

(log rank = 0.02). 10% of patients who had tacrolimus developed NODM compared to 3.1% of cyclosporine group. Univariate analysis identified mean prednisolone, cyclosporine, and tacrolimus dose, number of rejection episodes and graft failure as important. Multivariate analysis revealed age, graft failure, number of rejection episodes and tacrolimus as independent risk factors.

**Conclusion.** NODM adversely affects graft survival while patient survival was not affected. Tacrolimus and number of rejection episodes (probably a surrogate marker for bolus steroid doses) play major role in the pathogenesis of NODM. Our study did not reveal any significant relationship between HCV and NODM.

### P23.42 PENTOXIFYLLINE INHIBITS TUMOR NECROSIS FACTOR ALPHA GENE TRANSCRIPTION FOLLOWING LIVER ISCHEMIA-REPERFUSION

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**Background.** Pentoxifylline (PTX) has been shown to reduce liver injury after normothermic ischemia and reperfusion (I-R).

**Aim.** The aim of this study was to evaluate the effects of PTX on tumor necrosis factor-alpha (TNF-alpha) gene transcription following normothermic liver I-R. **Materials and Methods.** A segmental normothermic ischemia of the liver was induced by occluding the blood vessels including the bile duct to the median and left lateral lobes for 90 min. At the end of ischemia the nonischemic liver lobes were resected. Rats were divided into three groups: group 1, control Ringer's lactate administration; group 2, PTX treatment; group 3, sham-operated control rats. PTX (50 mg/Kg) was injected intravenously 30 min before and 60 min after induction of ischemia. Survival rates were compared and the serum activities of TNF-alpha, AST, and ALT were measured. Histology of the liver was assessed 6 h after reperfusion. Liver TNF-alpha-mRNA was assessed by PCR amplification at 0, 120, and 270 min after reperfusion.

**Results.** PTX treatment significantly increased 7-day survival (93.3%) compared with non-treated control rats (46.6%,  $P < 0.007$ ). The extent of liver necrosis and the release of liver enzymes were significantly decreased after PTX treatment. Serum activities of TNF-alpha were significantly decreased and liver expression of TNF-alpha-mRNA was inhibited after PTX treatment.

**Conclusion.** PTX protects liver from ischemic injury by inhibition of TNF-alpha gene transcription.

### P23.43 POSITIVE IMPLICATION OF APPLYING EXTENDED DONOR CRITERIA IN LIVER TRANSPLANTATION

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**Background.** Organ shortage has driven many transplant programs to extend their criteria to accept donors, and graft allocation policies have been modified accordingly.

**Objective.** To analyze the effect of extended donor criteria (EDC) on both graft and patient survival, and to propose a strategy to prioritize recipients who benefit from such grafts.

**Methods.** Prospectively collected data from all consecutive cadaveric liver transplantations (LT) between December 2001 and December 2004 at the University of Heidelberg were analyzed. The EDC included ventilation >7 days, ALT or AST >3 × normal, bilirubin >3 mg/dL, anti HBe or HBs Ag positivity, donor age >65 years, steatosis >40%, BMI >30, cold ischemia time >14 hours, Na >165 mmol/L, history of extrahepatic malignancy, and previous drug abuse. Variables include recipients' demographics, indication for LT, waiting time, urgency, MELD score. Outcome has been focused on early and late graft survival, patient survival, retransplantation, ICU/IMC stay, duration of ventilation, complications, and post-transplant laboratory findings.

**Results.** One hundred and ninety two grafts were used for 165 primary, 23 secondary, and 4 tertiary LT. Up to three EDC were present in 55% of all grafts. Twenty-four livers were transplanted after rescue allocation to HU (8%), T2 (17%), and T3 (75%) patients. Almost 90% of these T3-listed recipients had hepatocellular carcinoma (HCC), who would otherwise have had a much longer waiting time. Both uni- and multivariate analysis revealed that EDC had no impact on outcome. The recipient age (<55 vs. ≥55 years) was the only independent prognostic factor for survival ( $p = 0.02$ ), regardless of EDC.

**Conclusion.** The use of grafts with EDC is safe. Rescue-allocated livers meet the need of HCC patients for a timely transplantation. Further, the recipients' age is an independent factor for survival after transplantation.

### P23.44 PRELIMINARY RESULTS OF LIVING RELATED LIVER TRANSPLANTATION IN 19 CASES: MANSOURA EXPERIENCE

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**Background.** Living related liver transplantation is gaining acceptance in Egypt and is the only hope for end stage liver disease.

**Aim.** To show our experience in living related liver transplantation.

**Methods.** From May 2004 to February 2006, 19 cases of living related liver transplantation using the right lobe have been done. All cases were adults mean age 48 years, m/f ratio 16/3, 16 hcv cirrhosis, 2 hcc and one case Budd-Chiari syndrome.

**Results.** One year survival is 88%, no mortality in donors, 4 donors had bile leak: one case necessitates exploration, 5 cases collection and one case internal haemorrhage. In the recipient, we have 2 hospital mortality and one mortality at 6 months. Complications included: recurrent c and acute cellular rejection in 7 cases, vascular in 3 cases, biliary in 3 cases and internal hge in one case.

**Conclusion.** Living related liver transplantation is a good treatment of end stage liver disease in countries like Egypt but with more cost and needs more skills and training.

### P23.45 PRE-LIVER TRANSPLANT LOCOREGIONAL ADJUVANT THERAPY FOR HEPATOCELLULAR CARCINOMA (HCC) AS A STRATEGY TO IMPROVE LONG-TERM SURVIVAL

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**Background.** Pre-orthotopic liver transplant locoregional therapy (POLT) for HCC reduces drop-out rates while awaiting orthotopic liver transplant (OLT).

**Aim.** The aim was to investigate whether POLT improved long-term survival. We also reviewed our experience with OLT for HCC and correlated pre-OLT radiological staging with explant pathology.

**Methods.** A retrospective analysis of prospectively collected data identified 105 patients with HCC that underwent OLT between April 1985 and Feb 2006. 49 received POLT as transarterial chemoembolization, radio-frequency ablation, percutaneous ethanol injection or a combination.

**Results.** The 1-, 3-, and 5-yr survival, regardless of POLT, was 83.7%, 75.3%, and 68.6%, respectively; with a median survival of 117 months. Demographic data and waiting time were similar between POLT and untreated groups. Pre-OLT radiological stage was similar (POLT:  $2.29 \pm 0.86$  vs  $2.33 \pm 0.91$ ;  $p = 0.76$ ). At the time of transplant, POLT group had significant tumor downstaging ( $1.27 \pm 0.97$  vs Untreated:  $2.52 \pm 1.23$ ;  $p = 0.006$ ). POLT group had better 5-yr survival (84.9% vs 54.8%;  $p = 0.02$ ). Further, POLT was associated with a trend towards lower disease recurrence (12.2% vs 18.9%  $p = 0.33$ ). Eighteen POLT patients revealed no viable tumor cells on explant pathology (pT0). Radiological stage for these patients was T1 = 6, T2 = 10 and T3 = 2. No pT0 patients developed recurrence and all had significantly better long-term survival than untreated patients. Correlation pattern of pre-OLT radiological stage at listing with explant pathology distinctly varied (Accurate: POLT 24.5%, Untreated 56.0%; Underestimated: POLT 18.4%, Untreated 34.6%; Overestimated: POLT 57.1%, Untreated 9.4%;  $p = 0.03$ ).

**Conclusions.** OLT is a viable treatment option for primary HCC. POLT significantly downstages the primary tumor and improves long-term survival in patients with advanced disease. Pre-OLT imaging has low correlation with explant pathology that may be due to tumor down-staging with POLT or net tumor growth in the untreated group.

### P23.46 PROLONGED ANHEPATIC STATE AFTER EARLY LIVER GRAFT REMOVAL

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Two-stage liver transplantation, i.e. salvage emergent total hepatectomy with prolonged anhepatic state, and subsequent liver transplantation, has been described in the late 80's as a mean to stabilize some patients with fulminant hepatic failure, primary non-function after liver transplantation, or

massive hepatic trauma. The principal drawback of two-stage liver transplantation is the fact that anhepatic patient survival only depends on the future availability of a liver graft. The pathophysiologic alterations induced by total hepatectomy are not fully known, as it is not known how long a patient may be anhepatic before it is too late for hope of survival. In this report the authors describe the cases of four liver recipients who had to undergo salvage liver graft removal early during or after liver transplantation as a life-saving maneuver. All were afterwards registered for emergent liver retransplantation. Mean anhepatic period was 30 hours (Range: 17–60 hours). Two patients survived and fully recovered. From this experience and from other cases reported in the literature, the authors concluded that long (> 24 hours) anhepatic phase is compatible with survival without neurologic impairment.

**P23.47**  
**RECURRENCE AFTER SURGICAL TREATMENT OF HEPATOCELLULAR CARCINOMA: 13-YEAR OUTCOMES FROM A SINGLE CENTER**

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The natural history, treatment, and outcome after recurrence of hepatocellular carcinoma (HCC) following liver transplantation (LT) or resection (LR) is unknown.

**Methods.** 120 patients who developed recurrence after surgical therapy for HCC in 347 consecutive patients (LT = 155, LR = 192) from 09/1991 to 09/2004 were analyzed. Patients who underwent ablation or alone during this time period were not included. Characteristics of initial tumor, follow-up and management of recurrences were analyzed. Overall survival from initial procedure (OS) and survival after recurrence (RS) were the primary endpoints and variables were then tested for their prognostic significance with univariate and multivariate analysis.

**Results.** OS at 1, 3, and 5 years for all patients was better following LT (87, 74 and 65%) compared to LR (85, 68 and 53%) ( $p = 0.01$ ). 120 patients (35%) developed recurrence (LR:  $n = 98$ , 51%; LT:  $n = 22$ , 14%) with a median time to recurrence of 12.6 months following LR and 16.3 months after LT and a subsequent worse OS in both groups ( $p < 0.001$  respectively). Of the 98 patients who developed tumor recurrence following LR, 86 (86%) were confined to the liver. 53 (54%) underwent additional therapy (11 re-resection, 31 ablation, 8 TACE, 3 LT) with a median RS of 22 months. Multivariate analysis revealed that lack of pathological vascular invasion, time to recurrence > 12 months and additional therapy after recurrence was independently associated with longer OS after LR. In contrast, recurrences after LT presented with disseminated disease (73%); most were too sick for additional treatment and median RS was only 3 months ( $p < 0.001$  compared to resection).

**Conclusions.** If locally advanced, recurrences of HCC after surgery should be treated with multimodality therapy, if possible. Although the recurrence rate after LT is much less than LR, recurrences after LT have much poorer prognosis and rapid progression, independent of the stage of disease at the time of presentation.

**P23.48**  
**RESULTS OF INFERIOR VENA CAVA CROSS-CLAMPING IN LIVER TRANSPLANTATION BY PIGGYBACK TECHNIQUE**

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**Background.** Piggyback is orthotopic liver transplantation (OLT) technique where inferior vena cava (IVC) is preserved avoiding its cross-clamping. Nevertheless IVC can be temporally occluded in cases of hemorrhage.

**Aim.** To compare pre-operative liver function, intra operative aspects, immediate postoperative evolution, and graft and patient survival among patients submitted to OLT by piggyback technique with and without IVC clamping.

**Methods.** One hundred thirty-five OLT performed from January 2002 to September 2005 were evaluated. We evaluated 84 OLT with deceased donors performed in 84 patients with diagnosis of cirrhosis. They were divided in 2 groups; group 1 (G1): 60 cases without IVC clamping, and group 2 (G2): 24 with IVC clamping. IVC was occluded from the end of hepatectomy to the end of caval anastomosis, when the clamp was relocated. No extracorporeal venovenous bypass was utilized.

**Results.** Both groups were similar in mean age, gender, etiology, MELD and Child-Pugh scores, and donor nature (Briceno criteria). Mean time of IVC occlusion was  $60.2 \pm 11$  min. A significant reduction in G2 total hepatectomy time compared to G1 was observed ( $163.2 \pm 74.8$  min vs  $194.3 \pm 61.8$  min,  $p = 0.045$ ). The number of red blood cell packets transfused was significant higher in G1 compared to G2 ( $4.7 \pm 4.1$  units vs  $2.6 \pm 2.3$  units,  $p = 0.028$ ). No difference was observed between G1 and G2 in AST postoperative peak ( $1981 \pm 229$  U/L vs  $2825 \pm 439$  U/L,  $p = 0.3$ ), creatinine ( $1.4 \pm 1.0$  mg/dl vs  $1.8 \pm 1.5$  mg/dl,  $p = 0.23$ ), postoperative hemodialysis (3,3% vs 8,3%,  $p = 0.3$ ). There was no significant difference between G1 and G2 one year graft survival (76% vs 71%) and patient survival (91% vs 83%).

**Conclusion.** Inferior vena cava cross-clamping can be safely applied during liver transplantation by piggyback technique. This procedure can also avoid major surgical bleeding in some situations.

**P23.49**  
**RHO-ASSOCIATED KINASE INHIBITOR REDUCES TUMOR RECURRENCE AFTER LIVER TRANSPLANTATION IN RAT HEPATOCELLULAR CARCINOMA MODEL**

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**Background.** Calcineurin inhibitor cyclosporine itself promotes the invasiveness and metastasis of tumor cell by increasing cancer-cell motility independent of host immunity, but it remains unresolved whether calcineurin inhibitor tacrolimus itself promotes the invasiveness and metastasis of tumor cell or not. The small GTPase Rho/Rho-associated kinase (ROCK) pathway plays an important role in motility and invasion of tumor cell.

**Aims.** We examined the effect of tacrolimus on rat hepatocellular carcinoma cell invasion and whether tacrolimus activated the Rho/ROCK signal pathway. Furthermore, we investigated whether ROCK inhibitor Y-27632 suppressed tumor recurrence after experimental liver transplantation in rat hepatocellular carcinoma model.

**Methods.** We used rat morris hepatocellular carcinoma cells. Cell motility was evaluated with cell migration assay. Cell growth was assessed by MTT assay. Western blotting was performed to determine the level of phosphorylation for myosin light chain (MLC) and MAPK. Orthotopic liver transplantation was performed with cuff method.

**Results.** Tacrolimus enhanced the cancer cell migration and stimulated the phosphorylation of MLC, a downstream effector of Rho/ROCK signaling. Y-27632 suppressed the cancer cell migration and the phosphorylation of MLC induced by tacrolimus. On the other hand, tacrolimus did not enhance the cell proliferation and phosphorylation of MAPK. Y-27632 suppressed the tumor recurrence after liver transplantation and prolonged significantly the survival of liver transplant rats, compared with non Y-27632-treated liver transplant rats.

**Conclusion.** Tacrolimus stimulates the Rho/ROCK signal pathway to enhance invasiveness of hepatocellular carcinoma and ROCK inhibitor can be a new antimetastatic agent for tumor recurrence after liver transplantation.

**P23.50**  
**RIGHT LOBE ADULT LIVING DONOR LIVER TRANSPLANTATION**

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**Background.** Living donor liver transplantation is an alternative to cadaveric liver transplantation in adult patients.

**Aim.** We report the outcome of 35 right lobe adult living donor liver transplantations (ALDLT).

**Method.** We analyzed 35 ALDLT at our institution between April 2003 and December 2005 retrospectively.

**Results.** The age of the recipients ranged from 18 to 61 years (mean,  $41.7 \pm 12.5$  years). The median graft-to-recipient weight ratio was  $1.2\% \pm 0.4\%$  (range, 0.8 to 2.1). In the recipients, the mean operative time was  $10.6 \pm 2.7$  hours, the number of blood transfusions administered was  $4.1 \pm 5.1$  Unit, the mean hospital stay was  $25 \pm 22.9$  days, and the mean intensive care unit stay was  $2.3 \pm 1.5$  days. In the recipients, five vascular and 5 biliary complications occurred during the early postoperative period, and 4 vascular and 2 biliary complications developed in the late postoperative period. Eight of the 35 recipients studied died within 4 months after surgery. The age of the donors ranged from 23 to 50 years (mean,  $36.6 \pm 9$  years). In the donors, the mean operative time was  $6.4 \pm 1.6$  hours, the residual liver volume was  $43.3\% \pm 6.1\%$ , and the mean hospital stay was  $9.5 \pm 4.5$  days (range, 5–23 days). Two donors required an intraoperative blood transfusion. No donors died as a result of having undergone the procedure, although 4 experienced 6 complications. The mean postoperative follow-up period was  $12 \pm 4.6$  months (range, 1–32 months).

**Discussion.** In Turkey, the demand for ALDLT is beginning to exceed donor availability, and graft size presents a problem for adults who require LDLT. Because of the greater understanding of hepatic physiology and anatomy, right lobectomy can now be performed safely in experienced hands. Right lobe LDLT can be a lifesaving option for some adult patients with hepatic disease.

**P23.51**  
**SAFETY OF MODIFIED EXTENDED RIGHT HEPATECTOMY IN LIVING LIVER DONOR**

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