was demonstrated to result from de-novo C4 activation: (I) Cleavage of the internal thioester of C4 by treatment of sera with the nucleophile methylamine completely abolished C4 fragment deposition. (II) C4 fragment deposition was not observed when beads were incubated with C4-free immunoadsorption eluates obtained from highly sensitized dialysis patients subjected to preemptive immunoadsorption therapy. C4 fragment deposition was partially restored by addition of normal serum but not C1q-depleted serum. As observed for alloantibody-binding to FlowPRA beads, deposition of C4 fragment binding was temperature- and time-dependent with maximal binding after 60 min incubation at 40C. Similarly maximum C1q deposition was observed at 40C. In contrast, maximum C3 fragment deposition was found at 370C. At this temperature, C3 fragment deposition occurred in an alloantibody-independent fashion presumably as a result of alternative complement activation.

Conclusions: In summary, we herein present a novel cell-independent and easy to perform PRA test which enables flow cytometry-based detection of alloantibody-induced classical complement activation. Future studies testing larger patient cohorts will have to elucidate its relevance as an alternative to CDC-PRA testing and, moreover, as a non-invasive test to evaluate the presence of complement-activating alloreactivity in allograft rejection.

P11.
Tubulointerstitial but not Glomerular Expression of Endothelial Cell Activators in Donor Kidney Biopsies Predict Early Allograft Dysfunction

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Background: Delayed allograft function is among the highest risk factors for reduced long term graft survival. The adequate regulation of endothelial cell activity is of key importance for prevention of this process.

Methods: Biopsies from seven living donor kidneys (LIV) served as reference tissue, biopsies from six cadaveric donor kidneys with primary function (CAD-PF) and from six cadaveric donor kidneys with delayed graft function (CAD-DGF) were studied. In order to determine whether glomerular or tubulointerstitial markers of endothelial cell activation in donor kidney biopsies are predictive for the development of subsequent delayed graft function, we analyzed laser captured microdissected transplant biopsies (P.A.L.M.) by real-time PCR (TaqMan) for the expression of the following markers: ICAM, ET-1, iNOS, eNOS, IL-1ß. GAPDH was used as reference gene, a homogenous mix of universal human mRNA served as calibrator.

Results: The cold and warm ischemia time was not different between the cadaveric donor kidneys. All individual experiments were performed in triplicates. The overall coefficient of variation of repetitive measurements was < 0.05, ANOVA and Scheffe's test was used to evaluate differences between groups. Numbers are mean ± SD, and represent x-fold expression of LIV (normalized to 1).

Table 1.

Gene	LIV	CAD-PF	CAD-DGF
Tubulointerstitium			
ICAM	1.00 ± 0.02	22 ± 3*	5 ± 3
ET-1	1.00 ± 0.07	22 ± 3*	5 ± 2#
iNOS	1.00 ± 0.08	45 ± 5*	8 ± 7
eNOS	1.00 ± 0.06	25 ± 5*	6 ± 5
IL-1β	1.00 ± 0.08	–2 ± 6	2 ± 5
* ... p < 0.05 CAD-PF vs. other groups, # ... p < 0.05 CAD-DGF vs. other groups.			

There was no difference in the glomerular expression of the investigated markers between the donor groups, but the tubulointerstitial expression was manifold higher in the cadaveric kidneys.

Conclusions: These data suggest, that delayed allograft function in recipients of cadaveric kidneys is associated with a different expression profile of vasoreactive endothelial cells markers in the tubulointerstitium.

P12.

Abstract zurückgezogen.

LEBER/DÜNNDARM

P13.
Erfahrungen mit der kombinierten Leber-Nieren-Transplantation

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Grundlagen: Die kombinierte Leber-Nierentransplantation gilt als etablierte Behandlungsmethode beim Vorliegen eines Leberversagens in Verbindung mit einem nicht reversiblen Nierenversagen.

Methodik: Zwischen 28. Dezember 1983 und Juni 2002 wurden insgesamt 26 kombinierte Leber-Nierentransplantationen bei 21 Männern und 5 Frauen in einem mittleren Alter von 47,2 (24–66) Jahren durchgeführt. Chronische Hepatitis C (n = 7) und Hepatitis B (n = 5) waren die häufigsten Indikationen zur Lebertransplantation, und eine Glomerulonephritis zur Nierentransplantation. Zwei Patienten erhielten diese beiden Organe wegen einer primären Oxalose Typ I und ein Patient bei Tetrachlorkohlenstoffvergiftung, nachdem das Toxin das erste Lebertransplantat und die patienteneigenen Nieren schwerst geschädigt hatte.

Ergebnisse: Das Patientenüberleben nach einem und fünf Jahren ist 75%. Der erste Patient, der weltweit je einer kombinierten Leber-Nierentransplantation unterzogen worden war, wie auch die folgenden vier Patienten sind immer noch am Leben mit zwei völlig normal funktionierenden Organen. Der sechste Patient starb an einem Tumorrezidiv 11 Monate nach Transplantation, und Patient Nummer sieben an einer Gastrointestinalblutung ausgehend von einer Refluxösophagitis vier Monate nach Transplantation. Drei Patienten verstarben aufgrund einer septischen Komplikation 1, 2 und 6 Monate nach dem Eingriff und einer an einem Hepatitis B-Rezidiv. Ein Patient mußte sich wegen eines Hepatitis C-Rezidivs einer Retransplantation unterziehen, ein weiterer wegen einer Gallengangskomplikation. Abstoßung wurde in keinem der Nierentransplantate beobachtet, auch nicht bei einem Patienten, der mit 100% HLA-Antikörpern und positiver Kreuzprobe transplantiert worden war.

Schlußfolgerungen: Diese Ergebnisse zeigen, daß die kombinierte Leber-Nierentransplantation mit einer akzeptablen perioperativen Mortalität machbar ist und hervorragende Langzeitergebnisse liefert. Septische Komplikationen sind verantwortlich für die frühen Todesfälle, ein Wiederauftreten der Grundkrankheit für Spättodesfälle. Weiters scheint die Leber gleichzeitig vom selben Spender transplantierte Organe immunologisch zu schützen.

P14.
Combined Liver-Kidney Transplantation: A Case Report

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Background: Since the first combined liver-kidney transplantation was performed at the university hospital Innsbruck in 1983, this therapeutic option has gained increasing popularity for the treatment of patients with chronic hepatopathy combined with renal insufficiency. We report about the first combined liver-kidney transplantation in our center which was performed in May 2002.

Methods: Our patient (38 years, male) suffered from chronic hepatitis C infection since 1983 and developed a cirrhosis with Child's score B (9 points) at the time of transplantation. He was on dialysis treatment since February 2002 because of renal insufficiency on the basis of shrunken kidneys of unknown origin. In May 2002 he received a liver and a right kidney graft from a 29 year old male donor. The liver transplantation was performed in modified Piggy-back technique with retrograde reperfusion. After completion of the liver transplantation the kidney was implanted extraperitoneally from a separate incision according to standard techniques. The immunosuppressive induction was performed with low-dose anti-T-lymphogobuline (200 mg/d) for 7 days and prednisolone, which was tapered and removed on day 16. The long-term immunosuppressive therapie was started with tacrolimus and mycophenolate mofetil on day 1 with low serum levels (tacrolimus < 3 ng/ml until day 6, mycophenolate mofetil < 0,2 mg/ml until day 5, 0,38 mg/ml on day 6).

Results: The operation was performed without any problems in 9 hours 10 minutes (ischemic time liver 5 hours 10 minutes, kidney 8 hours 5 minutes) and the initial function of both organs was favourable (GOT 430 U/L, GPT 300 U/L, GGT 149 U/L, CHE 3290 U/L, PZ 96%, Kreatinin 4.7 mg/dl at day 1). Oral nutrition and mobilisation of the patient was started on day 1. There was no need of hemodialysis treatment after the operation. The patient left the hospital on the 8th postoperative day in excellent condition and very good organ function (GOT 27 U/L, GPT 101 U/L, CHE 2970 U/L, Kreatinin 1.5 mg/dl). He was not hospitalized again since that time. There was no evidence for rejection of the kidney, although the tissue match was not perfect (5 mismatches, but negative crossmatch).

Conclusions: Combined liver-kidney transplantation from the same donor is a valuable method for the therapy of chronic liver failure in patients with end stage renal failure. Since animal experiments and retrospective studies have shown that the liver allograft offers immunologic protection to the renal allograft, a bad tissue matching can be accepted for combined organ transplantation.

P15.
Need in Liver Transplantation for Adult Population in Ukraine

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Background: Liver transplantation (LT) is a modern treatment's standard for patients with liver diseases. The determination of the need in liver transplantation is the first step toward the successful implantation of LT in clinical practice.

Methods: The aim of our research is to calculate the yearly number of possible liver recipients among adult population of Ukraine (as an example in Lviv region) and to investigate the regional nosology structure and index of LT need. 3166 protocols of autopsies made by Lviv Regional Pathological Bureau during the 1995–2000 years were retrospectively analyzed. The criteries of inclusion to the group of possible candidates for LT were: primary chronic liver disease, primary biliary cirrhosis, progressive chronic liver disease, solitary hepatocellular carcinoma with a diameter of 5 cm or less. The absolute criteries of exclusion to the group of possible candidates for LT were: hepatocellular carcinoma with a diameter of more than 5 cm, an extrahepatic cancer or metastatic hepatocellular carcinoma, sepsis, HIV infection, viral hepatitis in active stage, intravenous drug abuse, active alcoholism. The relative criteries of exclusion to the group of possible candidates for LT were: lack of certainty of absolute abstinence of alcohol, insulin dependent diabetes mellitus, prior complex hepatobiliary surgery or major abdominal surgery, mental retardation. The index of LT need was determined as relation between yearly number of possible candidates for LT and each 1 million of adult population in the region. At the time, we established the maximal and minimal index of LT need. The maximal index includes persons with relative criteria of exclusion to the group of possible candidates for LT, the minimal index – does not include these persons.

Results: In Lviv region the approximate number of possible recipients for LT is 18.3 (maximum) and 14.8 (minimum) people per year. The highest index of the need in LT for adult population of Lviv region is 8.3 transplantations per 1 million of citizens. In Ukraine the approximate maximal number of possible recipients for LT was 338.88 people per year, the approximate minimal number of possible recipients for LT – 274.69 people per year. The nosology structure of LT need in the region are included with cirrhosis (62.7%), hepatitis (20.0%), hepatic cancer (12.7%) and other liver pathologies (4.3%).

Conclusions: The approximate yearly numbers of possible recipients for LT and index of the need in LT for adult population in Ukraine are significantly less in compare with European and world data. The regional nosology structure of LT need is corresponded to world experience.

P16.
Liver Transplantation for Hepatocellular Carinoma: A Single Center Experience

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Background: The hepatocellular carcinoma (HCC) is one of the most common cancers worldwide. Although HCC is potentially curable by surgical resection, this therapy option is limited because it can only be implemented in a small number of patients. Other treatments include locally ablative therapies, chemotherapy and rarely, radiation therapy. Liver transplantation can be an effective treatment for small, unresectable HCC, also in patients with liver cirrhosis. When comparing liver transplantation and resection in retrospective studies, liver transplant patients had better survival and reduced tumor recurrance. It has been proposed that locally ablative regimes, such as radiofrequency ablation or chemoembolisation, may be beneficial prior to transplantation and allows patients to wait for an appropriate donor. Several studies have shown that tumor size greater than 5 cm, vascular invasion and poor differentiation of the tumor affect tumor recurrence. We report about the experiences with liver transplantation for HCC in our center.

Methods: Between August 1998 and July 2002 9 patients have been transplanted because of HCC in our center. All patients were male with a mean age of 58 (43–68) years. The underlying diseases were HBV infection (n = 4), HCV infection (n = 1), combined HBV and HCV infection (n = 1), toxic liver cirrhosis (n = 2). In eight of the nine patientes the hepatocellular carcinoma was known at the time of transplantation, in one patient is was found incidentially in the explanted liver. Selection criteria for orthotopic liver transplantation (OLT) were unresectability of the liver tumor (multicentric tumor in 6 cases, unresectable location of the tumor in 2 cases) and severity of the underlying liver disease (Child-Turcot-Pugh-score A (n = 1), B (n = 7), C (n = 1)). Diagnosis of the tumor was confirmed by histology, imaging techniques (sonography, computer tomography, magnetic resonance imaging) and tumor marker (alpha-fetoprotein). All patients received an orthotopic liver allograft in modified Piggy-back technique with retrograde reperfusion. The donor characteristics were as follows: gender 7 male, 2 female; mean age 27.5, causes of death: trauma capitis (n = 5), cerobrovascular accident (n = 3), brain tumor (n = 1). The immunosuppressive induction was performed with low-dose anti-T-lymphogobuline for 7 days (200 mg/day) and prednisolone, which was tapered and removed in the mean after 87 days (40–180). The long-term immunosuppressive therapie was performed with tacrolimus and mycophenolate mofetil in 7 cases and with cyclosporin and mycophenolate mofetil in 1 case.

Results: 6 out of the 9 patients are alive, 1 died at day 102 due to acute rejection, 1 died at day 993 and one at day 1102 from recurrant HCC (1 metastasis in the skin and in the transplanted liver,1 recurrency in the transplanted liver). 1 out of the 7 patients alive has evidence of recurrant disease (os sarum). The mean time until recurrancy was 2.33 years. In all 3 patients with recurrant disease vascular invasion could be shown histologically in the expalnted liver, whereas only in 2 out of 6 patients without evidence of recurrancy vascular invasion of the tumor could be found. Since there is a possible benefit of chemoembolisation and/or radio frequency ablation for patients with HCC waiting for OLT, we successfully performed chemoembolisation in 8 patients and in 1 of those also radio frequency ablation. To prevent recurrancy after OLT the immunosu-

pressive regime was adjusted to the underlying disease by early removal of aprednisolone and reduction of long term immunosuppressive drugs. Patients were screened for recurrency by sonography and compute tomography. Recurrant HCCs were treated symptomatically in 2 cases and with local radiation therapy in 1 case (metastasis os sacrum). In 2 cases additional hyperthermic therapy was performed.

Conclusions: OLT is an effective treatment for subgroups of patients with hepatocellular carcinoma. It might be possible to downstage the liver tumor by chemoembolisation and/or radio frequency ablation and allow the patients to wait for a suitable donor. After OLT the early withdrawal of aprednisolone and the reduction of other immunosupressive is feasible. OLT can be a potentially curative therapy for HCC.

P17.
Impact of Liver Allograft Quality and Donor Demographics on Survival for HCV-Related Liver Disease

Bonatti H., Machicao V., Krishna M., Aqel B., Lukens F., Harnois D., Hellinger W., Nguyen J., Hughes Chr., Dickson R., Steers J. (Mayo Clinic, Transplant Center, Jacksonville, USA)

Background: Shortage of organs has caused increased utilization of marginal donors, living related liver donation and allograft splitting. The use of liver allografts from older donors remains controversial because of the potential risk of primary non-function. Whereas most studies in HCV focused on recipient factors such as viral load only few reports on the long-term faith of marginal grafts in terms of recurrence of HCV are available.

To determine the effect of donor age, graft steatosis and reperfusion injury on the outcome after liver transplantation (LT) in HCV-related liver disease.

Methods: Between 1998 and 2001, 467 liver transplants (LT) were performed at our center. A total of 195 transplants were carried out in individuals with HCV-related liver disease. Protocol liver biopsies were performed 1 hour after reperfusion, at one, sixteen and fifty-two weeks after LT. Specimens were scored for degree of steatosis (0–4), reperfusion injury (0–3), rejection (0–3), inflammation (0–4), and fibrosis (0–4).

Results: Marginal grafts in general were given preferably to less sicker patients. The donor age groups were well matched with regard to recipient age (48.5 vs. 52), mean MELD score (14.1 vs. 14.8), or cold ischemia time (6.9 vs. 7.2 hrs) in HCV and non-HCV patients. Increased donor body mass index or graft steatosis as well as degree of reperfusion injury did not promote recurrence of HCV. Graft survival according to donor age in non-HCV patients did not differ. In contrast, in HCV patients older-donor grafts showed a significantly decreased survival (figure) with recurrent disease accounting for the majority of graft losses. Mean fibrosis score was higher in older-donor recipients in comparison with younger donor recipients at 16 weeks (1.0 vs. 0.4, $p = 0.001$) and at 52 weeks (1.7 vs. 0.9, $p = 0.003$). The patient survival was not affected by the age of the donor in either group.

Conclusions: Advanced age of the donor is associated with more rapid progression of fibrosis and decreased graft survival in patients transplanted for HCV. Neither reperfusion injury nor graft steatosis were associated with earlier HCV recurrence. As survival using older grafts in non-HCV patients was not negatively affected, older-donor grafts should be considered preferentially for these patients.

P18.
Promising Outcome of Liver Transplantation for Malignancies using the Piggy Back Technique without Resection of the Retrohepatic IVC

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Background: The piggyback technique has been increasingly accepted by liver transplant centers due to its simplicity and the avoidance of major hemodynamic changes caused by cross clamping of the inferior vena cava (IVC). Patients with hepatic malignancies if meeting certain criteria benefit from liver transplantation (LT); however, due to the issue of radical resection the piggyback technique for these patients has only reluctantly been accepted. This study comprises our experience with LT using exclusively piggyback technique in patients with hepatic malignancies.

Methods: Between March 1998 and December 2001, 467 LT were performed at our center. Out of these 103 (22%) were undertaken in 81 patients with hepatic malignancies. A total of 72 patients carried a diagnosis of HCC, of which 33 (45.8%) did not meet the Mazzaferro criteria defined by either a single lesion < 5cm or less than 3 lesions. Six patients were diagnosed epitheloid hemangioendothelioma, the remaining patients had secondary liver tumors or extrahepatic malignancies. Extrahepatic spread for primary liver tumors was excluded in all cases on pretransplant evaluation. All LT's were performed using the piggyback technique without resection of the retrohepatic vena cava and without veno-veno bypass.

Results: 38 patients had a concomitant diagnosis of HCV, 11 of HBV, 17 of alcoholic liver disease, 2 of autoimmune hepatitis, 2 of primary sclerosing cholangitis and 2 of overlapping syndrome. In 4 patients cryptogenic cirrhosis was diagnosed. In three cases a tumor had been surgically removed within 3 months anticipating LT. In 14 cases the tumor was incidentally found on the hepatectomy specimen. 57 of 72 patients (79%) with HCC had undergone chemoembolization prior to LT, in 17 of these cases no viable tumor was found at LT. In this series a total of ten split grafts and 41 marginal grafts were utilized: non-heart beating donor (3), pediatric donor (6), donor age > 70 years (12), morbid obese donor (14), hypernatremic donor (6). There were 17 reLT in 14 patients (Primary non-function: 5, vascular complications: 2, biliary complications: 4, HCV recurrence: 3, tumor recurrence 1, venous outflow obstruction: 2). The latter occurred twice in a patient with EHE. During second reLT infiltration of the pericardium by a tumor nodule causing IVC compression was found. This is the only patient in whom IVC resection was necessary. An atriocavostomy (upper IVC anastomosis) and a standard suprarenal cavocavostomy (lower anastomosis) were performed. A total of 16 patients (19.7%) died during a median follow up of 650 days (range 180–1600). Nine of these were related to tumor recurrence (HCC: 7, EHE 1, metastatic neuroendocrine tumor 1), two to intraabdominal sepsis, two to HCV recurrence, one to necrotizing pancreatitis and two to cardiac arrest. Patient survival for patients with HCC who met the Mazzaferro criteria was excellent (89% at one year). Six of 33 (18%) patients who did not meet the Mazzaferro criteria died from tumor recurrence.

Conclusion: The piggyback technique safely can be used in patients with liver tumors. Compared to published data no increased recurrence rate was observed. In specific retrohepatic tumor recurrence was not observed in any case. The theoretical increased recurrence risk is out weight by the hemodynamic advantages offered by this simpler technique.

P19.
Hepatic Ischemia Caused by Torsion of a Large Accessory Liver Lobe: A Rare Indication of Orthotopic Liver Transplantation

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Background: Abnormalities of the liver are rare and generally without clinical signifance. An accessory lobe has its own mesentery, can be large in size and symptomatic or small and asymptomatic. Although the majority of cases with an accessory liver are not detected clinically, it can give rise to various symptoms like recurrent abdominal pain and fluctuating impaired liver function by torsion. We present a case of orthotopic liver transplantation in a patient with hepatic ischemia caused by complete vascular occlusion due to a twisted large accessory liver lobe.

Methods: A 19-year-old woman with a past history of an umbilical cord hernia and a left side renal aplasia presented with acute abdominal pain, nausea and vomiting. Physical examination revealed a painful tumor in the right mid-abdomen. Portal vein thrombosis and hemorrhagic infarction of a large accessory liver lobe

with inhomogenous contrast enhancement of the liver was discovered by computed tomography and ultrasound scanning. Lactate and liver serum transaminases deteriorated rapidly and clotting factors dropped. The patient was therefore transfered to our center and was operated on soon after admission.

Results: At laparotomy, approximately 20 hours after the onset of symptoms, an accessory liver lobe, weighing 1000 gr, with the gallbladder embedded was encountered. This accessory lobe was twisted and completely necrotic. Torsion of the lobe caused strangulation of the vascular supply to the whole liver with consecutive portal vein thrombosis and complete hepatic ischemia. Resection of the necrotic accessory lobe and reconstruction of the vascular structures and the bile duct as well as portal vein thrombectomy were performed. At day two function continued to deteriorate. Doppler ultrasound showed decreased portal and arterial perfusion with necrosis of the liver. The patient was listed for high-urgency liver transplantation and received a liver graft from an ABO-compatible donor. Despite postoperative renal failure requiring temporary hemodialysis, the course was uneventful and the patient discharged with normal liver and kidney function on day 21 after transplantation.

Conclusions: Though rare, an accessory liver lobe may cause serious troubles and should therefore be kept in mind in patients presenting with acute abdominal pain.

P20.
Orthotopic Liver Transplantation for Acute Liver Failure: The Innsbruck Experience

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Background: Acute liver failure is a rare clinical syndrome associated with high mortality, approaching 70–80%. A number of conditions can cause a sudden severe liver dysfunction, which finally triggers a multiorgan response. Among these viral hepatitis, acetaminophen toxicity and idiosyncratic drug reactions are the most common.

Methods: From 1977 to July 2002 602 liver transplants were performed in 558 patients. Among these 16 (2.7%) were performed in 3 children and 13 adults (median age 16 years) for fulminant hepatic failure. The underlying causes were as follows: drug toxicity (n = 5), fulminant hepatitis (n = 4), acute Wilson's disease (n = 2), acute Budd-Chiari syndrome (n = 1), liver ischemia (n = 1), primary haemophagocytotic syndrome (n = 1), amanita falloides poisoning (n = 1) and carbon tetrachloride intoxication (n = 1). All patients were encephalopathic, 8 grade I or II and 8 grade III or IV. Four patients required ventilation and 6 renal replacement therapy.

Results: Fourteen fullsize liver transplants, 1 living related and 1 reduced size transplantat were performed. Two patients underwent retransplantation, one combined with kidney transplantation because of liver and renal failure after carbon tetrachloride intoxication on day 34 and another after embolization of hepatic artery because of an arteriobiliary fistula on day 65. Both patients developed aspergillus sepsis and died from multiorgan failure. A third patient with grad IV encephalopathy died on day 4 after transplantation from intracranial bleeding. The other 13 patients (81%) are alive and doing well.

Conclusions: Orthotopic liver transplantation was successfull in 13 of 16 patients (81%) with acute hepatic failure and represents the therapy of choice for this life-threatening condition.

P21.
Hepaticojejunostomy as Therapy of Biliary Complications after Liver Transplantation

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Background: Biliary tract complications are a major problem in liver transplantation and have been reported to occur with an incidence of up to 30%. Bile duct strictures or lithiasis can be treated by interventional therapy. Necrosis of the common bile duct, biliary leakage or disruption of the biliary anastomosis require a surgical therapy. In these cases, as well as in recurring bile duct strictures and lithiasis the conversion of the biliary anastomosis from choledocho-choledochostomy to a biliary enteric diversion might be the therapy of choice.

Methods: We conducted a retrospective analysis of 51 conversions from choledocho-choledochostomy to hepaticojejunostomy (HJS) in a series of 878 liver transplantations in a period of 15 years. Indications and timing of surgery in the therapy of biliary tract complications were analysed as well as the incidence and management of complications occurring postoperatively.

Results: From 1987 to 2001 787 patients underwent a total of 884 liver transplantations. In 51 patients (6.4%) conversion of the choledocho-choledochostomy to hepaticojejunostomy was performed in cases of bile duct strictures (n = 15), biliary sludge or concrements (n = 10), a combination of strictures and concrements (n = 17), biliary cast (n = 8), bile duct necrosis (n = 7), biliary leaks (n = 4). Mean age of the patients was 52 years (range: 2–68). These operations were performed after a mean time of 113 days (range: 1–3804) from transplantation. Biliary continuity was achieved in a functional side-side fashion in 23 cases and as functional side-end anastomosis in 28 patients. Biliary enteric anastomosis for acute indications (biliary leaks, and bile duct necrosis) was performed in 11 patients at a mean of 12 days after transplantation (range 2–99 days), 40 patients underwent electively planned hepaticojejunostomy at a mean of 176 days post transplant (range 11–3804 days) for bile duct strictures, biliary sludge and concrements or biliary cast. After a mean follow-up of 581 days after HJS 34 patients were still alive, 5 patients had been re-transplanted for biliary abscesses (n = 2) or chronic rejections (n = 3). Postoperative complications occurred in 13 patients (25%) with a higher incidence of complications after acute surgery (45%) compared to elective surgery (20%). Mortality at 30 days was 2%. In 64.7% of the patients undergoing hepatico-jejunostomy no more further interventions were needed.

Conclusions: Hepatico-jejunostomy is the treatment of choice in common bile duct necrosis or leakage as well as in recurring bile duct strictures and lithiasis. Uncertainty exits in which cases of biliary tract strictures or lithiasis a primary interventional therapy should be preferred to an surgical approach.

P22.
Woran denken Sie bei AFP 120.000 kU/l 3 Monate nach Leberresektion eines HCC? Ein Fallbericht eines Hepatitis-C-positiven LTX-Patienten

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Grundlagen: Im Rahmen einer Routineuntersuchung 1990 fallen bei dem Patienten A, männlich – 50 Jahre, erhöhte Leberwerte auf. Der Patient wird Leber biopsiert und die Diagnose Hepatitis C gestellt. Die Leber ist zirrhotisch umgebaut. In den folgenden Jahren wird der Herr A mit Interferon und Ribavirin therapiert, spricht jedoch nicht darauf an. Die Kontrollen zeigen keinen Hinweis auf ein malignes Geschehen. Im August 1998 werden zum ersten Mal erhöhte Tumormarker (AFP 292 kU/l) im Labor festgestellt und in der CT läßt sich eine 3 cm große, nur unscharf abgrenzbare fokale Parenchymläsion der Leber darstellen. Die anschließende Biopsie und histologische Auswertung beschreibt ein HCC.

Methodik: Im gleichen Monat wird eine intraoperative Kryotherapie der Läsion und eine Segment-III-Resektion der Leber durchgeführt. Der postoperative Verlauf gestaltet sich komplikationslos.

Ergebnisse: Im November wird Herr A mit Uretersteinen aufgenommen und dabei werden auch die Tumormarker kontrolliert. Es findet sich ein Anstieg des AFP in wenigen Tagen von 21.599 bis zu einem Maximalwert von 120.000 kU/l. Es besteht der dringende Verdacht eines Rezidives und die anschließende CT und MRT bestätigen diesen, indem eine hochgradige suspekte Raumforderung im Sinne eines Rezidives mit Lymphknotenvergrößerungen im Bereich der Porta hepatis beschrieben wird. Eine Lebertransplantation

wird auf Grund des fortgeschrittenen Stadiums der Tumorerkrankung nicht durchgeführt. Der Patient erhält anschließend eine Chemotherapie mit Doxorubicin (12 Zyklen über einen Zeitraum von 1 Jahr). Zusätzlich begibt sich Herr A in komplementärmedizinische Behandlung, bei der ihm Mikroimmuntherapeutika, immunstimulierende Enzym- und homöopathische Präparate verabreicht werden.

Schlußfolgerungen: Im November 2000 wird der Patient erneut in der Transplantationsambulanz vorstellig. Das AFP befindet sich im Normbereich; es finden sich in der CT 3 verdächtige Herde (Seg. VII/VIII, IV+II), die alle bioptisch nur narbig fibrosiertes Lebergewebe ohne Hinweis auf Malignität zeigen. Der Patient wird am 29. 3. 2001 auf Grund seiner fortgeschrittenen Hepatitis-C-bedingten Lebererkrankung transplantiert. In der explantierten Leber finden sich keine neoplastischen oder dysplastischen Veränderungen. Der postoperative Verlauf gestaltet sich komplikationslos. Der Patient steht derzeit wegen eines Hepatitis-C-Rezidives unter Therapie mit Interferon und Ribavirin.

P23.
Rare Cause of Renal Failure after Liver Transplantation due to Mushroom Poisoning

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Background: Amanitine, the toxin of Amanita phalloides, is taken up by hepatocytes and interferes with messenger RNA synthesis, suppressing protein synthesis and facultatively resulting in liver failure. Orellanine, the toxin of Cortinarius orellanus, attacks the proximal tubular cells leading to interstitial nephritis and renal failure (RF). Both are extremly heat resistent. A 55-years old man picked, cooked and ate some mushrooms. 7 hours later he developed colicky abdominal pain, diarrhoea and vomiting.

Methods: Gastric lavage was performed and the diagnosis of mushroom poisoning was confirmed by identification of typical fungal spores in the gastric juice by a toxicologist. Both A. phalloides and C. orellanus spores were found. Hemoperfusion and administration of silibinin and N-acetyl-cysteine were started. On the 3rd day after ingestion the laboratory findings included an asparate aminotransferase 1610 U/l, alanine aminotransferase 3090 U/l, lactate 10 mmol/l and prothrombin activity 5%. He developed oliguric RF, and encephalopathy. The patient was transferred to transplant ICU and listed for urgent liver transplantation (OLT). An orthotopic OLT was performed on 4th day. However, RF did not resolve and the patient remained anuric.

Results: After 34 days of renal replacement therapy (RRT) provided by continuous hamodiafiltration the creatinine declined from 3.25 to 1.66 mg/dl, blood urin nitrogen from 109 to 48 mg/dl and urin output increased from 0 to 2500 ml/d. However, creatinine clearance remained (22 ml/min) low. 4 months after discharge from the hospital the patient did not require RRT and his renal function is still sufficient (crea 0.8 mg/dl, BUN 30 mg/dl). Additionally FK 506 is often cause of RF after OLT, but the plasma level of FK 506 never reached levels considered to be toxic.

Conclusions: Use of hemoperfusion may be effective in treatment of A. phalloides poisoning removing the toxins not yet taken up by hepatocytes. Orellanine is dialyzable only 24 h after ingestion of mushroom, thus any RRT later is not effective to prevent RF because the toxin is already bound to renal tubular cells. Nevertheless some previous studies showed a positive impact of hemoperfusion on outcome in both A. phalloides and C. orellanus poisoning when started shortly after mushroom intoxication. We believe that the early begin of hemoperfusion saved the patient from chronic RF commonly seen after C. orellanus poisoning. Early diagnosis and prompt commencement of hemoperfusion treatment may help to avoid severe long-term complications of RF in patients with A. phalloides and C. orellanus poisoning. Poisoning with C. orellanus should be considered as a rare cause of RF after OLT due to mixed mushroom intoxication.

P24.
Langzeitergebnisse der Mycophenolat-Mofetil-Rescuetherapie bei Calzineurin-Inhibitor-induzierter Nephropathie

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Grundlagen: Der Langzeitverlauf nach Lebertransplantation (LT) wird im wesentlichen durch die Nebenwirkungen der Immunosuppression, im speziellen der Calzineurin Inhibitoren (CI), FK506 und Cyclosporin A (CyA) bestimmt. In Vordergrund steht hierbei die Nephropathie. Einige Publikationen zeigten eine Verbesserung der Nierenfunktion nach Dosisreduktion oder Ersatz von CI durch Mycophenolat Mofetil (MMF), allerdings ist nur wenig über den Langzeiteffekt bekannt. In dieser Studie präsentieren wir erstmals Langzeitergebnisse von LT Patienten mit CI-induzierter Nephropathie, welche über einen Zeitraum von durchschnittlich 4,8 Jahren (3,1–6,0 Jahren) beobachtet wurden.

Methodik: In dieser Studie wurde bei 32 Patienten (m: 22/f: 10; Alter: mean 57 a; 33–74 a) wegen erhöhter renaler Retentionsparameter die Dosis der CI reduziert (25 mit CyA; 7 mit FK) und mit MMF in einer Dosis von 2 g/d durchschnittlich 25,6 Monaten post LT begonnen. Bei 14 Patienten (m: 13/f: 1) wurde innerhalb der ersten 6 Monate nach OLT(*early switch*), bei 18 Patienten (m: 9/f: 9) nach 6 Monaten (*late switch*) auf MMF umgestellt. Die Dosis von CyA und FK506 wurde im Schnitt um rund 2/3 reduziert, bei 9 Patienten (7 CyA, 2 FK506) abgesetzt. Ursache für die LT war eine HBV/HCV-(11), eine autoimmune Zirrhose (2), eine PBC (2), Hämochromatose (4), eine Fettleber (2) und eine kryptogene Lebererkrankung (4). In 2 Fälle lag ein CCC, in 4 ein HCC und in einem Fall Lebermetastasen eines neuroendocrinen Tumors vor.

Ergebnisse: Kreatininwerte verbesserten sich in der Gesamtgruppe von durchschnittlich 2,63 auf 1,53 ($p < 0,01$). In der *early switch* Gruppe zeigte sich, daß Kreatinin von 2,77 (1,96–6,62) auf 1,55 (1,22–1,76) [$p < 0,001$] und in der *late switch* Gruppe von 2,36 (1,99–3,1) auf 1,54 (1,38–1,74) [$p < 0,01$] reduziert werden konnte. Während in der *early switch* Gruppe 8 Patienten (57%) eine Normalisierung der Nierenfunktion zeigten, konnte dies in der *late switch* Gruppe nur bei 4 Patienten (22%) erreicht werden. Zu einer dialysepflichtigen Niereninsuffizienz kam es in der *early switch* Gruppe bei einem Patienten (mit zusätzlicher diabetischen Nephropathie), in der *late switch* Gruppe bei zwei Patienten (einer mit histologisch verifizierter IgA-Nephropathie). MMF wurde gut vertragen, nur in vereinzelten Fällen war auf Grund von Nebenwirkungen eine Dosisreduktion erforderlich. Es kam zu keinen Abstoßungsreaktionen. Insgesamt starben 4 Patienten, einer an Sepsis, einer an einem Tumorrezidiv und zwei wegen cardiogener Ursachen.

Schlußfolgerungen: Zusammenfassend zeigt diese Studie, daß bei Patienten mit einer CI-induzierten Nephropathie mittels Konversion auf MMF mit gleichzeitiger Reduktion der CI eine signifikante Verbesserung der Nierenfunktionsparameter erreicht wird. Dieser Effekt bleibt auch im Langzeitverlauf bestehen. Eine Normalisierung der Nierenfunktionsparameter konnte vor allem bei frühzeitigem Beginn einer MMF-Rescuetherapie erreicht werden.

P25.
Sirolimus in Kombination mit Mycophenolat Mofetil nach Lebertransplantation

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Grundlagen: Sirolimus (SRL) ist ein neu eingeführter immunsuppressiver Wirkstoff, der sich klinisch in der Vorbeugung von Abstoßungen nach Nierentransplantationen bereits als effektiv erwiesen hat. Wir präsentieren eine retrospektive Studie zur Evaluierung von SRL statt Calcineurininhibitoren in Kombination mit Mycophenolat Mofetil (MMF) als Immunsuppression bei Patienten nach Lebertransplantation (LTX).

Methodik: Von Juli 2001 bis Juli 2002 wurden 10 Patienten nach LTX (4 Frauen, 59 [41–66] Jahre alt) auf SRL umgestellt. Indikationen zur LTX waren Hepatitis B und/oder C (5), alkoholische Zirrhose (4) und Morbus Wilson (1). Die Umstellung auf SRL erfolgte 86 (37–118) Monate nach LTX. Bei einem Patienten wurde die immunsuppressive Therapie mit SRL am 3. postoperativen Tag begonnen. Indikationen für den Wechsel von Cyclosporin A oder Tacrolimus auf SRL waren Funktionsstörungen der Niere (9) oder neurologische Störungen (1). Die Immunsuppression setzte sich aus SRL mit einem Talblutspiegel von 4 bis 10 ng/ml und MMF mit einem Zielblutspiegel von 1 bis 5 g/ml zusammen. Der durchschnittliche Beobachtungszeitraum unter SRL-Therapie lag bei 261 (26–311) Tagen.

Ergebnisse: Patienten- und Transplantatüberleben waren 100%. Es traten keine Abstoßungsepisoden und keine Infektionen auf. Eine Verbesserung der Nierenfunktion konnte bei 8 von 9 Patienten mit Nierenfunktionsstörungen (88,8%) nachgewiesen werden. Bei dem Patienten mit neurologischen Störungen waren die Symptome regredient und die Nierenfunktion verbesserte sich. Nebenwirkungen (Exanthem, Hypertriglyzeridämie, Hypercholesterinämie) traten bei 3 Patienten (33,3%) auf. Bei 2 Patienten mußte das Medikament abgesetzt werden (Exanthem 1, Hypertriglyzeridämie 1).

Schlußfolgerungen: Die Kombination aus SRL und MMF bietet eine ausreichende Immunsuppression nach LTX. Nebenwirkungen sind mit Dosisreduktion oder Absetzen der Therapie reversibel. SRL stellt eine Therapiemöglichkeit für Patienten mit Nebenwirkungen durch Calcineurininhibitoren dar. Eine maßgeschneiderte immunsuppressive Therapie für Patienten nach LTX mit eingeschränkter Nierenfunktion und neurologischen Störungen wird ermöglicht.

P26.
4 Monate C-2-Monitoring im Ambulanzbereich, Organisation und praktische Erfahrungen bei lebertransplatierten Patienten

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Grundlagen: Seit mehreren Jahren werden die C-0-Talspiegel im Vollblut zur Überwachung der medikamentösen Therapie mit Cyclosporin verwendet, obgleich nie eine Korrelation zwischen Talspiegel und Abstoßung bzw. Toxizitätszeichen nachgewiesen werden konnte. Nach Literatur korrelieren C-2-Spiegel sehr gut mit der „Area under the curve" (AUC) und damit mit Abstoßung und Toxizität. Im stationären Bereich wurde das C-2-Monitoring bereits implementiert, seit Mai 2002 wurde nun auch im ambulanten Bereich für alle Neoral einnehmenden Patienten die C-2-Messung übernommen.

Methodik: Es wurde ein Informationsblatt für die Patienten erstellt, welches vom Leitstellenpersonal allen Patienten die Neoral einnehmen gegeben wird, worauf der komplette Ablauf des C-2-Monitorings dargestellt ist. Ein eigens dafür abgestellter Mitarbeiter koordiniert die Blutabnahmen der Patienten: Der Patient registriert bei der Leitstelle, nimmt seine Morgendosis an Neoral und folgt dem Routineablauf im Ambulanzbereich. Nach 2 Stunden kommt der Patient nun entweder von selbst oder aufgerufen zur Blutabnahme wo nun außer dem Medikamentenspiegel die gesamte Blutabnahme erfolgt und der Patient nur einmal gestochen werden muß. Danach ist für den Patienten der Ambulanzbesuch meist erledigt, und er bekommt alle für ihn wichtigen Daten und Mitteilungen mittels Briefsendung nach Hause zugesandt. Die Genaue Protokollierung erfolgt mittels Laptop, worauf alle zu monitierenden Patienten eigens erfaßt werden und in weiterer Folge die Auswertung erfolgen kann. Zielwert nach LTX in den ersten 3 Monaten 1000 ng/ml ± 200 ng/ml, vom 3.–6. Monat nach LTX 800 ng/ml ± 200 ng/ml, und ab dem 7. Monat 600 ng/ml ± 200 ng/ml. In der Analyse wird zwischen neu transplantierten Patienten (NP) und Patienten unterschieden, deren LT schon länger zurückliegt (AP).

Ergebnisse: Bis heute wurden 86 Patienten in der LTX-Ambulanz C-2-monitiert, 21 sind direkt von der Station (NP) übernommen worden, 65 (AP) sind ambulant umgestellt worden. 19 von 21 NP (= 90,4%) waren sofort im gewünschten Spiegelbereich. Alle AP wurden doppelt monitiert (C-0 + C-2): 34AP (= 52,3%) erreichten nicht den Zielwert und zeigten im mittel einen C2-Spiegel, der 50 ± 13% unter der Sollwertuntergrenze lag; eine Dosisanpassung bei AP erfolgte vorerst nicht. Aus dieser Differenz kann in Zukunft möglicherweise ein neuer Zielbereich empirisch erarbeitet werden.

Schlußfolgerungen: Die Durchführbarkeit des C-2-Monitoring in der LTX-Ambulanz wurde nun dank der sehr guten Zusammenarbeit von Pflegepersonal und C2-Team bewiesen. In der LTX-Ambulanz werden im Schnitt 20 Neoral-Patienten pro LTX-Ambulanz C-2-monitiert, wobei eine Zahl bis zu 80 Patienten pro „Monitor" vorstellbar wäre. Hier ist jedoch eine sehr aktive Mitarbeit der Patienten notwendig, welche das Medikament schon 1 Stunde vor dem Eintreffen in der Ambulanz einnehmen müssen. Nach der Einlaufphase in der LTX-Ambulanz wurde diese Art von den Patienten, die regelmäßig in die Ambulanz kommen, voll akzeptiert. In weiterer Folge kann diese Mitteilung der Einnahme auch auf den Patientenbrief vermerkt werden, so das alle Patienten die Neoraldosis schon eine Stunde vor dem Eintreffen in der Ambulanz einnehmen können.

P27.
Effects of Treatment for Osteoporosis after Orthotopic Liver Transplantation

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Background: Bone disease is a common problem in orthotopic liver transplant (OLT) patients. The cause is multifactorial, however, two main issues have been discussed: (a) endogenous hepatic osteopathy due to calcium malabsorption, hypogonadism and cholestasis and (b) exogenous causes such as immunosuppression, in particular corticosteroids. Several authors have recently described a massive loss in bone mineral density (BMD) after OLT, especially within the first 4 months, in the majority of patients. Furthermore, a fracture incidence of 24–65% has been reported. In this study we evaluated the efficacy of either biphosphonates or calcium/vitamin D3 supplementation on the natural course of osteoporosis after OLT.

Methods: We conducted a prospective study enrolling 58 patients (44 m, 14 f; mean age: 55 ys.) who underwent OLT in our center. Fourty-four patients received alendronate 10 mg qd (group Al) and 14 calcium/vitamin D3 (group CvitD) immediately after OLT. BMD was measured 4 months (median) preoperatively and 4 months and one year, respectively, following OLT. A placebo control group was not included, as the occurrence of osteoporosis after transplantation is well documented. Statistical analyses were done using SPSS. For statistical significance Chi Square test, the student's t test, ANOVA and the Kruskal-Wallis-Test, depending whether the parameters were equally distributed or not, were used.

Results: Patients treated with either alendronate or calcium/vitamin D3 showed a stable BMD 4 months after OLT compared to pre OLT values. Group Al gained 1%, group CvitD lost 0.6% (mean) of BMD in the lumbar spine, which was not statistically significant. In the femoral neck, group Al gained significantly more BMD in the first 4 months after OLT than group CvitD ($p = 0.002$). Patients treated with cyclosporin A gained markedly more BMD than patients on other immunosuppressants ($p = 0.024$). Thirty seven patients had a further follow up BMD one year after OLT. There was no significant difference between group Al and group CvitD concerning BMD in the femoral neck and the lumbar spine. A 5.4% gain of BMD could be seen within the first year in both groups. Pathological fractures were rarely diagnosed, only 3 patients showed a fracture after OLT: 7 patients already had a pathological fracture before OLT but had no deterioration afterwards.

Conclusions: In conclusion, we are able to demonstrate that consequent osteoporosis therapy can prevent the naturally occurring bone loss in the first year after OLT. Therefore, it seems to be useful to treat patients with biphosphonates or alternatively with calcium and vitamin D after OLT.

P28.
Lebensqualität nach Lebertransplantation

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Grundlagen: Seit 1972 bis Dezember 2001 wurde am Wiener AKH an 851 Patienten eine Erst-Lebertransplantation durchgeführt. Die Einjahresüberlebensrate liegt bei ca 80%. Ziel der Studie war es, die Lebensqualität der transplantierten Patienten und ihre Lebenssituation vor und nach der Transplantation zu untersuchen. Wie haben sie die LTX erlebt und konnten sie in ihr früheres Berufsleben zurückkehren? Spielt die private Lebenssituation (Kinder/Lebenspartner) im Heilungsprozeß eine Rolle? Wie haben sich ihre Lebensgewohnheiten verändert. Und vor allem, wie ist ihre Lebensqualität heute?

Methodik: An 301 im Dezember 2001 noch lebende lebertransplantierte Patienten (188 Männer/113 Frauen im Alter zwischen 22 und 79 Jahren) wurden anonyme Fragebögen verschickt (n = 301). Die Patienten wurden anhand von 23 Fragen über Diagnose, Wartezeit auf die TX, familiäres Umfeld, Beruf, Wiedereinstieg ins Berufsleben, private Aktivitäten vor und nach der TX sowie Alkoholkonsum und Medikation befragt. Sie wurden auch gebeten anhand eines Schulnotensystems ihre Lebensqualität vor und nach der TX zu bewerten (1 – sehr gut; 5 – schlecht). Die befragten Patienten hatten überdies noch die Möglichkeit zu einer persönlichen Stellungnahme.

Ergebnisse: Drei Wochen nach der Aussendung der Fragebögen wurden 174 (von n = 301; entspricht 57,8%) retourniert (155 beantwortete Fragebögen, 19 als unzustellbar). Die Befragung ergab, daß das Durchschnittsalter der Patienten bei der Transplantation bei 50,6 Jahren lag (jüngster Patient 18, ältester 68 Jahre). 48 Personen, entspricht 31% (davon 24 über 60 Jahre) waren zum Zeitpunkt der Transplantation schon in Pension (jüngster Pensionist 38 Jahre). 125 Patienten hatten einen Partner, der bei 120 Patienten eine große Hilfe während der Zeit der Transplantation war. 40 Patienten (25,8%) von den 155 Befragten sind wieder ins Berufsleben zurückgekehrt, aber nur 26 Personen (16,8%) davon bekleideten die gleiche Position wie vor dem Eingriff. Durchschnittlich traten diese Patienten nach 5,4 Monaten wieder in das Berufsleben ein. 22 lebertransplantierte Patienten (14,2%) arbeiten auch heute noch. Insgesamt 65 Patienten (41,9%) betreiben heute zwischen 1 bis mehr als 3mal pro Woche Sport Die Lebensqualität wurde von den Patienten vor der Transplantation als durchschnittlich mit der Note 4 bewertet (Schulnotensystem 1 – sehr gut, 5 – schlecht), nach der Transplantation war die Bewertung der Lebensqualität durchschnittlich 1,7.

Schlußfolgerungen: Grundsätzlich hat sich nach der Bewertung der Patienten die Lebensqualität für den einzelnen signifikant verbessert. Die Beschwerden vor der Tansplantation, wie z. B. Aszites, Müdigkeit, Appetitlosigkeit und Juckreiz wichen einem stark verbesserten Allgemeinzustand. Erstaunlich ist in diesem Zusammenhang, daß 25,8% der transplantierten Patienten wieder ins Berufsleben zurückkehrten, aber nur 16,8% (von 155) wieder die gleiche Position in ihrem angestammten Beruf besetzten wie vorher.

HERZ/LUNGE

P29.
The Impact of Induction Therapy and the Donor Specific Crossmatch on Outcome after Heart Transplantation

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Background: HLA matching is associated with better graft survival in renal transplantation. Its role in cardiac transplantation (Tx) is still unclear. Nothing is known about the potential impact of induction therapy on outcome of well vs. poorly HLA matched cardiac recipients. The combined effect of histocompatibility and type of induction was analysed to determine their influence on graft survival, incidence of rejection and severe graft sclerosis in patients who underwent cardiac Tx in our centre.

Methods: Donor HLA crossmatching was performed for 849 cardiac Tx. Completed data for HLA-A, -B and -DR mismatches exist for 623 patients. Postoperative management consists of induction therapy and triple immunosupression with calcineurin inhibitors, azathioprine or MMF and corticosteroids. 593 patients, collected in Group 1, were treated with thymoglobuline and other 256 recipients (Group 2) with different poly- (ATG Fresenius, ATGAM) or monoclonal (OKT-3, BT563) antibodies.

Results: The cohort had a mean number of 5.03 ± 0.93 (5) HLA mismatches. The distribution of mismatches (MM) to different HLA loci was as follow:
1. HLA-A: 0 MM – 7%, 1 MM – 35%, 2 MM – 58%;
2. HLA-B: 0 MM – 1%, 1 MM – 16%, 2 MM – 83%;
3. HLA-DR: 0 MM – 3%, 1 MM – 23%, 2 MM – 74%.

Statistical analysis demonstrates significantly better results for the Group 1 in: overall survival for HLA-A zero-MM ($p = 0.0011$), HLA-A 2-MM ($p = 0.02$), HLA-B 2-MM ($p = 0.002$), HLA-DR 2-MM ($p = 0.03$); freedom from severe graft sclerosis for HLA-B 2-MM ($p = 0.04$); freedom from clinical rejection for HLA-A 1-MM ($p = 0.03$), HLA-A 2-MM ($p = 0.0001$), HLA-B 1-MM ($p = 0.037$), HLA-B 2-MM ($p < 0.0001$), HLA-DR 1-MM ($p = 0.0005$), HLA-DR 2-MM ($p < 0.0001$).

Conclusions: Our experience demonstrates considerable positive impact of induction therapy with thymoglobuline compared with another types of induction on outcome, degree of acute and chronic rejection after heart transplantation despite of HLA-mismatch.

P30.
Long-Term Follow-Up of Three Prospective Randomized Trials Comparing Different Antibody Induction Protocols

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Background: Short-term data from randomised trials have shown significant differences in outcome between various antibody induction therapies. The purpose of this study was to investigate potential long-term influences of different antibody induction treatments.

Methods: Patients who underwent three different prospective randomised trials conducted between 1987–1992 were included in this analysis. A total of 222 patients (OKT3 n = 30, Fresenius-ATG (F-ATG) n = 88, thymoglobuline (THG) n = 77 and BT563 n = 27) were analysed for survival, incidences of rejection, infection, cancer, graftsclerosis and adverse events. Results were computed by Kaplan-Meier estimate and compared by log rank test.

Results: Overall survival was borderline significantly different between all groups (OKT3: 52.4%, F-ATG: 44.3%, THG: 67.5% and BT563: 51.8%; $p = 0.095$). Causes of death were different between the four groups. OKT3 treated patients had the highest rate of death from graftsclerosis (40%) and BT 563 the highest rate in death from acute rejection (23%). In the THG group there was the lowest incidence of acute rejections (57.3%, 29.5%, 18% and 50%; $p = 0.002$). There was no difference in overall freedom from severe infections (90.5%, 81.8%, 92.4% and 88.9%; $p = 0.232$) and CMV-disease (80.9%, 79.6%, 83.6% and 77.8%; $p = 0.822$). The incidence of cancer was similar in all groups (14.3%, 22.8%, 11.7% and 11.1%; $p = 0.146$), whereas there was a clear trend of lower incidence of graftsclerosis in THG treated patients (52.2%, 38.0%, 25.7% and 41.2%; $p = 0.053$).

Conclusions: Different Antibody induction protocols seem to be dissimilar in their immunmodulating function. Although all three studies were powered to detect differences in early rejection, long-term data show different incidence of development of graftsclerosis and on survival. Long-term adverse events were comparable and tolerable. These data clearly show that early immunmodulating influence of induction antibodies have long-range effects on the immune system.