methods: Thirty seven patients were retrospectively studied who underwent conversion from choledocho-choledochostomy to hepatico-jejunostomy for biliary strictures and concrements in a series of 807 liver transplantations. Resolving of cholestasis and the incidence of recurring biliary obstruction were analyzed.
Results: Surgery was performed due to anastomotic strictures in 11, ischemic strictures at the donor common bile duct in seven, strictures involving the bile duct bifurcation in 10, hepatolithiasis without structures in one and biliary sludge formation diagnosed by t-tube cholangiography in eight patients. Cholestasis instantly improved in 82% of the patients. After a long-term follow-up of median 33 months (range 3–149), 28 of the patients (76%) required no further intervention for recurring biliary obstruction following hepatico-jejunostomy. Anastomotic structures were observed in six (16%), recurring biliary concrements in two patients (5%).
Conclusion: HJS did prevent re-interventions for recurrent biliary obstruction in the majority of the patients. We therefore recommend early hepatico-jejunostomy for complicated post-transplant biliary tract obstruction not treatable by a limited number of endoscopic interventions.

P18 CLINICAL IMPACT OF OBESITY (BMI > 30) AFTER LIVER TRANSPLANTATION

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Introduction: Obesity appears to be a risk factor affecting overall outcome in organ transplantation. Pulmonary, cardiovascular and surgical complications following liver transplantation (LT) have been associated to obesity. Aim of this study is to review retrospectively our experience focusing on the role of BMI postransplant complications and retransplantation rate.

Methods: Between May 1999 to August 2007, a total of 397 patients underwent LT in our institution. Primary whole LT were performed in 214 (54.0%) adult recipients and considered for statistical analysis. Patients were divided into 2 groups: G1 (BMI?30), $n = 187$ (87.0%) and G2 (BMI>30), $n = 27$ (13.0%). Overall mean BMI was of 27(range 16–49). Differences were evaluated using the T-Test and the Fisher Test when appropriate. Survivals were analyzed by Kaplan-Maier curves (Log-rank test for differences).
Results: After a medium follow up of 46 month (range 1–100), 185 patients were alive (159 in G1 and 26 in G2). Donor and recipient characteristics were similar in both groups except for recipients? age (54 years vs. 57 respectively, $P = 0.025$). ICU and hospital stay were also similar. Finally, we did not find any significant differences between groups when looking at the expected early postoperative complications occurring in the obese (pneumoniae and ARDS). However, the need for renal replacement therapy was significantly higher in G2. Retransplantation rate was similar in both groups (G1: 4.8%, G2: 11.5%) as well as the incidence of PNF. 1 and 5-years overall graft and patient survival were: 89%/85% and 89% / 83% for G1 and G2 respectively ($P < 0.01$; $P = 0.43$). Conclusion: According to our experience mild obesity (BMI from 31 to 49) did not significantly impair overall graft and patient survival nor retransplantation rate. However, liver transplantation in obese patients may result in a higher incidence of incisional hernias and early postoperative renal replacement therapy.

P19 PHARMACOKINETICS, EFFICACY AND SAFETY OF INTRAMUSCOLAR AND INTRAVENOUS OF HEPATITIS B IMMUNOGLOBULINS COMBINED WITH NUCLEOSIDE ANALOGUES IN PROPHYLAXIS OF HEPATITIS B AFTER LIVER TRANSPLANTATION

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Background: In absence of prophylaxis, HBV recurrence after liver transplantation (LT) develops in up to 75% of cases. The use of hepatitis B immune globulins (HBIG) in combination with nucleoside analogues (NA) has improved outcomes of LT for HBV, reducing the 1-year recurrence rate to approximately 10%. In originally HBsAg-positive recipients of LT, HBIG schedule should be aimed to maintain HBsAg negative and anti-HBs serum titer >100 IU/L after surgery.
Aims: Safety and efficacy of intravenous (iv) and intramuscular (im) HBIG (virus inactivated with solvent/detergent method) treatment in patients transplanted for HBV-related cirrhosis and treated with NAs and immunoglobulins were evaluated by assessing the proportion of patients who maintained HBsAg-negative and anti-HBs titers above >100 IU/L while on im or iv administration.
Methods: In an open-label, multicenter study, iv or im HBIG pharmacokinetics and 6 months efficacy (persistent HBsAg-negative and anti-HBs titer > 100 IU/L) were evaluated in 31 patients treated with NAs and HBIG post-surgery, with a post-LT follow-up > 12 months.
In the First Part of the study : 1) 16 subjects received iv HBIG (VENBIG 2500 IU/50ml) at 5000 IU every 4 weeks for six months; 2) 15 subjects received im HBIG (IMMUNOHBs 540 IU/3ml) at 2160 IU every 2 weeks for the same period. At the end of the first part of the study a pharmacokinetic evaluation has been performed.
In the Second Part 15 patients received 2000 IU every 2 weeks of im HBIG (IMMUNOHBs 1000 IU/3ml) for 6 months and at the end of the study, a pharmacokinetic evaluation was performed.
Throughout the study anti-HBs levels were tested immediately before and after two next injections.
Results: All patients remained HBsAg-negative during 12 months follow-up and 29 of them maintained stable anti-HBs>100 IU/L. Fifteen adverse events were recorded, only three of them correlated with the investigational products. At the end of the study the mean titers of anti HBs resulted 396 IU/L.
Conclusions: These results confirm a comparable efficacy and safety of iv and im (540 IU/3 ml or 1000 IU/3 ml) HBIG treatments and their effectiveness on HBV recurrence.

P20 ANTIMICROBIAL PROPHYLAXIS IN LIVER TRANSPLANT PATIENTS- A MULTICENTER SURVEY SUPPORTED BY ELITA

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Introduction: Infection remains a major problem for patients undergoing liver transplantation. However, data regarding perioperative prophylaxis are lacking. The aim of the study was to gain insight into prophylactic antimicrobial strategies used in European liver transplantation (LT) centers.
Methods: The study was performed by means of an electronic and postal survey sent out to all European LT centers that are member of the European Liver and Intestine Transplantation Association (ELITA). In the survey, we asked for the prophylactic antibiotic, antifungal and Cytomegalovirus (CMV) regimen used in LT recipients. We also asked for other prophylactic measures performed (isolation post LT, selective bowel decontamination (SBD), mupirocin nasal ointment and chlorhexidine body washes for MRSA skin decontamination) and for microbiological surveillance by culture sampling of different sites. The questionnaires were treated anonymously.
Results: Of the 128 centres who were sent the survey, 61 centers (47,7%) from 16 different countries completed it. 62.3% of the centers answered by email, 18% by post and 19.7% by fax. 10% of the centers reported to perform < 25 LT, 36.7% 25–50, 28.3% 50–75, 10% 75–100 and 15% > 100 LT annualy.
Antibiotic prophylaxis for recipients with elective LT was provided by one single antibiotic in 48.3% of the centers. In 50%, a combination therapy was given and in 1.7%, the antibiotic prophylactic regimen was switched between mono-therapy and combination therapy every 6 months. The mean duration of antibiotic prophylaxis was 3.3 ± 2.5 days. 18.6% of the centers restricted antibiotic prophylaxis to the first postoperative day, 55.9% of centers administered antibiotic prophylaxis during 2 to 3 days, and 23.1% of centers for more than 3 days (one center didn't answer this question).
Mono-therapy was small spectrum (1st and 2nd generation cephalosporin, or aminopenicillin) in 42.9% of centers, and broad spectrum (3rd generation cephalosporin, piperacillin, or carbapenem) in 57.1% of centers.
Antifungal prophylaxis was administered by 33.9% of centers in all LT recipients, and by 55.9% of centers in patients at risk for developing fungal infection. The remaining 10.2% of centers never administered antifungal prophylaxis. Fluconazole was administered most frequently.
CMV prophylaxis was never administered in 10.3% of the centers. In 12.1% of the centers all patients receive CMV prophylaxis, and 77.6% of the centers only gave CMV prophylaxis to risk groups. Most centres who never gave CMV prophylaxis, started pre-emptive therapy when CMV PCR or antigen detection was positive.
For the other prophylactic measurements, 40.7% of the centres isolated the patients post LT, 37.3% gave SBD, 45.8% did mupirocin nasal ointment (10.2% always, and 35,6% when nasal carriage of staphylococcus aureus) and 50.8% did chlorhexidine body washes (20.3% always and 30.5% only in case of MRSA skin contamination).
Culture sampling occurred in 96.6% of the centres, with a mean number of sites 5.7 (76.3% of the centres took cultures of the blood, 64.4% of throat, 35.6% of perineum, 62.7% of nose, 89.9% of urine, 72.9% of sputum or endotracheal aspirate, 30.6% of stool, 78% of abdominal fluid when available, and 67.8% of chest drain fluid when available).
Conclusions: In Europe, there is a considerable variation in the different antibiotic, antifungal and CMV prophylactic strategies used for LT. These findings underscore the need for development of specific guidelines.