1 LIVING-RELATED LIVER TRANSPLANTATION (LRLT) IN EUROPE: REPORT OF THE EUROPEAN LIVER TRANSPLANT REGISTRY (ELTR)
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INTRODUCTION: Owing to organ shortage, LRLT is increasingly performed worldwide. Results from individual centers have been reported but multi-center data are lacking. METHODS: From October 1991 to June 2002, the ELTR cumulated the results of 928 LRLT performed in 52 centers from 15 European countries. Data were prospectively registered, updated every 6 months and controlled by audit visits of contributing centers. The aim of this study was to assess donor and patient outcome and to compare LRLT to cadaveric LT. RESULTS: There were 433 LRLT performed in adults and 495 in children. By the last 2.5 years adult LRLT largely exceeded pediatric LT (358 vs 157). The graft used was mainly the right hepatic (88%), left lobe (9%) and the left lateral lobe for children (84%). Donor operative mortality was 0.4% (4/928) with 4 postoperative deaths related to pulmonary embolism (1), sepsis (2) and cardiac failure (1). Donor morbidity accounted for 19% early postoperative complications, higher for right liver donation (34%) than for left lobe donation (16%) (p < 0.0001). As compared with cadaveric LT, there were more cancers (22% vs 10%, p < 0.0001), less acute hepatic failures (4% vs 8%, p = 0.05) and less retransplantations (1% vs 10%, p < 0.0001). Overall 5-year graft survival was 75%, better for children than for adults (80% vs 65% at 3 years, p = 0.003). While survival of LRLT was better than cadaveric LT for children (80% vs 70%, p < 0.01), it was similar for adults (65% vs 68% at 3 years). The size of the graft significantly affected the outcome of adults (2-month graft loss: 28% for right livers, 46% for left livers, 64% for left lobs, p < 0.001). Overall, graft loss included more primary non-functions (15% vs 9% of all graft loss, p < 0.01) and more technical complications (16% vs 13%, p < 0.05) but less rejection (1% vs 7%, p < 0.05) after LRLT than after cadaveric LT. CONCLUSIONS: In Europe, LRLT includes a mortality risk of 0.4% and an early complication rate of 19% for the donor. Compared with cadaveric LT indications for LRLT differ significantly. Results are better for children but similar for adults. Graft size is a critical factor for outcome.

2 LIVING DONOR LIVER TRANSPLANTATION AS A MODALITY FOR EXPANDING DONOR POOL
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BACKGROUND: Liver transplantation from a living donor (LDLT) is now widespread as an alternative therapy for end-stage liver diseases. The quick development of LDLT, however, raised serious ethical dilemmas, especially as regards donor safety. To evaluate the feasibility of LDLT, the results in a single institute were retrospectively analysed. MATERIALS AND METHODS: In total 249 LDLT procedures were performed for 245 patients at the University of Tokyo from January 1996 to November 2003. They consisted of 175 adults and 70 pediatric patients. The common indications included biliary atresia in 73, viral hepatitis and cirrhosis with or without hepatocellular carcinoma in 67 and cholestatic disease in 62, including primary biliary cirrhosis, autoimmune hepatitis and primary sclerosing cholangitis. Most donors were related to the patients, and consisted of 91 parents, 70 children, 13 siblings, 27 spouses and others in 24. The most common procedure was left liver with or without caudate lobe resection (n = 97) followed by right liver resection (n = 77). RESULTS: The rates of acute rejection and vascular and biliary complications were 31%, 6% and 27%, respectively. Eleven patients died during hospitalisation. The postoperative hospital stay among the surviving patients was 55 ± 28 days. Nine patients experienced late death and the 3-year cumulative survival rate was 88%. Four patients underwent re-transplantation. The most frequent complication in donors was bile juice leakage from the dissection plane of the liver or stump of the bile duct in 13, and six of these donors underwent re-operation for drainage. CONCLUSIONS: The long-term results of the recipients seemed to be satisfactory and no major complications were experienced in the donors. From a technical standpoint, refinement in biliary reconstruction will be necessary. For better long-term outcome, the strategy for hepatitis C virus must be established.

3 FIVE-YEAR SURVIVAL AFTER RESECTION OF HEPATIC METASTASES FROM COLORECTAL CANCER IN PATIENTS SCREENED BY POSITRON EMISSION TOMOGRAPHY WITH 18F FLUORODEOXYGLUCOSE (FDG-PET)
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OBJECTIVE: The 5-year overall survival (5yOS) after liver resection for colorectal cancer metastases without preoperative FDG-PET has been established in 19 studies (6070 patients). The median 5yOS in these studies is 30% (range 12–41%) and has not improved over time. FDG-PET detects unsuspected tumors in 25% of patients considered to have resectable hepatic metastasis by conventional staging. We report the first 5yOS survival results in a cohort of patients evaluated preoperatively by FDG-PET. METHODS: From 3/99 to 6/02, all patients having liver resection for colorectal cancer metastases had preoperative FDG-PET. A prospective database was maintained. RESULTS: We studied 100 patients (56 men, 44 women). The metastases were synchronous in 57, single in 63, unilateral in 78, and <5 cm in diameter in 60. Resections were major (3 segments) in 74 and resection margins were >1 cm in 52. Median follow-up was 31 mo (0.1–96 mo), with 12 actual >5-year survivors. There was one postoperative death. The actuarial 5yOS was 58% (95% CI 44–72%) (Figure).

4 RESECTION OF NON-RESECTABLE LIVER METASTASES AFTER CHEMOTHERAPY: PROGNOSTIC FACTORS AND LONG-TERM RESULTS
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INTRODUCTION: Surgery of primarily non-resectable (NR) colorectal liver metastases (CRLM) after downstaging chemotherapy is still questioned and prognostic factors of outcome are lacking. METHODS: From February 1988 to December 2000, 140 consecutive patients with CRLM...
were managed at a single institution. Of these, 29% (21%) were primarily resected from their CRLM and 1105 (79%) initially NR were treated by systemic chemotherapy (oxaliplatin or irinotecan regimens). They were prospectively reviewed every three courses of chemotherapy by the same multidisciplinary team and surgery was reconsidered in case of documented response to chemotherapy when the operative strategy could remove the tumoral tissue. In the group of patients resected after chemotherapy, 15 factors assumed to be predictive of survival (size, number and timing of metastases, main cause of initial non-resectability, tumour markers, type and duration of chemotherapy, of the operative procedure and pathology of the resected specimen) were evaluated by uni- and multivariate analyses. RESULTS: In the NR group, 139 ‘good responders’ (13%) were secondarily submitted to hepatic resection after an average of 10 courses of chemotherapy. CRLM were initially NR because they were too large (7%), ill-located (15%), multinodular (5%) or associated with extrahepatic tumour (22%). One hundred and four procedures (75%) were major hepatectomies (≥3 segments). Operative mortality within 2 months was 0.7% (1/139). Tumour recurrence could be treated by repeat hepatectomy in 50 patients (38%) or pulmonary resection in 27 (19%). After a mean follow up of 5.3 ± 3.2 years, overall 5-year survival was 56% (median 39 months) and disease-free survival was 22%. Sixteen patients (12%) were disease-free >5 years after resection surgery. Comparatively, 5-year survival of the 295 patients resected at once was 47% (p = 0.02). At multivariate analysis, four preoperative factors were independently associated with decreased overall survival: a rectal primary, a number of metastases ≥3, a carbohydrate antigen (CA 19-9) level >100 U/L and the presence of either peritoneal or lymph node concomitant metastases. Estimation of 5-year survival according to the presence of 0, 1, 2, 3 or 4 of these factors was respectively 60%, 35%, 15% and 2%. CONCLUSION: Chemotherapy allows 13% of patients with irresectable CRLM to be rescued by liver surgery with a 5-year survival of 36%. Four preoperative factors are able to predict long-term survival.

5 SURGICAL TREATMENT OF PANCREAS DIVISUM CAUSING CHRONIC PANCREATITIS: THE OUTCOME BENEFITS AFTER DUODENUM PRESERVING PANCREATIC HEAD RESECTION
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Based on ERCP a pancreas divisum (PD) can be found in 1–6% of patients. The correlation of this abnormality with pancreatic disease is an issue of continuing controversy. Nevertheless, in some patients this abnormality can lead to recurrent acute pancreatitis (RAP) or chronic pancreatitis (CP). We report of 36 patients (21 male, 15 female, mean age 57.9 years) with pancreas divisum in which the duodenum-preserving resection of the head of the pancreas (DPHPR) was carried out between 5/1982 and 2/2000. According to the classification of pancreas divisum, 10 patients demonstrated a complete PD, 25 a functionally incomplete PD and one a dorsal duct type. Histologically, 30 patients had chronic pancreatitis, 6 patients had recurrent acute pancreatitis without chronic pancreatitis. 97% of the patients suffered from upper abdominal pain. The preoperative pain score (visual analogue scale, VAS, [mean]) was 7.8 (CP) and 6.3 (RAP), respectively. 61% of the patients had endoscopic or surgical intervention prior to the DPHPR. There was no operative related mortality. Complications following DPHPR occurred in 28%, only 1 patient had to be reoperated. Follow-up (mean 39.3 month) was 100%, 4 patients died (1 suicide, 2 cancer of the oesophagus, 1 cardiac arrest). 50% of the patients were completely pain-free, 31% had a significant reduction of pain with a mean pain score of 2 (VAS) (p < 0.002). 6 patients (5 CP, 1 RAP) had further attacks of acute pancreatitis with need for hospitalisation (Table).

CONCLUSION: the DPHPR reduce pain and preserved the endocrine function in the majority of the patients with pancreas divisum. Therefore DPHPR should be the procedure of choice instead of other resective or drainage procedures.

6 REGIONAL VERSUS EXTENDED LYMPH NODE DISSECTION IN RADICAL PANCREATODUODENECTOMY FOR PANCREATIC CANCER: A MULTICENTER, RANDOMIZED, CONTROLLED TRIAL
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PURPOSE: The purpose of this study was to evaluate, in a multicenter randomized controlled trial (RCT), whether an extended lymph node dissection in radical pancreatoduodenectomy prolongs the survival of patients with pancreatic cancer. METHODS: From March 2000 to May 2003, 112 patients with carcinoma of the head of the pancreas were enrolled. After intraoperative investigation, patients were randomized to regional or extended (regional plus para-aortic) lymphadenectomy in radical pancreatoduodenectomy. None of the patients received any adjuvant therapy. All pathology specimens were reviewed and categorized, and morbidity, mortality, survival and quality of life were analysed. RESULTS: Of the 112 patients randomized, 11 were subsequently excluded because of the final pathology (7 chronic pancreatitis and 4 bile duct cancer), and the remaining 101 patients were analysed (51 regional vs 50 extended). There was no significant difference between the 2 groups with regard to age, gender and BMI. Although the mean operative time (426 minutes vs 547 minutes), intraoperative blood loss (1118 ml vs 1680 ml), number of retrieved lymph nodes (13 vs 40) and incidence of postoperative diarrhea (0 vs 24) differed in the 2 groups, there was no significant difference with respect to transfusion requirements, type of resection, overall morbidity excluding diarrhea, postoperative length of hospital stay (44 vs 42), mortality (0 vs 1), histological stage of the disease and QOL at 1 year after surgery. The 1-, 2- and 3-year survival rates for all 101 patients (78.7, 43.2, 32.4 vs 51.3, 39.9, 16.0%) and those with negative or positive node disease and disease-free survival (42.3, 17.8, 6.1 vs 48.8, 16.0, 12.0%) showed no significant difference between the two groups. CONCLUSIONS: In this multicenter RCT, radical pancreatoduodenectom- y with extended lymph node dissection did not provide any survival benefit in the treatment of patients with resectable pancreatic cancer.

7 CONNECTIVE TISSUE GROWTH FACTOR INFLUENCES THE PROGNOSIS OF CHOLANGIOCARCINOMA
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AIMS AND BACKGROUND: To analyse the expression and localization of connective tissue growth factor (CTGF) and to evaluate whether it influences the prognosis of cholangiocarcinoma. CTGF, which is regulated by transforming growth factor-β (TGF-β), has recently been implicated in the pathogenesis of fibrotic diseases and tumor stroma. Inasmuch as generation of desmoplastic stroma is characteristic for cholangiocarcinoma, it is not known whether it gives tumor cells a growth advantage, or it is an unpecific response to inhibit cancer cell progression. METHODS: Tissue samples were obtained from 55 patients (25 female, 30 male) undergoing curative liver resection for cholangiocarcinoma (25 klatkin tumors, 30
intra-hepatic/peripheral tumors). Tissue samples of 10 previously healthy organ donors (5 female, 5 male) and of 5 (3 female, 2 male) patients who had undergone liver resection for colorectal metastases were used as controls. The expression of CTGF was analysed by immunohistochemistry; CTGF expression levels were clustered using a score defined by semi-quantitative analysis. Perineural and vascular tumor infiltration were also evaluated overall. RESULTS: Immunohistochemical analysis revealed that cholangiocarcinoma tissue samples exhibited an increase in CTGF expression (p < 0.0001) over controls. CTGF immunoreactivity was constantly detected in fibroblasts surrounding tumor, while tumor cells showed weak to strong CTGF expression as scored above. Patients whose tumors exhibited high CTGF expression showed disease-free survival and overall survival that was significantly longer than those whose tumors expressed low CTGF levels (p < 0.0001). The presence of perineural and vascular tumor infiltration were related to a worse disease-free and overall survival (p < 0.05). At multivariate analysis CTGF was a significant independent factor for survival (p < 0.01). CONCLUSIONS: Our data indicate that CTGF, as a downstream mediator of TGF-β, is over-expressed in connective tissue cells and neoplastic cells of cholangiocarcinomas. In the present study patients with high CTGF expression had a better prognosis, indicating that CTGF could represent a novel prognostic factor for cholangiocarcinoma.

8 DOES THE PRETRANSPLANT MELD SCORE PREDICT POST-TRANSPLANT SURVIVAL? AN ANALYSIS OF THE UNOS LIVER TRANSPLANT DATABASE

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BACKGROUND: The Model for End-Stage Liver Disease (MELD) has been found to accurately predict pretransplant mortality and is a valuable system for ranking those in greatest need of liver transplantation. Whether higher MELD also predicts decreased post-transplant survival is unknown.

METHODS: We examined a cohort from the United Network for Organ Sharing (UNOS) database for whom the critical pretransplant recipient values needed to calculate the MELD score were available (international normalized ratio of prothrombin time, total bilirubin and creatinine). These patients were transplanted before the implementation of MELD-based liver allocation. In these 2565 patients, we analysed whether MELD score predicted graft and patient survival and length of post-transplant hospitalization.

RESULTS: In contrast to its ability to predict survival in patients with chronic liver disease awaiting liver transplant, we found that the MELD score was poor at predicting post-transplant outcome except for those with the highest 20% of MELD scores. In the patients that were in the highest quintile on MELD scores (MELD > 24), the one year patient survival was 77% versus 85% in the lower four quintiles. We did further modeling to determine what variables were better at predicting post-transplant survival, and found that recipient age, the need for mechanical ventilation or dialysis, and retransplantation were significant predictors of outcome. Recipients with any two of the three latter variables had a markedly diminished post-transplant survival rate.

CONCLUSIONS: MELD was a relatively poor predictor of post-transplant outcome. In contrast, a model based on four pretransplant variables (recipient age, mechanical ventilation, dialysis, and retransplantation) had a better ability to predict outcome. Our results support the use of MELD for liver allocation and suggest that statistical modeling such as that reported herein can be used to identify futile cases in which expected outcome is too poor to justify transplantation.

9 BILARY COMPLICATIONS AFTER LIVER TRANSPLANTATION IN CHILDREN WITH CYSTIC FIBROSIS

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INTRODUCTION: Cystic liver disease affects approximately 10% of children with cystic fibrosis (CF). Complications of cirrhosis, including portal hypertension, variceal hemorrhage, splenomegaly, thrombocytopenia, and malnutrition may lead to the consideration of liver transplantation. Advanced pulmonary disease in patients with CF and advanced liver disease may lead to the consideration for combined liver-lung transplantation. Post-liver transplant (LTx) biliary strictures affect approximately 10% of all recipients. Previous reports have demonstrated a higher incidence of biliary tract complications in CF recipients who underwent LTx.

METHODS: We report a single-center, retrospective, consecutive experience of 11 patients with CF with advanced liver disease who underwent LTx, and compare the incidence of biliary complications in this group to a consecutive contemporaneous cohort of children who received LTx for other indications. RESULTS: Between 2/90 and 9/03 our center has performed 106 LTx in 92 children (median age 3.2 years ± 5.8), 28% of LTx were from living donors. Actual patient survival over this 13-year period is 96%. Indications for LTx included biliary atresia (54%), CF (12%), alpha-1 anti-trypsin deficiency (9%), malignancy (5%), inherited metabolic disease (5%), PSC (4%), oxalosis (4%). Of 11 children with CF who received LTx, the median age was 13.4 years (range 8–18 years, ± 3 years). 5 received combined liver-lung transplant (LLTx), and 6 received LTx alone. 4/5 LTx recipients and 4/6 LTx recipients are alive. 3 received a LTx from a living donor, and had biliary reconstruction with a hepaticojejunostomy (HJ). All other CF LTx recipients (3) and all LTx recipients underwent biliary reconstruction with choledochocholedochojunostomy (CD-CD). 50% (3/5) of CF LTx recipients developed biliary stricture (CD-CD) vs 2/6 of LTx (1H, 1 CD-CD). All biliary strictures have been successfully treated with dilatation and temporary stenting. An age-matched cohort of children who underwent LTx for alpha-1 anti-trypsin deficiency (median age 8 years, range 0.4–15.4, ± 2.5) during the same time period, was used for comparison. All children are alive; 7/8 had a CD-CD and 1 (14%) developed a biliary stricture, vs 60% (CF recipients).

CONCLUSION: Excellent short- and long-term results can be achieved after both LTX and LTx in children with advanced liver disease from CF. Biliary stricture occurs more frequently in patients who have undergone LTx and CD-CD biliary reconstruction. Strong consideration should be given for biliary enterostomy (HJ or CD-jejunostomy) in CF patients undergoing LTx.

10 SHOULD HEPATOCELLULAR CARCINOMA BE TREATED DURING THE WAITING LIST PERIOD?

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BACKGROUND: In order to prevent tumor progression while waiting for a donor, adjuvant locoregional therapy has been recommended for patients with hepatocellular carcinoma (HCC) who are listed for liver transplantation. The aim of this study was to assess the efficacy of adjuvant therapy in patients with HCC while waiting for liver transplantation.

METHODS: We reviewed 77 patients with HCC and cirrhosis who were evaluated and listed for liver transplantation. We compared 36 patients (group 1) who received pretransplant locoregional therapy with 41 patients (group 2) who did not receive any pretransplant therapy. Treatments included 22 transarterial chemo-embolizations (TACE), 9 percutaneous ethanol injections (PEI), 4 radiofrequency ablations (RFA) and 7 liver sections. Groups were compared with respect to overall survival, recurrence-free survival and dropout from the waiting list. In addition, all explants were examined for viable tumor, grade and vascular invasion. RESULTS: There were no differences between the two groups with respect to age, gender, underlying liver disease, tumor stage (A/C), time on the waiting list, immunosuppression, and number of patients exceeding the Milan criteria. Sixty-two patients underwent liver transplant, 29 of whom received pretransplant locoregional therapy and 33 who did not. There were no differences in survival between the two groups at 1 year (84% vs 75%) and at 4 years (59% vs 51%) (p = 0.88). Recurrence- free survival at 1 year (86% vs 94%) and at 4 years (69% vs 63%) was also not significantly different (p = 0.08). Dropout from the waiting list due to tumor progression occurred with similar frequency in both groups (11% vs 12%) (p = 0.9). Viable tumor was found in 26/29 explants in group 1 and in all explants in group 2. CONCLUSIONS: These data suggest that pretransplant locoregional adjuvant therapy administered to patients with HCC while on the waiting list does not confer an advantage in terms of overall survival and disease-free survival after transplantation. Furthermore, adjuvant therapy does not appear to prevent patient dropout from the waiting list.
PREVENTION OF HEPATITIS B RECURRENCE AFTER LIVER TRANSPLANTATION USING HEPATITIS B IMMUNOGLOBULIN AND LAMIVUDINE COMBINATION THERAPY

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INTRODUCTION: Hepatitis B-related end-stage liver disease (ESLD) has been a relative contraindication for liver transplantation (LT) in the past because of the high rate of graft dysfunction and survival due to hepatitis B recurrence. However, after the introduction of passive immunoprophylaxis and antiviral drugs, it has recently become the most common indication in Korea, but there is still no consensus concerning types, dosage and duration of prophylaxis. Therefore, we investigated the efficacy of HBV recurrence prophylaxis using hepatitis B immunoglobulin (HBIG) and 1-year lamivudine combination therapy. MATERIALS AND METHODS: We performed a retrospective analysis of 160 patients who underwent LT for hepatitis B-related ESLD in our institution between January 1999 and December 2002. Forty-one patients with hepatocellular carcinoma (HCC) were included. HBeAg was positive in 51 patients (48%) and HBV DNA was positive in 28 (26%). Forty-four HBeAg-positive donors were used (42%). Mean follow-up duration was 31.7 months (range 12-59). Prophylaxis protocol included HBIG 10,000 IU i.v. intraoperatively, followed by 10,000 IU i.v. daily for 6 days and then 10,000 IU i.v. weekly three times. Afterwards 2000–6000 IU i.v. were given monthly with a target anti-HBs antibody titer of 350 mIU/L or above for the first year and 250 mIU/L thereafter. Lamivudine 100 mg po was given daily for 1 year postoperatively and discarded after confirming that HBeAg and HBV DNA were negative. RESULTS: There were 5 recurrent cases (4.7%) – 3 patients with inadequate HBIG administration and 2 with good compliance. Two patients had administration of 2 months. Therapy after HCC recurrence at 4 and 6 months, so HBIG was not given sufficiently according to the protocol and HBV recurred at 8 and 14 months, respectively. Both died because of cancer dissemination at 14 and 37 months. One patient was lost to follow-up and HBIG was not given adequately and HBV recurred at 27 months. Among patients who followed our protocol, recurrence was found in only 2 patients (1.9%). One patient had HBeAg/HBV DNA (+/-) and one (+/-) before transplantation and recurred at 25 and 28 months post-transplant, respectively. Both are under lamivudine therapy for over 12 months with normal liver function. CONCLUSION: Combination therapy using HBIG and 1-year lamivudine therapy is effective in controlling HBV recurrence and it can be kept to <2% if the protocol is followed appropriately. However, longer follow-up is needed and long-term HBIG administration needs to be elucidated.

ABLACTION AS A BRIDGE TO TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA

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BACKGROUND: Liver transplantation is an effective therapy for selected hepatocellular carcinoma (HCC). The shortage of donor organs has led to longer waiting times and some tumors progress to exceed transplant guidelines. Chemotherapy and/or embolization have been employed to control tumors during the wait. Ablative techniques including radiofrequency ablation (RFA) and percutaneous ethanol injection (PEI) are being effectively employed to treat unresectable hepatic malignancies. This study analyses the short- and long-term outcomes of ablation for control of HCC while awaiting transplantation. METHODS: From Jan 1999 to Sept 2002, 37 patients were transplanted for known or suspected HCC. All patients were considered for, and 14 patients (38%) received, pre-transplant percutaneous ablation (7 RFA, 6 PEI, 1 both). All patients were monitored with CT scans every 3 months until transplantation. Mean post-transplant follow-up is 31 months. RESULTS: Ages in the two groups were similar. Viral hepatitis was more prevalent in the non-ablated cohort (64% vs 78%). Ablated patients were more likely to have HCC as the primary indication for listing (86% vs 35%). Medical status at the time of transplant was equivalent. Median wait time was longer for the ablated group (125 vs 86 days). Pre-transplant radiologic mean tumor size was slightly larger in the ablated group (25.3 mm, range 10-51) than the non-ablated group (26.4 mm, range 10-50). Mean operative time (345 min) and median blood loss (2500 ml) were the same in the groups, but fewer blood products were administered to the ablated group. Major complications were more prevalent in the non-ablated group (29% vs 48%), although median length of stay was equivalent. In the non-ablated group, eight (34%) have died – four from tumor recurrence (17%). In the ablated group, only two (14%) have died – one of suspected recurrence (7%). Survival favors the ablated group (Figure): 93% vs 83% at 1 year and 77% vs 60% at 4 years (p < 0.18 log rank). Although adhesions to the ablation site were seen in half the patients, there was no evidence of needle tract seeding. However, each of the ablated lesions had residual tumor histologically. CONCLUSION: This initial experience suggests that percutaneous ablation of HCC prior to transplantation can be used safely without adverse effect on the transplant procedure or survival.

RESOURCE CONSUMPTION IN LIVER TRANSPLANTATION IS REDUCED FOR PATIENTS WITH HEPATOCELLULAR CARCINOMA

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PURPOSE: In February 2002, the United Network for Organ Sharing (UNOS) adopted the Model for End-Stage Liver Disease (MELD) scoring system for allocating donor livers. Preliminary reports have suggested that this system has changed the characteristics of transplanted patients, generally increasing the percentage of transplanted patients with the diagnosis of hepatocellular carcinoma (HCC), and increasing the acuity of non-HCC patients. This change is likely due to exception criteria which grant additional MELD points to patients with HCC. We investigated the relative resource consumption of HCC vs non-HCC patients at our institution, as well as the change in average MELD score for non-HCC patients after the implementation of MELD. METHODS: HBO/Trendstar patient charge data, MELD score and diagnosis were collected for each patient undergoing transplant between January 1999 and June 2003. Patients receiving transplants from living donors were excluded. The charges for the transplant admission were totaled. Charge data were adjusted for inflation using the medical component of the consumer price index. Average charges in the HCC group were compared to the non-HCC group. In addition, average MELD scores in non-HCC patients from January 1998 to June 2003 were compared. Lastly, the number of transplanted patients with the diagnosis of HCC pre- and post-MELD was determined. RESULTS: Patients with the diagnosis of HCC were found to have 39% smaller aggregate charges than non-HCC patients (p < 0.0021). In addition, the average MELD scores for patients receiving transplants for true MELD increased from 20.2 to 24.2 (p = 0.03). The percentage of transplanted patients with HCC as a primary diagnosis increased from 10% to 37% after the implementation of MELD, with p < 0.0021. 65% of patients receiving cadaver liver at our institution were men and the average age was 50. CONCLUSIONS: As a group, patients with the diagnosis of HCC have smaller aggregate charges for the transplant admission than patients without HCC. This is likely due to the fact that patients with HCC benefit from exception criteria that permit transplantation at an earlier stage of liver dysfunction than patients without HCC. MELD scores increased in non-HCC patients receiving transplants after the implementation of the MELD-based allocation system and a large increase in the percentage of transplanted patients with the diagnosis of HCC was observed at our institution. These findings suggest that the exception granted for HCC has considerably impacted the mix of patients receiving transplants and the resources consumed by liver transplantation.
14 OCCULT VASCULAR INVASION MAY LIMIT THE VALUE OF TRANSPLANTATION FOR LARGE HEPATOCELLULAR CARCINOMAS

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PURPOSE: Vascular invasion predicts poor outcome from transplantation for hepatocellular carcinoma (HCC). Expansion of the indications for transplantation to include tumors >3 cm has been proposed. This study examines the association between tumor size and vascular invasion in resected HCC. METHODS: A retrospective review of a prospectively collected international database of patients with resected hepatocellular carcinoma was performed. Data were then categorized into 2 large groups (<3 cm and >3 cm) with 4 subgroups: ≤3 cm, >3 cm to ≤5 cm, >5 cm to ≤8 cm, and >8 cm. Correlation between tumor size and the presence of major vascular invasion and microvascular invasion was made. RESULTS: 1073 patients were reviewed. Microscopic vascular invasion was identified in 48 of 190 (25%) patients with tumors ≤3 cm, 118 of 297 (40%) patients with tumors >3 and ≤5 cm, 126 of 231 (55%) patients with tumors >5 and ≤8 cm and 236 of 355 (67%) patients with tumors >8 cm. Differences among all groups were statistically significant (p < 0.005). The incidence of major vascular invasion also increased with size but did not reach statistical significance (3%, 4%, 12% and 18%, respectively, see Figure). Occult microvascular invasion was found in 62% of patients with tumors >3 cm, in contrast to 34% of those with tumors ≤3 cm (p < 0.001). CONCLUSIONS: Tumor size correlates with both microvascular and major vascular invasion. Based on the high incidence of occult vascular invasion in HCC >5 cm, expansion of transplant criteria to include HCC >5 cm will markedly increase the risk for recurrence and for poor outcome after transplantation.

15 LIVER TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA USING NON INVASIVE CRITERIA FOR THE PREOPERATIVE DIAGNOSIS

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Hepatocellular carcinoma (HCC) represents a frequent complication in advanced chronic liver disease. Tumour biopsy to confirm HCC is not always feasible and exposes the patient to the risk of haemorrhage and/or seeding of tumour cells. The arterialised feature of HCC and current advances in liver imaging have reduced interest in preoperative biopsy. The aim of this study was to assess the detectability of HCC by using non-invasive criteria in cirrhotic patients who qualify for liver transplantation (LT). Between 01/1995 and 06/2003, 480 patients underwent LT for liver cirrhosis. We retrospectively analysed 102 patients who underwent LT for HCC without preoperative tumour biopsy. The diagnosis of HCC was stated on the basis of at least one of the following features: recent appearance, arterialised nodules on CT scan, increased alpha-fetoprotein (AFP) blood levels. The accuracy of this policy was evaluated by comparing preoperative diagnosis with pathology reports of the explanted liver. Pathology examination confirmed HCC in 82 explanted livers (80.3%). The false-positive rate for the preoperative diagnosis was 20/102 (19.6%). However, for 10 patients, the indication of LT was justified, the histological examination finding either another cancer or a premalignant lesion (cholangiocellular carcinoma, n = 1; dysplastic nodules, n = 9). Conversely, in the remaining 10 patients (9.8% of cases), LT was not justifiable according to the current standard: in 4 cases, any lesion was found in the explanted liver, and in the 6 other cases, pathology analysis showed a benign lesion (regenerative nodules, n = 5; haemangiomata, n = 1). In these 10 false-positive cases without HCC or other cancer and without premalignant lesion, nodules were unifocal in 6 cases and bifocal in 4 cases. The mean diameter of these nodules was 1.57 ± 0.21 cm compared with 3.03 ± 0.12 cm in the false-positive group (p < 0.001). These false-positive nodules were arterioised in 6/10 cases and the mean AFP level in these patients was subnormal at 12.2 ± 4.1 mg/L. Overall sensitivity, specificity, positive and negative predictive value of our policy was of 76%, 95%, 82% and 93%, respectively. Overall, the indication for LT was excessive in 9.8% of cases. This substantial false-positive diagnostic rate exhibits the limitation of our policy, especially for nodular lesions smaller than 2 cm. Instead of biopsy that would be technically difficult for such nodules, either surgical resection (when possible) or repeat examination to show enlargement of the lesion should be considered in this subgroup of patients.

16 ENDOSCOPIC SCLEROTHERAPY (ES) AND ENDOSCOPIC VARICEAL LIGATION (EVL) IN THE ELECTIVE TREATMENT OF BLEEDING OESOPHAGEAL VARICES IN CIRRHOTIC PATIENTS - PROSPECTIVE RANDOMISATION STUDY

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AIM: The aim of the study was to compare the effectiveness and the safety of three forms of treatment (ES, EVL, ES + EVL) in patients with cirrhosis after variceal haemorrhage. METHODS: Between January 1999 and January 2003, 183 cirrhotic patients, soon after varical bleeding, were randomly assigned to either ES (n = 61), or EVL (n = 56) or ES + EVL (n = 66) groups. In the ES and EVL groups, we repeated procedures every 4–7 days until varical eradication, using 1% Polidocanol or MBL-6 Wilson-Cook shooter. In the EVL + ES group we repeated EVL procedures every 4–7 days until varices diminished to stage I and after this we followed with repeated ES until eradication. The differences between the three groups as regards Child-Pugh stage were not statistically significant. Patients have been observed for 12 months. RESULTS: The mean number of sessions required to obtain eradication was lowest in the EVL + ES group (ES, 5.35; EVL, 4.57; EVL + ES, 3.62) but not statistically significant. The bleeding rate was also lowest in the EVL + ES group (ES, 13.1%; EVL, 5.36%; EVL + ES, 2.56%) (p < 0.05). The rate of complications, mostly comprising stricures, was significantly higher in the ES than in the EVL and EVL + ES group (ES, 22.2%; EVL, 5.4%; EVL + ES, 2.56%) (p < 0.05). All stricures were successfully diluted. CONCLUSIONS: The advantages of combined EVL + ES treatment are the lower number of sessions needed to achieve varical eradication, lower reblooding rate and lower rate of complications than with ES and EVL alone.

17 VARIATIONS OF HEPATIC VEINS: APPLICATION IN LIVING DONOR LIVER TRANSPLANTATION

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The anatomic variations of the middle hepatic vein (MHV), left hepatic vein (LHV), and right hepatic vein (RHV) in 100 patients with normal liver were analysed using multidetector computed tomography (MDCT) to clarify the feasibility of resecting the right lobe or extended right lobe in living subjects for living donor liver transplantation. The umbilical fissural vein (UFV) draining the left part of the medial segment is recognized close to the confluence of the MHV and LHV. This tributary flows into the LHV
in 81% of cases, but into the MHV in 15% of cases. The liver transaction line should be established, in order to obtain the extended left lateral segment graft, including the drainage area of the UFV. Recently, it was reported that the right anterolateral portal vein (P8) bifurcated into P8v (the ventral branch) and P8d (the dorsal branch), and that segment 8 was divided into S8v (the ventral area) and S8d (the dorsal area). In this study, we identified the vein which runs between P8v and P8d, which crosses between S8v and S8d, and named ‘anterior fissural vein (AFV)’. The AFV and the UFV are bilateral symmetries. The AFV is recognized close to the confluence of the MHV and inferior vena cava (IVC). This tributary flows into the MHV in 97% of cases, but into the RHV in 3% of cases. To obtain a right lobe graft, most surgeons perform a right hepatectomy and leave the MHV intact in the donor. That is, there is a risk of venous congestion of medial and ventral part of segment 8 in almost all right lobe grafts. But in 98% of cases, the V8 that drains segment 8 flows into both MHV and RHV. And, in 72% of cases, the V8 flowing into MHV has a diameter > 0.5 cm, which is the minimal diameter of the hepatic vein to be reconstructed. In 11% of cases, the thick V6 that drains segment 6 flows into MHV only, and must be reconstructed to avoid congestion of the whole of segment 6. Preoperative delineation of this complex venous anatomy is of paramount importance because the hepatic veins have to be transected in the cutting plane of the liver. The location of this plane is determined by the optimal graft volume required, and both the graft and the remnant liver have to retain perfect function. The venous anatomy would change the cutting plane in the living donor and the surgical method of anastomosis for the recipient.

18 PORTAL VEIN EMBOLIZATION OF THE ENTIRE TUMOR-BEARING LIVER PRIOR TO MAJOR HEPATECTOMY IS NOT ASSOCIATED WITH SIGNIFICANT TUMOR GROWTH

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PURPOSE: Portal vein embolization (PVE) is used selectively to induce hypertrophy of the anticipated small liver remnant prior to major hepatectomy. The impact of PVE on intrahepatic tumor growth is unknown. This study examines changes in hepatic tumor volume after PVE. METHODS: Among 52 patients with malignant disease who underwent PVE at our center (1998-2003), 38 had measurable intrahepatic tumors (intrahepatic cholangiocarcinoma excluded). Three-dimensional CT was used for future liver remnant (FLR) and tumor volume measurement pre- and post-embolization. PVE was considered when anticipated FLR was ≤25% of the total liver volume in patients with normal liver, and ≤40% in patients with underlying liver disease. All portal vein branches to segments planned for resection were embolized (including segment IV when indicated) using a percutaneous technique. RESULTS: All patients were successfully embolized; segments IV-VIII in 28 patients, segments V-VIII in 10 patients. Median FLR volume increased from 17% of total liver volume to 26% after PVE (p < 0.0001), 13% to 24% in patients with normal liver, 30% to 37% for those with liver disease. The median interval between the two volumetric measurements was 37 days for patients with normal liver, and 43 days for patients with liver disease. There was no significant change in tumor volume pre- vs post-embolization (see Figure). p = 0.82). Tumor volume did not change in 6 patients, decreased in 14 patients (range 6-64% decrease) and increased in 18 patients (range 13-40% increase). Nine patients did not undergo resection: 1 with stable tumor but insufficient FLR hypertrophy, 2 with decreased tumor volume (insufficient FLR hypertrophy [1 patient], new findings on intraoperative ultrasound that precluded complete resection [1 patient]), and 6 with increased tumor volume (insufficient FLR hypertrophy [2 patients], extraportal disease [4 patients]). The remaining 29 patients were resected (76%). No patient was unresectable due to interval intrahepatic tumor growth. CONCLUSION: Portal vein embolization of all tumor-bearing liver prior to major hepatectomy is not associated with changes in tumor volume that impact resectability.

19 THE ROLE OF CHEMOTHERAPY AND SURGERY FOR HEPATOMBLASTOMA IN 49 PATIENTS

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BACKGROUND: Hepatoblastoma is a rare malignant tumor of the liver of childhood. The advent of chemotherapies specifically in the neoadjuvant setting has significantly improved the resectability and survival in these patients. AIM: To evaluate the impact of neoadjuvant chemotherapy on resectability in hepatoblastoma. METHODS: A retrospective analysis of 49 children with diagnosed hepatoblastomas from the age of 2 years to 11 years. RESULTS: The median age at diagnosis was 12 months. Of the 49 patients, 47 patients received chemotherapy in the neoadjuvant, adjuvant or palliative setting. Two patients underwent primary surgical resection and were kept on close follow-up only. In the chemotherapy group, 21 patients had received neoadjuvant chemotherapy. In the earlier 4 patients when definite chemotherapeutic protocols had not evolved, various agents were used. Two had received a combination of vincristine (VCR) and Endoxan; 1 had received the round cell tumor protocol and 1 had received a combination of VCR, Endoxan, ifosfamide and VP16. Fourteen children received a combination of cisplatin and Adriamycin (PLADO) and the last three received a combination of cisplatin, VCR and 5-FU. In this group 15 patients were successfully resected and R0 resection was achieved; one was unresectable at laparotomy on account of metastatic disease in both lobes of the liver; one had severe cardiotoxicity of Adriamycin and was unfit for surgery. Three patients were lost to follow-up and did not undergo surgical resection; one patient developed septicaemia after the first cycle of chemotherapy and died. A resectability rate of 94% was observed. Of the 2 deaths in the postoperative period, 1 died due to cardiac failure secondary to cardiotoxicity of Adriamycin and 1 died secondary to complications of a sustained intraoperative hypotensive episode. 13/15 patients (87%) who underwent surgery after neoadjuvant chemotherapy have survived with disease-free status for a range of 4-96 months. Chemotherapy related toxicity was mainly seen in the PLADO group (3/11 patients). No immediate or postoperative morbidity related to chemotherapy was seen in the last three patients who had received VCR, Plat and FU. The overall chemotherapy-related toxicity was seen in 4/18 patients. CONCLUSION: Those who were treated appropriately with neoadjuvant chemotherapy followed by curative resection had an excellent survival, thereby emphasizing the role of neoadjuvant chemotherapy in hepatoblastoma. The omission of doxorubicin from the newer protocols yields the same response but without its toxicity.

20 ABDICATION OF P53-INDUCED APOPTOSIS BY X PROTEIN OF HEPATITIS B VIRUS-UPREGULATED CYCLOOXYGENASE-2 EXPRESSION

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BACKGROUND: Cyclooxygenase (COX)-2 was over-expressed in nearly 80% of hepatitis B virus (HBV)-associated hepatocellular carcinomas (HCCs). We have previously shown that COX-2 over-expression reduced apoptosis and enhanced angiogenesis in HCC cells. Enhanced p53 expression repressed COX-2 transcription in fibroblasts but induced COX-2 expression under DNA damaging stress conditions. AIMS: We investigated the regulation of COX-2 expression by p53 and the viral transactivator X protein of HBV (HBx) and their interactions on apoptosis in HCC cells. METHODS: Hep3B HCC cell line was stably transfection with a doxycycline (DOX)-regulated p53-expressing vector (clone T15). Forced HBx expression was achieved by transient transfection. Expressions
of p53, HBx and COX-2 were examined by real-time quantitative RT-PCR. Western blot and immunofluorescence. Prostaglandin E2 (PGE2) was measured by ELISA. Apoptosis was determined by TUNEL assay in the presence or absence of a COX-2-specific inhibitor, NS-398. RESULTS: p53 mRNA and protein were highly expressed in T15 cells but reduced dramatically after treatment with 2 μg/ml DOX for 24 h. The protein level of a downstream target of p53, p21, was also decreased after DOX. COX-2 mRNA was increased by 2.3-fold when p53 was repressed by DOX. Forced HBx expression induced COX-2 mRNA by 6.4-fold at 48 h post-transfection even in the presence of p53. The levels of COX-2 protein paralleled with mRNA levels. Consistently, PGE2 levels were 1.5- and 2.1-fold higher after DOX addition and HBx transfection, respectively, when compared with the untreated condition. Intense staining of p53 was found mainly in the nucleus of T15 cells, of which COX-2 expression was barely detectable. In contrast, in HBx-expressing cells, the distribution of p53 mostly coincided with that of HBx in the cytoplasm where COX-2 was also localized. Of the p35-expressing T15 cells, 18% were apoptotic. The addition of DOX decreased the apoptotic cells to 9.5% while HBx transfection resulted in only 2.4%. More importantly, inhibition of apoptosis in both conditions was reversed by COX-2 inhibition with 10 micro-molar NS-398 treatment. CONCLUSIONS: HBx alleviated the p53 repression of COX-2 expression in HCC cells, which may act via sequestration of p53 in the cytoplasm. Furthermore, abrogation of p53-induced apoptosis by HBx was mediated at least partially by COX-2, thus emphasizing the importance of COX-2 in HBV-associated hepatocarcinogenesis.

21 SELECTIVE CHEMO-EMBOLIZATION IS SAFE IN HIGH-RISK PATIENTS WITH HEPATIC MALIGNANCIES

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BACKGROUND: Recent randomized trials have demonstrated that transarterial chemoembolization (TACE) improves survival in patients with hepatocellular malignancies. As a result, TACE is indicated for patients with unresectable tumors, significant underlying liver disease and/or as a bridge to liver transplantation. However, many of these patients are high-risk because of biliary obstruction, a serum bilirubin >2.0 mg/dl and/or major portal vein obstruction. Thus, whether TACE should be performed in these high-risk patients is unclear. AIM: Therefore, the aim of this analysis is to determine whether TACE can be performed safely in high-risk patients.

METHODS: Over a 4-year period, 132 patients underwent a mean of 2.6 TACE procedures at our institution. The chemotherapeutic agents were cisplatin, Adriamycin, and mitomycin C, and the embolization particles were polyvinyl alcohol. High-risk patients received more selective embolization with fewer particles and fewer procedures (mean 2.0, p < 0.04). The mean age for all patients was 60.6 years, and 61% were male. Hepatocellular carcinoma (HCC) was the underlying tumor in 60%, 28% had metastatic hepatic malignancies, and 12% had cholangiocarcinomas. 27% were Child-Pugh class B or C; and by the criteria defined above, 35 patients (27%) were high-risk. RESULTS: High-risk patients were slightly younger (59.2 vs 61.2 years, NS) and more likely to have HCC (86 vs 51%, p = 0.01). High-risk patients also were more likely to be Child-Pugh class B or C (50 vs 18%, p < 0.01). Procedure-related morbidity, 30-day mortality and mean survival for all patients and HCC patients are presented in the Table. CONCLUSIONS: These data suggest that high-risk patients undergoing TACE have 1) no increase in morbidity or mortality and 2) slightly, but not significantly, reduced survival secondary to more extensive liver disease. We conclude that transarterial chemoembolization can be performed safely in high-risk patients.

22 TECHNIQUES FOR LAPAROSCOPIC EVALUATION AND MANAGEMENT OF PRIMARY LIVER TUMORS IN PROSPECTIVE LIVER TRANSPLANT CANDIDATES

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INTRODUCTION: In the era of MELD, hepatocellular carcinoma (HCC) has become a prominent indication for liver transplantation. As radiofrequency ablation (RFA) has emerged as a modality in bridging patients with hepatic tumors to transplantation, we have aggressively developed a minimally invasive program to prospectively evaluate liver transplant candidates. A review of all RFA cases performed in liver transplant candidates in a single center was performed. Operative findings, morbidity and mortality data were focused upon. RESULTS: Forty-six procedures in 45 candidates were performed. All patients were Childs class B or C. Eight patients were placed in the lateral position with 38 in the supine position. In four patients lesions were not well visualized utilizing a laparoscopic intraoperative ultrasound probe (IOUS). All four patients had a hand assist port placed and a T-bar ultrasound probe utilized. This was sufficient to visualize lesions in three of the patients with the remaining patient requiring a conversion to an open procedure. The mean number of lesions at exploration was 1.6. Fifteen patients had prior abdominal surgery and dense adhesions. The mean tumor size was 2.5 cm. The mean estimated blood loss was 100 ml. There were no peri-operative deaths. The most common complication was a transient new onset of ascites in 11% (n = 5) or worsening of ascites in 50% (n = 23). Wound complications including ascites leak in 7% (n = 3) and wound infection in 7% (n = 3) were infrequent. 67% (n = 31) patients were listed for transplantation and 52% (n = 24) have been transplanted thus far. Two patients who underwent transplantation had subsequent cardiac complications and died after OLT. Explanted liver tumors have been documented to have 30-99% necrosis. Six deaths (43%) were observed in the group of patients not listed for transplant. Causes of death included: hepatic failure (n = 2), tumor progression (3), and massive variceal bleed (1). CONCLUSION: The laparoscopic approach for RFA offers a safe and effective approach for the evaluation and treatment of HCC. With the addition of the hand assist technique the major goal of patients are able to undergo RFA without conversion to a formal open procedure. An effective bridge to transplantation, patients receive adequate MELD scores for subsequent transplantation without incurring excessive morbidity or mortality.

23 COMPREHENSIVE EVALUATION OF THE PATIENT WITH VIRAL HEPATITIS AND POTENTIALLY RESECTABLE HEPATOCELLULAR CARCINOMA SHOULD INCLUDE DIAGNOSTIC LAPAROSCOPY AND LAPAROSCOPIC ULTRASONOGRAPHY

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INTRODUCTION: Despite significant recent improvements in liver imaging, preoperative evaluation of the potentially resectable patient with viral hepatitis and hepatocellular carcinoma (HCC) is often inaccurate. The degree of cirrhosis and presence of intrahepatic satellite lesions is frequently under-appreciated by transabdominal ultrasonography, magnetic resonance imaging (MRI) and computed tomography (CT). Diagnostic laparoscopy with laparoscopic ultrasonography may change management for patients with under-appreciated nodular cirrhosis or intrahepatic metastases, preventing unnecessary open exploration. The purpose of this study is to determine the effectiveness of routine laparoscopy as a separate procedure prior to resection in the evaluation of patients with potentially resectable HCC. METHODS: Patients with potentially resectable HCC were evaluated preoperatively with routine blood tests in addition to transabdominal ultrasound, triple phase CT, and/or MRI. All study patients also underwent diagnostic laparoscopy with laparoscopic ultrasonography. Laparoscopy was performed in an inpatient hospital operating room, with 23-h hospital stays in most cases. RESULTS: Among 65 patients evaluated with HCC between July 2001 and November 2003, 32 patients with potentially resectable disease were evaluated by diagnostic laparoscopy with laparoscopic ultrasonography. All patients had viral hepatitis: 16 with hepatitis B and 4 with hepatitis C. All hepatitis B patients were of Eastern Asian heritage, and all hepatitis C patients were of Western heritage. All study patients had cirrhosis: 18 were classified as Child's-Pugh class A and 2 as Child's-Pugh class B. Diagnostic laparoscopy changed the management in 9/20 (45%) cases. The management was
changed because of severe nodular cirrhosis in 4 cases, inaccurate assessment of intraduodenal metastases in 2 cases, inability to identify an HCC in 1 case, portal vein carcinoma in 1 case, and inability to tolerate general anesthesia in 1 case. CONCLUSIONS: Diagnostic laparoscopy and laparoscopic ultrasonography are useful in the evaluation of the potentially resectable patient with HCC. Information obtained from laparoscopy may change the clinical management in up to 45% of cases. Comprehensive evaluation of the patient with viral hepatitis and potentially resectable HCC should include diagnostic laparoscopy as a separate and independent component of the preoperative evaluation.

24 HEPATIC ARTERIAL INFUSION IS A SURVIVAL-ENHANCING STRATEGY IN SURGICAL MANAGEMENT OF HEPATIC METASTASES FROM COLORECTAL CANCER
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PURPOSE: The gold standard for treatment of hepatic metastases from colorectal cancer (CRC) is hepatic resection. In selected patients, the 5-year survival is 20–40%. However, most patients are unselectable at the time of presentation. Therefore, we have used alternative therapeutic strategies to optimize the operative management of these patients. The purpose of this study was to assess the benefit of these alternative strategies. METHODS: We studied a series of 273 patients with hepatic metastases from CRC in the period 1978–2001. A total of 134 patients were treated surgically: 87 patients underwent resection, 26 patients received hepatic arterial infusion (HAI) chemotherapy, and 21 patients underwent resection and HAI, and 8 patients underwent ablation with or without HAI. The remaining 139 patients received systemic chemotherapy and/or supportive treatment (historic control). Overall and median survival from surgical treatment of hepatic metastases or from diagnosis (in the non-surgically managed group) were calculated by the Kaplan–Meier method. RESULTS: See Table below. CONCLUSION: A multi-option strategy is essential in planning surgical management of hepatic metastases from CRC. The 5-year overall survival of 25% for hepatic resection can be enhanced by the addition of HAI. For patients with unselectable disease, tumor ablation with HAI, or HAI alone, can provide median survival of 29 and 17 months, respectively.

25 MANAGEMENT OF SPONTANEOUS HEMORRHAGE AND RUPTURE OF HEPATOCELLULAR ADENOMAS: IS IT TIME FOR A CHANGE?
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BACKGROUND: Hepatocellular adenomas (HCA) may present with spontaneous hemorrhage and rupture, which can be life-threatening. Our treatment policy for acute bleeding of ruptured HCA consisted of stabilization and initial, conservative management, or in case of hemoperitoneum and persistent bleeding, laparotomy and initial packing of the liver. Because of the risk of malignant transformation of HCA, a delayed partial liver resection was undertaken after the bleeding episode. There are, however, no data proving increased risk for recurrent bleeding or malignant transformation of HCA after acute hemorrhage and rupture. Also, the evolution of radiological selective arterial embolization in liver hemorrhage has changed the need for laparotomy and packing for uncontrollable bleeding. The aim of this study was to evaluate management in 17 patients with ruptured HCA and to assess a more expectant policy towards secondary resection. PATIENTS: Between May 1990 and August 2003, 17 female patients were diagnosed with acute hemorrhage and rupture of HCA (mean age 34 years, range 23–48 years). Nine patients remained hemodynamically stable and could be discharged after successful conservational management. One patient with signs of persistent intra-abdominal bleeding underwent laparotomy and partial liver resection at the first presentation, whereas four patients underwent laparotomy with initial packing of the liver to stop bleeding. 13 patients eventually underwent secondary resection varying from enucleation to extended hemihepatectomy after a mean of 7 months (range 2–24 months). In most patients the preoperative CT scans showed unspicuous, partly hypodense and hyperdense lesions consistent with organized parenchymal hematomas. Three patients were not operated after conservative treatment and showed no complications after a mean follow-up of 37 months (range 7–96 months). In one of these patients, the HCA showed regression from 5 to 1 cm after discontinuation of OCS. In 9 patients after elective resection, histopathological examination showed fibrosis at the site of the hemorrhage without a specific tissue diagnosis. In 4 patients, 7 lesions microscopically compatible with HA were identified (mean lesion size including area of previous hemorrhage 6.8 cm, range 1.5–18 cm). CONCLUSIONS: The absence of specific morphological findings in the resection specimens of the majority of patients after management of acute hemorrhage of HCA in this series casts doubts on the need for secondary liver resection. An expectant policy seems justified in these patients with regular follow-up imaging of the liver.

26 THE LEVEL OF DOUBLE-STRANDED RNA-ACTIVATED PROTEIN KINASE IS ASSOCIATED WITH ALPHA-FETOPROTEIN IN HEPATOCELLULAR CARCINOMA
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INTRODUCTION: Double-stranded RNA-activated protein kinase (PKR) is an interferon-induced, serine/threonine protein kinase. Recent studies have suggested that PKR is involved in the pathogenesis of hepatocellular carcinoma (HCC). Alpha-fetoprotein (AFP) is a well-known diagnostic protein generated by HCC cells and at a level higher than 500 ng/ml is generally accepted as a diagnostic marker for HCC. METHODS: In the present study, we examined the level of PKR in the liver samples from patients with HCC infected with hepatitis B virus (HBV). A total of 35 liver tumors was studied and the level of PKR was determined by Taq-Man PCR, a quantitative and reliable method to measure gene expression. Human G3PDH (glyceraldehyde-3-phosphate dehydrogenase), a constitutively expressed gene, was chosen as an internal control. The level of PKR was calculated as an index of PKR assay value over G3PDH. The measurement was done in both the normal tissue and the tumor tissue from the same liver and the PKR level in a given liver tissue was expressed as the ratio of tumor tissue value to normal liver tissue value. The level of AFP was measured before surgical resection of the tumor. RESULTS: Our results showed that the overall PKR level was much lower in tumor tissues than in non-tumor tissues, irrespective of whether the samples were infected with HBV or not, as measured by either branched DNA assay or anti-HBs antibody. According to the level of AFP measured, tumor samples were divided into two subgroups: AFP < 500 ng/ml and AFP ≥ 500 ng/ml. The concentration of AFP was significantly different between the two subgroups (50.6 ± 44.6 ng/ml vs 4024.2 ± 3485.9 ng/ml, p < 0.001). It appeared that the PKR level was increased in samples with AFP > 500 ng/ml compared with those with AFP < 500 ng/ml. The ratio of PKR in tumor tissues to PKR in non-tumor tissues was significantly lower in samples with AFP < 500 ng/ml compared with those with AFP > 500 ng/ml. CONCLUSION: The level of PKR was reduced in HCC tumor tissues, suggesting a possible role of PKR in the development of HCC. The association between PKR and AFP levels suggests that PKR may have a role in the production of AFP from HCC cells, as AFP promoter activity is repressed by p53 whose level is mediated by PKR. AFP levels may offer an alternative tumor marker for HCC.
27 COMPARING FDG-PET AND C11-ACETATE PET IN PATIENTS WITH HEPATOCELLULAR CARCINOMA
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The aim was to investigate if C11-acetate is more useful than FDG as a marker when PET is performed in patients with hepatocellular cancer. Twelve patients with newly diagnosed HCC were investigated with both types of PET markers. All HCC tumors were visible with C11-acetate while only two tumors were visible with FDG. In addition, a metastatic lesion not previously diagnosed with MRI or CT was discovered in the spine. In conclusion, C11-acetate seems to be a better marker for HCC. It could be useful when staging patients before liver resection or transplantation. The method merits further evaluation.

28 LEFT TRISEGMENTECTOMY WITH RECONSTRUCTION OF THE SEGMENT SIX HEPATIC VEIN
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Involvement of the hepatic veins by tumor has traditionally been a contraindication to hepatic resection. Advances in surgical technique gleaned from living donor liver transplantation, during which hepatic venous reconstruction is often required, allows hepatic resection with venous reconstruction in selected cases. We present a video case of a patient with a central cholangiocarcinoma that required left trisegmentectomy with reconstruction of the venous outflow to segment six. Hepatic resection with reconstruction of the hepatic veins extends the possibility for curative resection to patients that were previously unresectable with standard liver resection techniques.

29 NEOADJUVANT CHEMOTHERAPY FOLLOWED BY RIGHT EXTENDED HEPATECTOMY FOR CHILDHOOD HEPATOBLASTOMA
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Hepatoblastoma is a rare malignant tumor of the liver occurring in childhood. In the 1970s, surgical resection was the only treatment offered and the resection rate and survival were low. The advent of neoadjuvant chemotherapy has significantly improved both the resectability and survival in these patients. Many groups investigated the role of neoadjuvant chemotherapy. The Society of Pediatric Oncology Liver Tumor Study Group (SIOP-L1) conducted a large prospective trial using pre operative cisplatin and doxorubicin (PLADO) and achieved a resectability of 76%. To avoid the toxicity of doxorubicin other groups, chiefly the Children’s Cancer Group (CCG) and Pediatric Oncology Group (POG), used vincristine, cisplatin and 5 FU with similar results. In this video we demonstrate an extended right hepatectomy after neoadjuvant chemotherapy. We present a video of 5-year-old child who presented to us with a large hepatoblastoma in the right lobe and left paramedian sector of the liver. After a preoperative FNA diagnosis he received four cycles of neoadjuvant chemotherapy comprising of vincristine, cisplatin and 5 FU. After chemotherapy there was an over 50% response. We demonstrate an extended right hepatectomy in this child. The neoadjuvant chemotherapy had successfully downsized the tumor and had increased the resectability.

30 EXTENDED LEFT HEPATECTOMY WITH THE RECONSTRUCTION OF THE MIDDLE HEPATIC VEIN FOR INTRAHEPATIC CHOLANGIOCARCINOMA
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Intrahepatic cholangiocarcinoma has been reported to have very poor prognosis despite surgical excision. However, radical surgical resection is the only hope for cure in this disease. Most cases of intrahepatic cholangiocarcinoma have extensive invasion to bile duct and major vessels such as the portal vein, hepatic artery and hepatic vein. Combined vascular resection and reconstruction would be required for radical resection in some selected patients with expected curative resection and survival prolongation as compared with non-surgical treatments. In our institution, we have resected 64 patients with intrahepatic cholangiocarcinoma and obtained a 5-year survival rate of 39%. Twenty-two of 64 resected patients (34%) underwent combined vascular resection of the portal vein, hepatic artery, hepatic vein and inferior vena cava. As to the necessity of middle hepatic vein reconstruction in extended right or left hepatectomy, there is no consensus at present. In this video, we present the case of advanced intrahepatic cholangiocarcinoma existing in segment IV of diameter 6 × 5 cm in which involved hepatic duct confluence and also the middle hepatic vein. Extended left hepatectomy, caudate lobectomy and bile duct resection were carried out. The middle hepatic vein was involved by the tumor and therefore was also resected. The vascular clamp of the middle hepatic vein before resection brought about dark-redish discoloration of the extensive anterior part of the right hepatic lobe. We judged that the middle hepatic vein should be reconstructed after resection in this case for small remnant liver volume. The inferior mesenteric vein was harvested as an autograft vein 7 cm in length. The middle hepatic vein was reconstructed with the segmental graft of the inferior mesenteric vein. The inferior mesenteric vein graft was anastomosed with a newly incised orifice of the inferior vena cava. Postoperative course was uneventful. Reconstruction of the middle hepatic vein in extended left hepatectomy could be performed without any increased surgical risk in patients for whom the reconstruction might be required to maintain the remnant liver function as much as possible to avoid the occurrence of postoperative liver failure.

31 PERIOPERATIVE OUTCOME OF LAPAROSCOPIC LEFT LATERAL LIVER RESECTION IS IMPROVED BY USING STAPLE LINE REINFORCEMENT: A CASE REPORT
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BACKGROUND: Current laparoscopic stapling technology still cannot prevent hemorrhage or bile leaks (<5%) along the resection margin. A new staple line reinforcement technique was utilized in the present case. This technique incorporates an absorbable polymer membrane in the stapler staple, such that it butresses the transected solid organ. AIM: The objective of this novel procedure is to decrease hemorrhage at the staple line and to prevent bile duct leakage after liver resections. CASE REPORT: A 47-year-old man followed for status post biliopancreatic diversion with duodenal switch, presented with epigastric pain. On imaging, he was found to have a lesion in segment 2 of the liver which measured at least 3 cm in diameter. He was admitted to the hospital to undergo a laparoscopic left lateral liver resection for this hepatic lesion in segment 2. This procedure involved: laparoscopic ultrasonography of the liver and transection of the left hepatic lobe with endoscopic linear staplers. Liver capsule was incised. The staple cartridge 3.5, 60 mm long, reinforced with an absorbable polymer membrane was used for liver transection to catch the portal branches located mostly inferiorly. This required multiple firings in the liver parenchyma and also more division of some tissue anteriorly using the harmonic scalpel. The larger branch in the middle of segment 2–3 and the left hepatic vein were both transected with the novel staple line reinforcement technique. A smaller lesion on the surface was enucleated separately with the harmonic scalpel. No bleeding or bile leak in this area could be visualized. No drains were left. The patient’s postoperative course was uneventful. Pathology results showed a cavernous hemangiomata, 4.5 cm in diameter. CONCLUSION: Staple line reinforcement with the absorbable polymer membrane has the potential to decrease staple line hemorrhage and bile leak.

32 LAPAROSCOPIC LEFT LATERAL SEGMENT HEPATECTOMY
Jay Jan and Paul Hansen, Legacy Health System, Portland, OR, USA
This is a video presentation documenting a laparoscopic left lateral segment hepatectomy for metastatic colorectal cancer. Surgical technique will be described.

33 ARTERIAL AND PORTAL RECONSTRUCTION PRIOR TO LEFT HEPATECTOMY AND CAUDATE LOBECTOMY FOR HILAR CHOLANGIOCARCINOMA
Hiroshi Shimada, Itaru Endo, Daisuke Morio, Mitsuoka Sugita, Yasuhiko Miura and Shinji Togo, Department of Surgery II, Yokohama City University School of Medicine, Yokohama, Japan
Aggressive surgery such as extended hepatectomy with vascular resection
and pancreato-duodenectomy has increased resectability and curability of biliary malignancies. However, this aggressive surgical approach remains controversial in regard to the balance between risk and survival effect. Hepatocarcinoma has been performed in 26 patients in our department from 1991 to 2000. Portal vein and/or hepatic artery resection and reconstruction were performed in 10 patients. Two patients were portal vein alone, 3 were hepatic artery alone, and 5 were both portal vein and hepatic artery. Curability rates of the vascular resection group and no vascular resection group were 50% and 56.6%, respectively. Surgery-related death due to the thrombosis of the reconstructed portal vein occurred in one patient. On the other hand, there was one operative death in the no vascular resection group. The survival rates of the patients treated and not treated with vascular reconstruction were 52% and 42% at 3 years and 18% and 25% at 5 years, respectively, without significant differences between them. Two of 10 patients who underwent vascular resection survived >3 years. In conclusion, vascular resection can be considered a reasonable surgical approach in locally advanced tumor. In this video, combined portal vein and hepatic artery reconstruction prior to left hepatectomy and the caudate lobectomy is demonstrated. The patient is a 64-year-old male suffering from obstructive jaundice due to locally advanced hilar cholangiocarcinoma. Usually, vascular reconstruction was performed after the dissection of hepatic parenchyma and the hilar plate. In this case, vascular resection and reconstruction was carried out prior to hepatic dissection. It provided a good field to perform en bloc resection. The patient is doing well 4 months after surgery.

34 CENTRAL BISEMENTECTOMY WITH BILE DUCT RESECTION FOR ADVANCED GALLBLADDER CANCER
Keiichi Kubota, Junji Kita and Masato Kato, Second Department of Surgery, Dokkyo University Hospital, Tochigi Pref., Japan
Gallbladder (GB) cancer can easily invade the liver parenchyma or metastasize to the liver, requiring combined resection of the liver, such as extended cholecystectomy or right lobectomy. Portal embolization may increase the safety for patients undergoing right lobectomy. However, when the lateral segment is too small to perform trisegmentectomy or the lesion is too advanced to extirpate by resection of the inferior part of segment 4 and segment 5, central bisegmentectomy with bile duct resection (the procedure) is an option for such an advanced GB cancer. In this video, we will demonstrate our technique for the procedure. PATIENT AND DIAGNOSTIC IMAGING: A 74-year-old female was found to have an advanced GB cancer invading segment 4 and the anterior segment without jaundice. ICG retention rate at 15 min was 10%. Abdominal angiography showed no invasion to the hepatic arterial and portal venous branches to the posterior and lateral segments, which occupied 25% and 26% of the whole liver volume, respectively. In order to perform a right trisegmentectomy, portal embolization is necessary. Taking the tumor progression into consideration, we decided to perform the procedure, although it was complicated. TECHNIQUES: First, the duodenum was mobilized to confirm no metastasis to para-aortic lymph nodes (LN). The retro-pancreatic LNs were dissected, followed by the division of the common bile duct at the entrance to the pancreas. The LNs along the proper hepatic artery, the common hepatic artery and the celiac trunk were dissected. The right hepatic artery and the portal vein were dissected until they ramified into the anterior and posterior branches. Then the respective anterior branches were divided. Since the middle hepatic artery ramified branches to the lateral segment, only the branches to segment 4 were divided. Under hemihepatic clamping, the liver parenchyma between the lateral segment and segment 4 was divided, followed by the division of the left hepatic duct. Then the liver parenchyma between the posterior and anterior segments was divided, followed by the division of the bile duct to the posterior segment. The bile ducts were reconstructed by hilar-enteric anastomosis. The operation time was 12 h and 2 min, and the bleeding amount was 997 ml. She recovered uneventfully and is doing well without signs of recurrence 5 months after surgery. Surgeons should be armed with the technique of the procedure as a treatment option for an advanced GB cancer.

35 NEOADJUVANT CHEMOTHERAPY FOLLOWED BY RADICAL CHOLECYSTECTOMY FOR ADVANCED GALLBLADDER CANCER
Prashant M Mullerpatan, Rajiv C Shah, Deepak G Chhabra and P Jagnnath, Lilavati Hospital and Research Centre, Mumbai, India
Carcinoma of the gallbladder is one of the commonest biliary tract malignancies. The dismal outlook of this malignancy is primarily due to its late presentation and lack of effective treatment options. Currently the only available treatment option is surgical resection. The role of neoadjuvant chemotherapy to downstage the disease is not yet clearly defined. A 48-year-old male patient with locally advanced gallbladder cancer was initially treated with 8 cycles of neoadjuvant chemotherapy comprising gemcitabine and cisplatin. On re-assessment, the tumour was found to be downstaged and resectable. A radical cholecystectomy that involved complete clearance of the porta hepatitis along with a wedge resection of the liver (segments IVb and V) was performed. The patient had an uneventful postoperative recovery. The histology revealed large areas of necrosis with foci of carcinoma. This video presentation demonstrates the response of neoadjuvant chemotherapy in an advanced gallbladder cancer and the subsequent procedures of radical cholecystectomy.

36 LAPAROSCOPIC SURGERY FOR CHOLEDOCHAL CYSTS: EXPERIENCE WITH 16 PATIENTS
Masao Tanaka, Shoji Shimizu, Kazuhito Mizumoto, Hiroyuki Konomi, Masahiko Kawamoto and Koji Yamaguchi, Department of Surgery and Oncology, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan
Choleodochal cyst is a congenital malformation usually associated with pancreaticobiliary malformation. Due to the high prevalence of biliary carcinoma, ranging from 2.3 to even 52.0%, choleodochal cyst resection with cholecystectomy, not cystenteric anastomosis, should be advocated to prevent carcinogenesis. Resection of the choleodochal cyst can be done by minimally invasive laparoscopic surgery. The only prerequisite for successful laparoscopic resection is the type of the cyst. A type I choleodochal cyst, the most common type, joining the pancreatic duct preferably through a substantially long narrow segment is a good candidate. The first laparoscopic resection of a choleodochal cyst was performed by Farello in 1995 in a 6-year-old girl. The authors operated on the first adult patient in 1996 and have accomplished the whole procedure in 12 of 16 patients attempted until November 2003. Causes of the failure to accomplish the resection were too heavy pericholecdochal adhesion due to recurrent severe cholangitis (1 patient), diathermy injury to the main pancreatic duct (1 patient), too small hepatic duct to perform hepaticojejunostomy under laparoscopy (1 patient), and bleeding due to rupture of a pseudocyst remnant formed within the cyst wall during dissection (1 patient). Postoperative complications in the 12 successful patients included bile leakage (1 patient) and bleeding from the plane of dissection of the pancreas (1 patient). The latter patient underwent successful haemostasis by emergency laparotomy. There was no mortality. Recent refinements of the surgical procedure including the use of a 5-mm mini-laparotomy for Roux-en-Y anastomosis and hepaticojejunostomy with the use of a moving retractor (OmniTract®) have made the procedure easier and faster. Although laparoscopic resection and Roux-en-Y anastomosis are relatively demanding, this approach deserves further evaluation because this entity is a good candidate for minimally invasive surgery.

37 BILIARY CANCER ASSOCIATED WITH CONGENTIAL CHOLEDOCHAL CYST FOLLOWING CYSTODUODENOSTOMY
Takanobu Hoshino, Takashi Ishida, Fumiaki Ozawa and Daigo Hashimoto, Saitama Medical Center, Saitama Medical School, Kawagoe-city, Saitama Prefecture, Japan
Surgical treatment of biliary cancer associated with congenital choleodochal cyst (CCC) is presented. CASE: A 37-year-old female patient suffering from fever (40°C) and jaundice was admitted emergently. This patient had undergone choleodocho-duodenostomy (choledocho-duodenostomy) for CCC and associated cholangiitis at the age of 13 months. Laboratory data demonstrated jaundice, liver dysfunction, and elevated CA 19-9 (455 U/ ml). CT, MRI and MRCP demonstrated marked dilatation (40 mm in diameter) of the common bile duct (CBD) and tumour (35 mm in diameter) in this dilated CBD. This tumour was histologically diagnosed as
Adenocarcinoma by endoscopic biopsy via the anastomosis of cysto-duodenostomy. No distant metastasis was detected preoperatively. **SURGICAL OPERATION:** Pylorus-preserving pancreatico-duodenectomy was performed, and pathology revealed no lymph node metastases. The postoperative course was uneventful, and the patient is disease-free at 15 months after surgery. **CONCLUSIONS:** Since patients with CCC, particularly following cysto-enterostomy, may well develop biliary cancer at substantially higher frequency and lower age (49 years old, on average) than the normal population, these patients require careful and frequent follow-up (by CT, MRI, tumour markers), and immediate radical operation is needed following diagnosis of biliary cancer.

### 38 A PRELIMINARY STUDY OF THE THERAPEUTIC VALUE OF UPA, UPAR, PAI-1 AND PAI-2 mRNA EXPRESSION IN PANCREATIC ADENOCARCINOMA

Aikan Nielsen, Christopher J Scarlett, Jawinder S Samra, Anthony Gill and Ross C Smith, Royal North Shore Hospital, St Leonards, Australia

Urokinase-type plasminogen activator (uPA), its cell surface receptor (upAR), and two specific inhibitors, plasminogen activator inhibitor type 1 (PAI-1) and type 2 (PAI-2), have been identified as novel tumour prognostic factors in breast cancer. These may also be important mediators in human pancreatic adenocarcinoma. The aim of this study was to analyze uPA, upAR, PAI-1 and PAI-2 mRNA expression in pancreatic cancer and correlate this with tumour type and stage of disease. Invasive pancreatic adenocarcinoma (n = 21), ampullary carcinoma (6) and benign mucinous cystadenoma (10) samples, all with adjacent normal tissue (n = 37), were obtained from the pancreatic tissue bank at Royal North Shore Hospital, uPA, upAR, PAI-1 and PAI-2 mRNA expression was measured using real-time quantitative RT-PCR. Expression of uPA, upAR, PAI-1 and PAI-2 mRNA in pancreatic cancer tissue was significantly higher when compared with their adjacent normal tissue samples (p < 0.001). Increased expression was not observed in ampullary or benign tumours, except for PAI-1 in ampullary carcinoma. Using the Kruskal-Wallis ANOVA, we observed a significant difference in expression between tumour types for uPA, upAR and PAI-1 and PAI-2. Data were expressed as median and range. These observations suggest that significant over-expression of uPA, upAR, PAI-1 and PAI-2 correlates closely with the rapid progression and invasiveness of pancreatic cancer and that components of the uPA system may provide future therapeutic targets for pancreatic cancer treatment (Table).

### 39 THE UTILITY OF ENDOCOSCOPIC ULTRASOUND (EUS) IN PREDICTING PATHOLOGIC DIAGNOSIS, NODAL STATUS AND MARGIN STATUS IN RESECTED PERIPANCREATIC NEOPLASMS

Julie E Marosky, Robert E Glasgow, Kathryn F Hatch, Courtney L Scaife, Iqbal S Sandhu and Sean J Mulvihill, University of Utah, Salt Lake City, UT, USA

The utility of EUS in the detection of vascular invasion in patients with pancreatic neoplasms has been established. Its accuracy in determining pathologic diagnosis, nodal status, and final margin status is less certain. We reviewed a consecutive series of 53 patients undergoing pancreatic resection (40 pancreaticoduodenectomies, 8 distal pancreatectomies, 1 total and 1 central pancreatectomy, 3 enucleations) for pancreatic adenocarcinoma (28), intraductal papillary mucinous tumor (15), other cystic pancreatic tumors (3), neuroendocrine tumors (6), and pancreatic cancer (1) from January 2001 to September 2003 who underwent preoperative EUS in addition to CT or MRI staging. A specific protocol to assess surgical margins was used by independent pathologists. Preoperative EUS-guided fine-needle aspiration biopsy (FNA) was obtained and read as malignant in 41, indeterminate in 5, and benign in 7. The EUS-FNA accurately predicted final pathology in 81%. EUS predicted the presence of nodal metastasis in 8 patients; however, after resection 16 (50%) were proven histologically to have nodal metastasis (sensitivity = 38%, PPV = 75%). EUS predicted the absence of nodal metastasis in 45 of 53 examinations, whereas final pathology showed benign nodes in 35, or 66% (NPV = 78%, specificity = 95%). EUS suggested resectability with negative margins in 49 of the 53 patients (92%). All 53 patients underwent resection with no gross residual tumor. Final microscopic margins, however, were positive in 24 patients (45%). The diagnostic accuracy of EUS prediction of resectability with negative surgical margins was 58% (sensitivity 13%, PPV 75%, specificity 96%, NPV 57%). We conclude that EUS-guided FNA is reasonably accurate in predicting the presence of malignancy. No false-positive examinations were found, but false-negative examinations were common. The sensitivity of EUS in predicting nodal metastasis is poor, and cannot be relied upon to direct patients into neoadjuvant therapy for this indication. EUS is poor at predicting final margin status following resection.

### 40 ANTITUMOR ACTIVITY OF THE MTOR INHIBITOR,CCI-779, IN PANCREATIC CANCER PRECLINICAL MODELS AS SINGLE AGENT AND IN COMBINATION CHEMOTHERAPY WITH GEMCITABINE

Koji Fujimoto, Daisuke Ito, Ryuichiro Doi and Masayuki Imamura, Kyoto University, Kyoto, Japan

**INTRODUCTION:** The mammalian target of rapamycin (mTOR) plays a central role in cell proliferation. Disregulation of mTOR signaling occurs in diverse human tumors, and can confer higher susceptibility to inhibitors of mTOR. In this study, we investigated whether or not the mTOR signaling is dysregulated in pancreatic cancer cells, and whether the mTOR inhibitor, CCI-779, has antiproliferative effects in in vitro and in vivo models of pancreatic cancer. **METHODS:** First, we examined the expression patterns of mTOR signaling pathways including PTEN, Akt, mTOR, p70S6K, in 6 human pancreatic cancer cell lines (AsPC-1, BxPC-1, KMP-3, Panc-1, Suit-2) and 20 tissue specimens of pancreatic ductal adenocarcinoma (PDAC) by immunohistological determination of activated mTOR. Next, we examined the cytotoxicity of CCI-779 in the 6 cell lines in vitro as a single agent and in combination with gemcitabine. Finally, the antitumor effects of CCI-779 and gemcitabine in vivo were examined using AsPC-1 s.c. xenografts and Suit-2 peritoneal dissemination xenografts. Nude mice were divided into 5 groups: (1, 2) CCI-779 (10 and 20 mg/kg, 5 times/week × 2); (3) gemcitabine (125 mg/kg, biweekly × 2); (4) CCI-779 with gemcitabine (20 and 125 mg/kg) and (5) vehicle alone, were administered by i.p. injection. Tumor volumes and survival were measured. **RESULTS:** Among the 6 cell lines examined, PTEN expression was detected in 4 cell lines except for KMP-3 and KMP-4 cells. Interestingly, Akt was strongly phosphorylated even in the 4 cell lines, which showed positive expression of PTEN. mTOR and p70S6K were activated in all of the 6 cell lines examined. In the tissue specimens of PDAC, the expression of p-Akt, p-mTOR and p-p70S6K was detected in 50%, 55% and 65%, respectively. Regulating the cytotoxicity of CCI-779, AsPC-1 cells were highly sensitive to the treatment, and BxPC-3 and Suit-2 cells were slightly resistant. Intriguingly, CCI-779 and gemcitabine had additive effects in BxPC-3 and Suit-2 resistant to the treatment with CCI-779 alone. Furthermore, CCI-779 induced antitumor activity in AsPC-1 s.c. xenografts. The average tumor volume was 1514 mm³ in the control group, 1249 mm³ in the group treated with gemcitabine alone, 375 mm³ in the CCI-779-treated group, and 444 mm³ in the group treated with CCI-779 with gemcitabine. Also in Suit-2 peritoneal dissemination xenografts, the treatment of CCI-779 combined with gemcitabine produced the best results.

<table>
<thead>
<tr>
<th>Tumor type</th>
<th>uPA</th>
<th>upAR</th>
<th>PAI-1</th>
<th>PAI-2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pancreatic adenocarcinoma</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>17.1</td>
<td>20.1</td>
<td>4.7</td>
<td>7.4</td>
</tr>
<tr>
<td>Stage 1</td>
<td>4.0</td>
<td>3.1</td>
<td>0.3</td>
<td>2.5</td>
</tr>
<tr>
<td>Stage 2</td>
<td>4.2</td>
<td>0.03(4.3)</td>
<td>4.0</td>
<td>2.0</td>
</tr>
<tr>
<td>Stage 3</td>
<td>75.4</td>
<td>66.7</td>
<td>9.1</td>
<td>29.0</td>
</tr>
<tr>
<td>Ampullary carcinoma</td>
<td>3.9</td>
<td>1.9</td>
<td>3.0</td>
<td>0.6</td>
</tr>
<tr>
<td>Mucinous cystadenoma</td>
<td>1.9</td>
<td>3.4</td>
<td>2.5</td>
<td>1.6</td>
</tr>
</tbody>
</table>

*p < 0.05 significantly different from normal and pancreatic adenocarcinoma tissue.*
survival among the 5 groups. CONCLUSIONS: These results suggest that mTOR may be a good target for pancreatic cancer therapy and CCI-779 with additive cytotoxicity in combination therapy has great potential in the treatment of pancreatic cancer.

41 VASCULAR RECONSTRUCTION DURING PANCREATIC RESECTION OF MALIGNANT PERIAPPLYAL TUMOURS WORTHWHILE?
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From January 1968 to December 2001, 257 patients underwent pancreatoduodenectomy (241) or total pancreatectomy (16) for malignant peripancreatic tumours. Fifty-four patients (group I 21%) underwent vascular reconstruction (VR) while 233 did not (group II). Vascular reconstruction concerned the portal vein or the superior mesenteric vein in 43 patients, the superior mesenteric artery in 2 patients and both superior mesenteric vessels in 9 patients. Preoperative diabetes and biliary stenting, pancreatic adenocarcinoma and total pancreatectomy were significantly more frequent in group I. In the subgroup of patients with pancreatic ductal adenocarcinoma (125 patients), TNM staging was similar in both groups. Microscopic vascular invasion was confirmed in 50%. The 2 months hospital mortality was 6% in the whole group, not significantly different in group I (9%) and group II (5%), with a significant improvement in the last study period (group I: 6%; group II: 4%). The mortality was 0% for arterial reconstruction alone, 5% for venous reconstruction alone and 33% for combined arterial and venous reconstruction. (p = 0.021). The overall postoperative complication rate was 50% in group I and 58% in group II, with no significant improvement during the last study period. The incidence of postoperative pancreatic fistula was 15% in group I and 25% in group II (not significant). During a mean follow-up of 24 months (range 2–98) in group I and 33 months (range 2–250) in group II, the 5-year survival was 15.4% and 20.5%, respectively (not significant). The median survival time was 11.7 and 16.9 months in patients who underwent arterial and venous reconstruction, respectively (not significant). CONCLUSION: vascular reconstruction must be considered as an acceptable tool to achieve radicality in malignant peripancreatic tumors. Arterial reconstruction could be justified in highly selected patients.

42 EXPRESSION OF INTERFERON RECEPTORS IN PANCREATIC CANCER
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AIM: Interferons (IFN) are known to have antiproliferative and immunoregulatory activities that are modulated through specific cellular surface ligands, known as IFN-alpha, IFN-beta, and IFN-gamma receptors. We hypothesized a correlation between IFN-receptor expression in patients with pancreatic adenocarcinoma and overall patient survival. METHODS: Slides were prepared from 36 patients with pancreatic adenocarcinoma. Immunohistochemistry (IHC) was subsequently used to determine the expression of IFN-alpha/beta receptor-chain 2 (IFNalpha/betaR and IFN-gamma receptor (IFNgammaR) in 2 slides each of 36 patients, moderate expression in 19.4% of (7/36) patients, and faint or no expression in 77.8% (28/36) of patients. IHC confirmed a high expression of IFNgammaR in 58.3% (21/36) of patients, moderate expression in 30.5% (11/36) of patients, and faint or no expression in the remaining 8.3% (3/36) of patients. By comparison, 27.3% and 44.2% of the corresponding non-cancerous pancreatic tissue showed a high expression of IFNalpha/betaR and IFNgammaR, respectively. Clinico-pathological survey did not demonstrate a significant correlation between IFNalpha/betaR and IFNgammaR expression with regard to tumor size, vascular invasion, perineural invasion, lymph node metastasis, and disease stage. The Kaplan–Meier analysis demonstrated a significant survival advantage in those patients whose tumors expressed moderate-high IFNalpha/betaR expression compared with those with faint or no IFNalpha/betaR expression (26 months vs 16 months; p = 0.212, log rank test). The expression of IFNgammaR, however, had no impact on patient survival (20 months vs 17 months; p = 0.656, log rank test).

CONCLUSION: Patients who have pancreatic adenocarcinomas that express moderate to high IFNalpha/betaR have improved survival.

43 THE ROLE OF VASCULAR ENDOTHELIAL GROWTH FACTOR (VEGF)-C AND -D IN PATIENTS WITH INVASIVE DUCTAL ADENOCARCINOMA OF THE PANCREATIC HEAD
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AIM: The aim of this study was to evaluate the role of VEGF-C and VEGF-D in the process of lymphatic metastasis from pancreatic ductal adenocarcinoma. We assessed the precise expression pattern considering intratumoral heterogeneity of VEGF-C and VEGF-D in invasive ductal adenocarcinoma of the pancreatic head and analysed the relationship between the expression patterns and clinicopathological factors and prognosis. METHODS: Formalin-fixed, paraffin-embedded blockS were obtained from 58 patients with pancreatic head cancer. All of the patients underwent macroscopically curative resection with lymph node dissection. All of the resected primary tumors and lymph nodes were histologically examined by hematoxylin and eosin staining. The total number of resected lymph nodes was 1053, and median number was 18.2 per patient. Immunohistochemically, primary tumors and lymph nodes were examined by using antibodies against VEGF-C and VEGF-D. Tumors were judged as a high expression when over 25% of tumor cells showed positive staining. RESULTS: The expression level of VEGF-C and VEGF-D in the marginal portions were both significantly higher than those in the central portions, respectively. High expression VEGF-C group in the marginal portion of the tumor had significantly higher incidence of the involvement of lymphatic invasion (p = 0.028), and lymph node metastasis (P = 0.015). Both VEGF-C and VEGF-D expression had a significantly higher incidence of lymph node metastasis compared with the negative/low expression group (p = 0.007). The 5-year survival rates of patients with both high expression group were significantly lower than for the negative/low expression group (p = 0.017). CONCLUSION: VEGF-C and VEGF-D might be molecular targets for treatment to reduce lymph node metastasis and to improve the prognosis of patients with pancreatic adenocarcinoma.

44 PANCREATIC CANCER (MIAPACA-2) CELLS INCUBATED WITH N-3 FATTY ACID ENHANCED MEDIA DEMONSTRATE CELL CYCLE ARREST (G2/M) AND PROGRESSION TO APOPTOSIS
Thomas Dekoj, Tricia Babcock, W Scott Helton and N Joseph Espar, University of Illinois at Chicago, Chicago, IL, USA

INTRODUCTION: n-3 fatty acids have been proposed as antiproliferative therapies for specific gastrointestinal tract (GI) malignancies. Besides demonstrated in vivo anti-inflammatory properties via NFkB mediated inhibition, n-3 lipids regulate cell cycle progression/arrest. Previously we have observed accumulation of cell cycle at G2/M in MiaPaCa-2 cells; but cellular incorporation of lipid and subsequent cell cycle events have not been defined. HYPOTHESIS: Incubation of MiaPaCa pancreatic cancer cells with an n-3 lipid enhanced media results in media n-3 lipid depletion, G2/M cell cycle arrest (cdc2) and is associated with apoptosis. METHODS: MiaPaCa-2 pancreatic adenocarcinoma cells were seeded in 100 mm
dishes and treated with media alone, media with 100 μM n-6 lipid emulsion, or 100 μM n-3 lipid emulsion for 18, 24, 30, 48, and/or 72 h. HPLC lipid analysis was performed on resultant fatty acid methyl esters from treated cell cultures at the following time points: 24, 48 and 72 h of treatment. Total cd2 Western blot was performed by standard methods using PhosphoPlus cd2 (Tyr15) at 18 and 30 h of treatment. The Annexin V-FITC/propidium iodide staining flow cytometry was performed following specific kit specifications at 18 and 30 h. RESULTS: The media lipid analysis demonstrates that media alone and n-6-treated media maintained a consistent level of lipid; in contrast, the n-3 lipid-treated media showed a marked decrease of n-3 lipids in a time-dependent manner, under all time and concentration conditions. Total cd2 levels at both time points (18 h with increased change at 30 h) were decreased by approximately 50% (Figure). The annexin V-FITC/PI flow cytometry data showed an increase in cell death, early apoptosis, late apoptosis and death from apoptosis regions of the data field, as compared to media alone and n-6-treated cells. The increase in total apoptotic cells was approximately fourfold for both the 18- and 30-h time points. CONCLUSIONS: n-3 lipids are depleted from the media of n-3-treated cells, suggesting that the cells are absorbing and for metabolizing the lipid, cd2 levels are lower in the n-3-treated cells, supporting the proposition that n-3 lipids promote cell cycle arrest at G2/M. Annexin V flow cytometry demonstrates progression to apoptosis in only the n-3-treated cells, supporting the proposition that n-3 lipids are absorbed, act on cell cycle to progress to apoptosis.

45 ENDOSCOPIC ULTRASOUND DOES NOT ACCURATELY ASSESS PATHOLOGIC STAGE OF PANCREATIC ADENOCARCINOMA AFTER NEOADJUVANT CHEMOTHERAPY

Nicolas Betini, Vincent Moutardier, Olivier Turriti, Christian Pesenti, Bernard Lelong, Erwann Bories, Jérôme Guiramand, Marc Giovanni and Jean Robert Delpero, Institut Paoli-Calmettes, Marseille, France

BACKGROUND: Accuracy of endoscopic ultrasound (EUS) staging in pancreatic ductal adenocarcinoma (PDA) is demonstrated. In patients with PDA treated preoperatively with preoperative chemoradiation therapy (CRT), efficiency of EUS staging is controversial. The aim of this study was to compare preoperative EUS staging of PDA after CRT with pathologic examination. PATIENTS AND METHODS: From November 1996 to October 2003, we retrospectively reviewed the medical charts of 30 patients who underwent a neoadjuvant CRT for PDA after initial EUS staging. All patients were restaged by EUS before resection. Tumor location was pancreatic head in 24 patients and pancreas body in 6 patients. RESULTS: 24 pancreaticectomies and 6 distal pancreatectomies were performed. EUS accurately predicted the tumor stage in 6 patients (30%) and lymph nodes involvement in 6 patients in 6 patients (30%). EUS suggested vascular involvement in 12 patients but operative findings and pathologic examination were in negative in all cases. CONCLUSIONS: EUS appears to be inaccurate in PDA restaging after CRT. Tumor size, lymph node and vascular involvement cannot be predicted by EUS after CRT because of radiation-induced pancreatic changes.

46 DETECTION OF K-RAS POINT MUTATION BY PCR/RFLP ANALYSIS – IS THE SENSITIVITY HIGHER THAN HISTOLOGY IN A HAMSTER EXPERIMENTAL Pancreatic CANCER MODEL?

Cintia Yoko Morioska, Marcel Cerqueira Cesar Machado, Seiji Saito, André Siqueira Matheus, Renato Soares Godoy, Márca Saldanha Kubrusly, José Jukemura and Akiharu Watanabe, University of São Paulo, São Paulo, Brazil, Toyama University and Toyama Medical and Pharmaceutical University, Toyama, Japan

K-ras mutation has a relationship >80% with pancreatic cancer. We have previously established a curative resection model in hamster experimental pancreatic cancer. However, in cases with no histological evidence of metastasis, recurrence occurs in several cases. Thus, a method of early diagnosis would be helpful for better follow-up. The purpose of this study was to verify whether the sensitivity of histopathological and molecular studies differ in the diagnosis of metastatic sites. HaP-T1, a cell line derived from nitrosamine-induced pancreatic cancer was used in these experiments. Subcutaneously growing tumor in exponential phase was resected and orthotopic tissue implantation was performed. Partial pancreatoduodenectomy and splenectomy were done. Hamsters were divided into 3 groups: (A) positive control (n = 33), (B) surgery performed at day 7 (n = 30) and (C) surgery performed at day 14 (n = 27). Three animals from each group were sacrificed every 7 days until day 77 and necropsy was performed. Surgically resected and necropsied specimens such as pancreas, liver, lung, kidney, testis, and ovaries were sent for histopathological study and for detection of K-ras point mutation by PCR/RFLP analysis. Positive controls showed metastases in the histopathology starting from day 35 to 13 cases (30.4%) and at the molecular level starting from day 21 to 22 cases (66.6%). Groups 2 and 3 showed free margins in the surgically resected specimens. In group 2, tumoral recurrence was detected from day 42 in one case (3.3%) in the histopathological findings and in 2 cases (6.6%) at the molecular level. In group 3, metastases were detected from day 35 in one animal (3.3%) in the histopathology and in 2 cases (6.6%) at the molecular level. This study suggests that the PCR/RFLP analysis sensitivity rate was higher when compared with histopathological findings. These experiments show the importance of the possible use of this method for better staging and follow-up of pancreatic cancer.

47 SIGNIFICANCE OF LYMPH NODE MICROMETASTASES IN PERIAMPULLARY CARCINOMA

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PURPOSE: The purpose of this study was to investigate the clinicopathological significance of lymph node micrometastases compared with conventional study and to clarify the pathway of lymph node metastasis in periampullary carcinoma. METHODS: A total of 72 pancreatoduodenectomies (62 pylorus-preserving pancreatoduodenectomies, 8 Whipple operations, 2 total pancreatectomies) for periampullary carcinoma (pancreas 28, bile duct 24, ampullary 19, duodenum 1) between 2002 and 2003 were prospectively enrolled in this study. Lymph node metastasis assessed included groups #8, #9, #12, #13, #14 and #16. Dissected lymph nodes, after embedding in paraffin, were stained with hematoxylin-eosin (H-E) and then with pancytokeratin (pCK) by immunohistochemical staining. Micrometastasis was defined as <2 mm in diameter and not detectable by H-E staining. RESULTS: After H-E staining, 38 of 72 periampullary carcinomas had lymph node metastases (pancreas 24/28, bile duct 8/24, ampullary 8/19, duodenum 1/1). By pCK staining, 7 cases (pancreas 3, bile duct 4), which were lymph node negative by H-E staining, turned out to be positive (H-E-N/pCK+N+). Comparing clinicopathological data for the H-E/N/pCK N0 group (27 cases) and H-E/N/pCK N1 group (7 cases), there was no difference in many factors but there were more endolymphatic tumor emboli in H-E N0/pCK N+ (7/27 vs 6/7; p = 0.04). In periampullary cancer, 24 of 28 cases were lymph node positive in the H-E/N/pCK N+ group and by the drawing of pathway of lymph node metastasis, there were two frequent pathways: #13 → #14 → #16, #13 → #12 → #8 → #16. In bile duct cancer, the #13 → #12 → #8 → #16 pathway was more frequent. CONCLUSIONS: We detected 20% of new cases of micrometastases in periampullary carcinoma with pCK immunohistochemical staining and those cases were related to the endolymphatic tumor emboli. The long term results of micrometastases are needed.

48 ‘EN BLOC’ EXCISION OF HEPATIC HYDATID DISEASE IS SAFE AND SHOULD BE THE PREFERRED APPROACH

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PURPOSE: Complete excision of liver hydatid disease is the most effective treatment. However, despite several advantages, it is not universally popular. This study was undertaken to assess the feasibility and results of radical resection of hepatic hydatid disease. METHODS: The study was prospectively conducted in 28 consecutive patients with hydatid cyst of the liver, who underwent surgery during October 2000 to November 2003. All patients were assessed for suitability to undergo total cystopericytectomy
(TCP) or liver resection. RESULTS: There were 28 patients (19 females and 9 males) in the age range 19-61 years. The cyst was present in the right lobe of liver in 16, left lobe in 8 and both lobes in 4 patients. One patient had associated splenic hydatid cyst and symptomatic gallstone disease was present in 2 patients. In bloc excision of the hepatic hydatid cyst (TCP or liver resection) was performed in 22 of 28 patients (78.5%). This included closed total cysto-pericystectomy in 20, left hepatectomy and right hepatectomy in one patient each. 6 of 28 patients (21.5%) were deemed unsuitable for radical operation and underwent more conservative drainage procedures. Reasons included cirrhotic liver, close proximity to major vascular structures, unfavorable location, and communication with major bile duct. Postoperative complications included wound infection in 2 patients; bile leak occurred in 6 patients which were minor in all except one case (3.5%) which needed endoscopic papillotomy. The median hospital stay after TCP was 3.5 days and after drainage procedure 4.5 days. Over a median follow-up of 17 months, there has been no recurrence of cyst in any of the patients. CONCLUSIONS: Radical en bloc excision of hepatic hydatid disease can be performed safely and should be the preferred approach. However, the procedure needs to be individually tailored as all patients are not suitable (21.5%) for closed total cysto-pericystectomy or liver resection.

49 HEPATECTOMY FOR HEPATOCELLULAR CARCINOMA WITH MAJOR PORTAL OR HEPATIC VEIN INVASION CAN RESULT IN LONG-TERM SURVIVAL

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PURPOSE: Invasion of a main portal or hepatic vein branch (major vascular invasion, MVI) by hepatocellular carcinoma (HCC) is a grave prognostic factor with a <10-week median survival for untreated patients. MVI is generally a contraindication to liver transplantation or percutaneous treatment, but the role of hepatic resection remains controversial. We examined patients who underwent resection for HCC with MVI to assess their overall prognosis, as well as to determine which factors impacted survival. METHODS: 101 patients from a multi-institutional international database who underwent hepatic resection for HCC with MVI were evaluated using univariate and multivariate analysis. RESULTS: There were 87 men and 14 women with a median age of 61 years. Most patients had Child-Pugh class A disease (92; 91%), positive hepatitis B serology (59%; 58%), and multiple tumors (58%; 57%). The median alphafetoprotein (AFP) level was 1159 ng/ml (range 2-950,000 ng/ml) and the median tumor size was 10 cm (range 2-22 cm). The perioperative mortality rate was 6% (n = 6). Median survival was 11 months (median follow-up, 93 months). The 1-, 3-, and 5-year survival rates were 45%, 15%, and 10%; the longest-living survivor was still alive at 14.8 years. Patients with grade 0-2 fibrosis had a significantly higher 5-year survival rate (23%) than those with grade 3-6 fibrosis or cirrhosis (3% (p = 0.022) (Figure). Severe fibrosis and advanced tumor grade predicted early death (<6 months) after resection (p = 0.001 and p = 0.04, respectively). A trend toward worse survival in patients with AFP > 1000 ng/ml was observed (p = 0.06). On multivariate analysis, severe fibrosis remained a predictor of both long-term (>6 months) and short-term (<6 months) survival (hazard ratio (HR) = 7.1, p = 0.01 and HR = 2.7, p = 0.03, respectively). CONCLUSIONS: This multi-center international study indicates that hepatic resection can provide long-term survival in a subset of HCC patients with MVI. The high incidence of early death, however, emphasizes the need for more effective adjuvant or neoadjuvant therapy.

50 MID-TERM RESULTS OF LAPAROSCOPIC LIVER RESECTION FOR HEPATOCELLULAR CARCINOMA (HCC) COMPROMISING CHRONIC LIVER DISEASE

Alexis Laurent, Claude Tayar and Daniel Cherqui. Hospital Henri Mondor, Creteil, France

INTRODUCTION: Laparoscopic liver resection was developed by a limited number of teams over the past 3 years. We report our experience with this approach in patients with HCC and chronic liver disease as part of a prospective evaluation. PATIENTS: From November 1998 to August 2003, 27 patients with chronic liver disease underwent laparoscopic resection of HCC. Tumors were 10 cm or less in size and located in anterolateral segments. Liver disease was due to hepatitis B or C in 17 patients, alcohol in 8 and other causes in 2. Five-port CO2 laparoscopy was used and the specimen was extracted in a bag through a separate lower abdominal incision. RESULTS: One segment or less was resected in 19 patients including an anatomic resection in 10. Seven patients underwent left lateral sectionectomy and one underwent right hepatectomy. Seven conversions (26%) to laparotomy occurred for moderate hemorrhage in 4 cases and insufficient exposure in 3. All but one conversion occurred in resections of one segment or less. One patient received 2 units of red cells intraoperatively and two other patients were transfused postoperatively. Mortality and morbidity rates were 0% and 44% respectively. Transient liver failure and ascites occurred in 2 (7%) patients and there were no bile leaks or postoperative hemorrhage. Mean surgical margin was 11 mm (range 1-47 mm). After a mean follow-up of 2 years (range 0.5-4.7), 9 patients (33%) developed intrahepatic tumor recurrence, of which one died. One patient underwent orthotopic liver transplantation. Overall and disease-free 3-year survival rates were 93% and 71% respectively. CONCLUSION: Our study shows that laparoscopic liver resection for HCC in selected patients is a safe procedure with very good mid-term results. This approach could have an impact on the therapeutic strategy of HCC complicating chronic liver disease, especially as a bridge to liver transplantation.

51 SEQUENTIAL PREOPERATIVE ARTERIAL AND PORTAL VENOUS EMBOLIZATIONS IN PATIENTS WITH HEPATOCELLULAR CARCINOMA

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AIM: The purpose of this study was to investigate the preoperative biological and clinical course of 17 patients with hepatocellular carcinoma (HCC) who underwent sequential selective transcatheter arterial chemembolization (TACE) and portal vein embolization (PVE) prior to major hepatic resections, and to assess the postoperative patient prognosis. BACKGROUND: Hepatic resection, especially major hepatic resection, is the only curative treatment for large HCC. However, major hepatic resection is often contraindicated in HCC patients due to the underlying chronic liver disease. Preoperative PVE has been introduced to broaden the indications for hepatic resections; however, application of PVE to HCC patients with chronic liver disease has been debatable. PATIENTS AND METHODS: 17 HCC patients who underwent preoperative selective TACE and PVE for scheduled major hepatic resections were enrolled. The indications for PVE were determined using the volumetric ratio of the future remnant liver parenchyma and the indocyanine green retention ratio at 15 min (ICG R15). Tumor characteristics and blood test results before and after TACE and PVE, changes in the volumes of the liver segments after PVE, the feasibility of major hepatic resections, and the short- and long-term patient prognoses were examined. RESULTS: The liver function test results transiently worsened after the TACE and PVE, but returned to baseline levels within 1 (after TACE) or 2 (after PVE) weeks. Within 2 weeks after PVE, a 22 ± 4% of hyperfusibility of the non-embolized segments was obtained; subsequent major hepatic resections were feasible in 16 patients. Four (25%) minor complications were experienced postoperatively; however, liver failure did not occur. The 5-year overall and disease-
free survival rates after curative resection were 55.6% and 46.7%, respectively. CONCLUSIONS: Sequential TACE and PVE contribute to both the broadening of surgical indications and the safety of major hepatic resections performed in HCC patients with damaged livers. The long-term outcome of this treatment strategy is satisfactory.

52 PRIORITY OF PORTOSYSTEMIC SHUNT IN BUDD-CHIARI SYNDROME AFTER 22 YEARS OF EXPERIENCE
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PURPOSE: The purpose of this report is to describe our experience in treating the primary form of Budd-Chiari syndrome over a 22-year period to present a rationale for treatment by either portosystemic shunting or liver transplantation. METHODS: From 1979 to 2001, 58 patients with Budd-Chiari syndrome were treated at our institution. Of these, 41 were treated surgically by either surgical (n = 41) or medical (n = 17) means. Charts were reviewed of those treated surgically by either surgical shunting (n = 34) or liver transplantation (n = 4). RESULTS: A total of 41 patients underwent surgical treatment by either portosystemic shunting (n = 34), liver transplantation (n = 4), or other procedures (n = 3). 34 patients underwent portosystemic shunts: 29 mesenterico-caval, 4 portal-caval, and 1 mesenterico-atrial. The clinical classification of disease was as follows: 1 fulminant, 16 acute, 14 subacute, and 3 chronic. One death (13%, 1/34) occurred at postoperative day 38. The general condition of all but one patient (97%, 32/33 surviving patients) improved by 6 months. Ascites gradually regressed in 94%. All patients demonstrated clinical improvement in hepatosplenomegaly. Four patients experienced either primary shunt failure (6%), or portosystemic shunt thrombosis (6%, 2/34). Three of these patients underwent successful secondary liver transplantation. Following a mean follow-up period of 9.0 ± 6.4 years (range 0.08–22 years), all patients without primary shunt dysfunction or shunt thrombosis remain symptom-free. 85% (29/34) of patients are alive 0.08–22 years after surgery. Four patients underwent liver transplantation. The clinical classification of disease was as follows: 1 fulminant, 2 acute, and 1 chronic. The indications for transplantation included a failed portosystemic shunt, progressive hepatic failure with cirrhosis, or the fulminant form with fulminant hepatic failure. All four patients underwent uneventful liver transplantation. There was no postoperative mortality. The mean follow-up period following transplantation is 4.9 ± 4.7 years (range 0.2–11.3). All (100%) patients are currently alive and doing well. CONCLUSION: We have demonstrated that portosystemic shunting effectively controls symptoms and offers prolonged survival for those with the acute or subacute form. In those with the fulminant form, the standard approach is timely liver transplantation; however, we have demonstrated that in selected cases, portosystemic shunting can be feasible if treatment is undertaken rapidly. Liver transplantation should be undertaken in those with chronic disease and deteriorating hepatic function, although portosystemic shunting has a role in those with stable hepatic function.

53 SAFETY AND EFFECTIVENESS OF IPSILATERAL TRANSEPTIC RIGHT PORTAL VEIN EMBOLIZATION EXTENDED TO SEGMENT IV WITH PARTICLES AND COILS
David C Madoff, Eddie K Abdalla and J Nicolas Vauthery, University of Texas MD Anderson Cancer Center, Houston, TX, USA
PURPOSE: Various approaches have been described for portal vein embolization (PVE). We evaluated the safety and effectiveness of ipsilateral transhepatic right PVE extended to segment IV with particles and coils before planned extended right hepatectomy. METHODS AND MATERIALS: From 10/98 to 10/03, 42 patients underwent ipsilateral percutaneous transhepatic right PVE extended to segment IV with particles and coils to promote hypertrophy of the left lateral segment (segments II, III ± I). All patients had hepatobiliary malignancy: metastases (n = 23); biliary tract cancer (n = 14); hepatocellular carcinoma (n = 5). Three-dimensional CT volumetry was used to assess FLR volumes pre- and post-PVE. Embolization of segments IV–VIII was considered if the FLR/total estimated liver volume (TELV) was ≤52%. All PVE procedures were performed with intravenous conscious sedation. Particles (polymethyl alcohol or tri-acyl microspheres) ranging from 100 to 700 μ were administered in a stepwise fashion; smaller particles were used first to occlude the distal branches and larger particles were used subsequently to occlude more proximal branches. Particulate embolization was performed until stasis was achieved. Coils were placed in secondary portal branches to reduce the risk for recanalization. RESULTS: Right PVE extended to segment IV was successful in all patients with mean absolute FLR volume and FLR/TELV increases of 52.2% (p < 0.001) and 8.2% (p < 0.001), respectively. Median hospital stay was 1 day (range 0–8 days). No patient developed post-embolization syndrome, liver insufficiency, non-targeted embolization to FLR, or hemobilia after PVE. Three complications (7%) occurred: portal vein thrombosis in a patient with a left portal vein anatomical variant who was treated successfully with thrombectomy (n = 1), subcapsular hematoma (n = 1), and coil and thrombus extension of right posterior sector portal vein into main portal vein treated by thrombectomy at the time of resection (n = 1). No complication precluded resection. CONCLUSION: Ipsilateral transhepatic right PVE extended to segment IV with particles and coils can be performed safely while providing significant increases in the size of the FLR. This method should be compared to other currently used PVE techniques.

54 SURVIVAL IS IMPROVED BY SURGICAL RESECTION FOR EXTRHEPATIC RECURRENCE OF HEPATOCELLULAR CARCINOMA
Denis Castaing, Gérard Pascal, René Adam, Daniel Azoulay, Didier Samuel, Pierre Magdalena and Henri Bismuth, Paul Brouse Hospital, HepatoBiliary Center, Villejuif, France
BACKGROUND AND AIMS: Resection of hepatocellular carcinoma (HCC) is associated with a high incidence of recurrence. The surgical resection for liver recurrence is actually considered as the only potentially curative possibility. The treatment of extrahepatic recurrence is much debated. This retrospective study evaluated the role of resection in selected patients with extrahepatic recurrence of HCC. METHODS: A total of 525 patients underwent one or several liver resections for HCC with or without cirrhosis at a single institution over a 30-year period. Of these, 364 (69%) underwent a partial hepatectomy and 161 a liver transplantation. A total of 364 recurrences occurred in 263 patients (50%) with 136 extrhepatic recurrences in 98 patients (19%). One resection at least was done in 37 patients (38%). Resection was not feasible during laparotomy in 9 patients (9%). Surgery was decided if the resection was potentially complete. Extrahepatic locations and resections are summarized in the Table.

<table>
<thead>
<tr>
<th>Location</th>
<th>Number of sites</th>
<th>Number of resections</th>
<th>Resection rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary</td>
<td>41</td>
<td>15</td>
<td>37</td>
</tr>
<tr>
<td>Peritoneal</td>
<td>25</td>
<td>12</td>
<td>48</td>
</tr>
<tr>
<td>Bone</td>
<td>25</td>
<td>9</td>
<td>36</td>
</tr>
<tr>
<td>Abdo lymph node</td>
<td>20</td>
<td>3</td>
<td>15</td>
</tr>
<tr>
<td>Adrenal</td>
<td>12</td>
<td>6</td>
<td>50</td>
</tr>
<tr>
<td>Brain</td>
<td>4</td>
<td>2</td>
<td>50</td>
</tr>
</tbody>
</table>

RESULTS: There were no complications and no operative mortality (≤2 months). The 3- and 5-year survival rates for 37 patients who underwent one or several extrahepatic resections were 38% and 19% respectively and were significantly better than those of 61 patients who did not undergo any resection for recurrence: 8% and 1.5% respectively (χ² = 13.6; p = 0.0002). CONCLUSIONS: In selected patients with localized extrahepatic recurrence of HCC, surgery is safe and offers, when potentially curative, the only chance of long-term survival.

55 PORTAL VEIN EMBOLIZATION PRIOR TO SURGERY – IT MIGHT HELP BUT ...
Masato Nagino and Yuji Nimura, Nagoya University Graduate School of Medicine, Nagoya, Japan
OBJECTIVE: Portal vein embolization (PVE) has become important in the preoperative management of patients who are to undergo extensive liver resection. Many reports on PVE have been published; however, it remains unclear whether or not this intervention has clinical benefits. The aim of this study was to review our experience with preoperative PVE, focusing on hepatocarcinoma for biliary cancer. PATIENTS: From 1991 to October 2003, PVE was performed in 187 biliary cancer patients who were to undergo extended hepatectomy (right hepatectomy, right trisectionectomy, or left trisectionectomy). 75 patients had advanced gallbladder cancer and 112 had cholangiocarcinoma. Almost all PVEs were done by ipsilateral approach (puncture of the right anterior portal branch under ultrasound guidance), 2–3 weeks before surgery. Before 2002, fibrin glue mixed with lipiodol was used as embolic material, while after 2001 absolute ethanol and steel coil was used. When a planned hepatectomy was right trisectionec-
tomy, the right portal vein plus the left medial portal branch were emboled as previously reported. Similarly, in case of left trisectectomy, the left portal vein plus the right anterior portal branch were emboled.

RESULTS: There were no serious complications requiring blood transfusion or emergency intervention. Portal and mesenteric vein thromboses developed after PVE in one particular patient with protein S deficiency. This complication was successfully treated with thrombolytic therapy. No patient died of complications related to PVE. Only laparotomy was done in 23 (30.7%) of the 75 patients with gallbladder cancer and 14 (12.5%) of the 112 patients with cholangiocarcinoma, due to dissemination and/or locally advanced tumor. The remaining 150 patients underwent planned hepatectomy. Fourteen patients (9.3%) died of postoperative complications: mortality was higher in patients with gallbladder cancer than those with cholangiocarcinoma (17.3% vs. 5.1% vs. 5.98%, p < 0.05).

CONCLUSION: PVE can be performed safely without serious complications. PVE is not an ‘omnipotent tool’ to reduce the mortality of extended hepatectomy. However, the concept of PVE is rational, and this intervention has clinical utility, especially as presurgical management of high-risk hepatectomy.

56 POSTOPERATIVE BILE LEAKAGE: RISK FACTORS OUT OF 610 HEPATECTOMIES

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PURPOSE: The aim of this study was to identify the perioperative risk factors for postoperative bile leakage after liver resections. METHODS: Clinical data for 610 patients who underwent liver resection in our department between January 1989 and January 2003 were reviewed. Hepatectomies associated with hepato-portal biliary resection and reconstruction were excluded from this study. The median age of patients was 63 years (range 2-80), 153 patients (25.1%) were older than 70 years. Preoperative diagnostic work-up did not routinely include imaging of the biliary tree. 167 patients had a chronic liver disease. Anatomical liver resections were 480, major resections were 258, extended resections were 60. Biliary fistula was defined as the drainage of 50 ml or more of bile from the surgical drain or from a drainage of an abdominal collection, lasting 3 days or more. RESULTS: The overall in-hospital mortality rate was 2.4% (15/610). The morbidity rate was 27.5% (168/610). Postoperative bile leakage occurred in 22 patients (3.6%). One patient with bile leakage (4.5%) died because of the onset of sepsis and liver failure; in the other group 14 patients died in the postoperative course, with a mortality rate of 2.3% (p = 0.52). Univariate analysis of preoperative factors showed that the incidence of bile leakage in patients with peripheral cholangiocarcinoma was higher than in those with other liver diseases (4/15 [26.6%] versus 18/595 [3%], p = 0.0000). The presence of liver cirrhosis was associated with a lower rate of leakage (2/167 [1.2%] vs 20/443 [4.5%], p = 0.05). The incidence of postoperative leakage was similar after anatomical and non-anatomical resections, but it was significantly related to the extension of the hepatectomy: it occurred in 14 of 258 major hepatectomies (5.4%) versus 8 of 352 minor hepatectomies (2.2%, p = 0.039) and in 7 of 60 extended hepatectomies (11.4%) versus 15 of 550 non-extended hepatectomies (2.7%, p = 0.005). Biliary complications were more frequent in left hepatectomy (7/66 [10.6%]) than in right hepatectomies (4/54, p = 0.012). Hepatectomies including segments 1 and 4 were found to be at high risk for postoperative bile leakage (5/16 included: 6/52 [11.5%] vs 16/532 [2.9%, p = 0.002]; 5/16 included: 14/238 [6.7%] vs 8/402 [2%, p = 0.0029]. Stepwise logistic regression analysis identified extended hepatectomy, left hepatectomy and peripheral cholangiocarcinoma as independent risk factors for development of postoperative bile leakage. CONCLUSIONS: The presence of a peripheral cholangiocarcinoma, scheduled major or extended resections, especially on the left side, should be considered at high risk of postoperative bile leakage.

57 SURVIVAL BENEFIT ASSOCIATED WITH HEPATIC ARTERIAL CHEMOTHERAPY DEPENDENT ON NUMBER OF CYCLES COMPLETED AND INDEPENDENT OF CLINICAL RISK INDICES

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INTRODUCTION: Patients completing a full course of hepatic arterial infusion chemotherapy (HAIC) are those most likely to experience a survival benefit. The purpose of this study was to determine whether improved survival in patients completing therapy is due to the effects of treatment or biologically favorable tumors as predicted by traditional indices used in clinical risk stratification. METHODS: 24 patients undergoing placement of HAI devices between 11/01 and 6/03 were entered into a prospective database and followed. At completion, or final discontinuation of FU/DR therapy, patients were placed into 1 of 3 groups: those receiving 6 or more, 2–5 or 1 or fewer cycles. Response to treatment and clinical risk indices were determined for each group and compared.

RESULTS: Seven patients completed at least 6 cycles of HAIC. 8 patients received 4 cycles which was then truncated due to toxicity in 7 and death in 1. 9 patients received 1 or fewer cycles due to toxicity or pump failure in 3 each, persistently elevated LFTs precluding initiation in 2 and death in 1. There were no significant demographic differences between groups and each group had an equal number of procedures with curative or palliative intent (RFA, resection + pump/pump only). FU/DR dose was 0.12 mg/kg/day. 4 patients receiving no therapy are dead of recurrent/persistent disease. 4 patients receiving a partial course have documented recurrence (3 alive) and 4 of 7 patients completing therapy have recurrent/persistent disease (all alive). Survival and clinical risk indices are shown in the Table below. CONCLUSION: Failure to complete HAIC is common and cannot be predicted on the basis of traditional prognostic indices. Patients who receive most or all of planned HAIC enjoy a significant survival advantage over similar patients who fail to initiate or do not tolerate therapy.

58 HEPATIC MICROWAVE ABLATION USING A CLUSTERED PROBE SYSTEM: RESULTS OF A PHASE I ABLATE AND RESECT CLINICAL TRIAL

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BACKGROUND: Hepatic tumor ablation has become a treatment option for patients with hepatic malignancies or as an adjunct to hepatic resection. Microwave ablation has been available for approximately two decades; however, it has not received as much popularity as radiofrequency (RF) ablation due to the limited size of tissue ablation with a single antenna. This study demonstrates the results of a phase I clinical trial for selected patients undergoing elective hepatic resection. The tumors were treated intraoperatively with a cluster of three microwave probes prior to resection. Pathologic analysis with gross and histological examination was performed on all treated lesions. METHODS: Microwave hepatic ablation was performed in 9 patients prior to hepatic resection from 4/03 to 12/03. Three microwave antennae (Vivant Medical, Mountain View, CA, USA) were configured in a triangular formation with probe to probe distance of 1.5–2.0 cm. Real-time intraoperative imaging was used to guide antennae into the central aspect of the lesion. Without hepatic inflow occlusion microwave energy was applied for 10 min at 40 W through each antenna once. The hepatic resection was then completed in the standard fashion. Specimens were sectioned and measured in the fresh state. Tissue was fixed in formalin, paraffin-embedded, and sections were stained with H+E. Microscopic measurements were made. Tissue was also frozen fresh for histochemical evaluation. RESULTS: 9 patients were treated in this ablate and resect protocol. There were 5 males and 4 females with an average age of 62.1 years (range 39–79). Tumor histology included 6 metastatic colon cancers, 2 hepatocellular carcinomas, and 1 focal nodular

Initial stage

<table>
<thead>
<tr>
<th>Group</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>DFI (months)</th>
<th>Largest tumor size (cm)</th>
<th>Number of metastases</th>
<th>CEA (ng/ml)</th>
<th>Mean survival (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤1 FUDR</td>
<td>3</td>
<td>4</td>
<td>2</td>
<td>21.6 ± 24.9</td>
<td>4.7 ± 2.3</td>
<td>3.2 ± 2.8</td>
<td>390 ± 749</td>
<td>8.2 ± 4.3</td>
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<tr>
<td>&lt;6 FUDR</td>
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<td>2</td>
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<td>184 ± 449</td>
<td>15.7 ± 7.1*</td>
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<td>6 or more FUDR</td>
<td>2</td>
<td>3</td>
<td>2</td>
<td>21.4 ± 18</td>
<td>3.8 ± 0.91</td>
<td>3.0 ± 1.6</td>
<td>94 ± 130</td>
<td>17.8 ± 3.2*</td>
</tr>
</tbody>
</table>

*Significantly (p < 0.05) longer than those receiving 1 or fewer treatments.
hyperplasia. Average treated lesion diameter and volume were 4.2 cm. (2.0–3.7 cm.) and 69.7 cc (4.4–145.6 cc) respectively. Grossly, the microwave areas showed clear coagulation/necrosis effect. Microscopically, there was marked thermal-like effect with maximum intensity closest to the probe and gradually diminishing for about 1.1–1.5 cm toward the uninvolved parenchyma. In six of the cases a thin rim of hyperemia 0.1–0.2 cm. thick could be seen grossly and microscopically. Mean zone of ablation diameter and volume were 5.3 cm. (3.5–6.6 cm) and 93.8 cc (80–128.2 cc), respectively. CONCLUSION: Hepatic microwave ablation with clustered microwave antenna appears to be a promising technique for tumor ablation. Clustering of the antennae allows for a larger field of ablation than a single antenna microwave probe or any current RF probe. Hepatic vascular inflow occlusion may provide a larger area of coagulative necrosis. Further ‘ablate and leave’ studies are needed to determine its clinical efficacy.

59 RAPID LARGE VOLUME MICROWAVE TISSUE ABALATION (MTA) OF UNRESECTABLE LIVER TUMOURS USING A NOVEL APPLICATOR

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BACKGROUND: There is increasing interest in the in situ thermal ablation of liver malignancies either as a single treatment modality or in combination with liver resection. However, the efficacy of current ablation systems is limited by tumor size or associated complications. METHODS: Eleven patients considered to have large unresectable liver tumours >4 cm in diameter were enrolled in this study. Preoperative cross-sectional imaging in combination with intra-operative ultrasound was used to identify the tumours. Patients were treated with MTA alone (n = 4) or MTA with liver resection (n = 7). A total of 67 liver tumours was treated in this group of patients, 53 with MTA and 14 resected. The tumour types included metastases from colorectal cancer (n = 6) and parathyroid carcinoma (1), hepatocellular carcinoma (2), adenoma (1) and carcinoid (1). Two patients were treated laparoscopically, the remainder being treated at open surgery. The largest tumour was 6.5 cm in diameter, necessitating a single treatment of 4 min. Lesions 4–4.5 cm in diameter were treated in 3 min or less. Most ablations were carried out with a single insertion of the applicator. Complications, tumour recurrence and survival were recorded. RESULTS: Mean age was 61.4 years (range 30–79). The mean tumour size was 5.0 cm (range 4.0–6.5) and the mean MTA treatment time was 4 min (range 2–7). Six patients were alive at mean follow-up of 10 months (range 1–27, median 8). There were no complications related to the MTA treatment. Two patients died of pre-existing cardiac conditions in the postoperative period. Successful ablation was achieved in all patients, and no obvious tumour recurrence was visible at 3 months on imaging. At 1 year, two patients had hepatic tumour recurrence distant from the original ablation site and one patient developed extrahepatic disease at 27 months. CONCLUSIONS: Successful large volume ablation was achieved in all patients using this novel microwave equipment. This was accomplished using a rapid, single insertion technique computing favourably with other currently available ablative modalities. It appears safe and effective with minimal complications.

60 RADIOFREQUENCY ABLATION VERSUS SURGICAL RESECTION FOR SINGLE HEPATOCELLULAR CARCINOMA: LONG-TERM OUTCOMES

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OBJECTIVES: Radiofrequency ablation (RFA) has been increasingly utilized for hepatocellular carcinoma (HCC). Some believe the results are similar to those of surgical resection; however, no prospective controlled studies have been performed and such a study may be difficult to conduct. We, therefore, retrospectively reviewed patients with single HCC and compared the local control efficacy and long-term outcomes between resection and RFA. METHODS: From 1995 to August 2003, a total of 87 patients underwent resection (n = 47) or RFA (n = 40). 36 patients with poor operative risk due to underlying liver dysfunction and 4 patients who refused resection underwent RFA. Each treatment arm was further divided into two subgroups based on tumor size. Group 1, resection, <5 cm (n = 18); group 2, RFA, <5 cm (n = 26); group 3, resection, ≥5 cm (n = 29) and group 4, RFA, ≥5 cm (n = 14). Follow-up ranged from 2 to 72 months. Patients’ characteristics (age, gender, race, liver function, etiology of liver disease, alpha-fetoprotein, clinical stage, Child-Pugh classification), recurrence rates and overall and disease-free survivals were analysed. RESULTS: Group 1 patients were significantly younger (61 vs 67, p = 0.048) and had significantly better Child-Pugh classification (p = 0.005) than group 2 patients. Similarly, group 3 patients were significantly younger (60 vs 72, p = 0.005) and had significantly better Child-Pugh classification (p = 0.011) than group 4 patients. The mean tumor size of group 3 was significantly larger than that of group 4 (10 vs 7 cm, p = 0.23). The other parameters did not differ significantly. Local recurrence developed in 1 of 47 patients treated with resection and in 4 of 40 patients treated with RFA (2.0% vs 10.0%, p = 0.12). New intrahepatic and extrahepatic recurrence developed in 13 of 47 patients treated with resection and 10 of 40 patients treated with RFA (27.3% vs 25.0%, p = 0.78). These recurrences were subsequently treated with multimodality therapy as indicated. The median overall survival (49 vs 51 months, p = 0.44) and the median disease-free survival (36 vs 22 months, p = 0.84) were not significantly different between groups 1 and 2, as were the median overall survival (47 vs ≥63 months, p = 0.94) and the median disease-free survival (28 vs ≥20 months, p = 0.67) between groups 3 and 4. CONCLUSIONS: Although the groups were not completely comparable, this retrospective study seems to indicate that RFA offered equivalent long-term results to surgical resection for single HCC when each was combined with multimodality therapy. Whether these two treatments are truly comparable will require a prospective controlled study.

61 LIVER RESECTION FOR INTRAHEPATIC CHOLANGIÖCARCINOMA

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Surgical resection of cholangiocellular carcinoma (CCC) is the only therapy with a curative intention. In contrast to hepatocellular carcinoma (HCC), CCC is only rarely associated with liver cirrhosis. Therefore, extended resections are also feasible and locally advanced tumors resectable. From 1988 to 2022, 2251 patients underwent hepatic resection in our institution, among these 84 patients (4%) suffering from CCC. The surgical procedures in these patients were wedge resections (5%), hemiepatectomies (42%), extended resections (33%) and trisec tionectomies (20%). The postoperative mortality (90 days) was 8% in all patients, 3% after hemiepatectomy, 12% after extended resection and 14% after trisectionectomy. The rate of formally curative resections (R0) was 59%. The 1-, 5- and 10-year survival rates after R0 resection were 64%, 38%, and 34%, respectively. The respective rates after R1 and R2 resections were significantly lower. The histopathological differentiation was moderate in most CCC (G2: 67%). Highly differentiated tumors (G1) occurred in 4 patients, and poorly differentiated tumors in 28 patients. All patients suffering from G1 tumors survived over the long term up to 14 years, compared with rates of 10-year survival of 34% in patients with G2 tumors and one patient with a G3 tumor. Extended resections had been performed in more than half of the patients with an acceptable postoperative risk. In CCC, biological properties as the histopathological differentiation have a major impact on the postoperative outcome.

62 PERCUTANEOUS RADIOFREQUENCY THERMOABLATION AS AN ALTERNATIVE TO SURGERY FOR TREATMENT OF LIVER RECURRENCES AFTER HEPATECTOMY

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BACKGROUND: Radiofrequency (RF) current, converted into heat through ion agitation and friction, can destroy liver tumors by means of coagulation necrosis. This study assesses if percutaneous RF is a useful and safe technique for the treatment of liver recurrences (LR) after hepatectomy. PATIENTS AND METHOD: Forty-seven patients presenting 58 after hepatectomy for malignant tumors were treated with percutaneous RF instead of repeat hepatectomy. Radiofrequency thermal ablation was performed under image guidance for 12–15 min. This group
represented 62.6% of 75 patients treated with a curative intent for liver recurrences (LR) in the same time period. The 28 other patients underwent repeat hepatectomy. The primary tumor was a colorectal cancer in 29 (61.7%) patients. RESULTS: The mean number of liver metastases destroyed was 1.38 (SD 2.7, range 1–3) and the mean diameter was 21 mm (SD 7.5, range 9–35). Twenty-six patients (55.3%) presented LR at least once but up to 3 times after the initial RF application. An incomplete local treatment with RF was observed in a total of 12.7% of patients. Nine patients developed extrahepatic recurrences. The mean interval between RF and the last follow-up visit was 14.4 months (SD 10, range 5.5–40). One death and 3 major complications occurred, representing 3.7% of 107 thermoablated lesions. Survival rates at 1 and 2 years were 88% and 55%, respectively. A retrospective study of the authors’ database over two similar consecutive periods showed that RF increased the number of curative local treatments for post-hepatectomy LR from 16.6% to 26.1% and decreased the number of repeat hepatectomy from 100% to 39%. CONCLUSION: Percutaneous RF increases the number of patients eligible for curative treatment. It should be preferred to repeat hepatectomy when feasible and safe as it is much less invasive. We consider that repeat hepatectomy is now indicated only when percutaneous RF is contraindicated or fails.

63 RECOMBINANT COAGULATION FACTOR VIII IN MAJOR LIVER RESSECTION – A RANDOMISED, PLACEBO-CONTROLLED, DOUBLE-BLIND CLINICAL TRIAL
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BACKGROUND: Treatment and prevention of bleeding episodes in non-cirrhotic patients undergoing hepatectomy remain unsatisfactory in spite of improved surgical techniques. Clinical data indicate that rFVIIa induces a haemostatic effect even in patients with normal coagulation systems. We conducted a randomised, placebo-controlled, double-blind trial to evaluate the haemostatic effect and safety of recombinant activated coagulation factor VII (rFVIIa) in major hepatectomy. METHODS: 204 patients were equally randomised to receive either 20 or 80 μg/kg rFVIIa or placebo. Hepatectomy was performed according to local practice in the participating centres. Patients were monitored for 7 days post-surgery. Key efficacy parameters were the total transfusion requirements and blood loss. Safety assessments included monitoring of coagulation-related parameters and Doppler examination of hepatic vessels and lower extremities. FINDINGS: The proportion of patients requiring perioperative red blood cell transfusion was 15% in the patients receiving placebo (9/60) versus 8% in the patients receiving rFVIIa (21/245), p = 0.031. Mean intraoperative blood loss was 1073 ml in the 80 μg/kg group compared with 1422 ml and 1372 ml in the placebo group and 20 μg/kg group, respectively (logistic regression model; p = 0.026). Mean intraoperative blood loss was 1073 ml in the 80 μg/kg group compared with 1422 ml and 1372 ml in the placebo group and 20 μg/kg group, respectively (logistic regression model; p = 0.026). The reduction in haematocrit during surgery was smallest in the 80 μg/kg group, with a significant overall effect of treatment (p = 0.043). INTERPRETATION: rFVIIa seems to be of benefit for decreasing the number of patients requiring red blood cell transfusions when undergoing major hepatectomy. Dosing with rFVIIa appeared safe.

64 LIVER HANGING PROCEDURE COMBINED WITH HEMOSTATIC PLATE TO COMPRESS THE LIVER CUT END FOR OCCLUSION
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BACKGROUND: Belghiti et al. (Am Coll Surg 2001; 193: 109) proposed a liver hanging maneuver using a tape passed through the retrohepatic tunnel between the anterior surface of the inferior vena cava (IVC) and the liver. We tried to improve the procedure from four aspects. METHODS: 1. We tried different methods including dissection under vision using endoscope; step by step dilatation using Fogarty catheter; and finger dissection. 2. We use a hemostatic plate combined with the sling. Both tips of the sling are threaded through the holes on both end of the plate. The cut end of the liver can be compressed circumferentially when the sling is pulled up while the plate is pressed down, resulting in the occlusion of the blood to the cut end. 3. Double slings can also be used through the same tunnel but separated on the liver surface at both sides of the transaction line. In the same way double hemostatic plates can also be used in combination with the double slings. 4. A suprapilar bifurcation tunnel was developed between the right hepatic pedicle and the liver. The lower tip of the tape is set with a clamp and pulled through the tunnel. The portal triad can thus avoid being compressed when the liver is used for control of bleeding. RESULTS: Since April 2003, 36 cases of hepatectomy using liver hanging maneuver including 16 right hepatectomy (3 with caudate lobectomy), 1 right trisegmentectomy with complete caudate lobectomy, 7 left hepatectomy, 1 extended left hepatectomy with hepato-pancreato-duodenectomy (HPD), 9 segmentectomy or bis-segmentectomy, 2 piggyback liver transplantsations were done. The development of retrohepatic tunnel was successful in all but one case due to tumor closely attached to the IVC. There were no major complications related to this procedure. CONCLUSIONS: The application of hemostatic plate, double tapes and suprapilar bifurcation tunnel can be helpful in expanding the indications for liver hanging procedure. Belghiti’s liver hanging maneuver is a milestone in the history of liver surgery.

65 FIFTY-FIFTY AT DAY FIVE CRITERIA: AN ACCURATE ASSESSMENT OF POST-HEPATECTOMY LIVER FAILURE
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BACKGROUND: The risk of postoperative liver failure (PLF) remains present in the context of expansion of liver resection in patients with large tumors and/or abnormal underlying liver parenchyma. Various clinical (ascites, encephalopathy, icterus) and biological factors (serum prothrombin time, bilirubinemia) were used postoperatively but the definition of PLF was not standardized. Using a large prospective database during a short period, the aim of this study was to define an accurate definition of PLF. METHODS: Between 1998 and 2002, among the 715 hepatectomies included in the database, 349 (49%) had diseased liver (steatosis >30%; fibrosis, cirrhosis or non-icteric cholestasis) and 444 (62%) were major resections (≥3 segments). In all patients serum bilirubin and prothrombin time (PT) were collected respectively on postoperative days (PD) 0, 1, 3, 5, and 7. Patients were classified as at risk of PLF when either serum bilirubin level was >50 μmol/L and/or PT ≤ 50%; the subgroup with both criteria was identified as the fifty-fifty criteria group. The mortality was considered during hospital stay. RESULTS: The overall postoperative mortality rate was 3.1%. Overall analysis of postoperative liver function tests showed that PT decreased to a minimum at PD1 and then regularly increased after PD3, while the peak of serum bilirubin level was observed on PD7. Therefore we analysed PLF on PD3 showing that bilirubin ≥50 μmol/L was present in 102 (14.3%) patients and a PT ≤50% in 42 (6%). The simultaneous presence of bilirubin ≥50 μmol/L and PT ≤50% (fifty-fifty criteria) was observed in 25 cases (3.5%) with a mortality rate of 44%. The mortality rate of patients with only one or none of these criteria was highly significantly lower (p < 0.001), only 3.9% of mortality in the group with bilirubin ≥50 μmol/L and PT ≥50%; 5.9% in the group with bilirubin ≤50 μmol/L and PT ≤50% and 1% mortality rate in the group with PT ≥50% and bilirubin ≤50 μmol/L. CONCLUSION: Our results showed that after liver resection, patients who fulfilled bilirubin ≥50 μmol/L and PT ≤ 50% at day 5 have a PLF leading to nearly 50% mortality rate. Because postoperative liver function tests have various and dissociated kinetic evolution we propose to define postoperative PLF as the presence of the fifty-fifty criteria at postoperative day 5.

66 CONTRAST ULTRASOUND OF FOCAL LIVER LESIONS – AN INITIAL EXPERIENCE
Ravi Matudanayagam, Dennis Cochlin and Nagappen Kumar, University Hospital of Wales, Cardiff, UK

INTRODUCTION: The accurate detection and assessment of focal liver
lesions (FLI) is a common problem in hepatic imaging. One of the latest developments in ultrasound (US) technology is the use of contrast agents. The advantages are lack of radiation exposure and the ease of repeatability. We report our initial experience with the use of contrast US for the assessment of FLI. Our aim was to see if contrast US can accurately predict the nature of the FLI. METHODS: This was a retrospective study of 43 patients with FLI over a period of 10 months from January 2003 to October 2003. One experienced radiologist (DC) performed all the contrast US examinations after obtaining informed consent. The scan was performed in pulse subtraction mode after administering intravenous injection of the microbubble contrast agent, Sonovue. These patients had previously undergone other imaging like computed tomography (CT) or magnetic resonance imaging (MRI) where the diagnosis was suspected. They subsequently underwent contrast US examination. In appropriate patients the definitive diagnosis was confirmed by needle biopsy or surgical resection. The results of the contrast ultrasound were compared with the ‘gold standard’ for that particular diagnosis and were not used to influence patient management. RESULTS: There were 43 patients with FLI. There were 24 males and 19 females, with a median age of 57 years (range 39–94 years). The definitive diagnosis was hepatocellular carcinoma (HCC) in 6, metastasis in 19, haemangioma in 7, focal nodular hyperplasia (FNH) in 2, adenoma in 2, abscess in 5 and cholangiocarcinoma in 2. Contrast US correctly predicted the diagnosis in all patients with HCC, haemangioma, FNH, adenoma and abscess. Seventeen of the 19 patients with metastasis were correctly predicted by contrast US. One patient with metastasis was diagnosed as liver cyst and the other one with solitary secondary was reported as normal liver. One patient with cholangiocarcinoma was wrongly diagnosed as FNH. The contrast ultrasound was 100% sensitive in diagnosing HCC and abscess. The sensitivity for diagnosing metastasis was 89.47%. The positive predictive value was 100% for HCC, abscess and metastasis. Negative predictive value could not be calculated because of the small number of patients studied. CONCLUSION: We conclude from our preliminary study that contrast US has characteristics to accurately predict HCC, abscess and liver metastasis in patients with FLI. Further studies are required with larger numbers to confirm our preliminary findings.

67 COMPLEX HEPATIC SURGERY AIDED BY A 1.5 TESLA MOVABLE MR SYSTEM: A PILOT STUDY

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Resection represents the standard treatment for potentially curable liver tumors. The role of radiofrequency ablation (RFA) in the treatment of these lesions is not well defined, as technical factors may limit the potential for cure. One obstacle is that ultrasound (US) does not clearly define the extent and boundaries of the burn zone. This is particularly problematic when larger lesions are targeted with multiple applications. It was postulated that intraoperative MRI (iMRI) would better assess the completeness of RFA, influencing intraoperative decisions. Four cases of open hepatic surgery in an operating room equipped with a unique, movable 1.5 Tesla MRI scanner were performed. With this MRI system, standard OR equipment can be used, although certain modifications in the conduct of the operation are required. Patients were selected because RFA was a planned option. The operative approach was decided based on findings at laparotomy. After all ablative maneuvers, the effectiveness of ablation was evaluated with iMRI. Additional treatments were administered based on iMRI findings. Patient 1 had Child A cirrhosis and had recurrent multifocal hepatocellular carcinoma. The lesions were treated by combined resection and RFA. Patient 2 had multiple functional liver metastases from a small bowel carcinoid, and these were almost isoechogenic on US. The presence of miliary micrometastases confirmed at laparotomy precluded a liver resection; 5 gross lesions were debulked by RFA. Patient 3 had a recurrent colorectal metastasis (after a previous resection and two unsuccessful RFA); he underwent iMRI-guided resection. Patient 4 had 2 recurrent colorectal metastases (one >10 cm), following a right hepatic lobectomy. These were treated by RFA. Immediate post-treatment images showed the RFA bed to be hyperintense on T1-weighted (T1W) images and hypointense on T2W images. In two patients (patients 2 and 4), the post-treatment iMRI findings significantly altered management, as additional applications of RFA were required to completely encompass the target lesions. Our initial experience identified several technical factors that will require development. Specifically, the left and anterior aspects of the liver are suboptimally visualized; large patients are not easily imaged; and digital subtraction images are essential. These ongoing pilot studies have identified the problems with the present technology. Our findings will determine the direction of future development.

68 COMPARING SURVIVAL RATES OF HEPATIC ARTERIAL CHEMO-EMBOLIZATION FOR HEPATOMOCYTE CARCINOMA WITH DIFFERENT EMBOLIC AGENTS: GELFOAM AND POLYVINYL ALCOHOL

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PURPOSE: To compare survival rates of patients who have undergone hepatic artery chemo-embolization (HACE) with either gel foam powder (GP) or polyvinyl alcohol (PVA) particles and ethiodol for hepatocellular carcinoma. MATERIALS AND METHODS: HACE was performed on 83 patients who underwent HACE using 50 mg epirubicin, 25 mg doxorubicin, and 10 mg mitomycin-C with either GP (n = 44) or 300–500 mcg PVA and ethiodol (n = 39). Length of patient survival was calculated from the patient’s first HACE procedure. Transplant recipients were censored at the time of surgery. CTP and MELD scores were calculated for both groups. All patients were categorized as either alive or deceased at time periods of 3, 6, 12, and 24 months. Survival differences were tested for statistical significance with the log rank test. All categorical and patient survival data were analysed using product-limit (Kaplan–Meier) survival analysis. Fisher exact tests were used to test patterns for statistical significance. RESULTS: Mean and median CTP and MELD scores were similar (p = 0.35 CTP, p = 0.13 MELD) for each group. Overall mean and median patient survival was 23.9 and 17 months. Mean and median survival with GP was 25.4 and 18 months, while with PVA it was 9.8 and 14 months. The difference in mean survival was not significant (log rank test, p = 0.27). Mortality within 30 days occurred in one GP patient (liver failure) and two PVA patients (variceal bleed, sepsis). A greater percentage of GP patients were alive at 3, 6, 12, and 24 months and were significantly greater at 24 months. CONCLUSIONS: Whole group mean and median survival were not significantly different based upon the embolic agent used. Patients who survived past 12 months had a survival advantage when emibolized with GP.

Outcomes

<table>
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<th>Embolic agent</th>
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69 A MODIFIED COMBINED PERCUTANEOUS TRANSHEPATIC AND ENDOSCOPIC TRANSPAPILLARY TECHNIQUE FOR DIFFICULT CANNULATION OF BILE DUCT

Wen Li, Enqiag Liighu, Zhiqiang Wang, Fenchguo Cai, Xiangfong Wang, Hong Du, Jiagang Meng, Liufang Cheng and Yunsheng Yang, General Hospital of the Chinese People’s Liberation Army, Beijing, China and Department of Gastroenterology, Beijing, China

BACKGROUND: Morbidity and mortality remain high for combined percutaneous transhepatic and endoscopic procedures to approach the bile duct when endoscopic deep cannulation of the bile duct fails. AIM: To modify the combined percutaneous and endoscopic procedures in order to decrease the procedure-related morbidity and mortality. PATIENTS AND METHODS: Sixteen consecutive patients with malignant biliary obstruction or benign bile stenosis with stones underwent attempted endoscopic biliary therapy using a modified combined percutaneous transhepatic and endoscopic transpapillary approach. All patients had failed endoscopy-alone procedures and had contraindications to surgery. The indication was palliation of malignant biliary obstruction in 15 cases (8 common bile duct, 7 hilar), assistance with sphincterotomy for the removal of common bile duct stones and management of benign bile stenosis in 1 case. The first procedure was percutaneous transhepatic access to the biliary tree guided under colour Doppler ultrasound. Subsequent attempts were to introduce a guidewire or a cannula through the cannula or the guidewire into the
duodenum. A duodenoscope is then positioned in the duodenum immediately after the percutaneous procedures. Lastly the wire or the cannula from the percutaneous transhepatic access guided (‘kiss’) the endoscopic catheter or wire to access the common bile duct. There is no need to grasp and extract the guide wire perorally. RESULTS: The percutaneous transhepatic access to the biliary tree was successful in all cases (100%). Subsequent attempts via common bile duct and papilla access to the duodenum were successful in all but two cases (88%). Twelve of the 14 patients (86%) then had successful cannulation and stent placement by the modified combined percutaneous-transhepatic and peroral-endoscopic procedures (kiss technique). Procedure-related morbidity and mortality were 6% and 0% respectively. CONCLUSION: The modified combined percutaneous and endoscopic procedures (kiss technique) to approach the bile duct showed a very low procedure-related morbidity and mortality.

70 A PALLIATIVE TREATMENT OPTION FOR UNRESECTABLE CHOLANGIOCARCINOMA – INITIAL EXPERIENCE WITH TRANSCATHETER ARTERIAL CHEMO-EMBOLIZATION (TACE) IN A SINGLE INSTITUTION

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PURPOSE: Unresectable cholangiocarcinoma carries a dismal prognosis with median survival ranging from 6 to 12 months. Palliative treatment options have been disappointing and have not been shown to significantly prolong survival. Transcatheter arterial chemoembolization (TACE) has been quite effective in prolonging the life of patients with primary and some secondary liver cancer but has not readily been used against cholangiocarcinoma. Thus, the purpose of our study was to assess the impact of TACE on the survival of patients with unresectable, intrahepatic cholangiocarcinoma. METHODS: Fifteen patients with unresectable cholangiocarcinoma were treated with one or more rounds of TACE between 1995 and 2003 at our institution. Follow-up MR imaging was performed on all patients at 4+6 weeks after each TACE to determine tumor response and need for further treatment. Survival was calculated using the Kaplan-Meier survival curve. RESULTS: The median survival for 15 patients treated with TACE was 20 months (12-28 months, 95% CI). Follow-up MR imaging demonstrated 25-75% tumor necrosis in a majority of patients. Two patients who were previously determined to have unresectable tumors were actually able to be resected following TACE treatments and tumor shrinkage. Complications immediately following TACE treatment occurred in a minority of patients and included transient nausea, vomiting, diarrhea, hypertension, tachycardia, and right upper quadrant pain. A majority of these complications were managed with conservative therapy alone. CONCLUSIONS: Our results suggest that TACE was effective at prolonging survival of patients with unresectable cholangiocarcinoma. It was also generally well tolerated and, when compared to other therapies, TACE offered the advantage of a minimally invasive approach. TACE may therefore be an appropriate and promising palliative therapeutic option for patients with cholangiocarcinoma.

71 COMPARISON OF MELD AND CTP SCORES TO PREDICT SURVIVAL FOLLOWING CHEMO-EMBOLIZATION FOR HEPATOCELLULAR CARCINOMA

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PURPOSE: To compare the value of the Model for End-stage Liver Disease (MELD) and Child-Turcotte Pugh (CTP) scores to predict patient survival rates from hepatic artery chemo-embolization (HACE) for hepatocellular carcinoma (HCC). MATERIALS AND METHODS: Eighty-seven patients underwent 169 HACE sessions. MELD and CTP values were calculated prior to the initial treatment. MELD and CTP scores were placed in high and low categories about their respective medians, with the low category including the median score. Patient survival was tracked at 3, 6, 12, and 24 months, and log rank tests were used to determine statistical significance within the survival differences. Survival length was tracked from the date of the first HACE. Transplant recipients were censored at the time of surgery. RESULTS: Mean and median survival for all patients was 24 and 17 months. Sixteen patients were censored for transplant at a mean of 12.9 months. MELD and CTP scores correlated well to each other (r = 0.68). CTP score (r = -0.35, p = 0.04) correlated more strongly to survival than MELD (r = -0.26, p = 0.12). After high/low score category division, a statistically greater survival difference was predicted by CTP (27.2 vs 10.3 months, p = 0.03) than MELD (27.5 vs 15.8 months, p = 0.19). Survival differences between high and low risk groups at the 3-, 6-, 12-, and 24-month intervals are displayed in the table above. CTP scoring showed the difference between high and low groups to be statistically significant for all time periods. Statistical significance was not approached for any of the time lengths with the MELD system. CONCLUSIONS: CTP correlates better than MELD to overall patient survival and is a better predictor than MELD of survival at specific time points.

72 A SINGLE-CENTER EXPERIENCE IN THE USE OF RADIOFREQUENCY ABLATION (RFA) IN THE TREATMENT OF HEPATOCELLULAR CARCINOMA (HCC)

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INTRODUCTION: RFA for patients with non-resectable HCC is increasing in use as first-line treatment. Whilst there is evidence of improved survival rates with good quality of life for some, in others, patterns of recurrence and complications remain less predictable. PATIENTS AND METHODS: Over a 2-year period (2001-2003), we have managed 29 patients with HCC. Patient selection, severity of cirrhosis, treatment approach, number of treatments, recurrence rates and complications were identified. RESULTS: In those with viral aetiology 1 received liver transplant, 3 received best supportive care. In the non-viral group 1 received hepatectomy, 14 received best supportive care. CONCLUSION: Our data suggest that RFA may be of benefit to some patients with HCC, in particular those with small volume non-viral Child’s B/C cirrhosis who are not fit for surgical resection or transplant. Failure to see a fall in AFP after RFA is indicative of poor prognosis. We have also witnessed the phenomenon (reported by others) of rapid tumour progression throughout the liver and portal vein replacement within weeks of RFA. We advocate early follow-up CT at 4 weeks post RFA to detect this change and also question the use of RFA for HCC with portal vein proximity (see Table below).

73 ARTERIO-ENTERIC FISTULA AFTER SIMULTANEOUS PANCREAS AND KIDNEY TRANSPLANTATION (SPK)

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INTRODUCTION: Pseudoaneurysm rupture with an arterio-enteric fistula after pancreas transplantation is an infrequent event. We describe a case of arterio-enteric fistula after SPK transplant with a dramatic
enterontraphia treated with embolization of the Y graft and prompt removal of the pancreas. CASE REPORT: A 50-year-old man with a 31-year history of insulin-dependent diabetes mellitus and chronic renal insufficiency was admitted to our unit 8 months after a SPK transplant for a massive lower gastrointestinal bleeding. After reanimation the patient was transferred to the radiological unit and submitted to a selective angiography using a left femoral arterial approach. Contrast injection showed a large arterio-duodenal fistula at the level of the anastomosis between the mesenteric artery and the Y graft. As there was persistent severe hypotension we decided to embolize the mesenteric artery and the Y graft (Guglielmi detachable coils). The procedure was successful and the patient progressively recovered an acceptable hemodynamic condition. Once hypovolemia was completely corrected we proceeded to the graft removal. DISCUSSION: Pseudoaneurysm rupture must be suspected in patients with a history of pancreas transplantation and unexplained hypotension, cardiac arrest, or gastrointestinal tract bleeding. While Doppler ultrasound is an excellent diagnostic tool to identify these vascular complications in an elective setting, in an emergency angiography has the advantage of allowing diagnosis and treatment at the same time. In our case angiography recognized the site of the arterio-enteric fistula at the level of the anastomosis between the graft and the mesenteric artery, probably due to the rupture of a pseudoaneurysm. Prompt embolization of the graft could stop the hemorrhage. Although rare, pseudoaneurysms and arterio-enteric fistulas after pancreas transplantation are sources of significant morbidity and mortality. Based on our experience and review of the literature an endovascular approach to these complications may be considered as first treatment both in the emergency and elective setting.

74 COMPARISON OF THE SURGICAL BYPASS PROCEDURES AND PERCUTANEOUS TRANСПHASIC STENTING FOR NON-RESECTABLE MALIGNANT BILIARY OBSTRUCTIONS: A PROSPECTIVE CLINICAL TRIAL

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BACKGROUND: Unresectable malignant biliary obstruction results in a number of untoward physiological effects that can negatively impact on a patient’s health regardless of its etiology. Adequate drainage will result in an improvement of jaundice and pruritus and may improve a patient’s remaining quality of life. Available methods of biliary decompression include surgical bypass and non-operative drainage. METHODS: A total of 451 patients with unresectable malignant biliary obstruction was palliatively treated in our institute between January 1993 and December 2003. In this prospective study, we performed a surgical bypass (hepaticojejunostomy, choledochojejunostomy and choledochocholedochostomy) in the first group (n = 120). In the second group of patients (n = 331), prothetic stents were inserted by the percutaneous transhepatic route. We analysed the demographic data, diagnosis and patients’ status before the procedure, morbidity and mortality rates, complications, hospital length of stay and survival. RESULTS: Of the 451 patients, 261 were male and 190 were female. The mean age was 59 years (range 31-84) in the first group and 63 (range 31-90) in the second group. Diagnosis for biliary obstruction was pancreatic head carcinoma (n = 68, 56.6%), Klatskin tumor (19, 15.8%), tumors of ampulla of Vater (16, 13.3%) and gallbladder carcinoma (14, 11.6%) in the first group. In the second group patients were diagnosed as having pancreatic head carcinoma (n = 198, 59.9%), tumor of ampulla of Vater (88, 26.3%) and cholangiocarcinoma (42, 12.6%). Total bilirubin levels before the procedure ranged from 17 to 65 mg/dl (median 22 mg/dl) in the first group and 14 to 62 mg/dl (median 28 mg/dl) in the second group. Length of stent stay was 2-18 weeks. Overall morbidity and 30-day mortality rate were higher in the first group, 22-38% vs 1-30% and 12-32% vs 6-18%, respectively. Major complications such as cholangitis, bile leak, hemobilia, and biloma occurred in 16 patients (3.3%) in the first group and 64 patients (19.3%) in the second group. Median hospital length of stay was significantly shorter in the second group (25, 11-52 days vs 14, 3-32 days). Total bilirubin levels 1 month after the procedure ranged from 5.2 to 12.8 mg/dl vs 4.2-11.6 mg/dl in the groups, respectively (p = 0.38). Mean survival were 5.2 vs 3.8 months, respectively. CONCLUSION: Percutaneous transhepatic stenting offers palliation of malignant biliary obstruction with a shorter hospital stay; it is also a safe and effective technique for total biliary drainage and it is strongly indicated in high surgical risk patients.

75 TRANSPULSAR INTRAHEPATIC PORTOSYSTEMIC SHUNT IN BUDD-CHIARI SYNDROME: RESULTS OF A PROSPECTIVE STUDY

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BACKGROUND/AIMS: Transsplanlar intrahepatic portosystemic shunt (TIPS) is an interventional radiologic procedure widely accepted in the management of portal hypertension and its complications. Its use in Budd-Chiari Syndrome (BCS) remains controversial. The aim of our study was to evaluate the long-term clinical outcome of patients with BCS who underwent TIPS and to determine a subgroup of patients where this procedure is indicated. METHODS: Fourteen BCS patients with severe life-threatening complications and refractory to maximal medical support therapy underwent TIPS procedure along with assignment to the liver transplant list. The indication for TIPS was severe liver failure in 2 patients, refractory ascites and or portenitis in 10, and variceal bleeding in 2. Patients were followed clinically and had TIPS patency regularly checked during an average follow-up of 20 months. RESULTS: TIPS was placed in 11 of 14 (79%) patients among which 3 after 2 attempts. There were 5 technical complications (36%) for a total of 14 procedures. With the exception of one death (7%), all procedure-related complications were successfully treated. One patient with an acute form of BCS was transplanted 3 weeks after TIPS. In the remaining 9 patients ascites resolved (90%), and liver function and Child-Pugh class improved (100%). The mean decrease in pressure gradient (from 29 to 11 mmHg) after 2 months was 62%. Two patients (22%) developed dysfunction of TIPS at 7 and 13 months and at 2 months, respectively. However, after angioplasty these 2 shunts remained patent on follow-up of 20 and 17 months, respectively, giving a primary and a secondary (at the end of the follow-up) shunt patency rate of 78% (9 of 7) and 100% (9 of 9), respectively. CONCLUSION: In patients with BCS who do not respond to medical therapy TIPS is an efficient treatment with beneficial long-term outcome. It should be considered the first option in view of its low morbidity and mortality rates and good impact on preserving liver functional capacities.

76 PREDICTING POST-TRANSPLANT GRAFT SURVIVAL IN LIVER TRANSPLANT RECIPIENTS USING PRETRANSPLANT CHARACTERISTICS

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INTRODUCTION: The ever-widening gap between the availability of donor organs and the number of liver transplant candidates requires optimization of post-transplant outcomes by matching donors and recipients on preoperative factors that maximize graft survival. The aim of this study was to evaluate graft survival based on preoperative donor, technical, and recipient characteristics and devise a practical model with which to predict post-transplant survival. METHODS: Demographic, clinical, and survival data were extracted from the UNOS standard transplant analysis and research files for adult liver transplants. Potential risk factors influencing outcomes including donor age, cold ischemia time (CIT), urgency status, and recipient diagnoses were evaluated. Data were analysed via Kaplan-Meier, chi square, and cox proportional hazards regression procedure. RESULTS: 49,020 grafts were transplanted between 1987 and 2003. The mean follow up was 42 ± 1 months. Five-year graft survival for recipients of donors <60 vs ≥60 years old was 64% and 52%, respectively (p < 0.001). Recipients of grafts with <12 vs ≥12 hours of CIT had 5-year survivals of 65% and 59%, respectively (p < 0.001). UNOS status 2B and 3 recipients had 5-year survivals of 67% compared with 56% for UNOS status 1 and 2A recipients (p < 0.001). Five-year survivals for recipient diagnoses categorized as viral, EtOH, autoimmune, malignancy, and idiopathic/cryptogenic were 60%, 64%, 70%, 44%, and 64%, respectively. Multivariate analysis with Cox regression yielded the results shown in the Table on top of page 22. CONCLUSIONS: Cold ischemia time, recipient status, and donor age as well as the etiology of the recipient’s liver disease independently influence post-transplant graft survival. Therefore, the relative risks of these pretransplant characteristics can be used to develop a practical model with which to match donors and recipients in order to improve post-transplant survival.
77 THE USE OF MICRODIALYSIS FOR MONITORING THE METABOLIC CHANGES THAT OCCUR IN THE LIVER AT TRANSPLANTATION

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BACKGROUND: A microdialysis catheter was inserted into the graft immediately following reperfusion at orthotopic liver transplantation (OLT). Metabolites of the ischaemia reperfusion injury and selected amino acids were studied. METHODS: Fifteen patients (8 males) undergoing elective OLT with a median age of 52 (38–62) years. The microdialysis catheter was perfused with an isotonie solution for 48 h. The dialysate was collected at 1-h intervals and lactate, pyruvate, glyceraldehyde and glucose levels were measured. In addition, concentrations of amino acids alanine (ALA), arginine (ARG), citrulline (CIT), γ-amino-butyric acid (GABA), glutamate (GLU), glutamine (GLN), glycine (GLY) and taurine (TAU) were determined. Routine liver function tests and indocyanin green (ICG) clearance were also done. RESULTS: Median cold ischaemia time (CIT) was 10 h 28 min, warm ischaemia time (WIT) was 39 min. All grafts worked well. 24- and 48-h ICG clearance correlated significantly with postoperative transaminase levels. High lactate, pyruvate and glyceraldehyde levels were observed in the immediate postoperative period. These showed a significant decrease and stabilized to baseline levels within 3–4 h. A rise in median glucose and pyruvate levels was noted after 48 h. For ALA, CIT, GLN and GLY, no significant changes were observed. There was a significant decline in the levels to a baseline of TAU, GABA and GLU. In contrast, ARG levels were low immediately post reperfusion and progressively increased reaching significantly higher values from 24 h onwards.

CONCLUSIONS: These data may represent ‘normal’ changes seen in the immediate post-transplant period, as all grafts functioned well. The rise in both glucose and pyruvate levels beyond 40 h may represent glycogen breakdown and increased rate of glycolysis. Two most important metabolic fates of ARG in the liver are in the detoxification of ammonia via the urea cycle, and in the synthesis of nitric oxide. Low extracellular ARG may reflect influx of the amino acid into hepatocytes resulting in either formation of supra-physiological levels of NO in the presence of inducible NO synthase or conversion to ornithine, in the presence of arginine in the urea cycle. As the organ stabilizes, restriction of ARG uptake may give rise to the observed rise in extracellular ARG.

78 A DIAGNOSIS-DRIVEN EVALUATION OF OUTCOME IN PEDIATRIC LIVER TRANSPLANTATION

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OBJECTIVE: To identify predictors of graft and recipient survival for pediatric liver transplantation in the UNOS transplantation information database. METHODS: The UNOS transplantation information database was queried for primary diagnoses, UNOS/PEDLD scores, recipient demographics, surgical techniques, retransplantation rates, graft and patient survival for all pediatric liver transplant recipients (6734 patients, 7772 grafts). Outcomes were compared between recipients in 5 diagnostic subgroups including biliary atresia, metabolic diseases, fulminant hepatitis, hepatoblastoma and other tumors, and other etiologies. Additionally, the recipients were stratified by age groups (infancy (ages 0–2), childhood (ages 3–12), and adolescence (ages 13–17)) and procedure type (living related vs cadaveric). Data were analysed via Kaplan–Meier survival analysis and chi-square tests of proportions. Summary data are given as mean ± SD and percentages. The overall effect of diagnosis on graft and patient survival was statistically significant (p < 0.001), with consistently better survival among patients with biliary atresia and metabolic disease in comparison to the other diagnosis categories (pairwise p < 0.05). Living donor grafts were associated with better graft and patient survival among recipients with biliary atresia (both p < 0.01). CONCLUSIONS: Patient and graft survival is related to the primary liver disease in the pediatric liver transplant population. Those patients with biliary atresia and metabolic diseases have improved survival in comparison with other etiologies of liver failure, especially among those receiving living-related transplants (see Table below).

79 SIROLIMUS ATTENUATES IL-6 SECRETION BY PRIMARY HUMAN HEPATOCYES

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INTRODUCTION: Acute liver injury has been associated with the elaboration of proinflammatory cytokines like IL-1α, IL-6, IL-8, and TNF-α. IL-6, an acute phase reactant, is upregulated in the ischemia-reperfusion injury of liver transplant and has both regenerative and cytoprotective effects. Sirolimus (Rapamune) is an antiproliferative agent that has been introduced in the immunosuppressive regimen of liver transplantation, but its mechanism of action and effect on cytokine secretion in human hepatocytes have not been studied. METHODS: Primary human hepatocytes were obtained from liver resections using a modified two-step collagenase perfusion. Hepatocytes were cultured as spheroids at 3.0 × 10^6 cells/ml in medium supplemented with or without sirolimus at 8 ng/ml. Supernatants were collected on days 3 and 5 and assayed for IL-6, IL-8, IL-1β, and IL-10 by ELISA. Cellular RNA was extracted and RT-PCR was performed for IL-1α, IL-6, IL-8, IL-10, and TNF-α mRNA. Comparisons using paired t-tests were considered significant when p < 0.05. RESULTS: Compared with untreated cells, hepatocytes cultured in sirolimus had decreased levels of IL-6 (15 ± 5 ± 10 pg/ml vs 19 ± 5 ± 2.3 pg/ml) at 3 days and IL-8 levels increased in sirolimus treated cells (104 ± 15 ± 15 pg/ml vs 52 ± 15 ± 15 pg/ml).
– 7 pg/mL, p < 0.001). Supersaturation levels of IL-1β and IL-10 were undetectable in either group, <15.6 pg/mL and <7.8 pg/mL, respectively. Only IL-6 and IL-6 mRNA were detected in the primary hepatocytes. Consequently, the hepatocytes were unable to elaborate IL-1β.

CONCLUSIONS: The harvesting of hepatocytes stimulates the secretion of IL-6, similar to the ischemia-reperfusion injury seen in vivo. Siroliimus significantly decreases IL-6 secretion, potentially abrogating the protective and regenerative effects of the cytokine. The increased secretion of IL-8 suggests a possible detrimental effect of sirolimus with a maintained stimulus for neutrophil recruitment without the cytotoxic effects of IL-6. The effect on transplant immunosuppression may be counterbalanced by the negative effects on regenerative cytokine secretion and requires further study.

80 HEPATIC VENOUS ANATOMY OF THE MEDIAL SEGMENT TO SET UP A SAFE GUIDELINE FOR EXTENDED RIGHT LOBECTOMY

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Preference of right lobe graft without middle hepatic vein (MHV) trunk for adult recipients and lateral segment for pediatric recipients did not lead to full attention being paid to anatomic evaluation of hepatic vein branches to the medial segment (V4, S4). We experienced that S4 parenchyma without MHV trunk underwent scanty regeneration in some donors. The same phenomenon may occur in extended lateral segment grafts. To set up indications criteria for safe procurement of right lobe with MHV trunk and for secure procurement of extended lateral segment, we performed a series of studies on the anatomy of V4. The first study was how to discern the draining territory of MHV and left hepatic vein (LHV) in S4 parenchyma. We devised an intraoperative method to clamp the draining vein trunk directly after interruption of hepatic arterial flow. When the MHV and LHV trunks were isolated separately, clamping of one trunk revealed direct discoloration or counter demarcation at the surface of S4. With this method, we found that the ventral portion of S4a and the small narrow area of S4b near the interlobar margin always belonged to MHV territory and other areas were variably drained. The configuration of MHV territory was transferred to preparative donor CT for anatomical matching and volumetry. As a second study, we analysed the V4 tributaries using dynamic CT images and 3-dimensional reconstruction in 102 consecutive living donors. We divided the S4 parenchyma as right and left halves of S4a and S4b (S4R, S4aL, S4bR, and S4bL). Dominance of MHV drainage was observed in 100%, 34%, 78%, and 11%, respectively. Simultaneous LHV dominance in 3 quadrants except for S4aR was observed in 19% and the MHV territory became <30% of S4 volume. MHV dehydration in this venous anatomy will induce the veno-occlusive area of <15% of remnant left lobe volume, and such a proportion becomes spontaneously resolved without significant deterioration of liver function. For procurement of extended liver graft hepatocyte anatomic atlas may serve as a definite guide for evaluation of the veno-occlusive area in S4. This evaluation method can be applicable to non-transplant hepatectomy requiring concurrent resection of MHV trunk.

81 BILIARY COMPLICATIONS AFTER VARIOUS RECONSTRUCTIONS IN LIVING DONOR LIVER TRANSPLANTATION

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BACKGROUND: Biliary complications remain one of the most serious problems after living donor liver transplantation (LDLT). Hepaticojjunostomy has been a standard procedure for biliary reconstruction. However, recently, duct-to-duct (DD) anastomosis has been used more widely, because DD anastomosis has more physiologic biloenteric continuity. PURPOSE: We performed this study to evaluate the safety of various biliary reconstruction methods for LDLT. MATERIALS AND METHODS: Between January 1999 and December 2002, 147 recipients were enrolled, >1 year postoperatively. Hepaticojjunostomy was performed in 85 cases (57.8%) and DD anastomosis in 62 cases (42.2%). In DD anastomosis, a T-tube was inserted via CBD in 33 cases (53.2%), an internal stent tube was pushed upwards in the anastomosis throughout CBD in 7 cases (11.3%), and no drainage tube was used in 22 cases (35.3%). RESULTS: Among 147 cases, 10 biliary complications developed (20.4%). In hepaticojjunostomy, the incidence of complications was 8.2% (7/85), comprising 3 cases of bile leak and 4 cases of biliary stricture. The reoperation rate was 28.5% (3/7) in complications of hepaticojjunostomy.

In DD anastomosis, the incidence of complication was 37.1% (23/62).

Conversion to hepaticojjunostomy was needed in 8.7% (2/23).

The complication rate in cases using an internal stent was 21.4% (5/24).

Complications consisted of 4 cases of bile leak and one case of biliary stricture. In this internal stent method, one case needed surgical correction. The complication rate in cases using a T-tube was 33.3% (11/33).

Complications consisted of 6 cases associated with tube removal, 5 cases of biliary stricture. In this T-tube drainage method, one patient needed surgical correction. The complication rate in cases without biliary drainage tube was 31.8% (7/22).

Complications consisted of one accidental ligation of right posterior duct and 6 cases of biliary stricture. In cases of DD anastomosis without a stent, all complications were corrected by radiologic intervention. The complication rate was lower in hepaticojjunostomy than in DD anastomosis (p < 0.05). However, surgical correction was more frequently needed in complications of hepaticojjunostomy than in those of DD anastomosis, especially in cases without a stent (p < 0.05). CONCLUSION: In LDLT, the complication rate of various biliary reconstruction was 20.4%. In hepaticojjunostomy, the complication rate was 8.2%, but the rate of surgical correction was 28.5%. In DD anastomosis, the complication rate was 31.8% and the rate of surgical correction was 8.7%.

82 VALUE OF MAGNETIC RESONANCE CHOLANGIOGRAPHY IN ASSESSING BILIARY ANATOMY OF POTENTIAL ADULT LIVING LIVER DONORS

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BACKGROUND: Although magnetic resonance cholangiography (MRC) is routinely used by some centers to assess potential living liver transplant donors (LLT), its accuracy has not been examined systematically. The purpose of this study was to determine the accuracy of preoperative MRC in assessing adult LLT graft biliary drainage. PATIENTS AND METHODS: A prospective cohort of LLT donors who underwent right lobe resection by a single surgeon was evaluated. MRCs were generated using a General Electric 1.5T Excite platform with multiplanar, multisquence post Tesla reconstruction and post processing to obtain thin slab maximum intensity projections. MRC interpretation by a blinded staff radiologist and a staff surgeon were used to predict biliary anatomy. These data were compared to the intraoperative biliary anatomy findings for all patients derived from cholangiography and biliary exploration. The sensitivity, specificity, positive and negative predictive values of MRC for aberrant biliary anatomy were calculated. RESULTS: From October 2000 to July 2003, 30 patients underwent right lobe resection for LLT at a single institution with preoperative MRC and assessment of intraoperative biliary anatomy. Eighteen patients, 12 normal and 6 had aberrant biliary anatomy on MRC. Intraoperative cholangiography revealed normal and aberrant biliary anatomy in 19 and 11 patients, respectively. MRC demonstrated biliary anatomy accurately in 27 of 30 patients. The sensitivity, specificity, positive predictive and negative predictive values of MRC in detecting an aberrant donor biliary anatomy were 92%, 100%, 100% and 94%, respectively.

CONCLUSION: Preoperative MRC accurately assesses donor biliary anatomy in potential adult LLT donors and may guide the intraoperative management of the graft biliary tract.

83 ENDOTHELIN-1 CONTRIBUTES TO RENAL DYSFUNCTION IN ACUTE LIVER FAILURE

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BACKGROUND: Endothelin-1 (ET-1) is a powerful vasoconstrictor released from the injured liver, that may contribute to the pathogenesis of the hepatorenal syndrome. This study sought to determine whether ET-1 has a role in the development of renal dysfunction from liver failure. METHODS: Acute liver failure was induced in Wistar rats by 1.1 g/kg intraperitoneal galactosamine; controls received normal saline. At 24, 36 or 48 h, arterial (ABP) and central venous pressure (CVP) were measured, then plasma, urine and tissue were sampled. Plasma endothelin was measured by ELISA, liver and renal function by standard methods. Two
blinded, independent observers quantitatively analysed liver and kidney ET-1, endothelin receptor-A (ET-RA) and endothelin receptor-B (ET-RB) immunocytochemistry, with agreement assessed using kappa and Bland-Altman plots. RESULTS: Galactosamine caused liver failure and secondary renal dysfunction, with progressive hepatic damage but minimal renal abnormality on light and electron microscopy. Galactosamine did not change BP or CVP. After galactosamine plasma ET-1 levels rose (mean ± SEM pg/ml control vs 42 ± 1.96 ± 0.17 to 2.17 ± 0.94, p < 0.01) and hepatic ET-1, ET-RA and ET-RB expression increased. There was no increase of renal ET-1 expression by 42 h, but there was a marked, progressive increase in renal ET-RA and some increase of renal ET-RB expression. High levels of agreement were present for all immunohistochemical observations. CONCLUSION: These results suggest a role for hepatic ET-1 in the development of hepatoensal syndrome.

84 EVALUATION OF INTRAOPERATIVE AUTOTRANSFUSION FILTRATION FOR HEPATOMEGALY AND PANCREATECTOMY

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BACKGROUND: Hepatomegaly and pancreatemy are normal the surgical treatment of choice in patients with liver and pancreatic malignancies. Intra-operative blood loss for these procedures remains in the range of 500–1000 mL in most series. Intra-operative and postoperative anemias have been demonstrated to lead to increased perioperative morbidity, prolonged length of hospital stay and decreased overall survival. Autologous blood transfusion has remained the standard of care but has the potential to induce transfusion-related complications, both known and unknown. The utilization of intra-operative autotransfusion has remained an absolute contraindication in malignancies because of the unproven concern of the re-infusion of malignant cells. Thus the aim of our study was to demonstrate the lack of malignant cells in autotransfused filtered blood in patients undergoing hepatomegaly and pancreatemy in order to obtain initial data to demonstrate the safety of autotransfusion in surgical oncology patients. METHODS: This was a prospective study of 20 patients evaluating the presence of malignant cells from autotransfusion filtered blood following resection. All intraoperative blood loss from opening to closure was collected, filtered and prepared for autotransfusion. All samples were then immediately taken for lysis and flow cytometry. Each patient had a small 5 mL aliquot of filtered blood removed during the operation for positive control. RESULTS: Ten patients underwent major hepatomegaly defined by 4 isometric tumour, 2 extended right lobectomy, 3 right lobectomy, and 1 left lobectomy for metastatic colorectal cancer, with a median blood loss of 500 mL (200–700 mL). Median admission hemoglobin (Hgb) was 11.5 (range 9.2–13.7) with median discharge Hgb of 10.0 (7.3–12.8). Three patients received a total of 6 units of packed red blood cells. Ten patients underwent a standard pancreaticoduodenectomy with retroperitoneal lymph node dissection for adenocarcinoma with a median blood loss of 600 mL (400–800 mL). The median admission Hgb was 13.7 (range 12.5–15.6) with a median discharge Hgb of 10 (8.1–13.9). Five patients each did not receive a total of 9 units of packed red blood cells. Flow cytometry did not demonstrate the presence of any cytokeratin-positive carcinoma cells. Each pre-filtered aliquot did demonstrate cytokeratin cells but none were positive for carcinoma. CONCLUSIONS: Intraoperative autotransfusion for major hepatomegaly in metastatic colorectal cancer and pancreatemy for adenocarcinoma is safe and should begin to be evaluated in a phase 2 study for efficacy.

85 DOES PREVIOUS LATERAL PANCREATICOJEJUNOSTOMY INCREASE OPERATIVE MORBIDITY FOLLOWING PANCREATOCOUDENECTOMY FOR CHRONIC PANCREATITIS?

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INTRODUCTION: Lateral pancreaticojejunostomy (LJP) is the mainstay of surgical therapy for dilated duct chronic pancreatitis and has an excellent success rate and low operative morbidity and mortality. However, many patients do not achieve pain relief after LJP, and failure to adequately drain the head of the pancreas has been called the Achilles heel of LJP. Resection of the head of pancreas solves the problem of drainage of the head of the pancreas and resolves coexisting problems associated with an inflammatory mass in the pancreatic head. The purpose of this study was to examine whether previous LJP increases operative morbidity in patients who undergo pancreatocoduodenectomy. METHODS: The records of 68 consecutive patients who underwent pancreatocoduodenectomy for chronic pancreatitis were retrospectively reviewed and analysed. There were 17 patients who underwent pancreatocoduodenectomy after failure of LJP to relieve pain (LJP group). This group was compared to 44 patients without any prior pancreatic surgery (control). 7 patients who previous underwent other pancreatic operations were excluded from the study. RESULTS: Both groups had a similar stage of disease measured by ERCP and clinical findings. The LJP group had a higher number of prior intra-abdominal operations (1.4 ± 2.5, p < 0.005). There were no perioperative mortalities in either group. The overall morbidity was 50.8%, which was significantly higher in the LJP group (43.2% vs 70.6%, p < 0.04, odds ratio 3.2). Intra-abdominal complications occurred more frequently in the LJP group (34.1% vs 64.7%, p < 0.003), including a difference in the occurrence of delayed gastric emptying and pancreatic leaks. There was no difference in extra-abdominal complications (13.6% vs 17.6%). Postoperative hospital length of stay was not significantly different in both groups (14.0 vs 19.0 days). In the control group, 9.1% required reoperation for failure to improve chronic pain. In the other group none of the patients underwent reoperation. CONCLUSION: Patients with a history of failed LJP who undergo pancreatocoduodenectomy have a threefold increased risk for perioperative complications. An increase in pancreatic leaks might be related to technical difficulties in performing the anastomosis between the pancreatic duct and the vein of the jejunal limb. More extensive operative trauma due to the higher number of prior intra-abdominal procedures could explain a higher frequency in postoperative delayed gastric emptying.

86 PERSISTANT ARTERIAL ENCAEMENT AFTER TUMOR RESPONSE TO RADIO-CHEMOTHERAPY IN PANCREATIC ADENOCARCINOMA: IS IT A CONTRAINDICATION TO RESECTION?

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INTRODUCTION: In Pancreatic carcinoma, arterial encaement still remains a contraindication to resection. Chemoradiotherapy can provide an objective tumor response with some patients. The aim of our study was to assess the response rate of radio-chemotherapy on the tumor and on arterial encaement and the percentage of patients who can finally benefit from a curative pancreatic resection. PATIENTS AND METHODS: From March 1998 to May 2003, 61 patients with locally advanced pancreatic head carcinoma (superior mesenteric artery or coeliac axis encaement) with histologic evidence of cancer, received chemotherapy (5 fluorouracil and capatin) and radiotherapy (45 Gy). At the end of radio-chemotherapuy, all patients were staged by helical CT scan. RESULTS: In these 61 patients, 23 (38%) presented an objective response after radio-chemotherapy with persistent arterial encaement on CT scan. 38 were non-respondeurs to radio-chemotherapuy (group 1). All these 23 patients underwent a laparotomy with dissection of the suspected involved artery and biopsies along this vessel were done with pathologlcal examination. In 10 patients (group 2), persistent tumor was shown in periarterial biopsies, and a palliative derivation was performed. In 13 cases (56%) (group 3) a total dissection of the involved vessel could be performed with no evidence of residual tumor on the histological examination. In these patients a Whipple procedure was carried out. 11 patients (85%) had curative resection (R0), 2 presented a microscopic residual tumor on retroperitoneal margins (R1). Final pathological examination shown 4 T4 (31%) (venous involvement), 6 T3 (46%), 1 T2 (8%), 2 T1 (15%), 8 patients N+ (57%). Median survival rate was 11 months in group 1, 20 months in group 2 and 28 months for curative surgery (group 3). Three patients in group 3 were alive at 37, 55, 68 months, respectively. CONCLUSION: In our study, a tumor response after radio-chemotherapy was obtained in 38% of patients. A curative pancreatic resection was possible in 21% of patients who presented pre-therapeutic arterial encaement.
87 CIGARETTE SMOKE COMPONENTS INHIBITED GAP JUNCTIONAL COMMUNICATION AND CELL DIFFERENTIATION IN HUMAN PanCREATIC DUCTAL EPITHELIAL CELLS
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Cigarette smoke contains about 4000 chemicals, about 60 of which have been identified as carcinogens. Of these, polycyclic aromatic hydrocarbons (PAHs) are one class of compounds in this complex mixture of combusted byproducts of tobacco that has been extensively studied. Although the most abundant PAHs in cigarette smoke are methylated anthracenes and phenanthrenes, the epigenetic toxicity of these compounds has not been extensively studied. To understand the epigenetic toxicity of PAHs related to pancreatic cancer, a clone of a human pancreatic ductal epithelial cell line, H6c7, derived after immortalization with human papilloma virus, was used to examine the effects of PAHs on these cells. Several reports showed that methyl- or chlorine-anthracenes, which possess a bay-like structure, affect epigenetic events such as an induced release of arachidonic acid, inhibition of gap junctional intercellular communication (GJIC), and induction of mitogen-activated protein kinases in a pluripotent rat liver epithelial stem cell line. Anthracenes with no bay-like structures were inactive. GJIC is a biomarker for measuring the epigenetic toxicity of chemicals on the cells. These biological effects are all molecular events associated with the promotion phases of cancer. In this present study, we used H6c7 which were GJIC-incompetent and high in telomerase activities. H6c7 cells did not express detectable messenger only genes when grown in medium containing hormones and growth factors. In the presence of the c-AMP signalling pathway ( forskolin and IBMX), a basal mediator of growth factors, the cells became GJIC competent and expressed connexins. Telomerase activity was also decreased by c-AMP-elevating drug treatment. After induction of c-AMP, 1-methylanthracene with bay-like structures inhibited GJIC, whereas the 2-methylanthracene lacking a bay-like structure had no effect on GJIC. Telomerase activity remained high in 1-methylanthracene treatment but not with 2-methylanthracene. These results indicate that a prominent component of cigarette smoke, namely methylanthracenes with distinct structural configurations, could be a potential etiological agent contributing to the epigenetic events of pancreatic cancer. Funded by the NIEHS Superfund grant #P42 ES04911-07 to JET and McLaren Foundation to DNR and JET.

88 SURGICAL TREATMENT OF PanCREATIC NEUROENDOCRINE TUMOR: A 12-YEAR SINGLE INSTITUTIONAL EXPERIENCE
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BACKGROUND: The aim of this study was to evaluate contemporary outcomes associated with the surgical management of pancreatic neuroendocrine tumors. METHODS: The medical records of 59 consecutive patients with pancreatic neuroendocrine tumors treated at our institution from 1/1991 through 10/2003 were reviewed. Diagnoses were histologically confirmed for all patients. Survival was analysed using the Kaplan–Meier method (mean follow-up period, 41 months). Prognostic factors were analysed using log-rank test, and Cox regression. RESULTS: Mean patient age was 51 ± 13 years. Twenty-eight (47%) patients were male. Twenty-three (39%) patients presented with abdominal or back pain, and 5 (8%) patients with weight loss. Twenty-three (39%) patients had a functional tumor with associated symptoms (14 patients had an insulinoma, 6 had a gastrinoma, 1 each had a glucagonoma, a PPoma, an ACTHoma). Thirty-six (61%) patients had a non-functioning tumor. Forty-three (73%) patients underwent surgical resection (9 pancreaticoduodenectomies, 23 distal pancreatectomies, 1 total pancreatectomy, and 10 tumor enucleations were performed). Three (5%) patients with locally advanced disease and 12 (20%) patients with distant metastases had biopsy with or without palliative bypass. Overall 5-year survival rate for the entire cohort was 69%, the 5-year survival rate for patients who underwent surgical resection was 83%. Using univariate analysis, we identified factors associated with a significant favorable effect on survival including complete tumor resection, the presence of a functional tumor, tumor diameter < 3 cm, and absence of distant metastasis. Complete resection was an independent prognostic factor on multivariate analysis. CONCLUSIONS: Surgical resection of neuroendocrine tumors of the pancreas is associated with excellent long-term prognosis.

89 EXPANDING THE APPLICATIONS OF LAPAROSCOPIC GASTRIC AND BILIARY BYPASS: A SINGLE-CENTRE COHORT PROSPECTIVE STUDY

OBJECTIVE: To expand the applications of laparoscopic gastric and biliary bypass surgery to include therapeutic as well as prophylactic roles in the management of benign and malignant gastric outlet and distal biliary obstruction. METHODS: Laparoscopic biliary bypass was applied in jaundiced patients when stent insertion had failed, if concomitant gastric bypass was required, or in patients with benign distal biliary stricture. In addition, laparoscopic biliary bypass was applied prophylactically in non-jaundiced patients with distal duodenal obstruction secondary to uncauterised process tumour, as well as in non-stented jaundiced patients (bilirubin >200 µmol/l) during staging laparoscopy for periampullary malignancy in preparation for resection. Laparoscopic gastric bypass was applied in patients with benign or malignant gastric outlet-duodenal obstruction either primarily or when endoscopic interventions (endoscopic dilatation or duodenal expandable stent insertion, respectively) had failed, as prophylactically in patients undergoing laparoscopic biliary bypass for a locally advanced, unresectable, non-metastatic periampullary malignancy. Data were collected prospectively and entered into a protected computer database. RESULTS: Between February 2001 and October 2003, some 28 patients (17 male) with a median age of 67 years (range 26–76) underwent laparoscopic bypass surgery for gastric, duodenal and/or biliary obstruction. Nine patients had had previous abdominal surgery. The procedures performed included 15 gastric bypasses, 4 biliary bypasses, and 9 combined gastric and biliary bypasses. The median operative time was 90 min (range 30–330 min). The median postoperative hospital stay was 3 days (range 1–19 days). There were no conversions to open surgery. One patient died postoperatively secondary to aspiration pneumonia (mortality 3.6%). Other complications developed in two patients and central line sepsis and transient hypoventilation. There were no anastomotic leaks. Jaundice recurred in one patient who had undergone a Roux-en-Y hepaticejunostomy and was associated with multiple hilar liver metastases. None of the patients experienced recurrence of their gastric outlet obstruction. CONCLUSION: The applications of laparoscopic gastric and biliary bypass surgery are associated with rapid recovery, and can be safely expanded to include prophylactic surgery as well as pre-resection relief of jaundice.

90 MANAGEMENT OF PERFORATION AFTER ENDOCOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY (ERCP): A POPULATION-BASED REVIEW
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Perforation related to ERCP is a rare but serious complication. Our study evaluates the management and outcomes of these perforations. Between July 1996 and December 2002, a total of 6620 ERCPs were performed at our regional Therapeutic Endoscopy Unit serving Southern Alberta (pop. 1.5 million). Thirty perforations (0.5%) were identified and retrospectively reviewed. Of the 32 patients, 5 (17%) died as a result of the perforation, and 12 patients in total required operative intervention. Seven patients with guidewire perforations were recognized during ERCP. All were successfully managed medically. Of the 11 peri-ampullary perforations, 5 patients underwent surgery and 3 of these had repeat surgery. All of them had drainage of the retroperitoneum, and most had insertion of a T-tube. Three of the four deaths occurred in the operative group from intra-
abdominal sepsis, and one had her care withdrawn because of advanced cancer and organ failure. Of the 3 duodenal perforations, all required operation, with one death from sepsis. The locations of 7 of these peri-
terinal perforations could not be determined. Two of these underwent common bile duct exploration and drainage of retroperitoneum with no mortality. The average length of hospital stay for the five patients with peri-
ampullary, duodenal and unknown groups were 4.4, 26.5, 13.7, and 12.6
days, respectively. One esophageal perforation and one small bowel perforation after a previous Billroth II were identified during ERCP. They recovered uneventfully after surgery. Guidewire perforations can be managed medically with little morbidity. Peri-ampullary and duodenal perforations carry a high morbidity and mortality rate. In particular, retroperitoneal fluid collections on CT scans, delay in diagnosis and failure of medical therapy requiring salvage surgery are associated with a bad outcome.

91 THE ROLE OF DIAGNOSTIC LAPAROSCOPY PRIOR TO PANCREATOCOUDENOTOMY
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PURPOSE: To evaluate the efficacy of simple diagnostic laparoscopy (DL) prior to pancreatocoduodenectomy (PD).
MATERIALS AND METHODS: The charts of 140 patients scheduled for DL and possible PD between January of 1998 and December of 2002 were reviewed. DL was performed through one 10-mm viewing port and one additional 5-mm port if biopsy was indicated. The surface of the liver and peritoneal cavity was quickly inspected and if no suspicious lesions were found, a laparotomy was performed. Data including presenting symptoms, preoperative diagnosis, preoperative diagnostic studies, preoperative interventions, operative findings, and procedures performed following DL were collected. Outcomes including complications, readmissions, and additional procedures required were analysed to determine the efficacy of DL prior to PD.
RESULTS: 140 patients underwent DL with possible PD over a recent 4-year period. 135 of the 140 patients (96.4%) had preoperative CT scans and 5 patients underwent preoperative MRI of the abdomen. 104 of 140 (74.2%) had ERCP and stent placement prior to surgery. DL was successful in identifying metastatic disease in 9 of 140 (6.4%) patients and these patients did not undergo laparotomy. Of those 9 patients 1 required subsequent cholecystectomy and drainage of liver abscess and 1 developed gastric outlet obstruction requiring endoscopic stenting. The remaining 7 patients required no further operative intervention except endoscopic stent change. DL was unsuccessful in identifying liver metastasis in 6 (4.3%) patients who were found to have liver metastasis during laparotomy. 131 patients (93.5%) had negative DL and underwent laparotomy. 81 (61.8%) patients underwent PD. 23 patients underwent both biliary and gastric bypass. 25 patients underwent biliary bypass alone. One patient underwent gastric bypass alone and one patient had no bypass performed. Four of the 25 (1.6%) underwent biliary alone, required biliary bypass due to anastomotic dehiscence for gastric outlet obstruction. Two of the 23 (0.8%) patients undergoing double bypass required reoperation for gastric outlet obstruction.
CONCLUSIONS: DL in patients with potentially resectable pancreatic tumors successfully identified metastasis in 6.4% of the patients reviewed. These patients were spared the morbidity and recovery period of a laparotomy with infrequent need for further palliative interventions.

92 RESULTS OF SURGICAL THERAPY FOR HILAR CHOLANGIOCARCINOMA: A SINGLE-CENTER EXPERIENCE
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AIM: Liver resection is the only potential curative treatment for hilar cholangiocarcinoma. The extension of surgical radicality remains an open issue. We evaluated preoperative work up, resectability rate, survival and prognostic factors in a recent series at a Western hepatobiliary centre.
METHODS: From 1991 to June 2003, among 64 observed patients 47 curative liver resections were performed. There were 28 male and 19 female patients. Mean age was 58.1 ± 10.3. Mean tumor diameter was 2.5 ± 0.2 cm. Symptoms were present in 95.3% of patients with Klatskin tumor; jaundice was the initial presentation in 76.2% of cases. CT scan and percutaneous cholangiography were performed in all patients; angiography was performed only in selected cases (35.6% of cases). RESULTS: Major hepatectomies plus caudate lobectomy were performed in 14 patients (29.8%), extended hepatectomies with CL in 29 (61.7%), isolated bile duct resection in 4 patients (8.5%). Portal vein resection was required in 4 patients, hepatic artery resection and reconstruction was done in 4 patients, and pancreatoduodenectomy in one. Due to this aggressive policy, resectability rate was 73%. Overall operative mortality was 6.5%, and postoperative morbidity was 48.5%. The 1-, 3-, and 5-year survival rates were 70.6%, 46.3% and 27%, respectively. The 5-year survival was 45% in patients without lymph node metastases and 11% in patients with LN involvement, respectively. The 5-year survival rate was 54.8% in patients without perineural involvement, and 25.6% in patients with perineural invasion, respectively. CONCLUSIONS: CT scan and percutaneous cholangiography are the 2 basic preoperative examinations. Liver resection is the treatment of choice for hilar cholangiocarcinoma. Curative procedure may be achieved by major hepatectomy with CL. Aggressive surgical approach with eventual vascular resection and reconstruction increase resectability rate with an acceptable mortality. Lymph node and perineural status seems to be the strongest predictors of long-term survival.

93 IS AMPULLECTOMY APPROPRIATE FOR T1 AMPULLARY CANCER?
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PURPOSE: Although ampullectomy has been attempted in early ampullary cancer, the indication for and extent of resection is not yet established. The purpose of this study was to evaluate whether ampullectomy can be an alternative operation to pancreatoduodenectomy in T1 ampullary cancer with clinicoapathologic study.
METHODS: Of 220 patients who had undergone pancreateoduodenectomy for ampullary cancer between 1976 and 2002, 65 patients with a histological diagnosis of T1 cancer were analysed retrospectively. Pathologic slides were reviewed for analysis of the spread pattern of cancer and medical records were reviewed for clinical outcome.
RESULTS: Mean age of patients was 56.5 years, with 39 men and 26 women. The 5-year survival rate was 78.3% and median survival duration was 59.2 months at a median follow-up period of 79.1 months. Recurrence (local and systemic, 3 cases; systemic, 5 cases) developed in 11 patients (16.9%), all of whom expired after all. Pathologic study showed 6 cases (9.2%) of lymph node metastasis and 1 case of perineural invasion.
The patients with ampullary cancer superficially spread into CBD or P-duct without invasion of duodenum and pancreas, respectively, were 12 patients (18.5%) and 4 patients (6.2%). Mean length of invasion into CBD or P-duct beyond ampulla of Vater was 5.7 mm (range 2-23 mm) and 8.5 mm (range 1-16 mm), respectively. As a result, 19 patients (29.2%) of all 65 patients with T1 cancer had at least one of the risk factors considered to be associated with failure of ampullectomy, such as lymph node metastasis, perineural invasion, and CBD or P-duct involvement. Moreover, these risk factors for the failure of ampullectomy had no correlation with tumor size, histologic grade, gross morphology (p > 0.05). CONCLUSIONS: T1 ampullary cancer had a good prognosis, but relatively high recurrence rate (16.9%) even after pancreatoduodenectomy. Moreover, when the recurrence developed, it had a dismal result. Not a few patients with T1 ampullary cancer had, not confined to ampulla, lymph node metastasis, perineural invasion, and CBD or P-duct involvement, which could not be predicted. Therefore, ampullectomy for T1 ampullary cancer cannot be an alternative operation to pancreatoduodenectomy because of the possibility of high recurrence rate and pancreatoduodenectomy should be preferably performed for adequate radical resection.

94 IMPROVED RESULTS OF RESECTION OF HILAR CHOLANGIOCARCINOMA (KLATSKIN TUMORS): A SINGLE-CENTER, 15-YEAR EXPERIENCE
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BACKGROUND: Radical resection of hilar cholangiocarcinoma (HC) is difficult due to its proximal infiltration into the biliary tree and its frequent involvement of the bifurcation of the portal vein. In the mid-1990s, several studies showed improved results of more aggressive resection of HC in combination with extended liver resection and portal vein reconstruction.
Based on these results, we changed our treatment strategy towards performing more resections in combination with (extended) hemihepatectomy, with particular emphasis on complete excision of segment 1 and with reconstruction of the portal vein when necessary. The aim of this study was to assess the outcome of this changed strategy in terms of postoperative morbidity and mortality, microscopic tumor clearance and patient survival. METHODS: A total of 99 patients underwent surgical resection of HC in a 15-year period (1988–2002). The patients were divided into 3 groups, according to 5-year intervals: group 1 (1988–1993, n = 45, mean age 62.6 ± 1.7 years), group 2 (1993–1998, n = 25, mean age 58.1 ± 2.3 years) and group 3 (1998–2003, n = 29, mean age 60.2 ± 2.1 years). Proximal isolation of HC was classified according to the Bismuth-Corlette system (I–IV) on the basis of preoperative imaging studies. Patients routinely received postoperative radiotherapy (55 Gy). RESULTS: Compared with group 1, there were significantly more patients with type III and IV tumors in groups 2 and 3 (38%, 64% and 72% in group 1, 2 and 3, respectively, p < 0.05). Hilar resection in combination with (extended) hemihepatectomy and complete excision of segment 1 has resulted in more margin-negative resections and an improved survival, without increasing postoperative morbidity and mortality.

95 SURGERY FOR HILAR CHOLANGIOCARCINOMA: 10-YEAR EXPERIENCE OF A TERTIARY REFERRAL CENTRE IN THE UK

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OBJECTIVE: To review the outcome of patients operated for hilar cholangiocarcinoma and analyse prognostic variables. PATIENTS AND METHODS: A prospectively collected database on patients with hilar cholangiocarcinoma, between 1992 and 2003, and relevant clinical notes were reviewed retrospectively. A total of 174 patients, 96 (55%) male, median age 63 years (27–86), were reviewed. Jaundice was the initial presentation in 167 (96%). RESULTS: ERCP was performed on 101 patients of whom 27 (16%) had locally advanced disease. 45 patients (30%) underwent potentially curative resections. A radical hepatectomy with portal vein reconstruction was done in 7 patients, 6 (9%) of whom had R0 resections, 5 patients had biliary reconstruction with partial hepatectomy with 19 (61%) R0 resections (p = 0.042). Five patients required reconstruction of the portal vein. Postoperative complications developed in 19 (42%) patients, and there were 4 (9%) 30-day mortalities (hepatic insufficiency/ sepsis, 3); thrombosis of the reconstructed portal vein, 1). The median survival of those with R0 and R1 resections was 26 months (median follow-up 17 months). Among the patients with R0 resections, the cumulative survival rates at 1, 3, and 5 years were 83%, 58%, 41%, respectively, and in those with R1 resections were 71%, 24%, 24%, respectively (p = 0.021). Overall survival was shorter in patients with positive peritoneal invasion (median survival 16 vs 43 months; p = 0.066: NS). There was no significant difference in survival between the node-positive and -negative group. Median survival of patients who underwent liver resection was longer than those with bile duct resection only (30 vs 24 months p = 0.43: NS). CONCLUSIONS: ERCP was associated with a high failure rate in achieving preoperative biliary decompression, which was subsequently achieved by PTC. Clear histological margins were associated with improved survival and were better achieved by liver resection as compared with extrahepatic bile duct resection. Positive level 1 lymph nodes did not adversely impact survival.

96 ROLE OF HEAVY METALS IN PANCREATO-BILIARY MALIGNANCY

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BACKGROUND: Heavy metals as environmental pollutants have been implicated in human carcinogenesis. Elevated levels of heavy metals have been found in bile collected from subjects with gallbladder cancer in India. AIM: To determine whether there is a correlation between biliary heavy metals and pancreato-biliary malignancy in patients living in an industrial area of the UK. METHODS: Patients admitted to a tertiary referral centre with malignant biliary obstruction were identified and bile was collected from them either during endoscopic retrograde cholangiography (ERC), percutaneous transhepatic cholangiography (PTC) or during surgery. Bile was also collected from patients with benign biliary disease to act as controls. The bile samples were analysed for concentrations of lead, copper, zinc, cadmium, chromium and nickel using atomic absorption spectrometry after pretreatment by acid digestion method. The mean levels of every metal in the study groups (biliary malignancy and pancreatic malignancy) and the control group were compared by 2 sample t-test using MINITAB® statistical software. RESULTS: 78 bile samples were analysed (24 cholangiocarcinoma, 33 pancreatic carcinoma and 21 benign). When the samples from patients with cholangiocarcinoma were compared with the benign group, the mean concentration of each metal was higher in the malignant group except copper but did not reach significant levels. Similarly, metal concentrations in patients with pancreatic carcinoma were not significantly different from the benign group. The mean level of cadmium (Cd) reached closest to statistical significance in each subgroup of cholangiocarcinoma and pancreatic carcinoma compared to the benign group. When all the samples from malignant pancreato-biliary disease were taken together as a group and compared with the benign group, the mean concentration of cadmium was significantly higher in the former (p = 0.03) (Figure). CONCLUSION: This study supports the possibility that higher levels of heavy metals in bile may be associated with pancreato-biliary malignancy. Enough evidence is not available to implicate heavy metals as a direct cause of these tumours, but the present study indicates need for further research to ascertain the significance of this association between heavy metals and pancreato-biliary malignancy.

97 MULTIDETECTOR-ROW HELICAL COMPUTERISED TOMOGRAM IN DETERMINING THE RESECTABILITY IN GALLBLADDER CARCINOMA

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OBJECTIVE: To evaluate the accuracy of multidetector-row helical CT (MDCT) with 3D reconstruction in staging and assessing resectability of gallbladder cancer by correlating MDCT and operative findings. METHODS: MDCT of the abdomen was prospectively done in 37 patients
with clinical or radiological suspicion of carcinoma of the gallbladder between May 2002 and November 2003. Patients considered resectable on MDCT underwent surgical exploration and operative findings were correlated with MDCT findings. RESULTS: Surgical exploration was performed in 22/37 patients and 10 of these 22 patients underwent radical resection. MDCT revealed hepatic infiltration in 29 patients and vascular involvement in 18 patients. Infiltration of duodenum was present in 26, extrahepatic bile duct in 18 and colon in 13 patients. Lymph node enlargement was noticed in 21 patients. Non-contiguous liver metastasis was present in 10 patients and 5 had ascites. Six patients had stage III disease, 15 had stage IVa and 16 had stage IVb disease. The operative correlation of MDCT for liver infiltration was 100% while for vascular invasion, sensitivity was 100%, specificity was 93.3% and accuracy was 99.3%. Sensitivity for duodenal invasion was 80% while specificity and accuracy were 41.7% and 59%, respectively. MDCT was 50% sensitive, 100% specific and 72.7% accurate in determining the resectability of gallbladder carcinoma. CONCLUSION: MDCT was an accurate technique for staging gallbladder carcinoma and planning radical resections.

98 BILIARY OBSTRUCTION IN GALLBLADDER CANCER IS NOT 'SINE QUA NON' OF INOPERABILITY

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PURPOSE: The presence of biliary obstruction/ jaundice in a case of gallbladder cancer (GBC) is generally viewed as a sign of inoperability. We have critically evaluated all patients with GBC with biliary obstruction for curative resection. METHODS: Prospectively collected data of patients operated for GBC with evidence of biliary obstruction were analysed. RESULTS: Over the last 2 years and 9 months, radical resection with a curative intent was performed in 7 patients with advanced GBC with biliary obstruction. There were 5 females and 2 males with an age range of 21–68 years (average 49.3 years). One patient received a biliary stent prior to referral. In 5 patients the bilirubin ranged from 17.7 to 25.8 mg%. All 7 patients underwent bile duct resection and lymph nodal clearance as part of the radical resection.Extent of liver resection varied from a modified segment IV B and V resection (6 cases) to an extended right hepatectomy (trisegmentectomy). Additionally, distal gastrectomy was required in one patient. There was no postoperative mortality. Morbidity included wound infection and ascitic leak. The longest survivor is 33 months. CONCLUSIONS: The presence of biliary obstruction in a case of GBC should not be viewed as a sign of inoperability. In the absence of any evidence of distant spread, most of these patients can be taken up for radical curative resection.

99 CLINICAL COURSE OF ULCERATIVE COLITIS IN PATIENTS WITH AND WITHOUT PRIMARY SCLEROSING CHOLANGITIS: A CASE-CONTROL STUDY

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BACKGROUND: Primary sclerosing cholangitis (PSC) is a complication of ulcerative colitis (UC) and the pathogenesis of neither of them is completely known. We noticed in our practice that the patients with UC who were developed PSC experience a milder course of colonic disease. Our objective in this study was to define whether there is any difference between UC activity and its course in patients with and without PSC. PATIENTS AND METHODS: 19 patients with UC and PSC (8 male, mean age at onset of UC 25 and at onset of PSC 33) in whom colonic involvement was more than rectosigmoid were enrolled. For every patient with UC and PSC, three patients with UC alone (a total of 57 patients, 28 male, mean age at onset of UC 24) matched for age at onset, duration of the disease, and extension of colonic disease were selected as the control group. Patients with known hepatic diseases were excluded. Patients had been regularly followed up every 2–4 months and the protocol for their management was identical. We used number of hospitalizations due to activity of UC and number of short corticosteroid administrations in various years of follow-up as variables indicating the course and severity of the colonic disease in this period. To compare trends of UC activity between two groups, we used repeated measures two-way analysis of variances. RESULTS: Mean duration of follow-up in case and control groups was 6.1 years and 4.4 ± 4.9 respectively. The two groups had no significant difference in use of sulfasalazine or aminosalicylates. 2 patients in the case group (10.5%) and 2 patients in the control group (3.5%) underwent colectomy for dysplasia. The number of hospitalizations and courses of steroid therapy because of UC activity was significantly higher in controls than in cases (see Table). CONCLUSION: We found that development of PSC in patients with UC might have a positive effect on clinical course of the colonic disease. In theory, emergence of PSC may result in an increase in biochemical mediators, which may reduce the activity of UC. Further animal and human studies in this regard are warranted.

100 COMPARISON BETWEEN HELICAL COMPUTERIZED TOMOGRAPHY (CT) AND ENDOSCOPIC ULTRASOUND (EUS) IN THE STAGING OF RESECTABLE PARADUODENAL TUMOURS

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BACKGROUND: EUS has been introduced in our institution over the last 4 years. The aim of our study was to compare staging accuracy of helical CT and EUS in patients with resectable paraduodenal tumours. METHODS: 53 patients underwent pancreaticoduodenectomy for paraduodenal tumours between January 2000 and July 2003. These patients were staged preoperatively using CT followed by EUS. Three reviewers independently compared reports of the CT scans, EUS, histology, and operation notes. Factors evaluated included: the nature of the tumours, the occurrence of lymph node metastasis and the presence of arterial and venous infiltration. RESULTS: The accuracy of CT and EUS to detect the presence of a malignant tumour was 85% compared to 91% respectively; lymph node metastases 45% and 52%; and arterial/venous infiltration 90% and 84%. CONCLUSION: EUS does not contribute any additional information to CT scanning in the staging of resectable paraduodenal tumours.

101 COMPARISON BETWEEN TWO METHODS OF ENDOSCOPIC SPHINCTEROTOMY IN THE TREATMENT OF PATIENTS WITH BILIARY TRACT DISEASES

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AIMS: ERCP has become widely available for the treatment of pancreaticobiliary diseases and endoscopic sphincterotomy is an established treatment for common bile duct stones sphincterotomy of Oddi dysfunction (SOD). Pancreatitis is the most common significant complication of ERCP. The aim of this study was to evaluate and compare the complications of the two different methods of sphincterotomy, METHODS: Between October 2002 and September 2003 patients undergoing ERCP and endoscopic sphincterotomy were randomly assigned to two groups: conventional sphincterotomy through the papilla (group A) and suprapapillary fistulotomy-sphincterotomy (group B). The procedures were done by expert endoscopists in ERC. Pancreatitis was defined as abdominal pain and amylase levels higher than 3 times of pre-procedure state. Cholangitis, post-procedure bleeding and perforation were also evaluated. RESULTS: In the study period, 183 cases (78 male and 105 female, with mean age of 57.07 ± 17.04) were enrolled in the study, 93 cases were studied as group A and the second group included 90 patients who underwent needle-knife fistulotomy avoiding the papillary orifice. Final diagnoses of these patients were: choledocholithiasis (69.4%), sphincter of Oddi dysfunction (15%) and others 15.6%. Cumulation was successful in 77% of patients in the needle-knife fistulotomy group and 62.4% of patients in the conventional sphincterotomy through the papilla (group A) in first step. In the second step 34 of 93 patients in group A underwent needle-knife precut papillotomy after conventional sphincterotomy failed and 11 of 20 patients
in group B were finally cannulated in the second step. The mean number of attempts for cannulation was significantly less in group B (1.2 ± 0.8 vs 4.6 ± 3.2, p < 0.001). The mean duration of attempts for cannulation was also less in group B (4.4 ± 5.0 minutes vs 9.4 ± 6.8 minutes, p = 0.018). The size of CBD in the group with successful cannulation was 14.81 mm compared with 12.21 mm in the group with unsuccessful cannulation (p = 0.053). There were 2 patients with post-ERCP pancreatitis in group A and one case in group B. Microperforation occurred in one patient in group B, which improved with medical support. Furthermore, there was no perforation or bleeding or cholangitis following the procedure. CONCLU-
SION: This preliminary study shows that complications of fistulotomy-
 sphincterotomy are similar to conventional sphincterotomy and the procedure can be safely performed in those who failed conventional sphincterotomy in experienced hands.

102 \hspace{1cm} LIVING DONOR LIVER TRANSPLANTATION IN ADULTS: THE DONOR OPERATION
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This video shows the sequence of a right hemihepatectomy in a living donor.
1. Transverse and median laparotomy.
2. Hilar dissection, with identification of bile ducts, portal vein, and hepatic artery.
3. Retrohepatic dissection of inferior caval and hepatic veins.
4. Sonography, with demonstration of left, middle and right hepatic veins, and identification of the resection plane.
5. Liver biopsy, right portal vein and hepatic artery occlusion for ischemic preconditioning.
6. Cholecystectomy, and cholangiography, with probing of the biliary system.
7. Parenchymal liver transection, with use of Erbe Hydro-Jet, and bipolar coagulation forceps.
8. In situ right portal vein perfusion, and hemihepatectomy (segments 5–8).

103 \hspace{1cm} PROCUREMENT OF RIGHT LATERAL SECTOR GRAFT FOR LIVING DONOR LIVER TRANSPLANTATION
Shin Hwang, Sung Gyu Lee, Kwang Min Park, Ki Han Kim, Chul Soo Ahn and Deog Bok Moon, Asan Medical Center, Seoul, Republic of Korea
Right lateral sector (right posterior segment, RPS) becomes an acceptable type of partial liver graft when the size of the left lobe is disproportionately small. Unlike other grafts, we think that the feasibility of RPS procurement depends on the anatomical characteristics of donor livers. In our institution, we have confined its indication only to living donors with separately originating RPS portal vein (type III variation). Out of 700 living donors, we had tried to procure RPS in 10 donors. However, we had to change the operation plane to procure the left lobe graft in 4 donors instead of RPS because of smaller RPS than expected. With our experiences on 700 donor operations including 6 RPS harvest, we summarized the knacks for RPS procurement. If the portal vein is type III, the only limitation for RPS procurement is the relative size of RPS itself. We have often found that some S8 glissorian branches over rode the right hepatic vein (RHV) on triphasic CT images, by which the territory of RPS becomes smaller than the RPS volume guided by RHV. The volume of RPS is not always far exceeding that of the left lobe even when the left lobe volume is as small as 30% of the whole liver volume. If there are type III portal anomaly and sufficient size of RPS, there will be no anatomical contraindication for RPS procurement. In our 6 RPS donors, there were 2 replacing RPS arteries and 4 early branching right hepatic artery giving long RPS arterial stump. The main type of bile duct branching was low-lying separate RPS duct or trifurcation with deep-seated descending RPS duct. However, the ductal branching can be normal bifurcation type in one-third, but most of the RPS duct can be divided safely from the anterior duct because such B6 + 7 runs superficially along the hilar plate. A large elongated RHV is ideal because exposure of the vein trunk itself means making of appropriate transection plane. In some donors with prominent middle hepatic vein, V6 can be originated from the vein and it should be reconstructed. We think that type III portal vein anomaly always meets the optimal conditions for RPS procurement except for the proportional volume of RPS. RPS can be an optional type of partial liver graft only in feasible liver anatomies.

104 \hspace{1cm} LIVER SECTIONECTOMY WITH TRANSECTION OF GLISSON’S PEDICLES AT THE HEPATIC HILUS
Masakazu Yamamoto, Takehito Otsubo and Ken Takasaki, Institute of Gastroenterology, Tokyo Women’s Medical University, Tokyo, Japan
The liver can be divided into three sectors (left, middle, and right) on the basis of the ramifications of Glisson’s pedicles (the portal pedicles wrapped in their Wadaean sheaths) at the hepatic hilus. The ramifications of Glisson’s pedicles are located outside the liver and the pedicles can easily be taped after blunt dissection. After clamping the middle pedicle, we can easily confirm the boundaries between the left and middle sectors and the middle and right sectors. Therefore, middle sectionectomy can be performed systematically without dissecting the hepatic artery, portal vein and hepatic bile duct at the hepatic hilus. Left or right sectionectomy can be performed as the same maneuver. This technique of transection of Glisson’s pedicles at the hepatic hilus is simple, easy and useful in liver surgery.

105 \hspace{1cm} RIGHT HEPATECTOMY FOR HILAR CHOLANGIOCARCINOMA
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PURPOSE: To present right hepatectomy in video that has proved the most effective procedure in the prospective study of surgical treatment of hilar cholangiocarcinoma according to newly established guidelines (Ann Surg, in press). METHODS: Between July 1999 and December 2002, 40 of 42 surgically explored patients with hilar cholangiocarcinoma underwent resection. They were managed with preoperative biliary decompression, portal embolization, cholangiographic evaluation, and a choice of surgical procedures and techniques. Four types of hepatectomies were employed: right hepatectomy (n = 17), left hepatectomy (9), isolated caudate hepatectomy (5), and hilar resection alone (9). All hepatectomies included caudate lobectomy and hilar resection. Healey’s trisegmentectomy (resec-
tion of Couinaud’s segments 4, 5, 6, 7, and 8; or 2, 3, 4, 5, and 8) was performed in 3 cases, in which preoperative evaluation indicated longitudinal spread extending beyond the separating limits of the hepatic ducts from the vasculature in the conventional right or left hepatectomy. Concomitant vascular resection was carried out due to macroscopic involvement in 14 patients, with portal vein resection in 8 patients, hepatic artery resection in 8 patients, and both procedures in 2 patients. Pancreatocholedochectectomy was necessary for intrapancreatic extension in 7 patients with Bismuth type I or II tumors. RESULTS: Hospital or 30-day mortality and morbidity rates were 0% and 48%, respectively. Hepatic failure was not encountered. Histopathological examination revealed no positive ductal margins in all 40 patients, but two, treated with left hepatectomy and hilar resection alone respectively, showed positive resection margins from the hilar hepatic artery. The overall 3-year survival rate and median survival time were 40% and 27 months. Survival of patients with Bismuth type III or IV tumors or of patients who underwent right hepatectomy was significantly better. Survival of patients who underwent concomitant vascular resection was similar to survival of those who did not. Univariate analysis indicated the type of hepatectomy, histopathologic grade, Bismuth classification, concomitant hepatic artery resection, and UKCC stage as significant prognostic factors. CONCLU-
SIONS: No postoperative mortality and no positive ductal margins were achieved according to the above guidelines in a high-volume expert center. Long-term results, however, have not been significantly improved. Because right hepatectomy is likely to have superiority over the other procedures, indication of right hepatectomy for Bismuth type I or II tumors should be considered.

106 \hspace{1cm} IN SITU HYPOTHERMIC PERFUSION HEPATECTOMY FOR GIANT HEPATOCELLULAR CARCINOMA
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In situ hypothermic perfusion hepatectomy after vascular isolation for a hypervascular huge liver tumor, so as to operate on a bloodless liver without
pressure of time, was introduced by Forster in 1974 and further refined by Pichlmayr in 1990. Unlike the ex situ approach for liver tumor near hepatic vein confluence, in the in situ approach is helpful for liver tumor invading hilar plate. Dissection of suprahepatic vena cava from diaphragm was not necessary. Hypothermic perfusion with HTK-Brecheler solution was accomplished after division of portal vein, while on venous bypass (Bio-pump). The hepatic artery was simply clamped and was not perfused. The ischemic situation allowed particularly difficult resection in the areas of hilar plate, where hilar radicals became paper-thin and easily torn by prolonged tumor compression. This hypothermic perfusion hepatectomy has been known not to apply to the cholestatic liver and the cirrhotic liver, in which the liver parenchymal damage might be aggravated by hypo-thermia and cold ischemia. We here present a case of in situ hypothermic perfusion hepatectomy for giant HCC, centrally located, with obstructive jaundice (serum bilirubin 11.4 mg/dl) and gastric variceal bleeding by tumor compression on hilar plate. The patient is alive without tumor recurrence and with normal liver function 1 year postoperatively.

107 AN ISOLATED CAUDATE LOBECTOMY BY TRANSHEPATIC ANTERIOR APPROACH FOR HEPATOCELLULAR CARCINOMA
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A hepatic malignancy located in the caudate lobe of a cirrhotic liver presents surgeons with a dilemma as regards therapeutic strategy, because the caudate lobe is situated so deep and surrounded by the important vessels. We present an isolated caudate lobectomy by transhepatic anterior approach by video. After laparotomy, intraoperative ultrasonography was performed to recognize no intrahepatic metastasis. Isolation of the liver from the retrohepatic IVC was carried out after complete mobilization of both lobes. When the fissure for the ligamentum venosum was completely separated, the Spiegelian lobe was liberated from the left lob, exposing the dorsal part of MHV. Under repeated total clamping with reperfusion, transection of liver parenchyma was performed along the Cantile line, exposing the MHV distally to the confluence to the IVC. The hilar branches to the caudate lobe were divided, completely exposing the upper surface of the hilar plate. Finally, after division of the caudate process from the right lobe and mobilization of the right lobe, paracaval portion was separated from right lobe, exposing the RHV and right Glissonian trunk. The isolated caudate lobe was removed. This procedure is not so dangerous to preserve the remnant hepatic function. We advocate that the trans-hepatic anterior approach provides a strategic alternative for an isolated caudate lobectomy on an anatomical basis.

108 SUCCESSFUL HEPATIC RESECTION WITH TUMOR THROMBECTOMY OF HEPATOCELLULAR CARCINOMA WITH TUMOR THROMBUS EXTENDING INTO RIGHT ATRIUM USING CARDIOPULMONARY BYPASS AND TOTAL VASCULAR EXCLUSION
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INTRODUCTION: Extension of HCC with tumor thrombus through the hepatic veins into the right atrium can cause sudden death by heart failure and pulmonary embolism, even the primary tumor is relatively localized. We report on a case of hepatic resection and tumor thrombectomy of hepatocellular carcinoma with tumor thrombus extending into right atrium using cardiopulmonary bypass and total hepatic vascular exclusion. CASE REPORT: A 65-year-old man visited Yeungnam University Hospital with a diagnosis of left liver mass. The patient had not noticed edema in the lower extremities and dyspnea on exertion. Laboratory studies revealed that platelet count was 162,000 K/μl, total bilirubin 1 mg/dl, albumin 4.1 g/dl and prothrombin time 14.7 s. In addition, the retention of indocyanine green at 15 min was 13.5%. The anti-HCV was positive; alpha-fetoprotein was 6.45 ng/ml and PIVKA-2 582 mIU/ml. An abdominal CT scan, hepatic angiogram and echocardiogram revealed a 3-cm HCC in the left lobe and 4-5-cm tumor thrombus extending into the right atrium through the left and middle hepatic veins. Other studies revealed no distant metastasis. We performed surgery: first, remaining middle and left hepatic vein pedicles, extended left lobectomy with caudate lobectomy was performed. And then cardiopulmonary bypass was started, cardiac arrest was induced. Tumor thrombectomy through right atriotomy and extraction of separated left liver were performed while total hepatic vascular exclusion was applied. The total operative time was 13 h. The total duration of cardiopulmonary bypass was 55 minutes, and the cardiopletic time was 24 minutes. Total hepatic vascular exclusion time was 18 minutes. We have succeeded in performing an extended left lobectomy with caudate lobectomy and removal of tumor thrombus extending into the right atrium through the middle and left hepatic veins, applying cardiopulmonary bypass with total hepatic vascular exclusion.

109 LAPAROSCOPIC LIVER RESECTION FOR RUPTURED HCC: A USEFUL MINIMAL INVASIVE APPROACH IN ELDERLY PATIENTS
Pierre Alain Clavien Sr, Markus Weber, Lucas McCormack and Markus Selner, University Hospital of Zurich, Zurich, Switzerland
BACKGROUND: Laparoscopic liver resection is a new technique to decrease postoperative morbidity in selected patients. While laparoscopic resection is becoming widely accepted in patients with benign diseases, the role of laparoscopic liver resection in presence of malignant tumors remains controversial.

METHOD: A 75-year-old male patient admitted to our service with hemorrhagic shock due to acute intra-abdominal bleeding. Abdominal ultrasound and CT scan identified a 10-cm tumor in SII/III with massive intra-abdominal free fluid. The patient underwent an angiography and the feeding artery of the tumor was embolized. The patient was stabilized and transferred to the ICU for preparation for later surgery. RESULTS: Five days after the tumor embolization the patient underwent an explorative laparoscopy, which demonstrated liver cirrhosis and the large mass in SII/III without any evidence of extrahepatic disease. The left lateral sector was freed from its ligaments end the hepatoduodenal ligament was incised. A Pringle maneuver was performed laparoscopically using a new approach, and the parenchyma transection was done with the harmonic scalpel. The specimen was removed form the abdominal cavity using an endobag and extracted by a transverse supraceliac incision. The patient recovered well from surgery and the postoperative course was uneventful except for a mild upper respiratory tract infection. The patient was discharged 5 days after surgery. The histologic evaluation of the tumor showed a ruptured HCC without vascular invasion. CONCLUSION: Laparoscopic liver resection can be performed safely with minimal morbidity in elderly patients with ruptured HCC.

110 LAPAROSCOPIC PLACEMENT OF A HEPATIC ARTERIAL INFUSION PUMP
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This video demonstrates a completely laparoscopic approach to the placement of a hepatic arterial infusion pump for liver-directed chemotherapy. The patient is a 77-year-old male who was found to have synchronous unresectable liver metastases after receiving chemoradiation for a primary rectal adenocarcinoma. He had a complete response in his rectum. The patient then received multiple regimens of systemic chemotherapy over the course of a year with slow progression in the liver. On our evaluation he had no rectal tumor and no evidence of extrahepatic disease on computed tomography and positron emission tomography. He was referred for the placement of a hepatic arterial infusion pump for liver-directed chemo-therapy. The video is approximately 9 minutes long and describes a completely laparoscopic approach to the placement of a hepatic arterial infusion pump. The video sequentially shows port placement, operative staging, cholangioscopy, and isolation of the hepatic and gastroduodenal arteries. We then demonstrate laparoscopic ligation of the distal gastroduodenal artery, placement of the pump catheter into the gastroduodenal artery, securing the catheter into place and testing perfusion with methylene blue injection. This is a unique and uncommon minimally invasive procedure that could have significant impact on the treatment of hepatic metastases.

111 TECHNIQUE OF LAPAROSCOPIC LEFT LOBECTOMY IN A LIVING DONOR FOR PEDIATRIC TRANSPLANTATION
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BACKGROUND: In order to minimize morbidity and invasiveness of major abdominal incision in living donors, in this video we describe a
technique of laparoscopic harvesting of the left lobe. METHOD: Under general anesthesia, the donor was in supine position with his legs apart. Pneumoperitoneum was created with CO₂ and maintained at 12 mmHg. Five ports were used (10, 12, 12, 10 and 5 mm diameter) allowing the insertion of various devices such as harmonic scalpel, ultrasonic dissector, clip forces and linear staplers. RESULT: The left lobe was mobilized by section of the falciform and triangular ligaments. Left branches of the middle hepatic artery and portal vein were dissected free and branches assigned to the caudate lobe were clipped and divided. The liver parenchyma was divided on the right side of the round and falciform ligaments without vascular clamping. Pedicles assigned to segment IV were clipped and cut. The left bile duct and hilar plate were cut. On the right side, the distal end of the left bile duct was closed with 5/0 absorbable running suture. Parenchymal division was completed up to the left hepatic vein which was dissected free. A 10-cm suprahepatic incision allowed the insertion of a 15-mm port and a large bag. The left branch of the hepatic artery was clamped and cut and left portal and hepatic veins were cut with a unilatera stapler in order to preserve vessels length for further anastomosis in the recipient. The left lobe was placed in the large bag gently exteriorized through the suprahepatic incision and immediately flushed with cold preservation solution after a warm ischemia time of 5 min. The suprahepatic incision was closed and pneumoperitoneum was reinsufflated to check for hemostasis and biliosis. Pneumoperitoneum was vented and the fascia of the port incisions was closed with absorbable sutures. The left liver lobe was graft after 2 h of cold ischemia time and recipient's recovery was uneventful with good liver graft function. CONCLUSION: This video reports a safe technique of left lobe harvesting which aims at becoming a standard technique in living donation for pediatric liver transplantation.

112 QUALITY OF LIFE OF PATIENTS UNDERGOING AUXILIARY LIVER TRANSPLANT AND STANDARD ORTHOTOPIC LIVER TRANSPLANT FOR PARACETAMOL-INDUCED ACUTE LIVER FAILURE – A PILOT STUDY

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INTRODUCTION: Paracetamol (acetaminophen) overdose (POD) is the commonest cause of fulminant hepatic failure (FFH) in the UK. Super-urgent liver transplantation is a well recognized form of treatment with a 1-year survival of 65-70% for those patients who fulfill King's College criteria. Long-term immunosuppression gives rise to significant morbidity. Auxilliary liver transplantation (ALT), with the potential for native liver regeneration and withdrawal of immunosuppression, is an attractive option, particularly as these patients often have serious psychosocial problems and non-compliance with treatment can be an issue. This technique has been successfully developed in our unit and we have assessed the quality of life (QOL) of this group, with comparison to a group of patients undergoing standard orthotopic liver transplantation (OLT) for POD FFH during the same time period, 1996–2003, and to a general population. METHODS AND METHODS: To assess QOL we used a well validated generic QOL questionnaire, the Short Form 36 Version 2 (SF36 V2). We sent this questionnaire to all the surviving patients who had undergone ALT and standard OLT for POD FFH since 1996. For each domain of the SF36 V2 the raw scores were transformed into scores on a scale of 0 (worst) to 100 (best). An algorithm was then used to calculate Norm Based Scores (NBS). This score allows comparison and interpretation with the general population. The mean NBS of each domain for the general US population, ALT and standard OLT were compared using the non-parametric Mann-Whitney U test. RESULTS: Since 1998 we have carried out 700 OLT/ALT. There have been 12 ALT and 13 standard OLT for POD FFH in our unit. Eight ALT and seven OLT patients are alive, but one ALT patient has been retransplanted and is therefore excluded from the analysis. Six of the remaining seven ALT patients are off immunosuppression with the most recent patient undergoing immunosuppression withdrawal currently. In each domain of the SF36 V2, ALT fared better than standard OLT and compared favorably with the general population (due to small numbers). CONCLUSION: ALT for POD FFH achieves the objectives of native liver regeneration and withdrawal of immunosuppression, with a similar survival rate. It gives a better QOL than standard OLT, although statistical significance could not be shown.

113 HYBRID ARTIFICIAL LIVER AND RECONSTRUCTION OF MINI-LIVER FROM PORCINE FETAL LIVER USING RADIAL-FLOW BIOREACTOR

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PURPOSE: The radial-flow bioreactor (RFB), developed our institution, is a high-function 3-dimensional culture system, which can be used for high-density culture. In this study, porcine fetal hepatic cells with proliferating capacity were cultured by RFB for extracorporeal medicine. METHODS: After intraportal infusion of collagenase + dispase using porcine fetal livers (5–8 weeks), the hepatic cells were isolated with shaking method. After separation into hepatocytes (hepatoblast) and non-parenchymal cells by centrifugation (50 g), these cells were mixed and infused into RFB. The porcine cells cultured with hepatocyte growth factor (HGF), epidermal growth factor (EGF), Oncostatin M (OSM), ascorbic acid, insulin and dexamethasone under various concentrations were examined. 1) Morphological analysis: The routine histological and electron microscopic findings (TEM, SEM). 2) Immunohistological analysis of the expression of connexin (Cx) 32.3) NH3 loading test after 1 week's incubation as ammonia metabolism, were examined. Adult liver was used as the control. RESULTS: In the histological findings of fetal liver, the extramedullar hematopoesis was predominant at 5 weeks as compared with 8 weeks of fetus. The oxygen consumption tended to be higher in those cells, reaching a level of 15 ppm (Do in-Do out: AO2) within 2 days and was maintained favorably during the incubation period without growth factors (FLCs, we have established 7 cell lines derived from hepatocellular carcinoma patients, take 30 days to become same level) and was maintained favorably during the incubation period. However, the culture of adult hepatic cells was hardly maintained for 1 week without growth factor. In a pulse-dosing group (HGF 100 ng/ml; IGF 25 ng/ml; HGF 100 ng/ml; 2 times for incubation period) the oxygen consumption reached the maximum level of 25 ppm. As for ammonia metabolism activities, a good function was evident in the pulse group. A liver resembled reconstruction was observed in a microcarrier, celllose, and a mini-liver-like tissue was floating in the lower layer of RFB. In the pulse group, hepatic tissue of 1 cm³ (floating mini-liver) was reconstructed with palisade parenchyma- and bile duct-reshaped structures histologically. In TEM findings, microvilli (bile duct) and functional complex were also observed. Cx 32 was also observed in the mini-liver. CONCLUSION: The combination of porcine fetal liver with a proliferating capacity, RFB system and HGF pulse was an interesting system for artificial liver and regenerative medicine.

114 SPLENCHIC HEMODYNAMICS AFTER LIVING DONOR LIVER TRANSPLANTATION: RELATIONSHIP WITH CLINICAL OUTCOME

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OBJECTIVE: To study the outcome of splanchic hemodynamics early after living donor liver transplantation and to evaluate the relationship between hemodynamic changes and liver function. METHODS: Portal vein velocity and diameter were measured prospectively using Doppler ultrasonod in 23 consecutive recipients with cirrhosis, before and 1, 7, 14 and 30 days after living-related right lobe liver transplantation. Portal blood flow (PBF) was calculated. Liver function tests were obtained at the same time periods. Hepatic venous pressure gradient (HVPG) was determined at day 7 and a transjugular liver biopsy was performed. Hemodynamic results were compared with those obtained prooperatively in donors. RESULTS: The mean graft/recipient weight ratio (GRWR) was 1.01 ± 0.23. Fourteen patients were Child class B and 9 were Child class C. The mean right PBF in recipients at day 1 was significantly higher than in donors (1.55 ± 0.34 vs 0.89 ± 0.26 L/min, p < 0.01). The main determinant of elevated PBF in recipients was the increase in right portal vein velocity (86 ± 21 vs 48 ± 13 cm/s, p < 0.01). GRWR did not differ between Child class B and C patients. However, PBF was significantly higher in Child class C patients (1.61 ± 0.33 vs 1.38 ± 0.35 L/min, p < 0.05). PBF decreased significantly at 1 month but did not achieve normal values. WH PBF was analysed in relation to right lobe volume (PBF/LV), the mean value of this ratio at day 1 significantly correlated with bilirubin value at day 7 (r = 0.78;
p < 0.01). HVPG on day 7 was increased (8.5 ± 2.7 mmHg) and correlated closely with PBF/RLV at day 1 (r = 0.70; p < 0.01). Histological findings were not related to hemodynamic or biochemical changes. Cardiac output was increased at all time points but did not correlate with PBF or biochemical changes. CONCLUSION: Portal blood flow markedly increases early after living-related right lobe liver transplantation. Changes in splanchic hemodynamics may influence the outcome of liver function. Doppler ultrasound is a useful tool for the early detection of hemodynamic changes in these patients.

115 LAPAROSCOPIC LIVING DONOR LEFT LATERAL SECTIONECTOMY FOR PEDIATRIC LIVER TRANSPLANTATION

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BACKGROUND: We reported the first two cases of laparoscopic harvesting of left lateral liver grafts (Lancet 2002; 359: 392–96). The aim of this study is to report our 2-year experience with this technique. METHODS: From 2001 to 2003, 7 donors underwent laparoscopic left lateral sectionectomy for transplantation in their children. There were 4 mothers and 3 fathers aged 19–37 years (mean 28). Surgical technique included 5-port laparoscopy (2–12 mm, 1–10 mm and 2–5 mm) with CO2 pneumoperitoneum, dissection of the left portal pedicle and liver transection without clamping. Grafts were retrieved in a bag through an 8-cm supra-pubic incision. The recipients were 2 girls and 5 boys, with a median age of 15 months (10–19) and a mean weight of 9.3 kg (7–11). The indication was biliary atresia with previous hepatoportoenterostomy in 6 cases and metabolic disease in 1. DONORS RESULTS: Mean operative time was 4.5 h (4–6) and mean warm ischemia time was 12 minutes (10–15). There was one intra-operative complication due to hemorrhage from the left portal branch which was immediately sutured (case 4), but conversion to laparotomy was undertaken because of suspected stenosis of the left portal vein. There were no other conversions or intra-operative complications. There was one postoperative complication consisting of a pelvic hematoma from the extraction incision, which required no treatment. No patient was transfused intra-operatively or postoperatively. Mean hospital stay was 6.2 days (4–10). RECIPIENTS RESULTS: All grafts were transplanted and functioned immediately. There were two arterial thromboses. One was asymptomatic (routine Doppler US finding), while the other was associated with poor portal flow leading to the child’s death. One child with choledangiitis had a percutaneous biliary drain placed. All children but one are alive with a functioning graft. CONCLUSION: This report demonstrates the feasibility and safety of living donor left lateral sectionectomy. The rate of arterial thrombosis in the recipient requires further evaluation.

116 RISK FACTORS IN THE DEVELOPMENT OF BILIARY STRICTURES AFTER RIGHT LOBE LIVER DONOR LIVER TRANSPLANTATION

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INTRODUCTION: The shortage of cadaveric hepatic allografts has led to an increasing use of live donor liver transplantation (LDLT) in both the adult and pediatric populations. The rate of biliary complications remains high and contributes to morbidity and mortality of LDLT recipients. METHODS: Data pertaining to LDLT recipients were collected prospectively and later analysed to determine the incidence and factors contributing to biliary stricture. Patients who died within 3 months post LDLT, with follow-up <3 months and/or underwent retransplant were excluded from this analysis. Biliary strictures were diagnosed by transhepatic or endoscopic cholangiogram in patients with elevated alkaline phosphatase and bilirubin. The influence of MELD score, graft-to-recipient-weight-ratio (GRWR), number of bile ducts (BD) in the grafts, and type of biliary reconstruction (duct-to-duct (DD) vs Roux-en-Y (RY)) on stricture formation was analyzed. Statistical analysis was performed using Fisher’s exact test for subgroup comparison. RESULTS: Between 5/1999 and 11/2003, 75 right lobe LDLTs were performed in 75 patients. Actual patient and graft survival are 88% and 86.7% with a mean follow-up of 672 days (range 8–1672). Nine patients were excluded from the analysis: <3 months follow-up (3), early death due to septic complications (5), and retransplantation for arterial thrombosis (1). Mean age was 52.3 years (range 7–69). Male-to-female ratio was 3:1.1. Sixteen (27%) of 66 patients, with a mean follow-up of 754 days, developed biliary strictures requiring intervention. Mean MELD scores of recipients with and without strictures were 14 and 13, respectively. Influence of biliary reconstruction, number of the BDs, and GRWR are summarized in the Table. The biliary stricture rate was not statistically affected by the type of biliary reconstruction or the number of bile ducts. There was a statistically significant difference in stricture rate between patients with GRWR <1.1 and GRWR >1.1 (40% and 8%, respectively). CONCLUSION: In our recipient population, the rate of biliary strictures was not influenced by the type of the biliary reconstruction or the number of bile ducts. A higher stricture rate occurred in patients with GRWR ≤1.1. This may imply the possibility of a new presentation of small-for-size syndrome in liver transplant recipients.

117 THE MAIN HEPATIC ANATOMIC VARIATIONS FOR THE PURPOSE OF SPILT-LIVER TRANSPLANTATION

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AIM: The aim of this study is to demonstrate the importance of an assessment of the hepatic anatomic structures for the split-liver transplantation. MATERIALS AND METHODS: Human cadaveric livers (n = 60) were obtained from routine autopsies. Resections were carried out en bloc with liver, celiac trunk, left gastric artery, lesser omentum, superior mesenteric artery, and head of the pancreas. The main anatomic structures of the liver were dissected out and recorded minutely, also correlating to hepatic segments for application of the liver splitting. RESULTS: The right, the median and the left hepatic vein were unique, respectively, in 59 (98.3%), 53 (88.3%), and 46 (76.3%) cases. The portal vein trunk was divided into right and left branches in 59 (98.3%) cases. A median branch appeared in 9 (15.2%) cases and no bifurcation of the portal vein occurred in 1 (1.6%) case. The right and left hepatic ducts were multiple in 47 (78.3%) and 57 (95%) cases, respectively; however, the median hepatic duct was unique in 16 (26.6%) cases. Looking at the intrahepatic distribution of the right hepatic duct we found four branches in 28 (59%) cases, towards segments V, VI, VII, VIII; two branches in 11 (23%) cases, towards segments V, VI and two branches in 8 (17%) cases, towards segments VII, VIII. 57 cadavers had multiple left hepatic ducts. The intrahepatic dissection showed that the major branches distribution was towards hepatic segments II and III. Three separate branches of the left hepatic duct were found, in 11 (19%) cases towards hepatic segments II, III and IV. Two intrahepatic ducts, coming from hepatic segments V and VI, drained separately to the left intrahepatic biliary tree in 1 (2%) case. The arterial irrigation of the liver was made basically by right and left hepatic artery, only in 9 (15%) cases there was a median hepatic artery. Right hepatic artery, coming from the superior mesenteric artery, was present in 15 (25%) cases and left hepatic artery originating from left gastric artery in only 2 (3.3%) cases. Left hepatic artery had two exceptional origins, in 1 (1.6%) case coming directly from the abdominal aorta and in the other from the superior mesenteric artery. The right and left hepatic artery was accessory in 11 (18.3%) and 2 (3.3%) cases, respectively. Right hepatic artery was dominant in 4 (6.6%) cases. The median hepatic artery directed to segment IV in 6 (10%) and to segment II and III in 3 (4.9%) cases. CONCLUSION: The anatomical and technical details of the splitting procedure are critical to the success of this technique. The absence of bifurcation of the portal vein is a rare anomaly and would certainly contraindicate the partition of the liver.
118 EMERGENCY SUBTOTAL HEPATECTOMY – A NEW CONCEPT FOR FULMINANT HEPATIC FAILURE DUE TO TOXIC LIVER INJURY. TEMPORARY HEPATIC SUPPORT BY AUXILIARY ORTHOTOPIC LIVER TRANSPLANTATION ENABLES LONG-TERM SUCCESS

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BACKGROUND: Toxic injury due to paracetamol (acetaminophen) overdose (POD) is the leading cause of fulminant hepatic failure (FHF) in the UK and despite maximal medical therapy, 5% of those who develop FHF require liver transplantation. There is no evidence for the development of chronic liver disease in the patients who survive this toxic injury without transplantation. METHODS: Beginning in June 1998 we have been piloting a clinical programme of subtotal hepatectomy and auxiliary orthotopic liver transplantation for toxic injury: 12 patients up to July 2003..Difficulty was based on the following: [1] subtotal hepatectomy to remove 70–75% of the injured liver; [2] auxiliary transplantation of a maximal liver volume – a whole liver graft was used in all cases; [3] gradual withdrawal of immunosuppression after recovery. FINDINGS: Eight of the 12 patients are alive with 6 of immunosuppression at 6–62 months and one going through immunosuppression withdrawal currently. One patient has been retransplanted for vascular thrombosis and will be maintained on full immunosuppression. One patient died from lung injury within 24h of surgery but with normalised intracranial pressure, and one died with an intracranial haemorrhage after 7 days. Two patients who received grafts from ‘marginal’ organ donors died from primary graft non-function (recurrent after retransplantation). Following immunosuppression withdrawal, native hepatic regeneration with transplant atrophy has been confirmed by isotope and CT scanning in the long-term survivors. All surviving patients have normal liver function and have returned to a normal life within a few months. INTERPRETATION: Our results with this new technique are encouraging: 67% survival and no long-term immunosuppression requirement to date for successful cases.

119 LIVING DONOR LIVER TRANSPLANTATION FOR PATIENTS WITH HEPATOCELLULAR CARCINOMA IN CIRRHOSIS

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INTRODUCTION: Liver transplantation (LTx) has been established as a viable treatment of hepatocellular carcinoma (HCC), but the results have been negatively influenced by the time on the waiting list for a suitable cadaveric graft. Living donor liver transplantation (LDLTx) constitutes a new therapy option for these patients. Patients who initially meet the UNOS criteria but experience dropout due to tumor progression while on the waiting list, patients outside current listing criteria at the time of presentation as well as patients meeting the criteria but not able to wait because of end-stage liver cirrhosis may be considered in this therapy option. PATIENTS AND METHODS: From 1998 to 2003, 367 patients underwent liver transplantation in our centre. Of these, 338 patients underwent orthotopic liver transplantation (OLTx), 77 split-LTx, 6 ‘reduced-size’-LTx and 116 patients underwent LDLTx. From 67 patients having HCC, 33 patients undergoing LDLTx were reviewed. Prior to LTx, 10 patients underwent chemo-embolization as tumor-specific bridging treatment for HCC. From the 116 patients undergoing LDLTX, HCC was incidentally found in the liver explant in 6 of them (5.1%). For 4 patients LDLTx was carried out because of tumor recurrence after liver resection. Sixteen patients (45.5%) ‘met’ the Milan criteria for LTx, whereas 17 patients (54.5%) ‘exceeded’ them. RESULTS: 12-month patient survival was 71.2%. Five patients (15.1%) died in the first 30 days after LTx, one because of pulmonary embolism and the other four because of multiple-organ failure. Three patients developed metastasis to the lungs within 10–17 months after LTx; one patient died 10 months after the LTx and the other two are alive and in good physical condition at 47 and 54 months, respectively. One-year tumor-free survival was 91%. Median survival is 21 months with a range from 3 to 49 months. Donor morbidity referred to wound infection (3 patients, 9%), pleural effusion (2 patients, 6.5%), bile leak (3 patients, 9%) and biloma (1 patient, 3%); no operation was needed. CONCLUSIONS: Living donor LTx for HCC in cirrhosis is a treatment option for these patients, offering several advantages in comparison to the standard LTx, such as optimal graft quality, possibility of extended indication for LTx, performance of the procedure in timely fashion and reduction of the necessity for bridging interventions. Although complicating factors such as donor voluntarism and selection criteria limit the role of LTx for HCC, LDLTx allows more patients to undergo early transplantation and results in a better outcome.

120 FPSA-PROMETHEUS SYSTEM IN THE TREATMENT OF THE LIVER FAILURE – PRELIMINARY REPORT

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BACKGROUND: Encephalopathy, coagulopathy and hepato-renal syndrome are the most important factors influencing the poor outcome and mortality in the patients with acute and acute-on-chronic liver failure. Clinical investigations are in progress as regards the devices and systems supporting liver detoxification and metabolism. One of them is the Transjugular Plasma Separation Adsorption and Dialysis system (FPSA). This report presents the preliminary results of the treatment of the first series of patients with acute and acute-on chronic liver failure with the Prometheus device. PATIENTS AND METHODS: From September to November 2003, 18 FPSA procedures were performed in 9 patients with end-stage liver disease. The most common indication were: acute liver failure following paracetamol intoxication – 2 patients, Amanita phalloides intoxication – 2 patients, liver graft failure – 2 patients, liver acute-on-chronic liver failure – 1 patient. Poor liver function in the course of Wilson disease and HBV cirrhosis – 2 patients. King’s College Hospital criteria were adopted. The procedures were carried out with a Prometheus 400HF device. Intravenous heparin infusion was applied as an anticoagulant. Prior to and after the procedure liver function tests (ammonia, bilirubin, aminotransferases, urea, creatinine, serum levels and pH) were controlled. RESULTS: The mean number of procedures per patient was 2. The average time of the procedure was 7.5h. The mean heparin dose was 850 UI/h. After the FPSA procedure a significant decrease in the liver function tests was observed: bilirubin 19.42 vs 10.86 mg/dl, ammonia 212.2 vs 131.3 µg/dl, AST 1370.2 vs 579.9 IU/l, ALT 2017.6 vs 864.4 IU/l, urea 49.1 vs 22.7 mg/dl, creatinine 1.9 vs 1.2 mg/dl. Mean values of pH, sodium, potassium, calcium and magnesium serum levels prior to and after the procedure were respectively: 7.35–7.29, 126.8–136.6 mmol/l, 4.04–3.87 mmol/l, 1.89–2.27 mmol/l, 0.53–0.76 mmol/l. The mean body temperature was 35.8 and 36.7°C prior and after the procedure respectively. CONCLUSION: Preliminary data suggest that the use of the FPSA-Prometheus device in patients with end-stage liver failure makes it possible to improve the general patient’s status as well as selected parameters of liver function: ammonia, bilirubin, aminotransferases, urea, creatinine and pH.

121 LIVER TRANSPLANTATION WITH NEOADJUVANT CHEMORADIOThERAPY IS MORE EFFECTIVE THAN RESECTION FOR HILAR CHOLANGIOCARCINOMA

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BACKGROUND: We developed a protocol combining neoadjuvant radiotherapy, chemosensitization and orthotopic liver transplantation (OLT) for patients with operatively confirmed stage I and II hilar cholangiocarcinoma (CCA) in 1993. Since then, patients with unresectable CCA or CCA arising in the setting of primary sclerosing cholangitis (PSC) have been enrolled in the protocol. Patients with CCA amenable to resection have undergone conventional resection. We reviewed our transplantation and resection experiences with a specific aim to compare patient survival between the two groups. METHODS: We reviewed records for all patients whom underwent OLT per the protocol from 1993 through 2001. CCA diagnosis was based on intraluminal brush cytology or biopsy or a CA 19.9 level >100 ng/ml in the presence of a radiographically malignant structure. Neoadjuvant therapy included external beam irradiation with radiosensitizing bolus 5-FU chemotherapy, followed by a transcatheter Indium-119 brachytherapy boost and either intravenous 5-FU or oral capecitabine therapy. A staging abdominal exploration with biopsy of regional hepatic lymph nodes was performed as close as possible to the time of transplantation, and patients with regional hepatic lymph node meta-
stases or extrahepatic disease were excluded from OLT. We compared results after OLT with results for patients who underwent potentially curative conventional resection (extraphelial bile duct including the bifurcation and hepatic resection) at our institution during the same time period. All resection patients had negative margins and absence of regional lymph node metastases. RESULTS: Seventeen patients were enrolled in the transplant protocol, had negative staging operations, and underwent OLT. 20 patients had negative regional lymph nodes and underwent potentially curative resection. CONCLUSIONS: Neoadjuvant therapy and liver transplantation achieved significantly better survival than resection for patients with hilar CCA. Liver transplantation with neoadjuvant therapy has emerged as an effective treatment for patients with localized, regional lymph node-negative, hilar cholangiocarcinoma.

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<td>Resection Transplantation survival from beginning of neoadjuvant therapy</td>
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122 OUTCOME AFTER PANCREATODUODENECTOMY FOR TUMOR IN PATIENTS WITH BILE DUCT POSITIVE CULTURE
Alexandre Cortes, Reza Kianmanesh, Alain Sauvant, Sylvie Janny, Philippe Sockel, Philippe Ruszniewski and Jacques Belghiou, Beaujon Hospital, Chiby, France
From 2002 to 2003, 79 patients underwent pancreatoduodenectomy (PD) for periampullary tumors. All received i.v. antibiotics prophylaxis (cefazolin + metronidazole) and routine bile duct exploration at the gallbladder and/or bile duct. Thirty-five patients had infected bile (B+ group) and were compared with 44 patients with sterile bile (B− group). The 2 groups were comparable for age, ASA, tumor size and pancreas consistency (soft/hard) and the type of tumors except for ampullomas which were more common in B+ (26 vs 2%, p = 0.001). Preoperative instrumental and non-instrumental biliary endoscopic procedures had been performed in 80% of patients in B+ vs 14% in B− (p < 0.001), including 9 isolated sphincterotomies (20 vs 5%, p < 0.03) and 20 endoprosthesis insertions (97 vs 0%, p < 0.0001). Serum bilirubin level was lower in B+ (p < 0.05). Operative time and blood loss were similar in both groups. One patient died postoperatively (B+). The rate of pancreatic fistula was similar in both groups. Overall morbidity was increased in B+ (77 vs 59%, p = 0.05). Postoperative infectious complications (all proven) included superficial wound infections (26 vs 5%, p = 0.005), intraperitoneal infectious collections (23 vs 7%, p = 0.035), and pneumonia (14 vs 2%, p = 0.045). To treat infectious complications, antibiotics (>7 days) were more often given in B+ (71 vs 43%, p = 0.02). In the B+ culture, the 3 most frequent bacteria were Escherichia coli, Enterococcus faecalis and Klebsiella pneumoniae. Among B+ patients, bile contained at least 2 micro-organisms in 54%, and in 94% micro-organisms were resistant to cefazolin + metronidazole. In patients with infectious complications, the same micro-organism was isolated in bile and another sampling in 49%. Micro-organisms isolated in bile were susceptible to the combination of piperacillin + tazobactam in 66% of patients. In B−, bile sterility was definitively established after a 48h culture, except in one patient. In patients undergoing PD, bile infection in 80% of cases is related to previous instrumental biliary endoscopic procedures. Micro-organisms found in bile culture were (i) resistant to cefazolin + metronidazole in 94% of cases (used as antibiotic prophylaxis), (ii) multiple in 54%, and (iii) responsible for an increased rate of infectious complications (superficial and deep).

123 LAPAROSCOPIC PANCREATIC RESECTION: A SINGLE INSTITUTION EXPERIENCE WITH 30 PATIENTS
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BACKGROUND: Potential applications of laparoscopy in pancreatic surgery include pancreatic resection for benign disease; cystic lesions and in situ neoplasms. We report a single institution series of 30 patients who presented pancreatic benign tumor treated by laparoscopy. RESULTS: All patients were operated at the Bordeaux University Hospital between 03/1999 and 05/2003. The median age was 45 (26–72). Our conversion rate was 13% (4 cases: one undetectable celiac insulinaemia, one undetectable corporeal insulinaemia, bleeding, and the last one for technical problem). In 26 patients (87%), the entire procedure was performed by laparoscopy. 12 patients had undergone an enucleation (10 insulinaemia, 1 serous cystadenoma, 1 mucinous cystadenoma), 3 patients had a distal pancreatectomy (2 insulinaemia, 1 included spleen) and 7 patients underwent a left pancreatectomy (3 mucinous cystadenoma, 1 serous cystadenoma, 1 cystic tumor and 1 insulinaemia, 1 gastrina). 2 patients had a spleno-pancreatectomy (1 malignant insulinaemia and 1 mucinous cystadenoma) and one patient had a total duodeno-pancreatectomy (mucinous polycystadenomatosis). One other patient underwent a median pancreatectomy with pancreatico-gastric anastomosis (mucinous cystadenoma). The median operating time was 140 min (60–480 min) and median intraoperative blood loss was 250 ml. Morbidity rate was represented by 3 pancreatic leakage (10%), a postoperative bleeding (reoperating) and a partial splenic ischemia (no reoperation). There were no deaths. Mean hospital stay was 12 days. CONCLUSION: Laparoscopic surgery for benign lesions, especially left pancreatectomies, appears to be a safe procedure.

124 REDUCING PANCREATIC DUCT LEAK AND HEMORRHAGE DURING LAPAROSCOPIC DISTAL PANCREATECTOMY AND PARTIAL SPLENECTOMY USING STAPLE LINE REINFORCEMENT WITH AN ABSORBABLE POLYMER MEMBRANE
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BACKGROUND: Laparoscopic distal pancreatectomy is not performed without significant risk. Bleeding may occur in 0.5–16% of patients. Perioperative complications like pancreatic duct leaks and fistula formation are reported in 16–23% of patients. A new technique of staple line reinforcement with an absorbable polymer membrane was tested in an animal model to investigate a reduction of perioperative hemorrhage and leaks after pancreatectomy. MATERIALS AND METHODS: Twenty female 40-kg pigs underwent laparoscopic distal pancreatectomy and partial splenectomy in the present prospective animal survival study. In 10 consecutive animals (group A), a staple line reinforcement technique with an absorbable polymer membrane, which buttresses the resection site, was used for transection. A conventional stapler without buttressing was used to transect the pancreas and spleen in a control group of 10 animals (group B). Necropsy was performed: pancreas and spleen were sent for histopathology after 6 weeks. RESULTS: Operative data did not differ between the two groups. Operative time was 118 minutes in group A and 116 minutes in group B. Periprobe blood loss after distal pancreatectomy (5 ± 1 ml vs 75 ± 5 ml) was significantly higher in group B (p < 0.04). Significantly higher bleeding rates were also encountered after partial splenectomy in group B (45 ± 7 ml vs 215 ± 12 ml) (p < 0.01). Mortality in group B was 10%. There was 1 death in group B (10%) due to extensive postoperative bleeding at the staple line region of the spleen. A retrogastric fluid collection with elevated amylase levels was encountered in 1 animal (10%, group B). At necropsy, results showed in group A, that reinforce- ment material was absorbed completely and no loculated inflammatory reactions or fibrosis in duodenum, stomach or colon could be demonstrated. Minimal adhesions were encountered in both groups. Histopathology results showed fibrotic changes and injury to vessels and pancreatic duct only in group B. Methylene blue test demonstrated a leak of the pancreatic duct at the transection site only in 2 cases of group B. No leaks or damage were encountered in group A. CONCLUSION: The results of the present study show that this staple line reinforcement technique with the absorbable polymer membrane reduces staple line hemorrhage and pancreatic duct leakage after distal pancreatectomies. This study supports future application of absorbable buttress material for pancreatic transection and partial splenectomy in humans. This may result in diminishing perioperative complications such as bleeding and pancreatic leaks.

125 LAPAROSCOPIC RESECTION OF PANCREATIC NEOENDOCRINE TUMORS
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Pancreatic neuroendocrine tumors are rare neoplasms with variable biologic behavior. Conventional treatment involves open exploration
with enucleation or resection. We describe a series of nine consecutive patients with pancreatic neuroendocrine tumors treated laparoscopically at a university hospital between September 2001 and November 2003. Diagnoses include five patients with insulinoma, two with gastrinoma, one each with ampullary carcinoma and non-functioning islet cell tumor. All lesions were successfully localized by surgeon-performed, intraoperative laparoscopic ultrasonography. All patients with insulinoma were treated by enucleation and were cured. One gastrinoma patient underwent successful laparoscopic enucleation with node dissection but recurred, requiring open reoperation. The tumor in a second gastrinoma patient could not be localized, requiring conversion to laparotomy with transduodenal excision.

The patient with ampullary carcinoma was successfully treated by laparoscopic transduodenal excision, but recurred twice later and required open pancreaticoduodenectomy for cure. The non-functioning islet cell tumor was cured with laparoscopic distal pancreatectomy. Mean (SEM) operating time was 201 (21) minutes. Mean (SEM) length of stay was 7.3 (2.3) days. Major morbidity included pancreatic leak in three of nine patients, all treated successfully with percutaneous drainage. One patient required readmission for bleeding from a Mallory Weiss tear. There were no deaths. Laparoscopic resection of pancreatic neuroendocrine tumors represents a technically challenging, but feasible alternative for treatment of these rare tumors. Success depends on accurate preoperative biochemical diagnosis, use of intraoperative ultrasound for localization, and patient selection. Lesions most suitable for a laparoscopic approach are solitary, benign lesions that are amenable to enucleation or limited pancreatectomy.

126 COMPARISON OF MESENTERIC ANGIOGRAPHY AND ENDOSCOPIC ULTRASOUND FOR DETECTION OF PORTAL VEIN INVASION IN PATIENTS UNDERGOING PANCREATICODUODENECTOMY

Jonathan F Finks, James P Dolan, Douglas O Faigel, John G Hunter and Brett C Sheppard, Oregon Health & Science University, Portland, OR, USA

METHODS: We performed a retrospective review of the medical records, preoperative studies, operative notes and pathology reports of 152 consecutive patients undergoing pancreaticoduodenectomy from April 1994 through December 2003. In 21 cases, no preoperative studies were available for review, and these patients were excluded from the study. Results of preoperative studies were compared to operative and histopathologic findings when available. Criteria for portal vein (PV) invasion on preoperative imaging studies included loss of interface, encasement or intraluminal mass. Operative findings of tumor invasion, or adherence to the PV without a surgical plane, were accepted as invasion unless disputed by pathologic findings. RESULTS: 131 patients were included in this study. Results were available from angiography in 119 and endoscopic ultrasound (EUS) in 83 patients. Six patients underwent PV resection for suspected invasion. In 3 of these cases, an assessment of PV involvement was not included in the pathology report. In 1 case, there was no tumor invasion and in 2 cases, the final diagnosis was pancreaticitis. Final pathologic diagnoses were pancreatic cancer (48), ampullary/duodenal cancer (27), cholangiocarcinoma (8), islet cell tumor (6), pancreatitis (13), benign lesion (28), and metastatic cancer (1). Operative findings indicated PV involvement in 13 cases. Study results are presented in the Table above. When results of angiography and EUS concurred (56 patients, 79%), the positive and negative predictive values for the combined tests improved to 75% and 98%, respectively. CONCLUSIONS: While neither test reliably predicted PV invasion in this group of patients selected to undergo a Whipple procedure, angiography and EUS were both highly effective in ruling out PV involvement. As EUS offers the added benefits of tissue diagnosis and lymph node staging, and can be paired with therapeutic endoscopic intervention, it should remain the study of choice following CT scan. In cases where EUS is equivocal with regard to PV involvement, or when planning PV resection, angiography may provide valuable information.

127 SYSTEMATIC APPRAISAL OF THE EVIDENCE FOR SYNCHRONOUS PORTAL/SUPERIOR MESENTERIC VEIN RESECTION AT PANCREATICODUODENECTOMY

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INTRODUCTION: Tumour clearance at pancreaticoduodenectomy (PD) may be enhanced by en bloc resection of the portal/superior mesenteric vein (PV/SMVR). However, vein resection is associated with increased peri-operative risks. Almost all available data come from cohort series and there is no clear consensus on which patients (if any) benefit from PV/SMVR and on overall outcome. The aim of this study was to undertake a systematic review of the available evidence on PV/SMVR to obtain an overview of procedure-related complications and outcome from pooled cohort data. METHODS: A computerised search of the MEDLINE database was conducted for the period between 1996 and 2002 using the keywords ‘pancreatic cancer’ and ‘portal vein’. The bibliographies of articles retrieved from this search were manually cross-referenced to identify further articles. For each MEDLINE citation, the title, abstract, authors, institution, journal, major and minor descriptors were downloaded. The search identified 514 abstracts. Non-English, animal studies, reviews and reports were excluded (381). Of the remaining 131 articles, a further 88 were excluded due to no data on outcome of PVR, leaving 43 articles. When 19 sequential reports/double publications were excluded, there were 24 non-duplicated datasets which comprised the study population. RESULTS: There were 952 PV/SMVR (39%) of 2462 patients undergoing pancreaticoduodenectomy. Overall operative details and outcome data are expressed as median (range) in the Table. In-hospital mortality of PV/SMVR in the pooled cohort was 38 (4%) and, 1-, 2-, 3- and 5-year survival were 38%, 15%, 12% and 7.5%, respectively. CONCLUSION: The results of pooled data suggest that synchronous portal vein resection may be carried out with pancreaticoduodenectomy with a relatively low peri-operative morbidity but without convincing evidence of any survival benefit.

128 SURVIVAL BENEFIT OF EXTENDED PANCREATECDOCURECTOMY FOR A LIMITED GROUP OF PATIENTS WITH PANCREATIC HEAD CANCER

Sonohi Takao, Hiroshi Shimsu, Kouei Marmura, Hiroshi Kourahana, Yusuke Matakai and Takashi Aikou, Kagoshima University, Kagoshima, Japan

OBJECTIVES: Whether an extended pancreateoduodenectomy can bring about a survival benefit for the patient with pancreatic head cancer is still controversial. METHODS: 101 patients underwent a pancreatectomy for pancreatic head cancer between 1980 and 2001. 40 patients in the extended resection (ER) group had an extended lymphadenectomy and neural plexus dissection, while 61 patients in the conventional resection (CR) group did not have these extended procedures. Tumor status, morbidity, mortality, survival, recurrent type, and micrometastasis of the lymph node were retrospectively studied and compared between both groups. RESULTS: Morbidity and mortality were not associated with an extended resection. The incidence of R0 operations in the ER group was higher when compared with that in the CR group (p < 0.01). The actuarial 5-year survival rate (32.6%) of patients with pT-stage IA or IB in the ER group was significantly higher than that (8.2%) in the CR group (p = 0.04) because local recurrence (47%) in the CR group was higher than that

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multivariate analysis were: identification of the pancreatic duct with separate suture ligation, hand-sewn suture in addition to stapling closure, spleen preservation, use of PTFE pledgets for reinforcing the suture, sex, age, indication for pancreatectomy, associated diseases. Fistula was defined as a drain output >5 ml with amylase level 5 times higher than the serum value after day 5. RESULTS: Overall mortality was 0%, morbidity 47%, pancreatic fistula rate was 33%, mean ± SD postoperative stay was 12 ± 7 days. All fistulas healed spontaneously (mean duration 54 days). Fistula rate was 34% after hand-sewn closure, 26% after linear stapler closure and 42% after Endo GIA II stapler closure (p = NS). None of the factors considered in the analysis proved to reduce significantly the onset of fistula. The best result was obtained in 13 patients with pledge suture (fistula rate 15% vs 36%, p = 0.07). Also spleen preservation (28 patients) seemed to be a protective factor (fistula rate 21% vs 37%, p = 0.12). Main duct ligation (46 patients) had no significant effect (30% vs 35%, p = 0.5). At the multivariate analysis no factor significantly influenced fistula onset. CONCLUSION: Pancreatic fistula after left pancreatectomy remains an unsolved problem. Mechanical closure of the pancreas did not reduce the onset of fistula. The use of pledgets to reinforce the suture is advisable.

131 THE ENDOCRINE CONSEQUENCES OF TOTAL PANCREATECTOMY: IS LABILE DIABETES INEVITABLE?
Paras Jethwa, Mikael Hans Sodergren, John AC Buckels and Darius F Mirza, University of Birmingham, Birmingham, UK

INTRODUCTION: The pancreaticoglicic diabetes associated with total pancreatectomy is frequently described as both unstable and ‘brittle’ with control inherently labile and a high risk of hypoglycemia. We, however, have not always found this to be the experience of patients that had undergone total pancreatectomy in our department. We therefore performed a retrospective analysis to establish the nature and lability of diabetic control, and any associated complications of diabetic control in this group. METHODS: Patients who had undergone a total pancreatectomy in our unit were identified from the departmental database (1989–2003). A review of the patient’s case notes provided basic data with further information obtained by liaison with the patient’s general practitioner. Data regarding postoperative diabetic control was augmented by a telephone interview where possible. Patients who had undergone total pancreatectomy for necrotizing pancreatitis were excluded from our study group. RESULTS: 46 patients underwent total pancreatectomy during the period of study. The average age was 56 years with 29 cases still alive and 23 available for further telephone assessment. Mean follow-up was 28 months (range 0.5–129 months); 35 were performed as primary operations with 11 as completion procedures; 32 were for malignancy (15 dead), 14 for benign conditions (1 dead). There were 9 perioperative deaths. Diabetic control was reported by the patients as excellent (8), good (12), fair (8) and poor (4). We were unable to document control in 14 cases. From initial treatment insulin dose was increased in 17, decreased in 7 and unchanged in 6. 11 reported minor episodes of hypoglycaemia or hyperglycaemia and a ‘settling’ period. The mean settling time was 13 months (range 1.5–81). Only two patients needed in-patient treatment for complications. One patient with poor control had a long history of unstable diabetes preoperatively and the other had a history of poor compliance. CONCLUSION: Our patients reported better glycemic control than previously. Fluctuations were common but in-patient treatment was rare. Good liaison between surgical and diabetic teams is essential for optimal control. Unstable diabetes is not necessarily the outcome of total pancreatectomy.

132 EFFECTS OF LIVER ISCHEMIA ON THE PROTOHEME OF PULMONARY ALVEOLAR TYPE II CELLS IN THE RAT
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INTRODUCTION: Recently, it has been demonstrated in experimental models that hepatic ischemia may cause injury to the lung. Because alveolar...
epithelial injury is an important mechanism in the development of acute
liver injury, in this study we investigated the impact of liver ischemia on the
proteome of lung epithelial cells. METHODS: Male lean Zucker rats (250–
300 g) were anesthetized with isoflurane under spontaneous ventilation.
Vascular supply to the left and medial lobe (75% of the liver) was clamped for
55 min with subsequent reperfusion. Sham-operated Zucker rats without
any hepatic manipulation were used as controls. After 8 h, bronchoalveolar
lavage (BAL) was performed and alveolar type II cells (ATII) were isolated (purity > 90%), lysed by sonication and fractionated. For comparison, proteins were labeled with stable isotopes, trypically
digested, purified by cation exchange chromatography. The biotin-tagged
cystine-containing peptides were extracted using an avidin-coated
column, separated by HPLC and identified using MALDI-MS and protein
sequencing by collision-induced dissociation. Spectra were interrogated
against the SwissProt database and quantified using LC-BatchTag and
SearchCompare from the ProteinProspector suite of programs. RESULTS:
After ischemia and reperfusion, there was an increased percentage of
neutrophils (17%) compared with sham-operated controls (<1%) in BAL.
Quantitative proteomics showed differential expression of >50 proteins
compared with controls with a sham operation. These included beta-
defensins, lysozyme, surfactant and niosomal proteins and Na, K-ATPase.
CONCLUSION: Liver ischemia leads to lung injury represented by an
increased percentage of neutrophils and differential protein expression in
ATII that can be detected by quantitative mass spectrometry. The
identified proteins have an important role in innate immunity, protein
production and the active clearance of pulmonary edema fluid. The altered
response of ATII after liver ischemia may be clinically relevant and
warrants further investigation.

LIVING DONOR TRANSPLANT IN A PATIENT WITH
TOTAL SITUS INVERSUS AND REPAIRED TETRALOGY
OF FALLOT: ANESTHETIC ISSUES
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Clinic College of Medicine, Rochester, MN, USA.
INTRODUCTION: Situs inversus totalis (SIT) is rare and involves right
left reversal of the abdominal and thoracic viscera. Tetralogy of Fallot
(TOF) is associated with early mortality without surgical repair. Both
present perioperative management challenges. We report the first case of
living donor liver transplant (LDLT) to an adult with SIT and TOF. CASE
REPORT: A 62-year-old man with SIT, TOF, and primary sclerosing
cholangitis presented for LDLT. TOF was reconstructed in a reconstituted
RV outflow tract, ventricular septal defect closure, and pulmonary valve
homograft. Tricuspid anuloplasty was also performed. Preoperative ECG
had normal sinus rhythm with right bundle branch block. Echocardiogram
revealed pulmonary and tricuspid regurgitation, RV dilation with reduced
function, and LV hypertrophy with normal function. Coronary angiography
showed mild atherosclerosis. Intraoperative ECG leads were reversed due
to the dextrocardia. Transesophageal echocardiography was used to guide a
pulmonary artery catheter past the repaired tricuspid annulus, and assess
preload and ventricular function. The operation was hemodynamically
uneventful. Postoperatively, he had 2 episodes of SVT with spontaneous
conversion to sinus rhythm. Twelve days post-discharge, he developed re-
entrant SVT requiring administration of adenosine. He was placed on
atenolol and has had no more episodes of SVT. DISCUSSION: There
are several issues to consider in LDLT with SIT and TOF: 1. A variety of
procedures are used for TOF repair, resulting in abnormal valvular and
coronary anatomy. Preoperative work-up should define anatomy and
coronary flow reserve. Echocardiography assesses anatomy and valvular
function. Stress echocardiographic and nuclear imaging to assess coronary
reserve are not feasible due to technical difficulties arising from distorted
anatomy. Coronary angiography is preferred. 2. With SIT, ECG leads
should be reversed to adequately assess for intraoperative myocardial
ischemia. 3. Valvular pathology may make pulmonary artery catheter
estimates of filling pressures suspect. Further, placement may be difficult
following TOF repair. Intraoperative echocardiography may facilitate
perfusion optimization and provide estimates of preload and ventricular function. 4. Conduction system abnormalities and dysrhythmias may occur after TOF repair. If significant, they should be
corrected preoperatively. Perioperative vigilance and careful postoperative
follow-up are required.

VERY EARLY EXTUBATION AFTER LIVER
TRANSPLANTATION: ANESTHESIA TRENDS AND
INTRAOPERATIVE FLUID MANAGEMENT THERAPY
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The need of postoperative mechanical ventilation after orthotopic liver
transplantation (OLT) is still debated controversially. Early tracheal
extubation has been safely performed after OLT, questioning the need for
routine postoperative ventilation. A randomized clinical trial (RCT) was
enrolled for early tracheal extubation. Very early tracheal extubation in the
operating theater was achieved in 80% of patients (n = 105). 15% of all patients required 6 h postoperative mechanical
ventilation. Mechanical lung ventilation lasted more than 24 postoperative
hours in 5% of patients with severe intraoperative coagulopathy, reperfusion
syndrome, retransplantation or preoperative encephalopathy. Aprotinin
(Trasyloil) infusion has been used in all 105 patients. The initial dose was
2 × 10^3 IU during the first hour, continuous infusion 0.5 × 10^3 IU
lasted up to the end of OLT. Thromboelastogram (TEG) and routine
coagulation panel monitoring were multiply provided during OLT. Meticu-
losa intraoperative control of the coagulation process allowed decreasing
blood and blood product transfusion rate from 10 ± 2 units to 2 ± 1.5 units
case. Fluid uncontrolled therapy is one of the reasons for ‘wet lung’
syndrome, which requires prolonged mechanical ventilation. Crystallloid
(Plasmalyte), albumin and mannitol combination is an anesthesiologist tenet
during OLT based on continuous pulmonary artery pressure (PAP), CVP and
urine output monitoring. Intraoperative TEE made it possible to optimize
fluid status after the reperfusion period. Fluid therapy during OLT (year
2001–2003) has been changed from 10.5 ± 21 to 5.6 ± 0.5 L. Balanced
anesthesia was provided based on opioid (Fentanyl) infusion at a rate of
5 mcg/kg/h to 1 mcg/kg/h with oxygen and isoflurane inhalation. Muscle
paralysis was achieved by continuous Cisatracurium infusion at a dose of 1–
0.8 mcg/kg/min. Muscle paralysis was reversed in 82% of patients at the end
of OLT. Fentanyl infusion decreased till 0.5 mcg/kg/h, the patient in optimized
pain control condition was extubated 15 min after the end of surgery.
Alveolar-arterial oxygen gradient (D(Aa)O2) was calculated before extuba-
tion. Very early extubation group D(Aa)O2 was <250 mmHg. CONCLU-
SION: Immediate tracheal extubation was safe and well tolerated. Special
attention should be given to intraoperative fluid transference therapy,
coagulation control and meticulous anesthesia technique.

EXPRESSION OF SURVIVIN, AN ANTI-APOPTOSIS
GENE, IN A FATTY RAT COLD ISCHEMIA MODEL
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PURPOSE: Molecular changes during cold ischemia and the impact of
ischemic preconditioning (IP) are incompletely defined. We used DNA
microarrays to survey gene expression profiles of rat livers in a cold ischemia
model. METHODS: Obese Zucker rats (250–300 g) were randomized
either to a control group or IP group. Rats in the IP group were subjected to
ischemic preconditioning via hepatic arterial and portal venous clamping for
10 min with subsequent reperfusion for 10 min. Livers were then harvested,
flushed and stored in UW solution. After 8 h of cold ischemia, liver total RNA was purified, labeled and hybridized to mouse DNA
microarrays containing 23,000 elements. RESULTS: Survivin, a gene
encoding an inhibitor of apoptosis protein, was strongly upregulated in the
ischemic preconditioning group, as were thymosin beta and heat shock
protein 60. Several genes of unknown function are also significantly
upregulated. CONCLUSION: We confirm in our model IP upregulated
genes, which have been shown in various other ischemia reperfusion
models to play important roles. Our study identifies potential therapeutic
targets to ameliorate cold ischemia damage during transplantation.

ISCHEMIC PRECONDITIONING IMPROVES
METABOLIC PROFILES DURING COLD ISCHEMIA AND
SURVIVAL AFTER TRANSPLANTATION UTILIZING FATTY
DONOR LIVERS
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INTRODUCTION: The aim of the study was to investigate the effect of
ischemic preconditioning (IP) on metabolism of fatty livers during cold
ischemia (CI) and its effect on survival after transplantation in rat model. METHODS: In one experiment, IP (10 min ischemia/10 reperfusion) was performed in obese Zucker rats (250–300 g) in the right lobe whereas the left lobe served as control (n = 3). Immediately after IP, organs were harvested and flushed and stored in UW solution. Tissue was sampled at different time points (0, 4, 6, 8 h) from the right and left lobes. Organs were frozen, extracted using acid/liquid extraction procedure and analysed by 

H-MRS and 3P-MRS with a Bruker 500 Avance system. In a further experiment, rats were randomized to undergo a 70% reduced liver transplantation without arteriolarization either with or without IP. Survival at 24 h was determined. RESULTS: High energy balance (ATP/ADP) was significantly better preserved immediately after 4 and 6 h of CI in the right IP lobe when compared to the left lobe (0.67 ± 0.47, p < 0.001 and 0.41 ± 0.30, p < 0.002, respectively). There was no difference in energy balance at 8 h of CI. Lactate was significantly lower in the IP lobe at 4 h of CI (p < 0.05) but not at 6 or 8 h. Based on these results, we performed liver transplantation after 4 h CI using fatty livers as donor grafts into lean recipients. We found that IP improved recipient survival after transplantation. Specifically, at 24 h post transplantation, only two of eight (25%) rats in the control group survived, whereas six of out of eight (75%) rats in the IP group survived (p < 0.05). CONCLUSION: Ischemic preconditioning improves the metabolic profile of fatty livers during early cold ischemia. Ischemic preconditioning also greatly improves survival after liver transplantation utilizing fatty livers.

137 LIVER TRANSPLANTATION AND THROMBOSIS
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Massive blood loss with coagulation abnormalities in liver transplant recipients is a well known entity, but TEE-documented intracardiac thrombosis has not been reported. We present two cases that developed intracardiac thrombosis. Case 1: This was a 58-year-old lady. Surgery proceeded uneventfully well into the anhepatic phase. While the portal vein anastomosis was underway, the patient developed marked hypotension and bradycardia and decreased ETCo2, which initially responded to fluids and small boluses of epinephrine and phenylephrine. This recurred shortly after stabilization. She also developed various forms of arrhythmias including junctional rhythm, bigeminy, non-sustained ventricular tachycardia and severe bradycardia. A TEE probe was placed, which showed hypovolumic left side, a large friable clot in the RA, attached to the IVC/RA junction extending through the TV. CT surgery was contacted. As preparations were being made for this, on the TEE, it was noted that the clot was decreasing in size and finally disappeared about 45 minutes after the TEE probe had been placed. Sternotomy was not required and the patient's hemodynamic status improved. Postoperatively she had difficulty weaning from the ventilator, requiring a tracheostomy, and developed renal failure requiring dialysis. She eventually developed septic shock, multiorgan failure and passed away. Case 2: This was a 51-year-old female who was felt to have a dysfibrinogenemia versus factor XI deficiency, by the hematologist service. The patient was coagulopathic and TEG showed fibrinolysis. After 3 h, a sudden increase in right-sided pressures was noted with marked hypotension. A TEE probe was placed which showed underfilled LV with grossly intact function, dilated RA and RV with leftward bulging of the intra atrial septum, a Chiari network in the right atrium with what appeared to be fresh clot and more web-like structures protruding through the tricuspid valve with a mitral valve stenosis (1.2 cm). As resuscitation continued, the patient continued to deteriorate and developed ventricular tachycardia and progressed to ventricular fibrillation, which did not respond to aggressive resuscitative efforts. DISCUSSION: In the first case, a sternotomy and cardiopulmonary bypass were prevented by continued surveillance by TEE, although the patient did have an unfavorable outcome. In the second case, this patient had a Chiari network in her right atrium and this may have put her at an increased risk for developing a thrombus on this network. This was not recognized preoperatively. Another important point in this case was that all blood products, including Amicar, were being given through the same I.V. access port.

138 CARCINOID CRISIS Versus TRANSFUSION REACTION DURING LIVER TRANSPLANTATION
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INTRODUCTION: Approximately 5000 orthotopic liver transplants (OLTxs) are performed yearly in the USA. About 84% of all transplanted patients are alive after 1 year. However, typical liver transplantation recipients have a multitude of serious comorbidities and intraoperative hemodynamic instability and other critical events are not uncommon.

CASE DESCRIPTION: This is a case report of a 69-year-old male patient with end-stage liver disease secondary to alcohol abuse who underwent OLTx. The patient was also diagnosed with intractable ascites and chronic renal insufficiency. Preoperative evaluation included a transthoracic echocardiogram that estimated ejection fraction of 65%. The patient was taken to the operating room, and general anesthesia was induced after radial and pulmonary arterial cannulations. After reviewing the first set of intraoperative laboratory test results, packed red blood cell and fresh frozen plasma transfusions were started to correct anemia and coagulopathy. The surgery progressed well and dissection of the cisthotic liver was almost complete. At this point, sudden onset of hypotension, tachycardia, increased airway pressure and hypoxemia were observed. There was no identifiable surgical cause for this event. ECG, cardiac output, central venous and pulmonary arterial pressures were not significantly different from base line. Systemic vascular resistance was decreased from baseline. High frequency ventilation with reduced tidal volume and 100% oxygen, airway pressure therapy, epinephrine and phenylephrine infusions were moderately successful and decision was made to progress with surgery. However, the respiratory and hemodynamic stability was short-lived. The patient's condition deteriorated and was complicated with severe metabolic and respiratory acidoses. Bicarbonate vasopressors, inotropes, oxygen concentration, airway pressure therapy were successfully weaned subsequently. After 4 days, the patient left the intensive care unit and went home 9 days later. CONCLUSION: Liver transplant candidates frequently present with several comorbidities and a long list of prior medical interventions. Preoperative collection of all available information is essential in the accurate diagnosis and effective treatment of these patients.

139 ROLE OF ENDOSCOPIC ULTRASOUND (EUS)-GUIDED FINE-NEEDLE ASPIRATION (FNA) IN DIAGNOSIS OF PANCREATIC MALIGNANCY – A RETROSPECTIVE STUDY
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INTRODUCTION: Pancreatic malignancy is the fourth leading cause of cancer mortality in the USA. Endoscopic ultrasound (EUS) is one of the modalities used in the evaluation and work-up of pancreatic masses. In cases of advanced disease, tissue acquisition is still crucial prior to initiation of therapy. HYPOTHESIS: EUS-guided FNA is an accurate method for tissue acquisition in patients with pancreatic malignancy. METHODS: All patients diagnosed with pancreatic malignancy at UMass Medical Center from January 2000 to December 2002, obtained from the tumor registry, were included in the study. The details of the work-up done to evaluate and diagnose pancreatic malignancy, including EUS-guided FNA and the pathology results, were obtained from the medical records of these patients. Patients with metastasis to pancreas from a different primary were excluded from the study. RESULTS: 72 patients were diagnosed with pancreatic malignancy in 2 years at our center. Out of 72 patients 28 (38.88%) were evaluated by EUS. The indication for EUS was abnormal radiological findings in 27 patients (96.4%) and jaundice in 1 patient (3.6%). 26 of the 28 patients who underwent EUS had primary pancreatic malignancy. Out of these 26 patients, EUS-guided FNA was diagnostic for malignant cells in 22 patients (84.6%) (adenocarcinoma in 19 patients, islet cell tumor in 2 patients and neuroendocrine neoplasm in 1 patient). This procedure was not diagnostic in 4 patients (15.4%). These 4 patients were subsequently diagnosed by different techniques (2 patients had positive liver biopsies, 1 patient underwent Whipple's procedure, 1 patient was diagnosed on laparotomy). Patients who underwent EUS-guided FNA did not develop any complications related to the procedure. CONCLUSION: Over a third of the patients with pancreatic malignancy were evaluated with EUS-guided FNA. EUS-guided FNA is a useful and safe method of tissue acquisition in patients with pancreatic cancer. How the results of EUS-guided FNA pathology change the management of patients with pancreatic malignancy needs further study.

140 LAPAROSCOPIC VERSUS OPEN GASTRIC AND BILIARY BYPASS FOR GASTRODUODENAL AND PANCREATIC DISEASES: A COMPARATIVE STUDY
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BACKGROUND: Whilst gastric and biliary bypass in patients with
gastroesophageal or pancreatic head diseases may be accomplished laparoscopically, the benefits of this minimally invasive approach remain to be demonstrated. The aim of this non-randomised study was to compare the open and laparoscopic approaches to gastric and biliary bypass. METHODS: Between 1998 and 2003 some 42 patients underwent 43 surgical drainage procedures. The indications for laparoscopic and open surgery included benign (n = 4, n = 4) and malignant diseases (n = 18, n = 17 respectively). Patients who underwent trial dissection were excluded from analyses. The procedures performed via the laparoscopic and open approach included 12 and 4 gastric bypasses, 4 and 9 biliary bypasses, and 6 and 8 combined gastric and biliary bypasses, respectively. The results were expressed as numbers or medians (interquartile ranges).

RESULTS: There were no conversions to open surgery in the laparoscopic group. Operative mortality included one patient in each group. The patients in the laparoscopic and open groups were comparable for age (67 and 60 years, respectively) and sex (male 14 and 11). Laparoscopic surgery was associated with shorter operating time (90 [59–145] vs 119 [85–165] minutes, p = 0.055), a more rapid resumption of dietary intake (2 [2–3] vs 5 (4–7) days, p < 0.001), and a reduction in postoperative complications (n = 3, 14% vs n = 9, 43%; patients, p = 0.035) and hospital stay [3 (3–4) vs 10.5 (7.5–19) days, p = 0.001]. CONCLUSIONS: The laparoscopic approach to gastric and biliary bypass is associated with a smoother and more rapid recovery and shorter hospital stay compared with open surgery.

141 PATIENT VARIABILITY IN INTRAOPERATIVE ULTRASONOGRAPHIC CHARACTERISTICS OF HEPATIC COLORECTAL METASTASES
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PURPOSE: It is known that hepatic colorectal metastases can vary in their echogenicity and appearance on intraoperative ultrasonography (IOUS). Despite this, it is not known whether these differences are associated with patient/primary tumor factors or tumor-specific factors. This question was evaluated by comparing the variance of ultrasonographic features between patients and within the same patient with multiple lesions. METHODS: IOUS images and clinical data from 194 tumors and 94 patients undergoing liver surgery for hepatic colorectal metastases were analysed. Each evaluable IOUS image was digitally recorded and randomly coded, then blindly reviewed and scored for echogenicity (E-score, 1–5) and appearance pattern (P-score, A–D) using three independent observers. Variability within groups (i.e. patients) was compared to the variability between groups (Kruskal–Wallis and permutation tests). RESULTS: Of the IOUS-evaluable lesions, 36% were scored as isoechogenic (E = 3), 52% as hypoechoic (E = 1–2), and 12% as hyperechoic (E = 4–5). Lesions within patients were more similar in echogenicity than lesions between patients (p < 0.0001). Similarly, intra-patient variability in appearance pattern was significantly less than the variability between patients (p = 0.002). Patients with response to chemotherapy were more likely to have a characteristic IOUS appearance pattern but not echogenicity. There was no association between any ultrasonographic characteristic and the tumor size, location, age, gender, or histology. Moreover, patients with hyperechoic or hypoechoic tumors were more likely to have small (<1 cm) additional lesions identified (p < 0.05). CONCLUSIONS: This study demonstrates strong evidence that the ultrasonographic characteristics of hepatic metastases are more similar within patients than between patients, independent of size or other features. These findings may have implications in the ability to recognize and detect otherwise occult lesions on IOUS evaluation of the liver.

142 RESULTS OF MAJOR AND MINOR LIVER RESECTIONS BY LAPAROSCOPY
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AIM OF STUDY: Assessment of feasibility and results of minor and major (>2 segments) laparoscopic liver resections for cancer and benign tumours (BT). METHODS: Retrospective study of the outcome of patients with uncertain or definite BT or with primitive or secondary malignant liver tumours treated by laparoscopy in a specialized department. RESULTS: From 1995 to 2003, 81 liver resections were performed by laparoscopy: 33 (40%) for BT and 48 (60%) for cancer (13 hepatocellular carcinoma (HCC) (6 on liver cirrhosis), 1 cholangiocarcinoma, 24 colorectal metastasis (CCM) and 10 no colorectal metastasis). The liver resection was a major hepatectomy in 22 cases (18 right hepatectomy (RH), 3 extended RH, 1 left hepatectomy) and a minor resection in 59 cases. 8 (9.8%) patients were converted to laparotomy. 5 (6%) patients were transfused with a global postoperative morbidity of 19% and a mortality of 1.2% due to the postoperative death of a patient after a RH for CCM on a cirrhotic liver. Mean diameter of lesions was 5 ± 4 cm. For patients with a follow-up of at least 6 months, in CCM, global survival and survival without recurrence was respectively 57% and 47% with a mean follow-up of 2 years. In HCC, median survival without recurrences was 19 months with a mean follow-up of 29 months. CONCLUSIONS: If they are performed by surgeons specifically trained and specialized in laparoscopy, laparoscopic liver resections, even major hepatectomy, are feasible with results which seem similar to laparotomy.

143 PAIN PERCEPTION AND NEUROPLASTICITY IN PATIENTS WITH CHRONIC PANCREATITIS
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BACKGROUND: Treatment of chronic pain in patients with chronic pancreatitis is troublesome. One of the main reasons for this is the lack of knowledge and understanding of the mechanisms of chronic pain in these patients. AIM: To find evidence for neuropathy in patients with chronic pain caused by chronic pancreatitis and to gain more insight in pain mechanisms responsible for the chronicity of pain. PATIENTS AND METHODS: In 23 patients (11 men and 12 women) with chronic pancreatitis and pain, Verbal Rating Scores (VRS) and medications were registered. To study neuropathy we used somatic Quantitative Sensory Testing (QST). We measured pain detection and pain tolerance thresholds to electrical skin stimulation and pain tolerance thresholds to mechanical stimulation at the pancreatic region (dermatome T10 ventral and dorsal) and the dermatomes C5, T4 and L2. Pressure thresholds were measured at bony prominences in the corresponding dermatomes. Age- and gender-matched patients without pain or pain syndromes, undergoing an operation for a benign gynaecologic or urologic disease served as controls. RESULTS: 18 patients with opioids (O-group) and 5 patients with non-opioids (NO-group) were tested. The opioid group had a significantly higher mean VRS (6.5, range 3–10 vs 4, range 0–4, p < 0.01) Electric thresholds were significantly increased in both groups at level T4 (+61% and +120% respectively, p < 0.01). At the level L2, thresholds were significantly increased in the NO group compared with the controls (+77%, p < 0.01). At T10 thresholds in the NO group were significantly increased in comparison with both the controls and the O-group (+149% and +89% respectively, p < 0.01). The mechanical thresholds were significantly increased in the NO-group compared with the O-group. Interestingly, however, at the pancreatic region the mechanical thresholds were reduced in both subgroups (−54% and 26% respectively, p < 0.01). CONCLUSIONS: Chronic pancreatitis patients show significant neuropathy, e.g. central pain sensitization. The results are consistent with the hypothesis that chronic pancreatitis is associated with chronic neuropathic pain, facilitated by upregulated pain transduction mechanisms. QST renders a better understanding of nociceptive neuropathy and possibly leads to a new mechanism-based approach to pain therapeutics in patients with chronic pancreatitis.

144 IMPACT OF 3-D RECONSTRUCTION OF LIVER ANATOMY AND VIRTUAL TUMOR RESECTION ON OPERATIVE STRATEGY IN MAJOR HEPATECTOMY
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INTRODUCTION: At present, standard planning of hepatic resection is based on the knowledge of the functional anatomy of the liver as described by Couinaud, and on two-dimensional (2-D) imaging of the liver. Recent developments in 3-D CT allow an improved visualization of the distribution of intrahepatic vascular branches and a better prediction of their independent territories. We therefore evaluated the impact of 3-D reconstruction and virtual tumor resection on operation planning and intraoperative strategy in major hepatectomy. PATIENTS AND METHODS: In 21 patients, operation planning was performed by use of 2-D CT determining the line of dissection and calculating the volume of the future liver remnant (rFLV). After 3-D reconstruction of the liver,
based on the intended resection line manually determined at 3-D CT, the volume of the future liver remnant (FLRv) was calculated and recalculated as if the future liver volume being not devascularized, but having both portal venous blood supply as well as hepatic venous drainage. Therefore, the deviation of remaining functioning liver tissue in 2-D and 3-D operation planning (FLV2+FLV3) was calculated and the data from 2-D CT and 3-D CT were compared. According to these results changes in resection planning were made. RESULTS: The deviation of FLV2 to FLV3 was below 20% (n = 14/21), between 20 and 30% (n = 3/21), and between 30–40% and 40–50% in two patients each. Most extensive deviations were found in extended left hepatectomy or when left hemipateectomy was combined with an additional wedge resection in the right lobe. In 7 patients, results of 3-D CT led to a change of operation planning with regard to extent of resection or need for vascular reconstruction. In six cases, these changes could be achieved intraoperatively, in one case there was irresectability due to peritoneal carcinomatosis. CONCLUSIONS: 3-D reconstruction is able to visualize the intrahepatic vascular structure, the number and extent of portal venous segments and their relation to hepatic veins. Thus, areas at risk for either devascularization or venous congestion may be identified and precisely calculated prior to resection. In selected cases with small liver remnants or marginal hepatic function, operation planning may be improved substantially by prospective 3-D reconstruction and virtual resection.

145 CLINICOPATHOLOGICAL STUDY ON 114 CASES OF RARE PRIMARY HEPATIC MESENCHYMAL TUMORS
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OBJECTIVE: To investigate the clinicopathologic characteristics of rare primary hepatic benign and malignant mesenchymal tumors, in order to improve the accuracy of pathological diagnosis. METHODS: A retrospective analysis was made on 114 cases of 18 kinds of hepatic mesenchymal tumors (not including cavernous hemangioma), which were surgically resected in our hospital from Jan 1982 to Oct 2002 and were confirmed by histopathology and immunohistochemistry. RESULTS: Hepatic benign mesenchymal tumors accounted for 46.5%, including 53 cases of 7 kinds. In this group, the ratio of male to female is 1:1.95, with a mean age of 31.2 years. The most common tumor is hepatic angiomylipoma, which occurred in 39 cases (33.6%). All the patients in this group were alive without recurrence. Hepatic malignant mesenchymal tumors accounted for 53.5%, including 61 cases of 11 kinds. In this group, the ratio of male to female is 1.54:1, with a mean age of 45.2 years. The 1-, 3- and 5-year survival rates were 67.7% (21/31), 32.2% (10/31) and 12.9% (4/31), respectively. The most common tumor is primary hepatic lymphoma (PHL). Interestingly, all the PHL occurred in males (n = 12, 19.7%), 58.3% (n = 7) of PHL were positive for serum HBsAg, and 2 of them were associated with hepatocellular carcinoma. CONCLUSIONS: Most kinds of soft tissue tumors can primarily occur in the liver. It is noteworthy that there is a somewhat different age and sex distribution between patients with benign and malignant mesenchymal hepatic tumors. In China, PHL is more likely to occur in males with HBV infection. The differential diagnosis between primary or focal sarcoma and change of hepatocellular carcinoma and intrahepatic cholangiocarcinoma, as well as secondary metastases of the liver. The reasonable use of immunohistochemical staining has important diagnostic and differential diagnostic values.

146 VALUE OF MAGNETIC RESONANCE CHOLANGIOPANCREATOGRAPHY WITH SECRETIN STIMULATION IN THE EVALUATION OF PANCREATIC EXOCRINE FUNCTION AFTER PANCREATICOGASTROSTOMY
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OBJECTIVE: The aim of this study was to assess the value of magnetic resonance cholangiopancreatography with secretin stimulation (secretin-MRCP) in evaluating the remnant pancreatic exocrine reserve after pancreaticogastrostomy with pancreaticoduodenectomy. METHODS: 43 patients who had undergone pancreaticoduodenectomies and were given pancreaticogastrostomies for reconstruction were studied. Dynamic MRCPs using a half-Fourier acquisition single-shot turbo spin-echo (HASTE) sequence were obtained before and up to 10 minutes after secretin administration. The morphologic features and diameter of the main pancreatic duct were monitored and graded before and after secretin stimulation. The results were compared with those of endoscopic findings, secretin stimulation testing with a collection of pancreatic fluid, BT-PABA excretion, and falc chymotrypsin concentration. RESULTS: The results of secretin-MRCP were divided into three distinct groups: a good-secretion group (group 1, n = 22, 51%), a moderate-secretion group (group 2, n = 10, 23%), and a poor-secretion group (group 3, n = 11, 26%). This MRCP classification significantly correlated with pancreatic enzyme concentration such as p-type amylase, lipase, and trypsin in the gastric juice. The BT-PABA test value was 59.8% in group 1, 46.1% in group 2, and 46.5% in group 3, respectively, and significantly higher in group 1 than in groups 2 or 3. Fecal chymotrypsin concentration was 20.5 U/g in group 1, 14.5 U/g in group 2, and 0.7 U/g in group 3, respectively, and there was a significant correlation between MRCP grade and falc chymotrypsin concentration. CONCLUSION: MRCP with secretin stimulation favorably reflected the presence of remnant pancreatic exocrine function. Therefore, secretin-MRCP is a feasible and effective follow-up examination method to evaluate the remnant pancreatic exocrine function after pancreaticogastrostomy.

147 ANALYSIS OF INTRAOPERATIVE FROZEN SECTION RESULTS IN INTRADUCTAL PAPILLARY MUCINOUS TUMOR OF THE PANCREAS
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BACKGROUND: Intraoperative frozen section analysis on pancreatic duct margin specimens is widely used for pancreatic cancer as well as for other disease processes. The purpose of this study was to evaluate our experience with the accuracy and usefulness of intraoperative frozen section analysis for intraductal papillary mucinous tumor (IPMT). METHODS: A search of the pathology database at Barnes-Jewish Hospital for pancreas resections from 1999 to 2003 was performed. Pathology results from 231 pancreas resections were examined, and records with a final diagnosis of IPMT were more closely evaluated with respect to intraoperative frozen section analysis. RESULTS: From 1999 to 2003, a total of 18 operations for IPMT were performed on 17 patients (9 men, 8 women). The study population ranged from 52 to 84 years of age with a mean age of 71 at the time of procedure. Operative procedures included 11 pancreatoduodenectomy, 3 distal pancreatectomy, and 3 total pancreatectomy procedures. In this study group, 11 resection specimens contained IPMT alone, 2 resection specimens contained IPMT with borderline atypia, and 5 resection specimens contained IPMT with invasive adenocarcinoma or carcinoma-in-situ. Intraoperative frozen section analysis of the pancreatic duct margin was performed in 14 cases. In all cases (100%) the intraoperative frozen section analysis was consistent with the final pathology for presence or absence of IPMT and/or adenocarcinoma. In 12 cases (92%) the pancreatic duct margin was negative and no further resection was undertaken. The pancreatic duct margin was positive in 1 case (7%) for malignancy and in 1 case (7%) for IPMT on intraoperative frozen section. In both cases further resection was undertaken, and the new pancreatic duct margins were positive for IPMT but not invasive malignancy; these results were confirmed at final pathology. Total pancreatectomy was not performed in either of these two cases. CONCLUSIONS: In patients with intraductal papillary mucinous tumors of the pancreas, intraoperative frozen section analysis of the pancreatic duct margin compared to the final pathology is highly accurate. However, the use of intraoperative frozen section analysis for IPMT remains controversial, since attempts at further pancreatic resection (short of total pancreatectomy) may not yield a new negative margin.

148 EMERGENCY REPAIR OF COMPLICATED UMBILICAL HERNIA IN PATIENTS WITH LIVER CIRRHOSIS AND ASCITES: MESH OR NOT?
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BACKGROUND: Repair of umbilical hernia (UH) in liver patients with ascites has received little attention in comparison with other problems of cirrhosis. The timing and methods of UH repair continue to be a matter of debate. AIM: To compare herniorrhaphy (primary suture) with hernioplasty (polypropylene mesh) in patients with a primary complicated UH in the
setting of liver cirrhosis and ascites. PATIENTS AND METHODS: The study was a randomized clinical trial including 40 consecutive adult cirrhotic patients, admitted to the Department of Emergency of the National Liver Institute with complicated cirrhosis. Patients with recurrent UH, malignant ascites or evident liver failure were excluded. Patients were randomly allocated into two groups: group A underwent direct suture repair whereas group B underwent hernioplasty with polypropylene mesh (on-lay technique). The population studied included 26 men and 14 women with a mean age at presentation of 51 years. Patients presented with complicated UH in the form of incarceration (42%), obstruction (30%), strangulation (22.5%), and rupture (27.5%). The majority of patients (n = 36) had surgery under general anaesthesia, while local anaesthesia was administered for only 4 cases. The in-hospital morbidity and mortality were reported. The mean postoperative follow-up was 24 months. Patients were followed for late mortality and hernia recurrence. RESULTS: There were no significant anaesthetic complications or surgical procedure-related deaths. The mean duration of surgery was greater for mesh than for suture repair (58.3 vs 40 min). The mean postoperative stay was longer for the mesh group (11.2 vs 9.2 days). Rates of early complications such as sepsis, haematoma, wound infection, fever, and ascitic fluid leak were similar in the two groups. Postoperative haematoma occurred in 2 (10%) patients of group B, while no group A patients suffered this complication. Hospital mortality reported in 4 (10%) patients, distributed equally between the 2 groups. The hernia recurrence rate (11%) was similar after both methods of repair. CONCLUSION: Umbilical hernia exposes cirrhotic patients to potentially life-threatening complications such as rupture and strangulation. Emergency surgery should be considered cautiously and preferably in specialised centres for such decompensated patients. Mesh hernioplasty is not a superior method concerning the mortality and hernia recurrence rates in such a group of patients. The direct suture procedure has the advantage of shorter operative time and lower cost.

149 EFFECT OF FOLLISTATIN ON LIVER REGENERATION AFTER PARTIAL HEPATECTOMY IN RATS
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BACKGROUND AND AIM: Various agents are being tried to increase liver regeneration after liver resection. Follistatin is an activin-binding protein which can be isolated from ovarian fluid. It blocks the effects of activin, which is an inhibitor of DNA synthesis in the hepatocytes. The aim of this study was to investigate the effects of follistatin on liver regeneration after partial hepatectomy in rats. MATERIALS AND METHODS: Sixty Wistar-Albino rats weighing 200–275 g were used for this study. The animals were divided equally into two groups, as follistatin study and control group. Then each group was divided into 3 subgroups of 10 rats. Initially, a jugular vein catheter was placed. Intraperitoneal ketamine and xylazine were administered for anesthesia following by resection of 70% of the liver. One mg of human recombinant follistatin was given through the portal vein to the study group. Normal saline (0.9% NaCl) infusion for 24 h after hepatectomy was administered to the control group. Resected liver portions were weighed and recorded. Rats were killed at the end of 24, 48 and 72 h. Blood samples were collected from the inferior vena cava and remnant liver tissues were weighed. AST, ALT, ALP, albumin and prothrombin time (PT) levels were measured. Histopathologic evaluation including relative liver mass, mitotic index and proliferating cell nuclear antigen (PCNA) was performed. RESULTS: At the end of 24, 48 and 72 h, relative liver weight, AST, AL and ALP levels were statistically significant between the study and control groups (p < 0.05). There was no statistical significance for PT values at the end of 24 and 72 h and for albumin levels at the end of 48 and 72 h. Mitotic index and PCNA labeling percentages were significantly higher in the follistatin group compared with the control group at the end of 24, 48 and 72 h (p < 0.05) (See Table). CONCLUSION: Follistatin, an activin blocker, increased both morphological and functional liver regeneration after partial hepatectomy in rats. Intraperitoneal administration of follistatin may become a therapeutic option to increase liver regeneration.

150 THE DEVELOPMENT OF A NEW PRESERVATION SOLUTION FOR MACHINE PERFUSION OF THE LIVER: A COMPARISON BETWEEN THREE DIFFERENT COLLOIDS
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INTRODUCTION: Machine perfusion (MP) has proven to be beneficial in the preservation of the liver. Currently the modified University of Wisconsin solution (UW-Gluconate) is used as the MP preservation solution of choice. However, this solution does not contain a sufficient amount of substrates for the decreased liver metabolism at 4°C. Therefore we have developed Polysyl, a MP preservation solution based on a colloid, containing the necessary nutrients for the liver. In a previous study we have shown that Polysyl results in equal or even better quality liver preservation when compared to UW-Gluconate. We sought to optimize Polysyl by substituting the colloid hydroxyethylstarch (HES), which is expensive, difficult to obtain and causes microvascularular obstructions. We therefore compared HES with the colloids dextran and polyethylene glycol (PEG). METHODS: In an isolated perfused rat liver model, hepatocellular damage was assessed during perfusion after 24 h hypothermic MP with P-HES, P-dextran or P-PEG. To determine hepatocellular damage ALT and LDH levels were measured during 60 minutes of normothermic reperfusion with oxygenated KHB. Liver function was assessed using oxygen consumption, bile production and ammonia clearance. Control livers were preserved for 24 h by MP with UW-G. RESULTS: Compared with the control (UW-G) MP with either P-HES, P-dextran or P-PEG resulted in significantly less hepatocellular damage, higher flow, bile production and oxygen consumption during reperfusion. MP with P-dextran resulted in less hepatocellular damage (U/L) as compared with MP with P-HES: ALT (t = 40) 2.17 ± 0.98 vs 3.50 ± 3.51, respectively. Livers perfused with P-PEG also sustained less hepatocellular damage as compared to P-HES: ALT (t = 40) 2.20 ± 1.30 vs 3.50 ± 3.51, respectively. Oxygen consumption (mmHg) was increased after MP with P-dextran as compared with P-HES: (t = 10) 447.80 ± 53.10 vs 399.28 ± 30.64. Neither these differences, nor differences in ammonia clearance or bile production were significant. CONCLUSIONS: 24 h MP of livers with UW-G results in more extensive hepatocellular damage and reduced liver function when compared with MP with either Polysyl-HES, Polysol-dextran or Polysol-PEG. MP with Polysyl-dextran or Polysol-PEG results in equal or even less hepatocellular damage when compared with MP with Polysyl-HES. Therefore substituting HES in Polysyl with either dextran or PEG can be considered feasible.
151 EFFECT OF AMINOQUANIDINE ON BLOOD AND TISSUE LIPID PEROXIDATION AND PROINFLAMMATORY AND TH2-CELL AGGREGATION IN LPS-INDUCED HEPATIC ISCHEMIA-REPERFUSION INJURY

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BACKGROUND: The morbidity associated with hepatic resections is partly a result of hepatic ischemia-reperfusion injury (HII). Endothelial and Kupffer cell swelling, necrosis, microvascular congestion, leukocyte entrapment, platelet aggregation within the sinusoids result in failure of hepatic microcirculation. Nitric oxide (NO) formation and increased expression of inducible nitric oxide synthase (iNOS) also take place in HII. NO triggered by the iNOS reacts with free oxygen radicals and this leads to the formation of the most harmful peroxynitrite anion (ONOO−) and this anion leads to lipid peroxidation, cellular damage and apoptosis. The aim of this study was to investigate the effects of aminoquinidine (Ag) on liver tissue iNOS, serum and tissue lipid peroxidation under unfavorable conditions which are created by LPS-induced HII injury. METHODS: The experiments described in this study were performed in adherence to National Institutes of Health guidelines on the use of experimental animals. We randomized 48 rats into 6 groups: A (sham), B (HII), C (HII + Ag), D (HII + LPS), E (HII + LPS + Ag), F (HII + Ag + LPS). The rats were subjected to 45 minutes of hepatic ischemia followed by 45 minutes of reperfusion period. Aminoquinidine (50 mg/kg) and LPS (10 mg/kg) were administered singly or in combination intraperitoneally 10 minutes before reperfusion. Serum myeloperoxidase (MPO), serotonin, malondialdehyde (MDA), serum ATPase, liver tissue MDA, MPO, ATPase levels were determined to assess the lipid peroxidation. Liver iNOS staining was detected immunohistochemically. RESULTS: Plasma and liver tissue MDA and MPO were higher in groups B, D, E than in the other groups. The levels of the decreased in the groups given Ag alone or before LPS (C, F). There was intense iNOS staining in the same groups when compared with groups A, C and F. CONCLUSIONS: Our study indicates that aminoquinidine has a protective effect which acts as an iNOS inhibitor and reduces lipid peroxidation. Our findings show that Ag has beneficial effects in HII injury if administered before LPS, but it failed to prevent the tissue iNOS expression and lipid peroxidation if there was established endotoxia in HII injury.

152 EXPERIENCE WITH HTK PRESERVATION SOLUTION IN LIVER DONOR LIVER TRANSPLANTATION

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Major advantages of live donor liver transplantation (LDLTx) are the quality of the graft as well as a standardized and well controlled organ procurement procedure. Since there are not many publications on the use of histidine-trypthanol-ketoglutarate solution (HTK) for liver preservation we prospectively studied its efficacy and safety in LDLTx. This consecutive series includes 21 patients (19 adults, 2 children; aged 9 months to 61 years), suffering from end-stage cirrhosis (14), malignant liver tumors (6), and acute hepatic failure (1). All donors (age range 22-69 years) had normal liver function, including 6 with hepatic steatosis between 5 and 20%. The donor operations were performed by the same surgeon, and resulted in 19 right lobes, one left lobe, and one left lateral graft (mean graft weight 0.37 ± 0.21 kg, graft-recipient body weight ratio 1.33 ± 0.74%). Liver preservation was done in a standard fashion by gravity perfusion with HTK, started in situ through the portal vein (4 ± 1.0 L), and continued on the backtable with infusion via the hepatic artery (1 ± 0.3 L) for 10 min each to allow for adequate equilibration. In addition the bile ducts were flushed with HTK. The first warm ischemia time (WIT) was <1 minute, the second WIT was 37 ± 15 min, and the total ischemia time was 194 ± 69 min. All liver grafts showed good primary function; maximum aspartate aminotransferase 574 ± 519 U/L, total bilirubin 13.97 ± 4.77 mg/ dl, and partial thromboplastin time 50.13 ± 9.83 s. One graft was lost from parenchymal fracture secondary to portal hyperperfusion after 6 days, and the patient was salvaged by retransplantation. Five patients died 14–111 days after surgery from various infectious complications, none of them related to impaired graft function. 7/21 recipients developed early biliary leakage within 8–45 days from the ressectional surface, and following multiple duct reconstructions. There was no late ischemic-type biliary lesion. The results of this study confirm earlier observations that HTK solution is effective and safe – also when used in LDLTx. Potential advantages of HTK in comparison with other preservation solutions are: low potassium concentration, low viscosity, no particles, in situ perfusion, no need to flush before reperfusion, improved biliary protection, better recovery of microcirculatory changes, ready to use, and lower costs. Since the risk-benefit ratio is of particular importance in LDLTx the use of HTK solution should be encouraged.

153 INTRAVENOUS GLYCINE AMELIORATES ISCHEMIA REPERFUSION INJURY IN THE Rabbit Liver Lobar ISCHEMIA REPERFUSION MODEL

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INTRODUCTION: Liver ischemia reperfusion injury (IR) is a major complication of liver resection and transplantation. Cytokine release by activated Kupffer cells (KC) plays a central role in the inflammatory response following hepatic IRI. Glycine, a non-essential amino acid, may protect against hepatic IRI by inhibition of KC activity. However, its effect on portal blood flow, bile flow, hepatic microcirculation and tissue oxygenation has not been reported. AIM: To investigate the effects of glycine administration on hepatic IRI. MATERIALS AND METHODS: A rabbit model of hepatic lobar IRI was used.3 groups of animals (n = 6) were studied: sham group (laparatomy alone), ischemia reperfusion (IR) group (1 h of liver lobar ischemia and 6 h of reperfusion), and a glycine I/R group (intravenous glycine 5 mg/kg prior to the I/R protocol). Systemic haemodynamics, portal blood flow, bile flow, hepatic microcirculation (by laser Doppler flowmeter) and intracellular tissue oxygenation (by near infrared spectroscopy) were continuously recorded. RESULTS: Systemic haemodynamic parameters remained stable throughout the experiment and were not significantly different between the 3 groups. The glycine group had increased bile flow (Figure) and portal blood flow as compared to the I/R alone group for the entire period of reperfusion. The hepatic microcirculation was significantly increased by the second hour of reperfusion (glycine I/R vs I/R alone: 210.66 ± 25.03 vs 151.66 ± 45.97; p < 0.05) and the hepatic intracellular tissue oxygenation after the fourth hour of reperfusion (glycine I/R vs I/R alone: −13.84 ± 6.72 vs −25.53 ± 7.65; p < 0.05). CONCLUSIONS: Intravenous glycine administration reduces the hepatic haemodynamic alterations of IRI and provides a novel therapeutic modality.

154 MACHINE PERFUSION PRESERVATION OF THE NON-HEART-BEATING DONOR LIVER: THE INTRODUCTION OF A NEW PRESERVATION SOLUTION

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INTRODUCTION: The current situation in organ transplantation, with patients succumbing to awaiting transplantation, has led to the attention for suboptimal donors, i.e. the non-heart-beating donor. In these patients the circulation has ceased before harvesting of the organ could be commenced, resulting in warm ischemic damage. In order to facilitate transplantation, these organs need a more optimal preservation method. Recent literature has shown advantages of oxygenated hypothermic machine perfusion (MP) over cold storage (CS) for these marginal organs. As a MP preservation solution the modified University of Wisconsin...
solution (UW-Glucosate) is used. However, this solution causes microvascular obstruction, is hard to obtain and expensive. We have therefore developed Polysol, a colloid-based preservation solution containing specific nutrients for the liver. In previous studies this solution has proven to result in equal to better preservation of optimal livers. The aim of this study was to compare Polysol with UW-glucosate, in a non-heart-beating donor rat liver model. METHODS: In an isolated perfused rat liver model damage and function were assessed after 24 h hypothermic MP in UW-G (n = 6) or Polysol (n = 6). To determine liver parenchymal damage ALT and LDH levels were measured during 60 minutes of normothermic perfusion with oxygenated Krebs-Henseleit buffer. Liver function was measured by collection of bile and clearance rate of ammonia. Wet/dry liver weight ratios were determined for evaluation of cellular edema. Control livers were reperfused after 24 h CS in UW (n = 6). RESULTS: Liver damage (UL/L) was significantly higher in the control group compared with MP using UW-Glucosate or Polysol (p < 0.05). Although the results appear in favor of Polysol as compared with UW-G, these are not significant. Flow at reperfusion (ml/min) was significantly higher when using Polysol as compared with UW-G (33.3 ± 0.92 vs 11.50 ± 2.71; p < 0.01). Bile production (μl/h) was highest when using Polysol as compared with UW-G (390 ± 22.66 vs 153 ± 54.72; p < 0.01). Ammonia clearance (%) was highest after MP using Polysol as compared with UW-G (92 ± 1.73 vs 53.5 ± 10.96; p < 0.01). There was less cellular edema (wet/dry ratio in %) after preservation with Polysol as compared with UW-G (73 ± 0.008 vs 75 ± 0.009); this was significant for Polysol compared with control (73 ± 0.008 vs 77 ± 0.01; p < 0.02). CONCLUSIONS: Machine perfusion using UW-G or Polysol results in less hepatocellular damage than cold storage with UW. Machine perfusion of rat livers using Polysol is superior to machine perfusion using UW-G.

155 BILARY RECONSTRUCTION UTILIZING VCS® CLIPS VERSUS CONVENTIONAL SUTURED ANASTOMOSIS IN ORTHOTOPIC LIVER TRANSPLANT

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PURPOSE: Our previous report on the experimental use of non-penetrating tissue evertting VCS® clips in a porcine liver transplant model demonstrated that good results were achievable with a shorter time to create the anastomosis compared with hand-sewn reconstruction and that there was less inflammatory reaction incited by biliary reconstruction with clips. We examined the incidence of biliary anastomotic complications in a group of patients in whom orthotopic liver transplantation was performed using VCS® clips for biliary reconstruction and compare those patients to a contemporaneous, matched cohort treated with hand-sutured end-to-end cholecystocholedochostomy. METHOD: Sixteen patients in whom clipped anastomosis were performed were matched to a comparison cohort in a 1:2 fashion by: age at transplantation, disease etiology, model of end-stage liver disease (MELD) score, Child-Turcotte-Pugh (CTP) score, cold/warm ischemia times, and organ donor age. Outcome measures included total operative time, time for biliary reconstruction, transfusion requirements, hospital and ICU days, and incidence of biliary complications. Statistical methods included t-tests, chi-square tests of proportions, and Kaplan-Meier survival analysis. Summary data are given as the mean ± SEM. RESULTS: Between-groups analysis demonstrated no differences in matching parameters, transfusion requirements, hospital or ICU stay, or total time of operation. Time from completion of hepatic artery anastomosis to completion of biliary anastomosis was 41 ± 3 minutes compared to 52 ± 4 minutes but did not reach statistical significance (p = 0.09). After a mean of 30 ± 2.8 months follow-up, no differences in incidence of biliary anastomotic complications, including leak or stricture, were observed (p = 0.73). Leak and/or stricture were observed in 3 patients (19%) in the clipped group and 8 patients (25%) in the conventional sewn group. There were no differences between groups when comparing time to onset of biliary complications (p = 0.69). Repeat operative biliary reconstruction was required in the clipped group and 3 patients (19%) in the sewn group. CONCLUSIONS: Biliary reconstruction can be performed clinically using VCS® clips as an alternative with good anastomotic outcomes.

156 LIVER'S NOBODY WANTS: SINGLE INSTITUTION EXPERIENCE IN LIVER TRANSPLANTATION WITH 30 MARGINAL LIVERS OVER A 3-YEAR PERIOD

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INTRODUCTION: The shortage of organs has led some transplant centres to expand their criteria for the acceptance of marginal donors. The combination of multiple marginal factors seems to be additive on graft injury. PATIENTS AND METHODS: From 2001 to 2003, 314 patients underwent liver transplantation (LTx) in our centre. Among them, 39 patients underwent a liver transplantation with a marginal liver, which was offered to at least 7 transplant centres according to the allocation rules of 'Eurotransplant' and was not accepted by any of the centres for their allocated patient. We mainly accepted these livers for patients in poor condition or tumor patients on our waiting list, who probably would not have survived the expected waiting time of 6–10 months. The data for these 30 patients were reviewed. RESULTS: Primary graft survival was 86.5%. Four patients (13.5%) underwent a second LTx after the LTx with the marginal liver because of ‘primary non-function’; one of them died. There were overall 6 deaths in this group of patients. One patient underwent an LTx with a marginal liver as ‘rescue’ transplantation after a normal LTx; this patient is still alive and in good physical condition. 24 patients (80%) survived the LTxs with these ‘marginal’ organs with good liver function. They are followed-up by our transplantation outpatient ward. CONCLUSION: Our data demonstrate that transplantation of marginal livers can be performed with acceptable graft and patient survival in selected patients. A critical appraisal of the livers 'nobody wants' and of the potential candidates can lead to successful transplantation in patients with poor chances of surviving the waiting time.

157 TAURINE IMPROVES GRAFT SURVIVAL IN RAT LIVER TRANSPLANTATION

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INTRODUCTION: The etiology of ischemia/reperfusion injury is unknown; however, its underlying mechanisms most likely include activated Kupfer cells. Most recently, it has been demonstrated that taurine binds to a chloride channel, inactivating Kupfer cells. Thus, this study was designed to assess its effects for the first time in vivo after liver transplantation. METHODS: Livers from female Lewis rats (200–230 g) were transplanted after cold ischemia. Some donors were treated i.v. with 1.5 ml taurine solution (30, 100, 300 mM). Controls were infused with 1.5 ml normal saline. Survival, serum transaminases, histology, data of intravital microscopy and blood distribution at reperfusion to index microcirculation have been compared. Two-way ANOVA and Fisher’s exact test were used for comparison between groups as appropriate. Results are presented as mean ± SEM. RESULTS: Taurine improved graft survival after liver transplantation in a dose-dependent manner from 60% in controls to 80% (30 mM), 100% (100 mM) (p < 0.05) and 100% (300 mM) (p < 0.05) with 30 ml taurine solution. Furthermore, after reperfusion, injury to livers were reduced significantly. Both AST and ALT increased to 3187 ± 1030/ 1632 ± 532 U/l, 1049 ± 252/829 ± 231 U/l (p < 0.05) and 692 ± 69/ 576 ± 129 U/l (p < 0.05) after 10, 100 and 300 mM taurine respectively, compared with controls (3260 ± 41/470 ± 432 U/l). Taurine had the same effect on LDH after reperfusion. While 30 mM taurine solution had no effect on LDH release, 1.5 ml taurine at a concentration of 100 mM and 300 mM significantly reduced LDH release at 8 h after reperfusion compared with controls to 33% and 13%, respectively. Similar effects were seen in histology taken after transplantation. The time for blood to reperfuse the liver homogeneously to index early microcirculation was reduced to 50% of controls after 1.5 ml taurine (300 mM) (p < 0.05). Further, intravital microscopy revealed that taurine improved microcirculation due to a significantly decreased interaction between leukocytes (sticking/rolling) and endothelial lining cells. Moreover, significantly less latex beads were taken up (phagocytosis) by Kupffer cells in taurine-treated livers, which indicates their inactivation. CONCLUSION: These data indicate for the first time that pretreatment of donors with intravenous taurine minimizes reperfusion injury after liver transplantation in a dose-
158 A SINGLE CENTER EXPERIENCE OF INTRAMUSCULAR HBV PROPHYLAXIS IN LIVER TRANSPLANTATION

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BACKGROUND: Passive immunoprophylaxis with hepatitis B immunoglobulin (HBIG) to control progression of disease has resulted in emergence of liver transplantation (OLTs) as an option for hepatitis B-related chronic liver failure. Anti-viral drugs now provide a potential for cure. Barnes-Jewish Hospital at Washington University School of Medicine has used an HBIG protocol for 10 years prior to use of antiviral medications. We review our experience comparing recipients with and without the use of HBIG. METHODS: A retrospective review of patients undergoing OLTs at Barnes-Jewish Hospital at Washington University between August 1985 and December 2000 was performed. During this period, 590 liver transplants were performed at our center of which 25 patients were hepatitis B surface antigen (HBsAg)-positive. Outcome information included patient and graft survival, post-transplant HBV serology, and HBV recurrence. HBV recurrence was defined as a failure to clear serum HBsAg after liver transplantation or the subsequent reappearance of serum HBsAg during follow-up. RESULTS: Patient characteristics were similar. The recurrence rate of HBV in the HBIG group was 37% compared with 120% in the no prophylaxis group (p = 0.002). The median time to recurrence was similar (p = NS), HBsAg-positive patients (group I, n = 6) transplanted between 1985 and 1992 did not receive prophylaxis and recipients between 1993 and 2000 (group II, n = 19) received 30 ml of HBIG intravenously during the anhepatic phase then 5–10 ml intramuscularly in varying intervals to maintain HBIG through titers >800 mU/ml. 13 patients developed hepatitis B recurrence, of which 5 expired (3 of recurrent disease, 2 of other causes). The remaining 8 patients are alive with good liver function despite recurrence. Six of these patients have received antiretroviral treatment and one, group 1 patient, remains on HBIG for control of recurrence. CONCLUSION: Long-term follow-up of patients receiving HBIG prophylaxis demonstrates a significant reduction in hepatitis B recurrence with HBIG. Recurrent hepatitis B tends to be mild and is amenable to treatment with antiviral medications. We are presently evaluating our results with preparative and postoperative use of antiviral medication in combination with HBIG.

159 IMPACT OF DUCTAL SECTION MARGIN STATUS ON LONG-TERM SURVIVAL IN PATIENTS UNDERGOING RESECTION FOR EXTRAPANCREATIC CHOLANGIOCARCINOMA

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BACKGROUND: To clarify whether residual carcinoma in situ at ductal resection margins differs biologically from residual invasive ductal lesions in patients undergoing resection for extrapancreatic cholangiocarcinoma. METHODS: A retrospective analysis was conducted of 114 patients with extrapancreatic cholangiocarcinoma. In 84 patients who underwent resection the ductal resection margin status was classified into negative (n = 64), positive with carcinoma in situ (n = 11), or positive with invasive carcinoma (n = 9). The median follow-up period was 105 months. RESULTS: Ductal margin status was a strong independent prognostic factor by univariate (p = 0.0002) and multivariate (p = 0.0039) analyses. The outcome after resection was comparable between patients with negative ductal margin (median survival time, 45 months; cumulative 10-year survival rate, 40%) and those with positive ductal margin with carcinoma in situ (median survival time, 99 months; cumulative 10-year survival rate, 23%; p = 0.4742). In patients with positive ductal margins, outcome was significantly better in patients with carcinoma in situ than in those with residual invasive carcinoma (median survival time, 21 months; cumulative 5-year survival rate, 0%: p = 0.0003). Of 11 patients with residual carcinoma in situ, 4 died of local recurrence and the median disease-free survival was 89 months. CONCLUSIONS: Among patients undergoing resection for extrapancreatic cholangiocarcinoma, those with residual carcinoma in situ may survive significantly longer than those with residual invasive ductal lesions. This suggests that the natural history of residual carcinoma in situ differs from that of residual invasive ductal disease in extrapancreatic cholangiocarcinoma.

160 PATTERNS OF VASCULAR INJURIES ASSOCIATED WITH CONCOMITANT IATROGENIC BILE DUCT INJURY

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BACKGROUND: One in 300 cholecystectomies continue to result in serious biliary injury. The aim of this study was to assess the frequency of associated concomitant vascular injuries. METHODS: Case note review of a single centre experience of 26 iatrogenic biliary injuries and a further 13 medicolegal case note reviews (all cases Strasberg grade E). Vascular injuries were documented following visceral angiography or from the operative notes (index operation or subsequent biliary repair). RESULTS: Visceral angiography was performed on 17 patients and demonstrated a major vascular injury in 11. All vessels involved were right hepatic artery (RHA) in 6, common hepatic artery (CHA) in 3 and RHA with right portal vein in 2. In 3, RHA injury was detected at the time of biliary repair. Injuries identified at index operation: 1 portal vein (PV) injury; 1 combined CHA + PV injury; 1 isolated RHA injury. Two of 6 patients undergoing angiography without associated vascular injury had abnormal anatomy: CHA arising from superior mesenteric artery (SMA) in 1, in the other the RHA arose from the SMA. CONCLUSION: Associated vascular injury occurs in at least 1/3 iatrogenic biliary injuries. The RHA is the vessel most commonly injured, usually in the absence of a vascular anomaly. Visceral angiography is therefore a mandatory investigation in the management of bile duct injury.

161 DIMINISHED GALLBLADDER MOTILITY IN ROTTUND LEPTIN-RESISTANT OBESE MICE

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BACKGROUND: Obesity is a major risk factor for cholesterol gallstone formation, but the pathogenesis of this phenomenon remains unclear. Most human obesity is associated with diabetes and leptin resistance. Previous studies from this laboratory have demonstrated that diabetic leptin-resistant (Leprdb−/−) obese mice have a low biliary cholesterol saturation index, enlarged gallbladders and diminished gallbladder response to neurotransmitters. Recently, a novel leptin-resistant mouse strain Leprdb−/− (Rotund) has been discovered. Rotund mice are also obese, diabetic and, like Leprdb−/− mice, have an abnormal leptin receptor. Therefore, we tested the hypothesis that leptin-resistant obese Rotund mice would have large gallbladders and reduced biliary motility. METHODS: 8-week-old lean control (C57BL/6), n = 12) and Rotund leptin-resistant (Leprdb−/−, n = 9) mice were fed a non-therogenic chow diet for 4 weeks. All animals were fasted overnight and underwent cholecystectomies. Bile was aspirated from the intact gallbladder (GB), and the volume (µl) was recorded. Contractile responses (n(µm) to acetylcholine (Ach 10−5 M) and cholecystokinin (CCK 10−5, 10−4, 10−3 M) were measured. RESULTS: Results were analysed using the Mann-Whitney rank sum test and are presented in the Table. CONCLUSIONS: These data suggest that leptin-resistant Rotund mice have 1) increased gallbladder volume and 2)
diminished response to acetylcysteine and cholecystokinin compared with the lean control mice. Therefore, this study in a new leptin-resistant mouse confirms that leptin resistance from a defective leptin receptor is associated with abnormal biliary motility. We conclude that diminished gallbladder emptying may lead to gallstone formation in leptin-resistant obesity.

162 THIOACETAMIDE-INDUCED INTESTINAL-TYPE CHOLANGIOCARCINOMA IN RAT: AN ANIMAL MODEL RECAPITULATING THE MULTISTAGE PROGRESSION OF HUMAN CHOLANGIOCARCINOMA

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BACKGROUND: Cholangiocarcinoma (CCA) is a lethal disease, affecting many thousands the world over. Human, CCA develops through a multistage progression model preceded by the onset of the proliferation of the cholangiolar ductal epithelium. An animal model of multistep carcinogenesis in the biliary tree will enable the study of genetic changes in human CCA, and provide an avenue for chemoprevention strategies. We describe an oral thioacetamide (TAA)-induced model of rat CCA that recapitulates the histologic progression of human CCA. METHODS: Male Sprague-Dawley (S-D) rats (n = 170), weighing 350 ± 20 g, were used in this study. Drinking water with TAA 300 mg/L was administered orally, and the liver was harvested and examined histologically at weekly intervals, beginning at 5 weeks after initiation of TAA. Harvested tissues were formalin-fixed and paraffin-embedded for morphologic and immunohistochemical studies. RESULTS: Multifocal bile ductular proliferation with intestinal metaplasia (presence of goblet cells) and increasing histologic atypia (biliary dysplasia) was observed by the 9th week of TAA administration. Biliary cytokeratin (CK19)-expressing invasive intestinal-type CCA with stromal desmoplasia was evident at the 16th week, and by the 22nd week, the yield rate for CCA had increased to 10%. Invasive CCA had exceeded the development of hepatic cirrhosis by at least 4 weeks; the earliest incidence of hepatic fibrosis was observed beginning at 20 weeks post-TAA administration. The progression from normal cholangioloites to biliary dysplasia to invasive CCA was accompanied by upregulation of the proto-oncogenes c-met and c-erbB-2, tyrosine kinase receptors overexpressed in human CCA. The study was terminated at 6 months, at which time no systemic metastases or deaths were observed. CONCLUSIONS: Oral administration of TAA in drinking water to male SD rats produces a reproducible animal model for developing a large yield of the neoplasms of the ductular proliferation to biliary dysplasia beginning at the 9th week, which progresses to invasive CCA, mimics the multistep model of human CCA. The TAA rat model may serve as a powerful pre-clinical platform for therapeutic and chemoprevention strategies for human CCA.

163 ROLE OF NEOADJUVANT CHEMOTHERAPY IN LOCALLY ADVANCED GALLBLADDER CANCER: AN EARLY REVIEW

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Gallbladder cancers are the commonest cancers of the biliary system. The presentation is most often in the advanced stages, precluding extensive surgical resection. The role of neoadjuvant chemotherapy to downstage the disease followed by surgical resection is yet unclear with no published information. We evaluated six patients who had presented with locally advanced gallbladder cancer (GBC). We included patients with locally advanced stage IV disease but without distant metastases outside the abdomen. All patients received a combination of gemcitabine at 1 g/m² on day 1 and 8 and cisplatin at 100 mg/m² on days 1-3 in divided doses. Each cycle was administered at 3-weekly intervals. Each patient received an average of 4.4 cycles. An excellent response was noted. Although a complete response was not seen, a >50% response was seen in 5/6 patients. 1 patient was lost to follow-up after the first cycle. Another patient showed a good response after 3 cycles but did not return for surgery. All the remaining 4 patients underwent radical resection and 3 patients were disease-free at 1 year post-surgery. The 4th patient had a recurrence at 3 years and was successfully treated with chemotherapy.

164 DIAGNOSTIC IMPACT OF LAPAROSCOPY ON GALLBLADDER CARCINOMA

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INTRODUCTION: The grave prognosis associated with gallbladder carcinoma has not changed in decades, despite the advent of minimally invasive techniques. Incidence remains approximately 1%, long-term survival is seldom reported past 5 years. Minimally invasive techniques have expanded indications, changed practice patterns and increased numbers of cholecystectomies performed. Shifting practice patterns potentially impact diagnosis; increasing incidence and reducing presenting stage. We sought to determine if practice patterns affected incidence and presentation stage, and indirectly, prognosis of gallbladder carcinoma. METHODS: Charts were analysed of 1929 patients undergoing laparoscopic or open cholecystectomy in a 5-year period (1997-2002). Thirteen patients were identified with gallbladder cancer intra-operatively or postoperatively. Analysis included incidence of cancer overall, as well as for laparoscopic and open procedures. Stage upon presentation for each category of procedure was analysed to determine if minimally invasive technique and changing practice patterns impact presentation and prognosis. RESULTS: From 1997 to 2002, 1929 individuals underwent cholecystectomy — either laparoscopically or open. 84 patients underwent open (84/1929, 4.3%) and 1845 underwent laparoscopic cholecystectomy (1845/1929, 95.6%). Three patients (13/1929, 0.7%) were found to have gallbladder cancer postoperatively. All patients diagnosed with gallbladder cancer were female with a mean age of 64 years (52-78 years). Five of 13 (39%) patients underwent completion laparoscopic cholecystectomy, 8/13 (61%) were converted to open technique due to high suspicion for malignancy or difficulty with the procedure. T-stage of the tumors who underwent completion laparoscopic cholecystectomy included two T1, two T2, and one T3. Of the 8 open, three had T3 and five had T4 disease with extension outside the gallbladder serosa. CONCLUSIONS: Laparoscopic approach to biliary disease and associated practice patterns do not appear to downstage nor increase the incidence of gallbladder cancer in our cohort. There was a trend towards lower stage disease in those undergoing laparoscopic surgery. In those with advanced disease there was a substantial increase in incidence year-on-year, the incidence compared to standard conversion rate, suggesting that gallbladder cancer often presents clinically at an advanced stage. Laparoscopic techniques do not negatively impact the surgical treatment of gallbladder cancer or its presentation and should remain in its treatment algorithm.

165 BILE FLOW AND COMPOSITION ARE MODULATED BY INTRAVENOUS GLYCINE IN AN IN VIVO WARM ISCHAEMIA-REPERFUSION INJURY MODEL

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BACKGROUND: Liver ischaemia-reperfusion (IR) injury is a major complication of liver resection and transplantation. The cytokine release by activated Kupffer cells (KCs) plays a central role in bile and glycine inhibits KC activity. The effect of glycine administration on bile flow and composition following IR has not been investigated. METHODS: A rabbit model of hepatic lobar warm IR was used. Under general anaesthesia, the sham group (n = 6) underwent laparotomy alone for 7 h. The control IR group (n = 6) underwent 60 min of left and median lobe inflow occlusion and 6 h of reperfusion. The glycine IR group (n = 6) underwent a similar procedure to controls after receiving glycine 5 mg/kg i.v. Bile output was measured and composition analysed by proton magnetic resonance spectroscopy. RESULTS: Bile flow was reduced following IR alone but was maintained in the glycine IR group (108.3 ± 28 vs 2145.0 ± 11.4 μL/min) in the glycine group, p = 0.011) 6 h post-reperfusion. Glycine administration prior to IR was associated with lower phosphatidylcholines (1.2 ± 0.8 vs 3.0 ± 0.5 μmol/L in controls, p = 0.001) and lactate levels (8.1 ± 4.3 vs 26.3 ± 7.8 μmol/L in controls, p < 0.001) and increased bile acid (17.9 ± 2.8 vs 8.9 ± 2.1 μmol/L in controls, p = 0.001), pyruvate (1.3 ± 0.3 vs 0.7 ± 0.1 μmol/L in controls, p = 0.005), glucose (3.9 ± 0.9 vs 1.6 ± 0.6 μmol/L in controls, p = 0.007) and acetate levels (0.7 ± 0.1 vs 0.4 ± 0.1 μmol/L in controls, p = 0.009) (p < 0.001, glycine
166 HILAR CHOLANGIOCARCINOMA: RADICAL RESECTION IN A WESTERN POPULATION

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PURPOSE: To review the experience with hilar cholangiocarcinoma to determine the results of a radical surgical approach, including resection and lymphadenectomy. METHODS: An analysis of all the patients treated for proximal bile duct carcinoma has been done. From January 1993 through October 2003, 52 patients with hilar cholangiocarcinoma received surgical exploration with a curative intent. Among these patients, 11 underwent preoperative radiological drainage (either ERCP, PTBD or combined). No portal vein embolization was performed in this group of patients. 47 (90%) of the 52 patients had surgical resection and 5 patients were considered unresectable. Regional lymphadenectomy was systematically carried out, and extended lymphadenectomy (para-aortic) in 17.

The histopathology reports and patients' notes were reviewed. The survival analysis was calculated by Kaplan-Meier test RESULTS: According to the TNM classification (UICC 6th edition) the tumours were staged as follows: stage I, n = 12; IIa, n = 4; IIb, n = 13; III, n = 10; IV, n = 7. Of the 47 patients who underwent surgical resection, 3 had bile duct resection alone; 39 underwent liver resection combined with bile duct resection (17 right transectionectomy, 2 right hemipancreatectomy, 11 left transectionectomy, 7 left hemipancreatectomy, and 2 had other liver resection); the remaining 5 underwent liver transplantation. In the resection group, 17 (41%) patients underwent portal vein resection; hepatic artery resection was performed in 3 (7%). From all the patients who had a liver resection or a bile duct excision (42), negative histologic margins (R0) were achieved in 19 patients and microscopic margin involvement (R1) was seen in 16. In 6 of these patients distant metastases were found (peritoneal deposits in 2, liver metastasis in 3 and positive para-aortic lymph nodes in 1); nevertheless the resection was performed and was considered R2. The cause of R1 was identified either as a bile duct margin positive (7), hepatic/vascular surgical resection margin (6) or both (3). The survival at 3 and 5 years for those patients who had a liver transplant was 60% and 20%. Overall survival at 3 and 5 years was 18%. 8 patients who underwent a resection were alive. 4 years were 47% and 30%. The 3- and 5-year survival rates for R0 and R1 resection were 76% and 52%, and 25% and 25%, respectively. For R2 the figures were 14% and 0%. CONCLUSIONS: Despite the high incidence of R1-R2 resection, the long-term survival suggests that these patients may benefit from an aggressive approach.

167 DEVELOPMENT OF A ROBOTICALLY ASSISTED 3-D ULTRASOUND SYSTEM FOR RF ABLATION OF LIVER TUMORS

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PURPOSE: Radiofrequency ablation (RFA) is a minimally invasive method for treatment of primary and metastatic liver tumors. This approach can often be limited by the ability to accurately and easily target the RFA probe using free-hand manual techniques. Here we describe a novel, inexpensive system that reconstructs 3-D ultrasound from a hand-held probe and a robot arm to accurately position the RFA probe at the selected target, thereby greatly increasing the visualization, simulation, and planning power of the surgeon. MATERIALS AND METHODS: Major system components include: 1) a PC-based surgical workstation providing overall application control, 2-D and 3-D ultrasound processing and surgeon interfaces; 2) a conventional 2-D ultrasound system (SSD-1450 ultrasound machine, Aloka Inc.); 3) a five degree-of-freedom robot for positioning the probe; and 4) an electromagnetic (EM) tracking system (Flock of Birds, model 60 FOB, Ascension Technology, Inc.). The EM base unit is fixed to the operating table and the EM probe is fixed to the ultrasound probe and needle holder. The imaging protocol starts with an exploration phase, in which the user decides on the volume of interest. Once the volume is available, we plan the treatment and then execute it using the robot. RESULTS: We first conducted experiments without an imager to test the accuracy of this system. We achieved 0.78 mm transaxial and 1.2 degrees rotational accuracy within 0.5–2 s. We then conducted needle placement experiments under 3-D ultrasound guidance using calf liver with pitted olives embedded in the liver at depths ranging from 5 mm to 40 mm, to simulate cancerous lesions. Finally, in order to assess the geometric accuracy of the system, we employed a phantom consisting of several plastic pins immersed in a water tank. The overall accuracy is 2.54 mm on average and a targeting success rate of 100%. CONCLUSIONS: We describe here a novel, low-cost needle guidance system based on a generic, mobile robot and free-hand 3-D ultrasound. This system offers the following advantages: (1) accuracy and stability from precise and steady robot motion, (2) the use of inexpensive robot components, and (3) the ability to be used immediately without prior calibration or registration. We are currently testing the system in a live pig model using both open and laparoscopic surgical techniques.

168 DIFFERENT MECHANISMS OF REPERFUSION INJURY IN MACRO- AND MICROVESSEL FATTY LIVERS—A PORTAL VEIN FLOW-DEPENDENT MECHANISM

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BACKGROUND: Due to the dramatic organ shortage fatty livers are commonly used for liver transplantation. The role of micro- and macrovesSEL steatosis in ischemia/reperfusion injury is unclear. METHODS: ob/ob mice and mice with choline-deficient diet were chosen as models for steatosis. 45 minutes of ischemia of 70% of the liver were performed in lean and fatty steatotic mice. The amount of micro- and macrovesSEL steatosis was determined by oil-red-O and Sudan red staining. The amount of total lipids was evaluated in the liver tissue. Liver injury was quantified by serum AST levels. Liver necrosis was determined by H&E staining and the ATP content of the liver tissue was quantified by bioluminescence assay. The blood flow in the portal vein was evaluated by laser Doppler. RESULTS: The amounts of total intrapathetic lipids were similar in ob/ob and choline-deficient mice (50 ± 48 mcg/mg, p = 0.5), while the total lipid values were 5 times lower in the lean control group (9.2 ± mcg/mg). ob/ob mice had more macro- than microvesSEL steatosis (75% vs 25%), while choline-deficient animals had less macro- than microvesSEL fat (30% vs 70%). After 45 minutes of ischemia and 4 h of reperfusion ob/ob mice had significantly higher AST levels (20,100 U/L) than choline-deficient (7,200 U/L) or lean mice (540 U/L). After 24 h reperfusion the AST levels of ob/ob and choline-deficient mice were comparable (17,200 ± 16,300 U/L), while the AST levels were decreasing in lean mice (310 U/L). After 4 h and 24 h of reperfusion ob/ob mice had more necrosis in the liver tissue than choline-deficient mice (4: 62% vs 41%; 24 h: 80% vs 65%). Lean mice had only minimal necrosis at this time point. ATP levels were comparable in ob/ob and choline-deficient mice prior to ischemia and after reperfusion. Lean animals had a rapid normalization of the portal vein perfusion after reperfusion (90% of the baseline with 1 h). Choline-deficient mice had 60% of the baseline portal vein flow within 1 h of reperfusion. In contrast, ob/ob mice had a decreased portal vein perfusion up to 24 h of reperfusion (15% of the baseline with 24 h). CONCLUSION: Macrovessel steatosis results in higher liver injury in the early phase after ischemia and reperfusion than microvesSEL steatosis. In contrast to lean livers both types of fatty livers result in a necrotic form of cell death. The decreased portal vein flow following reperfusion is a possible mechanism of the early severe injury in mice with macrovesSEL steatosis.

169 PREDICTORS OF SURVIVAL FOLLOWING HEPATIC RESECTION FOR COLORECTAL METASTASES: 10-YEAR EXPERIENCE AT A SINGLE INSTITUTION

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INTRODUCTION: Metastatic colorectal cancer limited to the liver can be resected with a cure rate of 30–50%. We examined the risk factors for disease recurrence and death in a large series of liver resections performed for colorectal metastases over a 10-year period at a North American hepatobiliary surgical oncology centre. METHODS: All patients who underwent liver resection for metastatic colorectal cancer between 1992 and 2002 at two university-affiliated hospitals were identified. A total of 425 hepatectomies were performed. Demographic, perioperative and survival data were retrospectively obtained through chart review. Major outcome variables were overall survival and disease-free survival. Risk
factors for disease recurrence and mortality were identified using multi-
variate analysis by the Cox proportional hazard method. RESULTS: A total of 425 hepatectomies were performed for metastatic colorectal cancer over the 10-year period. The median number of resected metastases was 1 (range 1–11), 101 cases (24%) had bilobar disease. The majority of operations performed 276 (65%) were major hepatectomies (4 or more seg-
ments). Procedures performed included: right hepatectomy 203 (48%); right trisegmentectomy 28 (7%); left hepatectomy 49 (9%); left tri-
segmentectomy 5 (1%); left lateral segmentectomy 52 (12%); non-anatomic resections 58 (14%); and other 39 (9%). Perioperative morbidity occurred in 62 (14.6%) patients. There were 7 (1.6%) perioperative deaths. The overall survival at 1, 3, and 5 years was 90%, 62%, and 45% respectively. The disease-free survival at 1, 3, and 5 years was 65%, 35%, and 26%, respectively. Multivariate analysis identified: size ≥5 cm (RR = 1.6, 95% CI = 1.1–2.3); a positive resection margin (RR = 3.0, 95% CI = 1.3–7.1); and previous chemotherapy (RR = 1.4, 95% CI = 1.0–2.0) as negative predictive factors for overall survival. Number of metastases and bilobar distribution were not significant prognostic variables. CONCLUSION: Hepatic resection for metastatic colorectal cancer is safe and provides good overall survival rates of 45% at 5 years. A history of previous chemotherapy, large tumors >5 cm or positive histologic margins are poor prognostic variables. A continued aggressive approach is justified by the low operative mortality rate, and good results, even in individuals with multiple, bilobar metastases.

170 MAJOR LIVER RESECTION SIGNIFICANTLY IMPAIRS THE HEPATIC RETICULO-ENDOTHELIAL CLEARANCE CAPACITY

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STUDY PURPOSE: Postoperative complications following major liver resection are related to residual liver volume but are difficult to predict. We hypothesize that part of the risk following major liver surgery may be associated with a reduction in hepatic reticulo-endothelial clearance capacity. This study describes a novel approach to residual liver and reticulo-endothelial clearance estimation following liver resection. PA-
TIENTS AND METHODS: Patients who underwent surgery for an intended liver resection were included in the study. Total and residual functional liver volumes were measured preoperatively by 3-D CT volumetry. Hepatocyte and reticuloendothelial clearance measurements were performed before and on day +1 after surgery by means of indocyanine green clearance (ICG-C15, %) and 99mTc albumin microspheres clearance (AM-C10, %) and related to functional liver volume. Patients with chronic liver disease (Child-Pugh C) and patients with open abdominal exploration served as positive and negative controls. RESULTS: 26 patients (6 with extended and 8 with standard liver resection, 8 explorations and 4 with chronic liver disease) were included in the study. After extended liver resection, absolute values of ICG-C15 and AM-C10 decreased significantly from 28.3% to 61.1% to 48.9% (p = 0.02), whereas relative-to-volume values increased significantly from 5.7%/100 ml to 16.2%/100 ml (p = 0.013) and from 4.5% to 13.7%/100 ml (p = 0.02). In spite of this compensatory effect, absolute values of AM-C10 (48.9%) on day +1 following extended liver resection fell within values from patients with chronic liver disease (AM-C10, 53.2%). No significant changes of absolute and relative values of liver function were found after standard resection and exploration. CONCLU-
SION: Combining functional measurement with liver volume allows insight into the compensatory responses of the liver following surgery. Absolute reticuloendothelial clearance capacity, although partially com-
pensated, is significantly impaired following extended liver resection.

171 CLINICAL UTILITY OF CHEMOTHERAPEUTIC SENSITIVITY TESTING IN HEPATIC TUMORS

Angela Marshall, Mark Thomas, Steve Rudich, Travis Doty and Joseph Buell, University of Cincinnati, Cincinnati, OH, USA

BACKGROUND: In the era of improved surgical techniques and patient survival, the use of adjuvant chemotherapy has become integral to patient care. A significant percent of patients are resistant to front-line therapy. Thus deciding appropriate chemotherapy regimens can be challenging. One novel method is the use of in vitro tumor growth and chemother-
apeutic sensitivity testing. METHODS: To assess the utility of this strategy we reviewed the last 75 hepatic resections performed in our practice. This included evaluating the growth of in vitro tumor, the selection of chemosensitivity and the impact on clinical practice. RESULTS: In the group of hepatic resections 34/75 patients had tumor specimen collected and shipped for testing. Seven (24%) tumor specimens failed to grow in culture. Those tumors that failed to grow in culture were breast (n = 2), lymphoma (1), pancreas (1), prostate (1), Stominal A rectum (1). Two (6%) specimens grew but were found later to be contaminated with bacteria. Tumor growth in culture was achieved with varying success. The following is the percentage of cultures grown in vitro and successful sensitivities obtained: colorectal cancer 4/4 (100%); ovarian cancer 5/5 (100%); cholangiocarcinoma 5/8 (63%); hepatocellular carcinoma 2/4 (50%), other 3/5 (60%). Of those patients with chemosensitivity profiles abnormal sensitivity patterns were detected in 7/19 (37%) of cultured tumors. In these 7 patients chemosensitivities were used to change the chemotherapy regimen administered to these patients compared to standard agents usually chosen as front-line. CONCLUSIONS: Chemo-
sensitivity testing is feasible in hepatic tumors including primary and metastatic disease. The incidence of tumor growth was greatest with ovarian, colorectal metastases while intermediate growth was noted in primary liver cancers (cholangiocarcinoma and hepatocellular cancer). Contamination was infrequent but ceased after increased experience with the isolation system. This new technology is beneficial to patient care, and especially in an era of chemoresistance, artificial chemosensitivity patterns have led to alterations in clinical practice patterns.

172 EARLY ONSET COLORECTAL LIVER METASTASES ASSOCIATED WITH A POOR OUTCOME DISPLAY A DISTINCT GENE EXPRESSION SIGNATURE

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In patients undergoing hepatic resection for colorectal liver metastases, multivariate analysis has demonstrated that detection of liver metastases within 12 months of primary resection is an independent indicator of poor prognosis. This phenotypic difference may reflect more aggressive tumour biology in metastases detected at an earlier stage. DNA microarrays now allow global tumour expression profiling in a single experiment. We investigated the gene expression signatures of liver metastases detected within 12 months of the primary compared with those detected thereafter. 31 colorectal liver metastases were snap-frozen at operation (18 metastases detected <12 months and 13 metastases detected >12 months after the primary). Total RNA was extracted, quantified and subjected to quality assessment. Microarray experiments were performed using the Affymetrix HG-U133A GeneChip (22,283 transcripts). Data analyses were performed using GeneSpring (version 6.0) 2065 genes were found to be differentially expressed between liver metastases detected within 12 months of the primary and those detected thereafter (Welch t test, p < 0.05). To identify candidate genes that exhibited the most significant and consistent expression changes we selected genes that were differentially expressed by at least 1.5-fold in >20% of the samples. A total of 395 genes satisfied these analysis criteria for differential expression between the two groups (200 genes over-
expressed and 198 genes under-expressed). These are principally genes involved in the key processes of cell adhesion, angiogenesis and growth factor-induced tumour proliferation. We have identified a highly significant and consistent gene expression signature of liver metastases detected within 12 months of the primary. These genes are pivotal in biological pathways associated with metastasis and may be responsible for the observed aggressive phenotype. Further work to evaluate the use of these genes as potential molecular markers or therapeutic targets is required.
### 173 DOES PRE-OPERATIVE CHEMOTHERAPY HAVE AN EFFECT ON HEPATOCYTE METABOLISM?

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**INTRODUCTION:** While it is well established that locoregional chemotherapy directed at colorectal liver metastases causes hepatocyte damage, little is known of the effects of systemic chemotherapy on the normal liver. With the advent of new chemotherapeutic agents such as oxaplatin and infusional 5-fluorouracil, which are specifically used in the neoadjuvant setting, it is important that any detrimental effects on hepatocytes are documented. Anecdotal evidence from liver surgeons suggests that there is a change in the parenchyma following systemic chemotherapy. This study was therefore undertaken in an attempt to establish the differential function of isolated hepatocytes taken from resected livers which have either been exposed to preoperative chemotherapy or not. **METHODS:** 41 patients undergoing hepatectomy for colorectal metastases between 1999 and 2003 were recruited. The patients were arranged into 4 groups according to their preoperative chemotherapy status: neoadjuvant oxaplatin (n = 10); neoadjuvant 5-fluorouracil (5FU) (n = 7); adjuvant 5FU (n = 17) or no chemotherapy (n = 7). Hepatocytes were isolated from sections of normal liver parenchyma taken from the region of the resected mass most distant from the tumour using a modified two-step collagenase perfusion technique. The initial cell viability and cell yield were calculated using trypan blue dye exclusion. The metabolism of 8 different compounds was then calculated using the rate of disappearance of the parent compound and the production of a specific metabolite over a 2-h time course. This reflected the function of individual CYP enzymes. Non-parametric statistical tests were then applied to the data in order to determine significance. **RESULTS:** When all 4 groups were compared it was seen that there were no significant differences in the initial cell viability and viable cell yield. There was also comparable metabolism of 7-ethoxycoumarin, testosterone, diclofenac, bufuralol, 5-methylthiopentoin, coumarin, chlorotoluzone, midazolam and 7-ethoxyconuramin, reflecting the function of CYP 1A2, 3A4, 2C8, 2D6, 2E1, 2C9, 2E1, 3A4, UGT and SULT, respectively. **CONCLUSION:** It is therefore seen that the administration of neoadjuvant systemic chemotherapy has no detrimental effect on the function of normal hepatocytes isolated at the time of surgery. This has implications for both the surgeon and oncologist with respect to treatment regimens, surgical technique and postoperative liver function.

### 174 CAUDATE HEPATECTOMY FOR CANCER: A SINGLE INSTITUTION EXPERIENCE WITH 146 PATIENTS

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**PURPOSE:** Caudate lobe resection is technically demanding with the disparate goals of preserving major vascular and biliary anatomy without compromising tumor clearance. Herein, we assess our results with caudate resection for malignant disease. **METHODS:** From 1992 to 2003, we performed caudate resection for malignancy in 146 patients. Clinicopathological correlates were analysed in these patients using chi-square or t-tests. Survival was determined using the method of Kaplan and Meier. **RESULTS:** Of the 146 patients identified, 20 (14%) underwent an isolated caudate resection 'Caudate only' and 126 (86%) underwent caudate resection as part of a more extensive hepatectomy 'Caudate plus' (Table). The most common other liver procedures were right trisegmentectomy (30%), left lobectomy (23%), and left trisegmentectomy (17%). The most common indication for caudate resection was metastatic colon cancer (59%) followed by cholangiocarcinoma (25%) and primary hepatocellular cancer (10%). 21 patients also underwent resection of the portal vein (n = 16) and/or vena cava (n = 13). The median estimated blood loss was 800 ml with a median transfusion of 2 units. The median length of stay was 9 days. At least one complication was reported in the majority of patients (55%). Nine patients (6%) died as a result of postoperative complications. Postoperative mortality was significantly higher in patients who underwent a major vascular resection (29 vs 2.5%, p < 0.001). Median survivals for patients with colorectal metastasis, cholangiocarcinoma, and hepatocelular carcinoma were 36, 28, and 32 months, respectively. **CONCLUSION:** Caudate resection of the liver can be performed safely but concomitant major vascular resection substantially increases the mortality of the procedure.

### 175 EXOGENOUS ADENOSINE INCREASES SPHINCTER OF ODDI MOTILITY, ACTING VIA CHOLINERGIC MOTOR NEURONS

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**BACKGROUND:** The sphincter of Oddi (SO) is a complex neuromuscular structure which regulates the flow of bile and pancreatic juice into the duodenum. Purines such as ATP and adenosine modify gastrointestinal motility but their actions in the biliary tree are poorly understood. Recently exogenous ATP was demonstrated to increase SO activity acting via cholinergic and nitricergic pathways. **AIM:** To determine if exogenous adenosine (1) modulates SO motility in vivo, (2) involves cholinergic neural pathways. **METHODS:** SO motility was recorded in fasted, anaesthetised, Australian brush-tailed possums (n = 17) with a multi-lumen manometry catheter. Adenosine (10-4 M, 1 µM-10 nM) was applied topically to the extraduodenal portion of the SO before and after pretreatment with hexamethonium (HEX; n = 6), atropine (ATR; n = 4) or the neurotoxin tetrodotoxin (TTX; n = 5). One-minute periods, representing the control period or the peak response, were analysed for area under the curve (AUC), contraction amplitude, frequency and basal pressure. The duration of the adenosine-induced response was also determined. Data were analysed using repeated measures ANOVA. **RESULTS:** Adenosine concentration-dependently increased SO activity for AUC (p < 0.05), amplitude (p < 0.05) and duration of response (p < 0.05), but had no effect on contraction frequency or basal pressure. Adenosine application (10 nM) increased SO activity to 293 ± 103% and 305 ± 44% of control for AUC and amplitude respectively, last 180 ± 93 s. Pretreatment with TTX and the muscarinic antagonist ATR blocked the adenosine-induced response (AUC, amplitude and duration: p < 0.05), whereas pretreatment with the nicotinic antagonist HEX had no effect. **CONCLUSION:** Exogenous adenosine increases SO activity acting via cholinergic motor neurons, suggesting that purinergic regulate SO motility. (Supported by NHMRC of Australia, grant #1021313, and the National Parks and Wildlife Service.)

### 176 ALTERED GLUCOSE METABOLISM IS ASSOCIATED WITH IMPAIRED GALLBLADDER MOTILITY

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**BACKGROUND:** Obesity, increased age, female gender, hyperlipidemia and diabetes all have been associated with increased risk for cholesterol gallstone formation. Biliary cholesterol hypersecretion, enhanced crystal formation and impaired gallbladder emptying are the key elements in gallstone pathogenesis. However, which risk factors are associated with specific pathogenic elements remains to be elucidated. In addition, data on biliary motility may be confused by existing gallstones. Therefore, the aim of this analysis was to determine which clinical risk factors were associated with impaired gallbladder emptying in humans without gallstones. **METHODS:** Gallbladder (GB) ultrasound examinations were performed on 180 adult Caucasian non-diabetic volunteers without gallstones. Volunteers had fasting blood drawn and then received a standardized fatty meal. GB volume was measured before and after the meal, and the ejection fraction (EF) was calculated. An EF of <25% was considered abnormal. **RESULTS:** 50% of the volunteers were overweight (BMI >30), and the mean age was 39 years (range 18–76), 55% were female, and 37% had an elevated cholesterol (XOL). Only 3% had a fasting blood sugar over 120 mg/dl, but 21% had an abnormal gallbladder EF. Risk factors stratified

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<th>Hepatocystomy</th>
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<th>Caudate plus</th>
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<tr>
<td>Number of patients</td>
<td>20 (14%)</td>
<td>126 (86%)</td>
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<tr>
<td>Vena cava resection</td>
<td>2 (10%)</td>
<td>11 (9%)</td>
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<tr>
<td>Portal vein resection</td>
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<td>14 (11%)</td>
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<tr>
<td>Median blood loss</td>
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<td>Median hospital stay</td>
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by EF are shown in the Table. CONCLUSIONS: These data suggest that among volunteers without diabetes or gallstones (1) 21% have impaired gallbladder emptying and 2) the only clinical risk factor associated with this abnormality is increased fasting serum glucose. We conclude that altered glucose metabolism, and not obesity, increased age, female gender or hyperlipidemia, is associated with impaired gallbladder motility.

**177 POSTOPERATIVE ERCP VS LAPAROSCOPIC CHOLEDOCHOTOMY CLEARANCE OF BILE DUCT CALCULI**

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Secondary biliary duct stones detected on cholangiogram during laparoscopic cholecystectomy are unable to be cleared via the cystic duct, require either a cholecystectomy or postoperative ERCP. This is a randomised study of these two approaches in the Brisbane metropolitan area. From June 1998 to February 2003, 372 patients had cholangiographically documented bile duct stones during laparoscopic cholecystectomy. 286 had successful trans-cystic duct clearance, leaving 86 patients randomised into the trial. Operative time was 154 min for the ERCP group (45 patients), 160 min for cholecystectomy (41 patients). Morbidity in terms of bile leak, retained stones, GI bleeding and sepsis occurred in 13% vs 14.6%. Hospital stay was 8.5 days for ERCP vs 6.5 days for cholecystectomy (ns). These data reveal a balanced outcome in terms of major morbidity and confirm our view that the majority of secondary biliary duct stones should be cleared trans-cystically, with those failing having either cholecystectomy or postoperative ERCP based on local surgical and gastroenterologic expertise, equipment availability and patient preference.

**178 LAPAROSCOPIC TRANSCYSTIC EXPLORATION OF THE COMMON BILE DUCT - A STRATEGIC ALTERNATIVE**

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BACKGROUND: Laparoscopic cholecystectomy has become the gold standard in Sweden. At the time of operation 5-10% of the patients have coexisting stones in the common bile duct (CBD). There are several alternatives in treating these patients. We have chosen to try to extract the stones at the primary operation, preferably by laparoscopic trans-cystic exploration of the CBD. METHODS: During the years 1994-2002 laparoscopic attempts at exploration of the CBD was made in 222 patients. A retrospective chart review was made and the patients in whom the operation could be completed using the trans-cystic technique were included in this study. RESULTS: In 40 patients a primary cholangiogram was chosen. In the remaining 182 of 222 patients an attempt at trans-cystic CBD exploration was made and it was successful in 135 cases (74%). The majority (68%) were women and their median age was 52 years (range 19–84 years) at the time of operation. In 126 patients one or more stones were extracted, in nine no stone could be found during cholecystectomy. The median operating time was 162 minutes (range 89–384 minutes) and the median postoperative hospital stay was one day (range 1–33 days). Eight patients had postoperative complications; three had cardiac pulmonary complications, three bleeding, one pancreatitis and one bile leakage needing percutaneous drainage. One of the patients with postoperative bleeding was reoperated due to infection of the hematoma. Otherwise there were no reoperations and no mortality 30-days postoperatively. Two patients had postoperative ERC with sphincterotomy, in one of them a retained stone was found. CONCLUSION: After laparoscopic trans-cystic exploration of the common bile duct the hospital stay is short. The frequency of retained stones is low. The papilla is saved and the potentially dangerous complications of ERC can be avoided. A single-stage laparoscopic procedure with trans-cystic common bile duct exploration is a traumatic alternative.

**179 TRANSCYSTIC STENTING FOR CBD STONES AT LAPAROSCOPIC CHOLECYSTECTOMY FACILITATES POST OPERATIVE ERCP**

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BACKGROUND: There are several strategies to treat stones in the common bile duct (CBD) at laparoscopic cholecystectomy (LC). The most frequent method is post LC ERCP. Transcystic stenting of the CBD was developed to facilitate post operative ERCP. AIM: To compare the efficacy and morbidity of conventional post LC ERCP to ERCP that has been facilitated with the insertion of a transcystic stent. METHOD: A prospective, non-randomized, single unit study from June 1996 until June 2002. The conventional ERCP group were referred from other surgeons for a post LC ERCP for CBD stones found at operative cholangiography (OC). The stented group had the LC done by the authors, a transcystic stent was inserted and proceeded to post LC ERCP. All ERCPs were performed by the authors. RESULTS: See Table. CONCLUSIONS: Insertion of a transcystic stent at LC does facilitate post LC ERCP for CBD stones. There is an increased rate of cannulation and clearance of the CBD and a significant reduction in the incidence of post ERCP pancreatitis.

**180 NATURAL PROGRESSION OF HEPATOLITHIASIS THAT SHOWS NO CLINICAL SIGNS AT ITS INITIAL PRESENTATION**

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BACKGROUND: Hepatolithiasis is common in East Asian countries and is more refractory to surgical treatment than most other benign diseases of the biliary tract. Long-standing cholangitis caused by retained and recurrent stones and the development of intrabiliary cholangiocarcinoma remain major problems in performing effective management. PURPOSE: To elucidate the natural progression of hepatolithiasis that showed no signs at the time of initial presentation. METHODS: Over a 20-year period, we observed 122 of 311 patients with hepatolithiasis who reported no symptoms and thus, who received no treatment at initial presentation. The follow-up periods were for up to 18 years (mean, 13 years and 1 month). RESULTS: Fourteen of 112 patients (11.5%) developed some symptoms attributed to hepatolithiasis. The interval until the onset of symptoms ranged from 9 months to 7 years and 4 months (mean, 3 years and 5 months). The developing symptoms included abdominal pain, hepatic abscess, cholangitis, and cholangiocarcinoma. Nine of the 14 patients (64.3%) developed stone migration to the extrahepatic bile duct at the onset of clinical symptoms. The incidence of liver atrophy on computed tomography in the patients with symptomatic hepatolithiasis (13 of 14 patients; 92.9%) was significantly higher than that in the patients with asymptomatic hepatolithiasis (14 of 108 patients; 13.0%). The prognosis of the patients with symptomatic hepatolithiasis was as follows: 2 died of cholangiocarcinoma, 1 died of hepatic failure, and 11 survived. Fifteen of the asymptomatic patients died, but none of these deaths were attributed to hepatolithiasis. CONCLUSIONS: Close observation is an alternative management at initial presentation for patients with asymptomatic hepatolithiasis without extrahepatic stones or liver atrophy.
**181 ENTRAL NUTRITION RICH IN FAT REDUCES INFLAMMATION AND GUT BARRIER FAILURE IN BILEDUCT-LIGATED RATS WITH SYSTEMIC HYPOPOTON**

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**BACKGROUND:** Cholestatic patients have an increased risk for septic complications after major surgery due to an increased susceptibility to endotoxemia and systemic hypotension. Thus far, no effective therapy has been reported to reduce postoperative complications. Recently, chologenic nutrition with high amounts of fat has been shown to be very efficient against endotoxia and inflammation. However, it is unknown to what extent an intact bile flow is required for the observed protection. **PURPOSE:** To study the effect of high-fat enteral nutrition on endotoxemia, inflammation and intestinal permeability in bile duct-ligated rats subjected to hemorrhagic shock. **METHODS:** Bile duct-ligated (BDL) Sprague-Dawley rats were either fasted or fed with a low-fat or high-fat enteral nutrition before hemorrhagic shock. At 90 minutes, endotoxin and TNF-α were determined in plasma. Distribution of the tight junction protein zonula occludens protein 1 (ZO-1) was assessed by immunofluorescence. Intestinal permeability to horseradish peroxidase (HRP) was determined ex vivo in the ileum. **RESULTS:** Plasma endotoxin significantly decreased after hemorrhagic shock in BDL rats fed with high-fat nutrition (15 ± 3 pg/ml) compared with rats that were fasted (32 ± 1 pg/ml, p < 0.001) or those fed with low-fat nutrition (26 ± 6 pg/ml, p < 0.01). In line, circulating TNF-α was reduced in rats pretreated with high-fat nutrition (61 ± 20 pg/ml) compared with fasted (188 ± 26 pg/ml, p < 0.05) or low-fat pretreated rats (105 ± 20, p < 0.01). A disappearance of ZO-1 was observed in intestinal epithelium cells of ileum and colon of non-treated rats demonstrating a breakdown of tight junctions. However, in high-fat pretreated rats ZO-1 distribution remained unaffected. In parallel, the increased intestinal permeability to HRP in low-fat pretreated (2.4 ± 0.3 μg/ml) and fasted BDL rats (7.6 ± 0.3 μg/ml) was reduced by high-fat enteral nutrition (0.9 ± 0.1 μg/ml, p < 0.001 and p < 0.001, respectively). **CONCLUSION:** These results suggest that an intact bile flow is not required for the protective effect of high-fat enteral nutrition on hemorrhagic shock-induced endotoxemia, inflammation and gut barrier loss. Pretreatment with high-fat enteral nutrition may be a new, simple and effective strategy to prevent endotoxin-mediated complications in cholestatic patients undergoing major surgery.

**182 ROLE OF TLR 4 IN CHOLANGITIS**

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**INTRODUCTION:** Cholangitis is a common clinical problem that can be fatal. We have developed a murine model of cholangitis and have shown that animals are very susceptible to biliary infection with E. coli or LPS in the obstructed bile duct. We now examine the role of TLR 4 in cholangitis. **METHODS:** 6-8-week-old C57BL/6J (TLR4−/−) or C57BL/6J (TLR4+/+) mice were subjected to bile duct ligation (BDL) and injection of 0.5 mg/mouse of LPS (Sigma). Survival was monitored. A cohort of animals was sacrificed at 6 h after induction of cholangitis. Liver injury was assessed by measuring serum ALT levels. Liver tissue was harvested and RNAe protection assay (Pharmingen) was used to examine mRNA levels of TNF-α and interleukin-6 (IL-6). Histologic analysis of liver was performed by standard H&E staining. **RESULTS:** TLR4−/− mice were resistant to biliary LPS – survival was 100% versus 13% in TLR4+/+ mice. Hepatic TNF-α and IL-6 mRNA levels were elevated in the TLR4−/− mice compared with the TLR4+/+ mice. However, liver injury, as measured by ALT and histologic examination of necrotic foci and neutrophil infiltrate in liver tissue, was similar between the two groups. **CONCLUSIONS:** Presence of TLR 4 is critical to LPS responsiveness in our novel murine model of cholangitis. Interestingly, despite increased hepatic pro-inflammatory cytokine profile and increased susceptibility to LPS in TLR4−/− mice, histologic liver injury was not different to that in TLR4−/− mice. This suggests that TLR 4−/− induced lethality is dependent on factors other than liver injury in cholangitis.

**183 PROGNOSTIC IMPLICATIONS OF PRESERVED BILE DUCT CONFLUENCE IN PATIENTS WITH CARCINOCOLIC LITHIASIS**

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**INTRODUCTION:** Biliary reconstruction is performed according to the level at which the injury occurred. A comparative study between patients in whom the biliary junction was preserved and another group where the biliary junction was not preserved was done. **METHODS:** A retrospective review of the biliary reconstructions performed for iatrogenic lesions between 1990 and 2002 was carried out. Postoperative outcome, functional status of the anastomosis, recurrent cholangitis, need for radiological instrumentations and/or reoperation were analysed. **RESULTS:** We reviewed 204 cases, 130 cases had a preserved biliary junction while in 74 the injury included the junction. All patients were treated with a Roux-en-Y hepatojejunostomy. In the first group, 4% required reoperation, 4% underwent radiological percutaneous instrumentations, 8% had anastomotic dysfunction and 4% had cholangitis. In the second group, 24% needed reoperation and 80% radiological instrumentation. Anastomatic dysfunction was observed in 64% and cholangitis in 55%. It is important to note that 52 of the 74 cases in the second group had a history of more than two reconstruction attempts. **CONCLUSION:** When the biliary junction is preserved after iatrogenic injury we found a significantly better outcome. The results of biliary reconstruction in this type of patient are better at long term compared to those where the junction was not preserved, evidenced by a lower reoperation and radiological instrumentation rate.

**184 EFFECT OF ISCHAEMIC PRECONDITIONING ON HEPATIC INTRACELLULAR TISSUE OXYGENATION DURING ISCHAEMIA REPERFUSION INJURY IN MODERATE HEPATIC STEATOSIS**

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Our previous study showed that ischemic preconditioning (IPC) significantly improves blood flow in the microcirculation during the reperfusion phase and preconditioned liver exposed to hypoxia maintains the cytochrome oxidase redox state. The present study aimed to investigate whether IPC could protect the liver with moderate steatosis form ischemia reperfusion (IR) injury through improving intracellular tissue oxygenation. Female New Zealand rabbits were subjected to a rich (2%) cholesterol diet for 8 weeks to induce moderate hepatic steatosis. Following which animals were subjected to 1 h lobar ischemia followed by 7 h reperfusion (IR). Animals were divided into three groups (n = 6 each): (1) sham laparotomy, (2) IR and (3) IPC with 5 min ischemia and 10 min reperfusion before IR. Hepatic microcirculation (HM) and tissue oxygenation including deoxymyglobin, oxyhemoglobin and cytochrome oxidase redox state were directly measured by laser Doppler flowmeter and near-infrared spectroscopy (NIRS). Fresh liver tissue samples were taken at baseline, 2 h and 7 h after reperfusion for the assay of activity of cytochrome C oxidase and citrate synthase. Hepatocellular injury was assessed by indoxaline green (ICG) clearance which was directly measured by NIRS. HM was significantly deteriorated in the IR group (94.0 ± 3.0 vs 73.3 ± 3.3 flux unit, p < 0.01), whereas it was significantly better in IPC after 7 h of reperfusion (73.3 ± 3.3 vs 118.3 ± 16.2 flux unit, p < 0.05). Cytochrome oxidase redox state measured by NIRS was better in the IPC group and that was also supported by higher cytochrome C oxidase activity in the IPC group (p < 0.05). The IPC group showed better ICG clearance as compared with the IR group (66.2 ± 3.9% vs 46.3 ± 11.6%). The data suggest that IPC protects steatotic liver from IR injury through improving HM and intracellular tissue oxygenation.

**185 GLYCINE MINIMIZES LEUKOCYTE-ENDOTHELION INTERACTION AFTER WARM ISCHEMIA VIA MECHANISMS INCLUDING INACTIVATION OF KUPFFER CELLS**

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Hepatic microcirculation is disturbed after warm ischemia via mechanisms including Kupffer cell-dependent injury which cannot be prevented during
major abdominal surgery, i.e. liver resection or transplantation. Since glycine, a non-toxic amino acid, prevents Kupffer cell activation this study was designed to assess its impact on leukocyte-endothelium interaction in detail. Sprague-Dawley rats (200-230 g) were infused with glycine (1.5 ml; 300 µM) to increase serum glycine levels about 4-fold to 1.2 ± 0.1 mM (p < 0.05) compared with controls treated with isonitrogenous saline, and amino acid without effects on Kupffer cells. Subsequently, warm ischemia of the left liver lobe was induced for 60 min. In vivo microscopy immediately after warm ischemia/reperfusion revealed that glycine totally prevented permanent adhesion of leukocytes in postischemic venules (p < 0.05) and significantly reduced this phenomenon in sinusoids from 267 ± 43 µm² in controls to 66 ± 13 µm². Further, at 2 h after warm ischemia glycine significantly reduced AST, ALT and LDH from 375 ± 24 U/L, 402 ± 27 U/L and 3773 ± 351 U/L in controls to 211 ± 27 U/L, 223 ± 31 U/L and 1374 ± 238 U/L, respectively. Warm ischemia increased both phagocytosis of fluorescent latex beads (1 µm) more than 3.5-fold to 85 ± 6 per microscopic field (p < 0.05) and [Ca²⁺], in Kupffer cells about 2-fold to 192 ± 5 µM (p < 0.05), which indicates Kupffer cell activation, being totally prevented with glycine. These results demonstrate for the first time that glycine dramatically reduces injury to livers after warm ischemia via mechanisms including minimized Kupffer cell-mediated leukocyte-endothelium interaction.

186 COMPUTER-BASED LIVER OPERATION PLANNING: 2 YEARS OF CLINICAL EXPERIENCE

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INTRODUCTION: For several years, computer-based liver operation planning has been offered by several informatics groups in Germany without being available in a routine clinical setting. Although there are two advanced systems in development (HepaVision by MeVis and LENA by DKFZ), there has been no reported experience of these systems in a clinical setting until recently. METHODS: Our LENA-System, which was developed and optimized especially with the clinical application in mind, is able to provide planning results just 2 h after image acquisition. For this purpose, CT and MRT images are sent via the teleradiology system Chili to the department MRI of DKFZ. Subsequently, the healthy liver parenchyma with lesions and the complete vessel systems – arteries, veins and bile ducts – are segmented, accomplishing an assignment of image regions corresponding to semantic units. After validation of these areas by a radiologist, a 3D image reconstruction is generated. This allows detailed insight into the individual liver anatomy, providing free interaction (rotation, zoom and translation). In addition to the 3D visualization, our system supports a calculation of vessel-dependent supplied areas, risk areas and a resection index. As a result, we obtain the dependent parenchyma with an exact specification of volume and a graphical presentation for every vessel section. These are the data supplied to the surgeon. Interdisciplinary meetings allow a definition of the operative concept. During the intervention, the planning data are available on a freely movable monitor in the operation theatre. RESULTS: During the development phase, the planning time was minimized from an initial 2 days to approximately 1 h. It is this optimization that allows the seamless integration of planning results into the clinical workflow. All in all, a total of more than 150 cases have been processed in our unit using this system. In 38 cases, the data became an integral component of the surgical therapy planning. In the meantime, this procedure is part of the standardized preparation of every living liver donor operation in Heidelberg. The visualization of all vessel systems, including bile ducts, with a 3D technique in clinical routine has been achieved for the first time.

CONCLUSIONS: Due to our unique system, we are able to add confidence in diagnosing surgical relevance of our operation plan, which forms a sensible supplement to traditional imaging in clinical routine.

187 INTRA-OPERATIVE ISOVOLUMIC HEMODILUTION IS SAFE AND EFFECTIVE IN ELIMINATING BANKED BLOOD TRANSFUSIONS DURING RIGHT HEPATIC LOBECTOMY: COMPARISON OF LIVING DONORS VS NON-DONORS

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Multiple studies have shown isovolumic hemodilution (IH) to be safe and effective during liver resection to limit the use of banked blood. However, no studies to date have looked at IH in living donor right hepatectomy. As blood vessels cannot be tied off prior to parenchymal dissection in living donors, thereby isolating the right lobe, blood loss may be significantly higher. Table below presents our data using IH in 10 consecutive patients undergoing living donor right hepatic lobectomy compared to 10 consecutive patients undergoing right hepatic lobectomy for primary or metastatic cancer. In all cases, the starting hematocrit was >30, central venous pressures were maintained no higher than 6 mmHg during the parenchymal dissection, and the patient was placed in the Trendelenburg position during dissection. No patients in either group required transfusion of banked blood or blood products. These data clearly demonstrates the following. 1) The use of intraoperative IH allows right hepatic lobectomy to be safely and effectively performed, both in donors and non-donors, without the use of banked blood/blood product transfusions. 2) As the OR time is significantly longer in living donors, blood loss and subsequent fluid replacement are higher, although not significant. 3) Overall length of stay is longer in the donor group; however, 2 patients had prolonged stays due to complications. One patient required emergent transplantation due to hepatic vein thrombosis related to previously undiagnosed factor V Leiden deficiency, and the other had a postoperative bile leak. If we remove these patients from analysis, the overall length of stay in this group is 7.25 days, virtually identical to the non-donor group.

188 IMPACT OF CONTRAST-ENHANCED INTRAOPERATIVE ULTRASONOGRAPHY DURING LIVER RESECTION

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AIM: Intraoperative ultrasonography (IOUS) is the most accurate diagnostic technique for detecting focal liver lesions but suffers from a few drawbacks in differentiating and detecting focal liver lesions (FLL). The aim of this pilot study was to evaluate the potentiality of contrast-enhanced IOUS (CE-IOUS) in this sense. MATERIALS AND METHODS: Twenty-nine consecutive patients underwent liver resection using IOUS and CE-IOUS. Mean age was 64.2 years (range 38–87); there were 19 males and 10 females. Seventeen patients had HCC, 10 colorectal (CRC) liver metastases, one GIST metastases and one had inflammatory pseudotumor preoperatively misdiagnosed as a peripheral mass-forming type cholangiocellular carcinoma. In all patients 4.8 ml of SonoVue (Bracco Imaging, Milan, Italy) was injected intravenously through a peripheral vein. SonoVue consists of sulphur hexafluoride-containing phospholipid microbubbles in saline. RESULTS: In the 10 patients with metastatic lesions CE-IOUS detected in 3 patients, 5 FLL undiagnosed by IOUS. In patients with HCC, CE-IOUS confirmed all but one of the preoperative FLL and in 10 patients depicted a total of 18 new FLL of uncertain origin: 12 had no enhancement peculiar to HCC at CE-IOUS pattern and at histology proved to be dysplastic nodules or did not show any change at postoperative follow-up (9–16 months); the remaining 6 in 3 patients had enhancement peculiar to HCC and histology confirmed this diagnosis. CE-IOUS added findings to those of unenhanced IOUS in 44.6% of patients (13/29). CONCLUSIONS: These preliminary results show that IOUS accuracy is improved by CE-IOUS with an impact on surgical strategy. In particular, CE-IOUS increases specificity in differentiating nodules detected in the

<table>
<thead>
<tr>
<th>Average no. of units IH</th>
<th>Average first postoperative HCT (%)</th>
<th>Average HCT 7 days postoperative (%)</th>
<th>Average estimated blood loss (ml)</th>
<th>Average fluid replacement (ml)</th>
<th>Average LOS</th>
<th>Average OR time</th>
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<tbody>
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<td>Donors</td>
<td>24</td>
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<td>31</td>
<td>1101</td>
<td>6261</td>
<td>11.2 days</td>
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<tr>
<td>Non-donors</td>
<td>3.4</td>
<td>29.45</td>
<td>27.98</td>
<td>690</td>
<td>4855</td>
<td>7.9 days</td>
</tr>
</tbody>
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p values for all but LOS are not significant.
cirrhotic liver by IOUS and the sensitivity of IOUS itself in detecting tiny fore-sites in patients who undergo surgery for CRC liver metastases.

189 NON-ALCOHOLIC STEATOHEPATITIS: A COMMON DISORDER IN PATIENTS WITH GALLBLADDER DISEASE

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BACKGROUND: Non-alcoholic fatty liver disease (NAFLD) affects up to 20% of the Western world. It is now one the commonest reasons for outpatient hepatology consultations. NAFLD is also known to progress to forms involving hepatic inflammation and/or fibrosis non-alcoholic steatohepatitis (NASH). AIMS: 1. To evaluate the prevalence of NAFLD/NASH in a group of patients undergoing laparoscopic cholecystectomy (LC). 2. To ascertain the accuracy/value of ultrasonography commonly used to diagnosis fatty liver. 3. To correlate liver enzyme abnormalities found in NAFLD/NASH. METHODS: 142 patients undergoing LC were recruited, and had simultaneous laparoscopic liver biopsy. Biopsy results were compared to preoperative abdominal ultrasound examination and correlated with liver enzyme tests. RESULTS: NAFLD was found in 76% whilst 41% of the study group had at least moderate to severe steatosis (Brunt classification). NASH was found in 22.5%, of whom 56.2% had some degree of peri-sinusoidal fibrosis. In diagnosing moderate to severe degrees of steatosis, ultrasonography has a sensitivity of 74.1% and specificity of 75.0%; OR: 8.6(3.9-18.5, p < 0.05), positive and negative predictive values of 77.9 and 75.0% respectively. Only 26% of the patients with NASH had an elevated ALT >60 IU/L, and only 21% with NASH had an elevated AST/ALT ratio (with ALT > normal). CONCLUSIONS: This represents to date the largest histologically controlled study evaluating the accuracy of ultrasound in hepatic steatosis. NAFLD is very common in the LC patient group and is likely to reflect the high population prevalence, and shared risk factors. The accuracy of ultrasonography as performed in the general outpatient setting has been shown to be reasonable in diagnosing hepatic steatosis. Liver enzyme abnormalities often used to aid the diagnosis of NASH may not be very sensitive.

190 ALL FAT ISN'T THE SAME: GC/MS ANALYSIS OF TWO COMMON STEATOTIC MODELS

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BACKGROUND: Hepatic steatosis is associated with diabetes, cirrhosis, and susceptibility to ischemia-reperfusion injury. It is a primary determinant in donor liver selection for transplantation. Evaluation of total hepatic fat content by H&E; staining and classification as macro- or microsteatosis may ignore underlying fatty acid (FA) variability. We hypothesized that the liver fatty acid profile of genetically fat (ob/ob) mice would be different to that of lean mice fed a high fat diet. By adapting a gas chromatography mass-spectroscopy (GC/MS) protocol for whole tissue hepatic analysis we believed we would observe different fatty acid profiles between the two models of steatosis. METHODS: 6-week-old ob/ob mice (n = 5), lean littermates (n = 4), and lean littermates given 60% by wt fat food for 14 days (n = 4) were sacrificed and liver tissue was collected. Frozen section slides were stained with Oil O O (ORO) stain. Lipid content in liver tissue was also homogenized and FAs were extracted in chloroform/methanol. Methyl esters were derived with BF3 and internal standards were added. Each sample FA methyl ester (FAME) mix was employed for instrument standardization. GC/FID instrument parameters were set based on internal standards at extinction. Samples were also standardized to protein.
cellular border) following 1 h ischemia and 6 h reperfusion. RG greatly decreases this occurrence. CONCLUSIONS: These data indicate that hepatocellular injury following 1 h of warm ischemia and 6 h of reperfusion occurs mostly in the form of necrotic cell death. RR pretreatment decreases hepatocyte injury as measured by AST and ALT levels via a mechanism which protects hepatocytes from necrotic cell death during ischemia. This action of RR implicates mitochondrial calcium overload in warm ischemic hepatocyte injury.

193 HEP-B HUMAN HEPATOCELULAR CARCINOMA CELLS EXHIBIT RESISTANCE THROUGH INCREASED PHOSPHO-ERK SIGNALING AFTER LONG-TERM EXPOSURE TO MEK INHIBITORS

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Human hepatocellular carcinoma (HCC) is associated with increased expression and activity of MAPK intermediates. Short-term treatment of HCC in vitro with MEK inhibitors results in a concentration-dependent decrease in phospho-ERK. The purpose of this study was to investigate the effects of U0126, PD98059, and PD184161 on HCC cell lines following long-term MEK inhibition. Treatment, U0126 and HepG2, were treated with MEK inhibitors U0126 (1.0–100.0 μM), PD98059 (1–20 μM), and a novel MEK inhibitor, PD184161 (0.1–1 μM) for 12–72 h. ERK and MEK expression were determined by Western blot. Activity of MEKK and MEK was determined by phospho-MEK and phospho-ERK immunoblots. Cell growth was determined by an MTS proliferation assay and confirmed by cell counts. HepG2 cells exhibited a concentration-dependent p-ERK downregulation with U0126, PD98059 and PD184161 that was similar at all time points observed. In HepB3 cells, however, p-ERK expression returned to control levels at all doses measured at both 24- and 48-h time points. When medium containing U0126 was removed from HepB3 cells after 24 h and placed on naïve HepB3 cells, there was a decrease in p-ERK that was equivalent to that seen following treatment with freshly prepared U0126, effectively ruling out degradation of the drug. Exposing previously treated HepB3 cells to new U0126 did not result in an equivalent decrease in p-ERK, as to that seen in naïve cells. Total ERK and MEK expression did not change with any of these manipulations. Phospho-MEK, however, was increased up to 5-fold over control in a concentration-dependent manner with U0126 treatment. Cell proliferation assays confirmed that within the first 24 h HepB3 cells were sensitive to the antiproliferative effects of MEK inhibitors, but this effect did not continue when the cells were examined after 48 and 72 h of treatment. The large increase in MEK activation as a result of U0126 treatment may alter the effectiveness of U0126 as an inhibitor of downstream ERK phosphorylation. HepB3 cells are able to circumvent the effects of pharmacologically active MEK inhibitor after 24 h, possibly through a hyperactive upstream positive feedback mechanism or by a novel MEK-independent mechanism.

194 COMPARISON OF MOLECULAR PATHWAYS BETWEEN LOSS OF HETEROZYGOSITY AND MICROSATELLITE INSTABILITY IN HEPATOCELLULAR CARCINOMA

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OBJECTIVE: The multiple genetic alterations involved in the tumorigenesis of human hepatocellular carcinoma (HCC) have not been well studied. The aim of this study was to explore the role of loss of heterozygosity (LOH) of tumor suppressor genes (TSG) and/or microsatellite instability (MSI) during hepatocarcinogenesis, as well as their correlation with clinicopathological features. METHODS: LOH on 6 TSG (APC, DCC, MCC, OGG1, p53 and RBl) in 36 informative HCC and 13 polymorphic microsatellite markers in 15 HCC were analysed by using microdissection-based PCR amplification and direct DNA sequencing. RESULTS: The overall incidence of LOH in HCC was 41.7% (15/36). The frequency of genetic alterations of TSG in informative HCC were p53 (87.5%), APC (58.8%), OGG1 (50%), RBl (37.5%), DCC (25%) and MCC (0%). 46.2% (6/13) microsatellites showed LOH in nine of 15 HCC (60%), but none of HCC showed MSI. If taking LOH of APC, OGG1 and DCC as type I (n = 6), and LOH of p53 and RBl as type II (n = 7), the mean tumor size of these two types were 2.9 ± 1.7 cm and 7.1 ± 3.4 cm, respectively (p < 0.01), and clinical outcomes were 72.6 ± 36.6 months and 51.0 ± 30.4 months, respectively (p < 0.05). No significant differences were found between genetic alterations and age, sex, serum AFP level, frequency of HBV infection, liver cirrhosis, tumor differentiation and tissue type (p > 0.05). CONCLUSIONS: Compared with MSI pathway, LOH pathway plays a more important role during the development of HCC. Based on the present study, a multistep model of hepatocarcinogenesis is proposed, in which, LOH of APC, OGG1 and DCC might be an early event, whereas LOH of p53 and RBl is an advanced event, whereas MCC may play no role in that process.

195 CLINICAL APPLICATION OF ANTI-ANGIOGENIC TREATMENT FOR HEPATOCELLULAR CARCINOMA – WITH SPECIAL REFERENCE TO MATRIX METALLOPROTEINASES AND CYTOKINE NETWORK

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PURPOSE: For the development of primary hepatocellular carcinoma (HCC), tissue remodeling and angiogenesis are key factors. In this study, angiogenesis-related matrix metalloproteinases (MMPs) and angiogenesis-related factor treatment, MMP-2, -9 and MT1,2-MMP were evaluated. MATERIALS AND METHODS: We examined the expression rates of angiogenesis-related MMP-2, -3, -7, -9 and MT1,2-MMP in the cancer and non-cancerous areas of resected tumors in 30 patients by immunohistological analysis. In addition, the serum cytokines (IL-6, IL-8, and TNF-α) were measured to confirm the source of hepatocarcinogenesis. Furthermore, using a diethylaminozone (DEN) HCC model in rats, MMP-M (Marimastat) was administered by 4 routes (systemic, hepatic artery, portal vein, local). The chemopreventive effect was also examined. The evaluation was made on tumor diameter, nodular number, immunohistochernistry (MMP-2, -9 and MT1-MMP), zymography (MMP-2, -9), Northern blotting and the hepatic microvascular casts (red: artery; blue: portal vein). RESULTS: The expression of MT1-MMP was frequently observed to a similar extent as that of MMP-2 in cancer areas. MMP-9 in HCC-infiltrated region was often observed. These findings in the DEN model are fundamentally the same as those for clinical cases. In the clinical cases, the expressions of MMP-7 and 9 were closely related to the cancer infiltration. In addition, enhanced expression of MMP-7 was interestingly observed in HCC viable cells after transcatheater arterial embolization. Furthermore, MT1-MMP appeared to be the most important factor in HCC because of its widespread pattern of expression. Serum cytokine study of the patients with HCC, a switch-on angiogenic status including decreased TNF-α and increased IL-8 was suggested (before and after carcigenogenesis). In the systemic group of MMPI as compared with the control, the number of red nodules (HCC) successfully decreased by 75%. In the intra-arterial and portal groups as well, the red nodules was significantly decreased. Chemoprevention was also observed. In the vascular casts by SEM, suppressed tumor angiogenesis of portal area and maintained sinusoidal structure were observed in the treatment groups. Expressions of MMP-2, -9, especially decrease of its activated type (zymography) and of MT1-MMP (Northern blotting) were evident in the treatment groups. CONCLUSION: Various anti-angiogenic treatments such as MMPI and its combinations seem to have a possible contribution to chemoprevention, tumor dormancy, and tumor shrinkage in cases of HCC.

196 ADJUVANT ARTERIAL INFUSION CHEMOTHERAPY AFTER RESECTION OF HCC WITH TUMOR THROMBOSIS OF THE PORTAL VEIN

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The prognosis of hepatocellular carcinoma (HCC) with tumor thrombosis of the main trunk or major branches of portal vein is extremely poor, even if it is resectable. Uncontrollable multiple metastases often appear in the residual liver within several months after the operation. Recently, arterial infusion chemotherapy has been attempted for HCC that resists conventional therapies. This study was designed to evaluate the efficacy of adjuvant
arterial infusion chemotherapy after resection of HCC with tumor thrombosis of the portal vein. The regimen consists of induction and following therapy. The induction therapy is daily administration of cisplatin (DDP 5–10 mg/day for 1–5 days) and continuous infusion of 5-fluorouracil (5-FU 250 mg/day for 5–10 days). In principle, patients receive four serial courses of chemotherapy. The following therapy is weekly or bi-weekly administration of DDP (5–10 mg) and subsequent infusion of 5-FU (750–1000 mg for 10 h). Between January 1997 and December 2002, 21 patients with intractable HCC were treated in our hospital by arterial infusion chemotherapy. 11 patients completed the regimen, 4 patients showed a complete response, and 2 patients showed a partial response. The response rate is 54.5%. Based on the encouraging results, we applied this regimen to the adjuvant chemotherapy after the resection of the HCC with portal tumor thrombosis. The adjuvant therapy was terminated when the cumulative dose of 5-FU reached 15 g. In a retrospective study, 12 patients had curative resection of HCC with tumor thrombosis of the main trunk or major branches of portal vein, and 6 patients received the adjuvant chemotherapy. Liver function and tumor pathology were not different between patients with adjuvant chemotherapy and without chemotherapy. The mean survival is 47.3 months with chemotherapy and 10.8 months without chemotherapy. The mean disease-free interval is 25.8 months with chemotherapy and 4.5 months without chemotherapy. The current pilot study indicated that adjuvant arterial infusion chemotherapy is a very promising strategy after aggressive surgery to the HCC with tumor thrombosis of the portal vein. However, a controlled study is essential to obtain conclusive evidence.

197 DIAGNOSIS AND SURGICAL TREATMENTS OF HEPATOCELLULAR CARCINOMA WITH TUMOR THROMBOSIS IN BILE DUCT: AN EXPERIENCE OF 34 PATIENTS FROM ONE CLINICAL CENTER

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AIM: Hepatocellular carcinoma (HCC) with bile duct tumor thrombosis (BDT) is a rare event. The prognosis of this type of patient is very dismal. This study aims to further improve the prognosis of these patients, and share our experiences on the diagnosis and treatment of HCC with BDT. METHODS: Thirty-four patients with HCC with BDT who received surgical treatment in the authors' institute from July 1987 to January 2003 were reviewed retrospectively. The diagnosis, treatment, and outcome of these patients were summarized. RESULTS: Thirty of the 34 patients (88.2%) were positive for alpha-fetoprotein (AFP) (>20 μg/L), and 12 patients (35.3%) were found to have obstructive jaundice before operation, 18 cases were suspected ‘obstruction of bile duct’ preoperatively. The primary tumors were frequently located at the left medial (13 cases) or right anterior lobe (14 cases). Thirty-one patients received liver resections and removal of BDT, while the other 3 patients received removal of BDT combined with hepatic artery ligation and cauterization (HAL + HA), or only removal of BDT because their liver function reservation and general condition could not tolerate the primary tumor resection. The 1-year survival rate was 71.4% (20/28). The longest disease-free survival was over 13 years. Intercurrent tumor recurrence within 1 year after operation was found in 14 patients (14/28, 50.0%). CONCLUSIONS: Surgical removal of primary tumors and BDT is safe and beneficial for HCC patients with BDT. Early detection, diagnosis, and surgical treatment are the key points to prolong the survival time of patients.

198 ACTIVIN A STIMULATES VASCULAR ENDOTHELIAL GROWTH FACTOR GENE TRANSCRIPTION IN HUMAN HEPATOCELLULAR CARCINOMA CELLS

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BACKGROUND AND AIM: Upregulation of vascular endothelial growth factor (VEGF) is known to play a critical role in hepatocellular tumor biology. In an attempt to identify factors responsible for VEGF induction in human hepatocellular carcinoma (HCC), we evaluated the effects of activin A on VEGF gene expression. METHODS: Expression of VEGF, activin A and its receptor was analysed by Northern blot, PCR, and enzyme-linked immunosorbent assay. Functional VEGF promoter analysis and gel shift assays were performed to define minimal promoter requirements and potential transcription factors. RESULTS: In vitro activin A, VEGF and its receptors were detected immunohistochemically in 9/9 HCC tumor specimens. In vitro the expression of VEGF the activin A receptor system was confirmed by ELISA and RT-PCR in three HCC cell lines. Incubation of HCC cell lines with activin A for 96 h led to time- and dose-dependent increase of VEGF protein and mRNA concentrations. Transient transfections with a human VEGF reporter gene construct (ΔVEGF –2018/+50) showed transactivation of the VEGF promoter through activin A. 5 deletional analysis revealed the –85 to –50 region of the human VEGF promoter to be responsible for basal as well as inducible promoter activity. CONCLUSION: This study identifies activin A as a novel stimulus of VEGF gene expression in HCC. Activin A indirectly stimulates angiogenesis in human hepatocellular carcinoma through up-regulation of VEGF gene expression by transactivation of the –85 to –50 region of the VEGF promoter.

199 RUPTURED HEPATOCELLULAR CARCINOMA: A TERMINAL OR SALVAGEABLE EVENT?

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PURPOSE: Ruptured hepatocellular carcinoma (HCC) is often regarded as a terminal event of the disease. Aggressive resection, the introduction of interventional radiology techniques and improved surgical outcome with surgical resection may have altered the outcome in this once dismal presentation. We reviewed our experience with treatment and outcome of this acute abdominal emergency to determine if this is a terminal or salvageable event. Methods: Between January 1996 and October 2003, 28 patients were admitted with the diagnosis of acute ruptured HCC. All patients were followed up for a minimum of 3 months. Clinical data were obtained and reviewed retrospectively. Definition of terminal event was classified as death during the same hospital admission for rupture of HCC. RESULTS: The mean age at presentation was 64 years (range 31–90 years) with male predominance (86%). The average maximal diameter of the ruptured tumour was 8.6 cm (range 4–10 cm). 60% of patients had a background of cirrhosis, largely secondary to hepatitis B infection. The most common presentation was abdominal pain, followed by abdominal distension and shock. Various modes of treatment were administered: conservative management (n = 1), surgery (6), transarterial embolization alone (6) and transarterial embolization followed by surgery (5). In-hospital mortality rate was 25% (7 of 28 patients), median survival time was 4 days. The only significant factors affecting outcome were presence of shock at time of presentation (p = 0.003), underlying cirrhosis and Child-Pugh grading. Survival time was substantially long in the remaining patients who were discharged after treatment (median survival of 365 days). CONCLUSION: Early mortality of ruptured HCC was associated with a poor pre-rupture disease state and presence of shock at presentation. In the majority of patients, rupture of HCC is not a terminal, but rather, a salvageable event. With current management and careful selection of patients, prolonged survival can be achieved.

200 SURGICAL RESULTS OF HEPATIC RESECTION FOR HEPATOCELLULAR CARCINOMA WITH DIAPHRAGMATIC INVOLVEMENT

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PURPOSE: Direct diaphragmatic involvement is not uncommon in patients undergoing hepatectomy for hepatocellular carcinoma (HCC). The purpose of the study was to retrospectively evaluate the surgical results of HCC with diaphragmatic involvement undergoing curative en bloc resection. MATERIALS AND METHODS: Between January 1989 and December 2002 53 patients who had HCC with clinical diaphragmatic involvement underwent curative en bloc resection in our hospital. During operation if a tumor was found to invade or densely adhere to the diaphragm, a cuff of the involved diaphragm was removed en bloc. The clinicopathological features, operative risks, 5-year disease-free and actuarial survival of the 53 patients were retrospectively studied. RESULTS: Of the 53 HCC patients with clinical diaphragm involvement, seven (13.2 %) were pathologically proved to have muscular invasion of diaphragm, the other 46 (86.8%) were fibrous adhesion only or free of tumor. Primary repair of diaphragm was adequate in 52 patients (98.1%)
and one needed mesh repair. Thirteen patients (24.5%) developed postoperative complication with the leading cause of pleural effusion and no operative mortality occurred. Until March 2003 after a median follow-up of 25.0 ± 26.4 (range 2.6-150.5) months the 5-year disease-free and actuarial survival were 11.0% and 21.0%, respectively. There is no significant difference between the patients with histological muscular invasion and those without muscular invasion in disease-free survival (p = 0.23) and actuarial survival (p = 0.59). CONCLUSION: En bloc resection of involved diaphragm in HCC patients with clinical diaphragm involvement is justified as it is associated with acceptable operative risks and may achieve long-term survival.

201 A PROSPECTIVE ANALYSIS OF PERIHEPATIC LYMPH NODE STATUS IN PATIENTS UNDERGOING HEPATIC RESECTION A. J. L. H. T. N. CHENG

Stephen R Grohmyer, Wang Liang, Yuman Fong, Ronald P Dametto, Michael D’Angelo, Mikhail Gonen, Lawrence H Schwartz, Leslie H Blumgart and William R Jarnagin, Memorial Sloan Kettering Cancer Center, New York, NY, USA

PURPOSE: Perihepatic lymph node metastasis is a significant negative prognostic factor in patients undergoing hepatic resection for malignancy. However, preoperative identification of patients with perihpatic nodal involvement is often difficult and previous studies have suggested a high incidence of occult metastatic disease. METHODS: Perihepatic lymph nodes were sampled from up to 3 stations (portal, hepatic artery, and perihocellular) at the time of hepatic resection in 79 patients undergoing partial hepatectomy for primary or secondary hepatic malignancy. Lymph nodes were measured on preoperative CT scan by radiologists blinded to operative and pathologic findings. Intraoperatively, lymph nodes were graded by the surgeon for suspicion of metastatic disease using a scale of 1–5 (1 = lowest suspicion of metastatic disease, 5 = highest suspicion of metastatic disease). For the analysis, grades 1 or 2 were considered ‘low suspicion’ and grades 3, 4 or 5 were considered ‘high suspicion’. For CT measurements hepatic artery and perihodional nodes were considered ‘positive’ if detectable; portal nodes were defined as positive if the cross-product of the dimensions was >0.65 cm³. Pathologic findings were then correlated with radiographic findings and intra-operative findings. RESULTS: Indications for planned hepatectomy were metastatic colorectal cancer (n = 29), hepatocellular carcinoma (9), peripheral cholangiocarcinoma (5), and other (5). The percentage of patients in this series having a histologically positive lymph node was 13.9%. None of these lymph nodes were considered ‘low suspicion’ by the surgeon and 50% were considered ‘negative’ by radiologic criteria. The incidence of truly occult metastatic nodal disease was 0%. There was no significant difference in the percentage of positivity at each station: portal (6.8%), hepatic artery (7.1%), and perihocellular (6.8%). Both clinical and radiologic assessments were valuable in assessing nodes (Table). CONCLUSIONS: Routine perihpatic nodal sampling in patients undergoing resection for primary or secondary hepatic malignancy has a low yield. Preoperative CT scans and intra-operative assessment of nodes are useful in identifying patients in whom nodal sampling has a high yield.

202 SELECTIVE INHIBITION OF IKK DEGRADATION BY CALPAIN-1 INHIBITOR AMELIORATES THE INDICES OF MURINE CERULEIN-INDUCED ACUTE PANCREATITIS

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INTRODUCTION: Prevention of NF-κB activation down-regulates inflammatory gene expression and oxidative stress in acute pancreatitis (AP). Calpain-1, an intracellular protease, plays an essential role in NF-κB activation by selectively degrading inhibitor factor B (IκB). Specific inhibition of calpain activation by calpain-1 inhibitor may permit selective modulation of inflammatory pathways upregulated in AP. METHODS: Studies conformed to American Physiology Association guidelines. Male wild-type mice had free access to food and water and were randomly allocated to one of four groups (n = animals): group 1 (n = 10) sterile normal saline intraperitoneally (i.p.; control); group 2 (n = 17) cerulein (50 μg/kg, in saline) i.p. hourly for 5 h; group 3 (n = 17) calpain-1 inhibitor i.p. (5–20 mg/kg) 30 min before induction of AP and thereafter hourly cerulein i.p. (x 5) and group 4 (n = 10) calpain-1 inhibitor (5–20 mg/kg) 30 min before normal saline i.p. hourly (x 5). Mice were sacrificed 6 h after AP. Pancreata and lungs were snap-frozen in liquid nitrogen and stored at −80°C until assessed. Histologic injury was quantified morphometrically. Principal end-points were: serum amylase and lipase, expression of adhesion molecule ICAM-1, nitrotyrosine, inducible nitric oxide synthase (iNOS), myeloperoxidase (MPO), malondialdehyde (MDA), and histologic evidence of lung and pancreas injury. Results were analysed by one-way analysis of variance with Bonferroni’s correction. Significance was at p < 0.05. RESULTS: Intraperitoneal cerulein caused severe AP characterized by neutrophil infiltration, hemorrhagic necrosis and elevated amylase and lipase. Calpain-1 pretreatment resulted in significant reduction in amylase and lipase (p < 0.001 vs cerulein; p = NS vs control). Immunohistochemistry demonstrated a marked increase in activity for nitrotyrosine, iNOS and ICAM-1 in pancreata and lungs of cerulein-i.p. mice, which was abolished by calpain-1 pretreatment. MPO and MDA in both lung and pancreas were elevated in cerulein-induced AP. Calpain-1 pretreatment reduced MPO activity in lung (p < 0.05 vs cerulein) and pancreas (P < 0.05 vs cerulein). Similarly, calpain-1 pretreatment reduced MDA in lung and pancreas. CONCLUSION: These findings provide the first evidence that calpain-1 inhibitor, a potent inhibitor of NF-κB activation, selectively attenuates both pancreatic and lung injury and the inflammatory pathways upregulated in experimental acute pancreatitis.

203 ANTIBIOTIC PENETRATION INTO PANCREATIC NECROSIS IN PATIENTS WITH NECROTIZING PANCREATITIS

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AIM: To evaluate the rate of antibiotic penetration into pancreatic necrosis in patients treated for necrotizing pancreatitis with prophylactic piperacilline/tazobactum antibiotic. MATERIALS AND METHODS: The study was performed on necrotic tissue of the pancreas and inflammatory peripancreatic ascites derived from 10 patients (m 2, f, m, 60) treated for necrotizing pancreatitis in 2001/2002. The treatment started with prophylactic piperacilline/tazobactum antibiotic that was maintained up to 14 days, in addition to TPN and intensive care, according to the prospective protocol. Patients were operated on day 18–21 of treatment for pancreatic necrosis. Samples of necrotic tissue of the pancreas and samples of the inflammatory ascites from omental bursa were collected during the operation and investigated for the concentration of the antibiotic by fluoroscopic/spectroscopic methods of registration in an HPLC system. The spectrometer was supplied with two independent monochromatic inductors and registration, xenon lamp and luminescence signal detector PMT with a spectrum range of 210–370 nm. Results: See Table below. CONCLUSIONS: The study indicates effective penetration of piperacilline/tazobactum to the inflammatory ascites surrounding the pancreas and to the tissue of the necrotic pancreas itself in acute necrotizing pancreatitis.

204 INTRAOPERATIVE SELENIUM MODULATES L-ARGININE-INDUCED EXPERIMENTAL ACUTE PANCREATITIS

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INTRODUCTION: Selenium is an essential cofactor in the antioxidant glutathione peroxidase pathway: one of the mechanisms of propagation of acinar cell injury in acute pancreatitis (AP). Serum selenium levels are

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<th>No. of patients</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>10</th>
<th>Med.</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pancreatic necrosis (mg/kg)</td>
<td>172</td>
<td>68</td>
<td>176</td>
<td>147</td>
<td>113</td>
<td>126</td>
<td>100</td>
<td>67</td>
<td>102</td>
<td>129</td>
<td>120</td>
</tr>
<tr>
<td>Omental ascites (mg/kg)</td>
<td>190</td>
<td>101</td>
<td>210</td>
<td>261</td>
<td>176</td>
<td>187</td>
<td>156</td>
<td>190</td>
<td>200</td>
<td>159</td>
<td>183</td>
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<tr>
<td>+/−34</td>
<td>+/−37</td>
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depleted in chronic acute pancreatitis with degree of depletion corresponding to severity. A clinical trial has suggested that oral selenium supplementation improves outcome in clinical AP but these findings remain unsubstantiated. This study tests the hypothesis that intravenous selenium supplementation given after disease induction modulates the course of experimental AP. METHODS: All studies complied with American Physiology Association guidelines for animal care. Male Sprague-Dawley rats were randomly allocated to one of three groups (n = 5 per group) as follows: group 1 (control), no intervention; group 2, acute pancreatitis (AP) induced by intraperitoneal l-arginine hydrochloride, 250 mg per 100 g body weight on day 0; group 3, AP + selenium (15 μg/kg) at 24 and 48 h after induction of AP. All animals were given buprenorphine for analgesia (previously demonstrated to have no effect on outcomes in this model) and sacrificed at 72 h. Samples for pancreatic and lung histology were snap-frozen in liquid nitrogen and examined after H&E staining by a histopathologist blind to group allocation. Biochemical end-points were: serum amylose, serum antioxidant levels, bronchoalveolar lavage (BAL) protein and lung myeloperoxidase activity (MPO). Statistical comparisons were by non-parametric tests with p < 0.05. RESULTS: L-Arginine induced AP characterized by edema, neutrophil infiltration, acinar cell degeneration and elevated serum amylose. Selenium supplementation had no effect on serum selenium levels. However, selenium supplementation was associated with a reduction in BAL AP (p < 0.01; Mann–Whitney U-test). In addition, acinar cell degeneration and pancreatic inflammatory cell infiltration were absent in selenium-treated animals. CONCLUSION: In this relatively prolonged study model intervention with selenium starting 24 h after induction of AP ameliorated histological signs of acinar cell injury and reduced pancreatic inflammatory infiltrate and had a protective effect on lung injury. These findings suggest that post-induction selenium can modulate pancreatic and lung injury in experimental AP.

205 SURGICAL TREATMENT OF CHRONIC PANCREATITIS WITH PANCREATIC MAIN DUCT DILATATION – LONG-TERM RESULTS AFTER HEAD RESECTIO AND DUCT DRAINAGE

Wolfgang Schlosser, Andreas Schwarz and Hans Beger, University of Ulm, Ulm, Germany

INTRODUCTION: Tissue and duct hypertension is considered as a major factor in the etiology of pain in patients with chronic pancreatitis (CP). Duct dilatation is a consequence of duct obstruction due to scars or duct stones. Nevertheless, the procedure of choice, drainage or resection, is still under discussion. We present long-term results of patients operated with duodenum-preserving pancreatic head resection (DPHR) combined with a Partington-Rochelle duct drainage in cases of chronic pancreatitis with multiple stenosis and dilatation of the side ducts. METHODS AND PATIENTS: From April 1982 to September 2001 in 55 out of 538 patients with chronic pancreatitis a DPHR with additionally Partington-Rochelle duct drainage was performed (44 male, 11 female, mean age 45.8 years). 92% of the patients suffered from alcoholic pancreatitis. Medical respective pain treatment for chronic pancreatitis was in median 64.5 month prior to surgery. The indications for surgery were in 87% pain, 39% of the patients had an inflammatory mass in the head of the pancreas, 36% had a common duct stenosis and 5% had a severe stenosis of the duodenum. The endocrine function (OGGT) was impaired in 79% of the patients preoperatively. Hospital mortality was 0%, postoperative complications occurred in 11 patients. FOLLOW-UP: All except 2 patients were followed up in the outpatient clinic with a mean follow-up time of 69.7 month (8–61 months), the late mortality was 9%. 68% of the patients were completely free of pain, 29% had occasional pain, 3% suffered from a further attack of pancreatitis. Body weight increased in 79%, 58% were professionally rehabilitated. Late postoperative endocrine function was unchanged in 85% (improved in 5%, deteriorated in 10%). CONCLUSION: The pain control in patients with multiple duct stenosis after duodenum-preserving pancreatic head resection with duct drainage leads to long-standing absence of pain and low recurrence rate of attacks of pancreatitis.

206 A CLINICALLY-BASED CLASSIFICATION SYSTEM FOR CHRONIC PANCREATITIS: ASSESSMENT IN COMPARISON TO THE MARSEILLES, CAMBRIDGE, HEIDELBERG AND ABC SYSTEMS OVER A 9-YEAR STUDY PERIOD

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INTRODUCTION: Classifications of chronic pancreatitis (CP) based on either histologic (Marseilles) or endoscopic (Cambridge) criteria are not widely used. The aim of this study was to design a clinically based classification (CBC) for CP and to evaluate this in comparison to other systems over a prolonged period. METHODS: Patients with a diagnosis of CP (577; L1CE-9) for 1994 were identified from the records of the Hepatobiliary Service of a University Hospital. Endoscopic (ERC/P) or CT evidence were mandatory for inclusion. Twenty-three new patients met criteria and were allocated a category according to the Marseilles, Cambridge, Heidelberg and ABC systems and also according to a novel clinically based 3-stage system. Mild CP: abdominal pain + either ERCP or CT evidence of CP + obligatory; no regular (weekly) opiate, preserved endocrine, exocrine (ex/end) function and no peri-pancreatic complications (PPC). Moderate CP: abdominal pain + at least one of: regular opiates, impaired ex/end function, no PPC. End-stage CP: ERCP or CT + at least one obligatory: biliary stricture, portal hypertension, duodenal stenosis ± one of: pain, diabetes, steatorrhoea. Charts were reviewed for the subsequent 9 years with annual categorical allocation. Principal outcomes were death and progression to end-stage CP. RESULTS: (See Table). The Cambridge, ABC, Heidelberg and clinically based systems all demonstrated a significant progression to end-stage disease over 9 years (p < 0.01 Kruskal-Walls with post-correction). CONCLUSION: This is the first study to compare multiple classification systems for CP, evaluating change in disease category over a prolonged observation period. The results confirm that for clinical categorization, the Heidelberg, ABC and clinically based scoring systems are valid and practical.

207 RESECTION VERSUS HEAD CORING FOR HEAD MASSES IN CHRONIC PANCREATITIS

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AIM: Comparative study of resection (Whipple procedure) versus head coring (Frey procedure) in treatment of head masses in chronic pancreatitis. PATIENTS: During the period 1991–1997, 34 patients underwent head resection and 123 patients, a head coring. The two groups were similar in age, sex, etiology of pancreatitis, preoperative pancreatic function, associated co-morbid illnesses and size of mass. METHODS: The parameters studied were: 1. pain relief using a pain grading system, 2. functional results (endocrine and exocrine), 3. quality of life estimation. RESULTS: The results are shown in the Table. Patients with head coring had comparable relief of pain, with greater preservation of exocrine and endocrine function. CONCLUSION: Head resection causes severe pancreatic insufficiency and a poor quality of life in >50% of patients. Parenchyma-conserving operations are more suitable for patients with chronic pancreatitis.

<table>
<thead>
<tr>
<th>Parameter</th>
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<tr>
<td>Number</td>
<td>34</td>
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</tr>
<tr>
<td>Mortality</td>
<td>1</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Hospital stay (days)</td>
<td>17</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Pain relief</td>
<td>116</td>
<td>0.016</td>
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<tr>
<td>Deterioration in endocrine status</td>
<td>21</td>
<td>22</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Deterioration in exocrine status</td>
<td>24</td>
<td>27</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Good quality of life</td>
<td>16</td>
<td>89</td>
<td>&lt;0.01</td>
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208 ORGAN-PRESERVING RESECTION OF THE PANCREATIC HEAD IN PATIENTS WITH CHRONIC PANCREATITIS
Gyuhas Farkas, Laslo Leindler, Gyuhas Farkas Jr and Maria Daroczi, University of Szeged, Faculty of Medicine, Szeged, Hungary
INTRODUCTION: In chronic pancreaticitis (CP), enlargement of the head of the pancreas develops as a consequence of inflammatory alterations. A new safe procedure has been developed for duodenum-preserving pancreatic head resection for CP. This report is concerned with the results attained with this operation in the median follow-up period of 24 months.

PATIENTS AND METHODS: In 94 patients (male 71; female 23; mean age 46.3 years), a new surgical management was performed after the development of an inflammatory tumour of the pancreatic head. The preoperative morbidity comprised frequent abdominal pain, a weight loss in all patients, jaundice in 8 patients, and latent insulin-dependent diabetes mellitus (IDDM) in 8 and 8 patients, respectively. The diagnosis was confirmed by ERC, sonography and CT. Pancreatic functions were checked by means of the amylase tolerance test (ATT), the glucose tolerance test and stool elastase (Pancreatic Elastase, SchleBo, Germany). The surgical procedure consists of a wide excision of the inflammatory tumour in the region of the pancreatic head, without division and cutting of the pancreas over the portal vein. Reconstruction, with drainage of the secretion from the remaining pancreas into the intestinal tract, takes place through a jejunal Roux-en-Y loop. In 8 patients and in 12 patients with stenosis of the common bile duct, prepancreatic bile duct and the jejunum loop. RESULTS: Only one reoperation was performed as a consequence of anastomosis bleeding, but no mortality was noted in the postoperative period. The duration of hospitalization ranged between 7 and 12 days, with a median of 8.5 days. In the median follow-up period of 24 months (range 6-24), all the patients became complaint-free, and their weight increased with a median of 10 kg (range 4-25). After 1 and 2 years of operation bilio-digestive anastomosis was performed in 2 patients owing to bile duct stenosis and 4 patients were performed with total stomach diversion. The ATT and the stool elastase level demonstrated an exocrine function improvement (155 ± 8.5 to 122 ± 7.8%); 126.3 ± 34 to 134 ± 36 µg/g, respectively). No change was noted in the preoperative endocrine function of 78 patients but 4 patients with latent diabetes mellitus (DM) became IDDM and in 4 patients the latent DM improved. CONCLUSION: The results clearly reveal that this organ-preserving pancreatic head resection is a safe and effective procedure for definitive control of the complications following the inflammatory alterations of CP.

209 APACHE II SYSTEM IS BETTER THAN RANSON SYSTEM IN PREDICTING SEVERITY OF ACUTE PANCREATITIS
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BACKGROUND: Accurate prediction of severity of acute pancreatitis is important as early therapeutic interventions, such as endoscopic papillotomy and antibiotics, have been shown to improve survival. The aim of the study was to compare the accuracy of the two commonly used multifactorial scoring systems, Ranson and APACHE II systems, in predicting severity of acute pancreatitis in a local population.

PATIENTS AND METHODS: Between January 2002 and September 2003, 101 consecutive patients with acute pancreatitis were prospectively studied. Scoring at the time of diagnosis and at 48 h was performed for both Ranson and APACHE II systems. Systemic and local complications were defined in accordance with the Atlanta classification. The diagnostic accuracy was evaluated by sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and positive likelihood ratio (LR). Statistical analysis was achieved by a chi-square test using two-by-two contingency tables to determine significant relationship between disease severity and predictive tests. RESULTS: 12 patients (11.9%) suffered from severe disease. The etiology of acute pancreatitis was biliary stones in 59 (58.4%), alcoholism in three (3.0%), idiopathic in 23 (22.0%) and other factors in 16 (15.5%). Systemic complications were multi-organ failure in five (5.0%) and respiratory and renal insufficiency in two (2.0%). Five patients with multi-organ failure died (5.0% hospital mortality). All five (5.0%) local complications were pseudocyst formation. Both Ranson and APACHE II systems predicted severe pancreatitis (p = 0.001 and p < 0.001, respectively). The PPV and positive LR for Ranson score, APACHE II score at diagnosis and APACHE II score at 48 h were 28.6%, 61.5%, 81.8% and 3.0, 11.9, 34.1, respectively. 48-h APACHE II score, but not Ranson score or APACHE II score at diagnosis, correlated with the occurrence of local complications (p = 0.009). CONCLUSION: The APACHE II system is better than the Ranson system in the prediction of severity in acute pancreatitis. The 48-h APACHE II score provides the best prediction of both systemic and local complications.

210 NECROTIZING PANCREATITIS: PROSPECTIVE STUDY OF 127 CASES
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INTRODUCTION: Necrosis is a non-viable area of pancreatic parenchyma, typically associated with peri-pancreatic necrosis. Infected necrosis is the presence of pancreatic necrosis with positive bacteriological tests, in a clinical setting characterized by a marked early inflammatory response. The aim of this paper is to report our experience and current approach to the treatment of this condition. METHOD: In severe AP and necrosis (diagnosis is performed by CT scan with IV contrast), early antibiotics were initiated. Enteral nutrition was started as soon as possible to avoid bacterial translocation and post-gastric infarction. At sterile pancreatic necrosis is only a local lesion, it must not be punctured or injured if mild AP does not get worse, when there is suspicion of infection, when severe necropancreatitis improves or when it does not require other treatment than the one previously mentioned. Local necrosectomy (10 cm-long annular incisions ciprofloxacin) and evolves well, etiological treatment is performed; however, if it gets worse or infection is suspected, a percutaneous puncture must be performed. If bacteriological tests are positive, necrosectomy is performed. RESULTS: From April 1987 to July 2003, we treated and studied prospectively 895 patients with documented AP, 127 of which presented necrosectomizing pancreatitis; 75 men and 52 women with an average age of 44 years (24-78). Out of 127 patients, 47 had sterile necrosis, some associated with liquid collections that had received the medical treatment previously mentioned. The mortality rate was 17%: 8 severe patients died before the second week from early systemic complications with negative percutaneous bacteriological tests. The other 80 presented infected pancreatic necrosis (all with positive bacteriological tests): 6 received only medical treatment, due to patient refusal of surgical procedure or anesthetic contraindications (2 deaths). One patient had percutaneous drainage and 73 patients underwent surgery: 20 with close and drainage method, 7 of these had to be re-operated to complete necrosectomy (3 deaths) and 50 through open procedure with an average of 6 re-surgeries before closure (3-59) (10 deaths). All patients had positive bacteriological tests in several cultures. The mortality rate for infected necrosis was 19% (at study entry, there were 15 severe patients, 2 of whom could not be operated on). CONCLUSION: The tactical combination of different methods is a rational approach to decreasing mortality for necrosectomizing pancreatitis (18%): 8 of 47 in sterile necrosis and 15 of 80 in infected necrosis.

211 EXTENDED HEPATICŒJUNOSTOMY BY AN ANTERIOR APPROACH: TECHNIQUE AND RESULTS
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AIM: To assess the outcome of biliary reconstruction using a new technique based on a combination of the methods described for left- and right-sided complex stricture and injury. The new technique was designed to offer a simpler method of surgical repair, but with an improvement in long-term outcomes. STUDY DESIGN: Analysis of cases operated on for high biliary stricture and injury in a tertiary referral hepatobiliary unit between 1993 and 2002. Comparison is made to published literature and also a contemporary series of standard repairs for low biliary strictures and injuries carried out in the same unit by the same surgeons. PATIENTS AND METHODS: All patients undergoing surgery for high biliary strictures and injuries during the study period were included. The new technique was based on a modification of published approaches, but represents a significant extension into both the right and left hepatic duct systems. Furthermore, all is achieved by a straight forward anterior approach. The outcome measures assessed were: clinical symptoms after repair, liver function tests and the need for re-intervention following surgery. RESULTS: 24 patients underwent biliary reconstruction using the new technique and these were compared to 26 patients who underwent standard surgery for low stricture and injuries during the same period.
Postoperative morbidity was regarded as significant in 6 patients (25%), of whom five were having a revision of a failed previous reconstruction. There was one in-hospital death (8.3%) at 19 days postoperatively. There has been no clinical, biochemical or radiological indication of recurrence of biliary stenoses to date in 21 patients after a follow-up of mean duration of months (23–108 months). In two patients with significant intrahepatic stricture and fibrosis, the liver function tests have not returned to normal, but good symptomatic relief has been obtained. These results compared favourably with the low stricture group. CONCLUSION: This extended hepaticejunostomy by an anterior approach for high biliary stricture and injury achieved a satisfactory outcome in 96% of cases.

212 PORTAL VEIN THROMBOSIS AFTER LAPAROSCOPIC SPLENECTOMY
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PURPOSE: To examine the clinical presentation and risk factors for portal vein thrombosis occurring after laparoscopic splenectomy. METHODOLOGY: Cases of portal vein thrombosis were identified by clinical audit. All cases of laparoscopic splenectomy by the surgeons involved in the study period were examined by retrospective chart review. RESULTS: There were 7 cases of portal vein thrombosis identified out of 136 cases with an incidence of 5.1%. Massive splenomegaly, specimen weight, myelofibrosis and postoperative thrombocytosis were all significantly associated with the development of portal vein thrombosis. Massive splenomegaly was the most important risk factor. Patients presented with abdominal pain, fever and altered liver function tests. All presented within 15 days postoperatively, and 5 presented after initial discharge. Diagnosis was by USS and CT. One patient died. Six were successfully treated with anticoagulation. CONCLUSIONS: Portal vein thrombosis is a potential complication of laparoscopic splenectomy associated with massive splenomegaly. It is a potentially fatal complication but when suspected can be diagnosed by non-invasive imaging and treated with anticoagulation. Prophylaxis should be considered for high-risk cases.

213 IS RADICAL SURGERY USEFUL IN CARCINOMA OF GALLBLADDER
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BACKGROUND: Carcinoma of gallbladder is regarded as a fatal disease; however, a few recent papers have reported long-term survival after radical surgery. The aim of this study is to evaluate the role of radical surgery and to elucidate nodal status, its prognosis influence and the efficacy of lymphadenectomy. METHODS: From 1997 to 2002 a total of 603 patients with gallbladder cancer were treated at the Cancer Hospital & Research Institute, Gwalior. Radical surgery was performed on 69 patients with intent to cure. In this study analysis has been done only for those cases who were operated with intent to cure. There were 11, 19 and 39 patients with pT1, pT2 and pT4 disease respectively. Segment 4 and 5 resection was performed in 19 cases, right hepatectomy in 7 cases, HDp in 9 cases and gallbladder bed resection was done in 30 cases. All patients underwent systemic lymph node dissection, resection of bile duct was in 13 cases. A mean of 9 regional lymph nodes and 4 para-aortic lymph nodes were dissected per person. RESULTS: Various postoperative complications including wound infection, bile leakage and hepatic failure occurred in 25 (35%) patients. Three patients died due to acute postoperative complications. The rate of hospital death was higher in unresected cases (55%) than in resected cases (15%). The 1-, 3- and 5-year survival rates for all 69 patients with curative resection were 75%, 46% and 25%, respectively. There were statistically significant differences in survival in these three groups, i.e. inoperable, unresectable and resectable groups. The 46 patients (31.74%) with node positive disease included 10 with pN1 disease and 23 with pN2 disease. Nine patients (6.21%) had positive para-aortic nodes; postoperative survival was poor in patients with positive para-aortic nodes (1-year survival 33%, median survival 7.3 months). CONCLUSION: Radical cholecystectomy with or without pancreaticoduodenectomy has a definite advantage as regards overall survival and disease-free survival. However, it is associated with a higher rate of complications, so meticulous preoperative work-up is essential. Regional and para-aortic lymphadenectomy does not provide a survival benefit for patients with advanced gallbladder carcinoma with para-aortic lymph node metastasis.

214 SURGICAL OUTCOME OF 412 HEPATOCENTEROSTOMIES
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Endoscopic treatment of biliary obstruction is preferred to surgical treatment because of the effective relief of jaundice and low complication rates. However, stent exchanges are needed frequently and therefore cause considerable morbidity. Surgical bypass procedures offer optimal long-term palliation of obstructive jaundice but are associated with higher initial morbidity and mortality rates. Recent data show improved results after surgical drainage procedures. The aim of this study was to analyse the surgical outcome of the three most important patient groups undergoing surgical biliary drainage. Perioperative parameters were analysed for 412 consecutive patients who underwent a hepatocenterostomy (HE) between 1992 and 2003. 277 patients underwent a HE for a peritumoural malignancy, 37 for chronic pancreatitis and 98 for a bile duct injury. Hospital mortality was 3% (7 patients), 0% and 0% and the median postoperative hospital stay was 10, 8 and 9 days after a HE for malignancy, pancreatitis and biliary duct injury, respectively. The overall complication rate was 29%, 27% and 23% and the rates for severe complications were 1%, 0% and 4% for anastomotic leakage, 3%, 5% and 1% for intra-abdominal hemorrhage and 3%, 0% and 2% for abdominal abscesses after a HE for malignancy, pancreatitis and bile duct injury, respectively. The incidence of a relaparotomy during the initial stay was 3%, 8% and 6%. The indications for a relaparotomy were mainly anastomotic hemorrhage, leakage and drainage of intra-abdominal abscesses. Mortality after surgical biliary drainage is relatively low, hospital stay is short and the rates of severe complications are acceptable. Therefore, surgical biliary drainage is a good alternative for the endoscopic treatment of biliary obstruction.

215 LONG-TERM OUTCOME OF ROUX-EN-Y HEPATICOJEJUNOSTOMY WITH STOMATIZED LIMB FOR BENIGN BILIARY STRUCTURES
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Benign strictures of the extrahepatic biliary tract represent a difficult problem with reported recurrence after resection in 10–30% of the cases. This report details the results obtained in patients managed by the technique of hepaticojejunostomy with access loop formation. During the period 1990-2003, 23 patients (16 females, 7 males) aged 40-74 years (mean 57.6 years) with benign strictures of the extrahepatic biliary tract were operated on. The iatrogenic injury was sustained at cholecystectomy – with or without bile exploration – in 21 cases. Two cases had a history of penetrating abdominal injury. All the patients had been undergone 1-4 (mean 1.8) biliary operations before they were referred to our department. For the precise localization of the obstruction, percutaneous transhepatic cholangiography (PTC) in the first 16 cases and PTC combined with MRCP in the last 7 cases were performed. According to the Bismuth classification, 18 of the strictures were level II, 4 were level III and one was level V. All the patients underwent Roux-en-Y hepaticojejunostomy with exteridion of the extended limb of the Roux loop to the skin. There was no 30-day mortality. Complications occurred in 5 patients: anastomotic leak in 2 (with biliary fistula closed spontaneously within 6-7 days), wound infection in 2, and one of each of pulmonary infection and incisional hernia. The mean postoperative hospitalization was 9.5 days (7-16 days). Postoperative trans-stoma cholangiogram or introduction of an endoscope via the stomaized jejunal limb was routinely performed to examine the anastomoses. During a mean follow-up period of 7.5 years (1-13 years), no recurrent stricture or intrahepatic stone formation occurred. Limb stomas, producing only minimal discomfort, were closed at 4 years. Their blind end remained subcutaneously. Roux-en-Y hepaticojejunostomy for Bismuth II, III and V benign biliary stenoses are often satisfactory long-term outcome. Routine stoma formation of the Roux loop secures direct access for radiological or endoscopic intervention, but our results show that it is unnecessary for lesions of level II.
216 OUTCOME FOLLOWING RIGHT TRISEGMENTECTOMY WITH CAUDATE LOBECTOMY FOR HILAR CHOLANGIOCARCINOMA

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BACKGROUND: The effect of combined liver resection for hilar cholangiocarcinoma (HC) was not proved until the late 1980s, because of both high postoperative mortality and the difficulty in obtaining pathological confirmation. Since the excellent paper of Dr. Naito published from Nagoya University in 1990, liver resection including caudate lobectomy (CL) has been accepted as an adequate treatment modality for HC. However, the optimal extent of hepatic resection has not been determined so far. PURPOSE: We conducted this study to assess the safety of right trisegmentation (RTS) with CL for HC through the analysis of postoperative mortality and morbidity and to evaluate the effect through the analysis of the pathological curability and overall survival. PATIENTS AND METHODS: Retrospective clinicopathological analysis was performed for 16 HC patients who underwent RTS with CL from June 1999 to April 2003 compared with 24 HC patients who underwent right lobectomy (RL) or extended right lobectomy (ERL). The 16 patients in the RTS with CL group consisted of 12 males and 4 females and the mean age was 59.6 years. Median follow-up period was 14.4 months and preoperative Biornuth-Corlette type was type II in 4, type IIIa in 10 and type IV in 2. 2 patients received additional pancreaticoduodenectomy owing to invasive carcinoma in the distal resection margin. Survival rates were obtained by the Kaplan-Meier method with the Breslow and Gart-Williams, Breslow's modified life table. Median surgical time estimated blood loss and transfusion amount was 510 min, 800 ml and 0 pint, respectively. Postoperative complications including 2 chronic liver failures developed in 12 cases, but no in-hospital deaths occurred. Postoperative pathological examination showed peripancreatic and pathological cancer invasion in the proximal resection margin, although 3 cases had carcinoma in situ lesions in the distal margin. During follow-up periods, 3 cases developed recurrences and 3 patients died. 1-, 2- and 3-year survival rates were 81%, 62%, and 49%, respectively. The ERL group had an in-hospital mortality rate of 8.3% (2/24), cancer positive proximal margin of 12.5% (3/24) and 3-year survival rates of 40%. CONCLUSION: RTS with CL is an effective and not dangerous surgical procedure achieving low mortality rates and high pathological curability for HC except type IIIb HC. Better survival rates following this procedure could be expected through long-term follow-up.

217 RE-SURGERY FOR INCIDENTAL GALLBLADDER CANCER – A SINGLE INSTITUTION EXPERIENCE

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BACKGROUND: Incidentally diagnosed gallbladder cancer is becoming increasingly common, especially with the advent of laparoscopic cholecystectomy. Depending on the histological staging, revision surgery is offered to patients who have infiltration beyond the muscular layer of the gallbladder. This re-surgery provides a statistically significant benefits comparable with per-primum resected cases. AIM: The aim of this study was to review our single-centre large experience in dealing with patients with incidentally diagnosed gallbladder cancer. PATIENTS AND METHODS: A prospective database of patients who underwent gallbladder resection for gallbladder cancer at our institute from 2000 until 2002. A total of 51 patients underwent surgery for gallbladder cancer: 31 had re-surgery for incidentally diagnosed cancer gallbladder who had undergone surgery elsewhere. This group was analysed with regard to whether the timing of the re-surgery or the nature of the previous surgery – laparoscopic or open cholecystectomy – had an impact on the peri-operative outcome in terms of resectability as well as on the long-term outcome. RESULTS: Out of the 31 patients, 22 (70.9%) had successful resection with the rest having unresectable disease. As compared to this, in the group undergoing per-primum surgery, 11 patients (55%) out of 20 had resectable disease. In the re-surgery group, 12 patients had undergone open cholecystectomy, 15 laparoscopic cholecystectomy and 4 some other surgery. In the laparoscopic group, 10 out of 15 (66.67%), in the open surgery group 9 out of 12 (75%) and in the other surgery group 3 out of 4 (75%) had resectable disease at re-surgery. The impact of the time lag between the cholecystectomy and the re-surgery as regards resectability was as follows. Re-surgery within 1 month of postoperative pathological examination showed no pathological cancer surgery between 1 and 3 months, 11/18 (61.1%) and re-surgery after 3 months, 8/10 (80%) had resectable disease. There was no peri-operative mortality in this series, and the major morbidities were wound infections (5.8%), bile leak (3.9%) and intra-abdominal collection (3.9%). At 1-year follow-up, of 27 evaluable patients, 19 were disease-free and 8 patients were alive with recurrence. CONCLUSIONS: It seems from our results that neither the approach of the previous cholecystectomy (whether laparoscopic or open), nor the timing of the re-surgery has any significant impact on resectability. Re-surgery can be performed safely at specialist centres and should be offered to patients who have incidential gallbladder cancer with infiltration beyond the muscularis layer.

218 MANAGEMENT OF CHOLEDOCHAL CYSTS IN ADULTS TREATED BY COMPLETE EXCISION: A WESTERN SINGLE INSTITUTION EXPERIENCE

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Cancer arising in choledochal cysts (CC) is in part related to the presence of pancreatico-biliary maljunctions (PBM) with pancreatic reflux into biliary tree. Preventive excision of the common bile duct including the CC is the recommended treatment. However, the extent of this resection is not well standardized. During the past 10 years we performed routinely as a policy, complete excision (CE) for type I or IV CC. The principal aim of this study was to evaluate the morbidity of CE, especially after extensive intraparenchymal dissection of choledochus. Among 30 consecutive adult patients presenting a CC, 23 (76%) had type I or IV CE was performed in 26 (87%) cases. In 13 cases (43%) all with demonstrable PBM, the CE was prolonged to the intraparenchymal portion of the end of choledochus. For the first cases this extensive dissection of the end choledochus was performed by passing through extra- or intramural plane of choledochus (classic technique), while the resection in the vascular plane of epchenal ductal plexus (Pediatric Ando's technique). Three patients (10%) presented cholangiarcinoma (2 with PBPM). In 2 of the 3 cases, preoperative investigations were considered as normal. Two patients died after 14 and 34 months. The overall morbidity of CE was 9/26 (35%). The proper morbidity of extensive intraparenchymal dissection was 4/13 (30%). Among 4 operated patients, 3 (75%) had extensive intraparenchymal dissection, according to classic technique. No major morbidity was observed for patients following extensive intraparenchymal dissection of choledochus when dissection was inside epchenal ductal vessels plane (p < 0.05). Amylase concentration in the bile was significantly higher in patients with individualized PBM vs those without (p < 0.005) and in unclear cases made it possible of revise the diagnosis of CC. Our results suggest that (i) CE with extensive intraparenchymal dissection of the choledochus in presence of PBM can be safely performed passing by the plane of epchenal ductal vascular plexus; (ii) in all cases, routine frozen sections should be performed so as to misdiagnose an early stage of cancer.

219 MICROCALCULI IN COMMON BILE DUCT: ANY ROLE FOR LAPAROSCOPIC ULTRASONOGRAPHY AFTER PRE-CHOLECYSTECTOMY DUCTAL CLEARANCE BY ERCP?

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Background: Laparoscopic ultrasound (LUS) during laparoscopic cholecystectomy (LC) has been a valid alternative to preoperative cholangiography in detecting stones in the common bile duct (CBD). The aim of this study was to determine the role of LUS and its clinical significance when CBD stones were detected by LUS after pre-operative ERCP with ductal clearance. Methods: LUS was performed in 25 patients undergoing LC for biliary pancreatitis (n = 11) or gallstones/CBD stones (n = 14). All patients received pre-operative endoscopic retrograde cholangio-pancreato-raphy (ERC/P)/sphincterotomy. The presence and the size of the CBD stones were recorded by LUS during operation. Microcalculi (<0.5 mm) in CBD were left behind and these patients were followed up with liver function tests and transabdominal ultrasound. RESULTS: During LC, LUS identified CBD stones in 4 patients (16%). One patient had a 1-cm stone and exploration of CBD was performed at the same setting. The other 3 patients who had microcalculi (<0.5 mm) in the CBD were simply put under observation. They all showed no abnormality in liver function and transabdominal ultrasound subsequently. They all remained symptom-free. Conclusion: LUS is a non-invasive way of identifying calculi in CBD during LC. Microcalculi detected in CBD intraoperatively (LC) can be managed safely without surgical exploration.
211 INCIDENCE AND IMPACT ON SURVIVAL OF LYMPH NODE METASTASES IN PATIENTS WITH COLORECTAL LIVER METASTASES
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AIM: Lymph node metastases are well known negative prognostic factors in oncologic surgery. The role of regional lymphadenectomy after liver resection for secondary malignancies is still unknown. We evaluated prospectively the incidence and the impact on survival of lymph node metastases in patients with colorectal hepatic metastases. METHODS: From April 1990 to January 2003, 92 patients with colorectal liver metastases were prospectively enrolled in this study. There were 28 (53.8%) male and 24 (46.2%) female. Mean age was 61.6 ± 9.5 years (range: 40–77 years). Mean number of metastases was 2.1 ± 1.2 (range 1–7). Mean diameter was 4.8 ± 2.0 cm (range 1–15). Preoperative CT scan evaluation of lymph node status and definitive histologic findings were also compared. Liver resection was performed together with lymphadenectomy around the hepatic pedicle, pancreatic space, common bile duct and celiac axis. All patients received adjuvant chemotherapy. Mean postoperative follow-up was 28 months. RESULTS: A wedge resection was performed in 12 pts (23.1%), segmentectomy in 23 (44.2%), and major hepatectomy in 17 (33.7%). The median number of dissected lymph nodes was 6.1 ± 4.1 (range 4-16). Mean postoperative stay was 9.2 ± 1 days. Postoperative complications appeared in 17 (32.7%) patients; none of them was related to lymph node dissection. One patient died postoperatively secondary to myocardial infarction. Tumor tissue in dissected lymph nodes was found in 7 (13.5%) patients. The 1- and 3-year survival was 53.5% and 35.7% in patients with lymph node metastases, and 95.3% and 68.7% in patients without metastatic lymph nodes, respectively (p < 0.01). Two (28.5%) patients with lymph node metastases survived >3 years. The sensitivity and specificity of CT scan in detecting LN metastases were 42.8% and 88.8%, respectively. CONCLUSIONS: Liver resection with regional lymphadenectomy is a safe procedure, which should be applied in patients with colohepatic hepatic metastases in order to stage the disease precisely. CT scan does not seem reliable in the evaluation of lymph node status. Despite the dismal results expected in patients with lymph node metastases, this latter should not be considered an absolute contraindication to surgical approach.
systemic treatment. METHODS: Eighteen breast cancer patients (aged 30–77, median 50.4 years old) with LM as the sole site of metastatic disease underwent resection and/or radiofrequency ablation (RFA) between May 1996 and February 2002. The stage of the breast primary was I in 1 patient, IIA in 4 patients, IIB in 2 patients, IIIB in 6 patients, and IV in 5 patients. LM developed after a median time of 49.2 months (range 15–136 months) from initial diagnosis in 13 patients. In 5 patients who presented with synchronous breast/liver lesions, liver surgery was performed 2–12 months prior to breast surgery. The number of LM was 1, 2, and 3 or more in 10, 6, and 2 patients, respectively. Most of the patients first metastasis (81%) was to the liver. These patients had a dismal median survival of 5–7 months if treated with surgery and conventional chemotherapy. PATIENTS AND METHODS: The department of ophthalmology in our hospital treats approximately 50 new cases of uveal melanoma each year. Patients are then followed for the occurrence of liver metastasis with quarterly liver function tests and biannual ultrasound scans. Between October 1994 and November 2003, 20 consecutive patients with uveal melanoma were referred for surgery with isolated liver metastasis. These patients underwent various hepatic resections. Operative times were classified as ‘curative’ if the entire tumor appeared to be excised or ‘tissue for vaccination’ preparation if the tumor was not fully resectable. In all cases some tumor was sent for attempted preparation of an autologous vaccination. A Port-Cath catheter was inserted into the hepatic artery for regional chemotherapy via the gastroduodenal artery in 17 patients. Data regarding the primary uveal melanoma, surgical procedures, neoadjuvant, immunotherapy, vaccination and outcomes were reviewed retrospectively. RESULTS: 20 patients with uveal melanoma presented with isolated liver metastasis. They presented on average 49 months (range 1–144 months) after initial treatment of their uveal melanoma. The median age at hepatocarcinoma was 57 (range 30–84 years). 23 operations (22 hepatectomies and one distal pancreatectomy) were carried out, without perioperative deaths. Early postoperative complications occurred in 32% of patients and included pulmonary emboli, bile leak, broken drain and wound infection. 9 patients underwent curative resections (11 operations), 11 patients were not fully resectable and underwent limited resections enabling vaccination preparation. The median crude survival for curative resection (range 11–81 months) was 100% at a half year, 88% at 1 year, 71% at 2 years and 33% at 5 years. The median crude survival for non-curative resection (range 2–19 months) was 82% at a half year, 40% at 1 year, 10% at 1.5 years and 0% at 2 years. Of our 20 patients: 4 are disease-free, 1 is alive with disease, and 15 are dead. CONCLUSION: Patients with uveal melanoma and metastases to the liver gain from an aggressive multimodal treatment. Complete surgical resection of metastatic uveal melanoma combined with neoadjuvant, immunotherapy or vaccination improves expected outcome. Early detection of liver metastasis is crucial. We found a crude survival of 57% at 4 years when curative resection is possible.

226  THE SIGNIFICANCE AND CLINICAL FACTORS ASSOCIATED WITH A SUB-CENTIMETER RESECTION OF COLORECTAL LIVER METASTASES

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INTRODUCTION: Prognosis after resection of colorectal liver metastases is influenced by various factors. A positive surgical margin has been shown to adversely influence prognosis. Although a 1-cm margin has been accepted as adequate, the data to support this are sparse. METHODS: Our hepatobiliary database was queried for patients undergoing liver resection for colorectal metastases between January 1992 and July 2003. Standard demographic, clinicopathologic, and outcome variables were recorded. All patients were divided into three groups: margin of resection (MOR) < 0.5 cm (group A), between 0.5 and 1 cm (group B), and >1 cm (group C). In addition, operative reports from each hepatic resection were analysed to determine local factors that may have contributed to a sub-centimeter resection. Standard statistical calculations were performed. RESULTS: 114 patients (67 males, 45 females), with a mean age of 64 (range 35–89) underwent liver resection for colorectal liver metastases, 53 patients were in group A, 26 patients were in group B, and 33 patients were in group C. Two patients had positive surgical margins and were excluded from analysis. There were no differences in age, sex, tumor location, tumor size, tumor differentiation, Duke’s stage, pre-operative CEA level, number of metastases, distribution of metastases, or need for blood transfusion between the three groups (p > 0.05). Group C patients demonstrated decreased local recurrence (LR) (z2 = 11.1, p = 0.003) and distant recurrence (DR) (z2 = 9.5, p = 0.008). In addition, Kaplan–Meier survival analysis confirmed significant differences in time to LR (p = 0.003) and DR (p = 0.003) by log-rank test. A trend towards improved survival was noted for group C (92.6 months), when compared to groups B (49.1 months), and A (27.6 months). After evaluation of the operative reports, factors associated with a sub-centimeter resection included non-anatomic resection (z2 = 6.309, p = 0.043), proximity to a major vessel (z2 = 1.442, p = 0.003) and location of the liver (p = 0.008). These characteristics were most prevalent in group A. CONCLUSION: A sub-centimeter resection for colorectal liver metastases is associated with increased local and distant recurrence, as well as a trend towards decreased overall survival. Considerations should be made for extended resections when tumors are centrally located or near major vessels. When a non-anatomic resection is being performed, MOR > 1 cm should be attempted as an adequate margin is often underestimated.

227  COMBINED MODALITY TREATMENT AT OPERATION FOR HEPATIC METASTASES OF NEUROENDOCRINE AND CARCINOID TUMORS

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BACKGROUND: Surgical cytoreduction and endocrine manipulation are the standard of care for neuroendocrine liver metastases. Recently, ablation has been used in conjunction with liver resection in patients who cannot be completely resected. METHODS/RESULTS: 82 patients (pts) undergoing operation for neuroendocrine liver metastases from 1995 to 2003 were identified from a prospectively gathered database. 45 (55%) were female. Mean age was 55.9 years (+/− SD 13.5), 49 (59.8%) of pts had carcinoid tumors; 31 pts (37.8%) had islet cell or non-carcinoid neuroendocrine tumors. 52% had evidence of endocrinopathy. Primary sites included pancreas (35.4%), small bowel (29.3%), colorectum (12.2%), and appendix/cecum (8.5%). Mean time from primary resection to hepatic operation was 40 months (median 15.9) (Table 1) overleaf. Mean length of

Operation | Number | %
--- | --- | ---
Lobectomy | 19 | 23.2
Segmentectomy | 8 | 9.8
Wedge | 5 | 6.1
Ablation | 14 | 17.1
Anatomic + ablation | 24 | 29.3
Non-anatomic + ablation | 3 | 3.7
Exploration/ biopsy only | 9 | 11
Total | 82 | 100
stay was 7.25 days (median 7, SD 3.4). 19.5% of pts had complications, including abscess (n = 4), hepatic insufficiency, biliary leak, and wound infection (n = 2 each). There were no perioperative deaths. Mean follow-up from liver diagnosis was 45.7 months (range 2.3–236.8). Kaplan–Meier survival curves were generated for pts with carcinoid versus non-carcinoid tumors. Mean survival for pts with non-carcinoid neuroendocrine tumors was estimated at 109.5 months after liver diagnosis (mean 90.2, SE 7.5). Pts with carcinoid tumors survived longer than patients with other neuroendocrine tumors; lack of deaths precluded precise estimates with current follow-up. CONCLUSIONS: Pts with neuroendocrine hepatic metastases can undergo surgical therapy with a moderate complication rate and hospital stay. Pts with carcinoid liver metastases may have longer survival than those with other neuroendocrine tumors. We recommend a combined strategy of liver resection performed together with ablative therapy of unresectable lesions, in order to debulk these progressive, often symptomatic tumors, because a significant proportion of affected patients will have meaningful long-term survival.

228 EVOLUTION OF MISSING COLORECTAL LIVER METASTASES FOLLOWING INDUCTIVE CHEMOTHERAPY AND HEPATECTOMY
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BACKGROUND: A dramatic response to chemotherapy in some patients with multiple bilateral and initially unresectable liver metastases (LM) from colorectal cancer sometimes leads to their disappearance from imaging studies. Our study was aimed at assessing the evolution of these metastases when they were also not found during liver surgery. PATIENTS: Among 104 hepatectomized patients for colorectal LM in 4 years, 15 patients were retrospectively eligible. Eligibility criteria were: initially unresectable LM, a dramatic response to chemotherapy and the complete disappearance of at least one LM on imaging studies (ultrasonography, computed tomography and magnetic resonance) during >3 months. In 4 patients (27%), the disappeared LM could be found and treated at laparotomy. The main selection criterion for the 11 studied patients of this series was the impossibility of finding and treating the disappearing LM sited in the remaining liver after hepatectomy, resulting in ‘missing LM’. RESULTS: After a median follow-up of 19 months (range 6–50) for the series, 8 patients among the 11 (73%) did not present any recurrence of the missing LM. The median follow-up was 20.5 months for these 8 patients. The 3 recurrences occurred respectively at 5, 5, and 8 months after surgery. CONCLUSION: The disappearance of LM after chemotherapy on high-quality imaging studies and after intraoperative liver exploration resulted in their definitive cure in approximately 70% of cases. The current dogma stipulating an obligatory resection of the initially affected part of the liver is no longer acceptable.

229 RESECTION MARGIN IN PATIENTS UNDERGOING HEPATECTOMY FOR COLORECTAL LIVER METASTASIS (A CRITICAL APPRAISAL OF THE 1-CM RULE)
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AIMS: To evaluate the influence of resection margin involvement and its width on survival and postoperative disease recurrence after hepatectomy for colorectal liver metastasis. PATIENTS AND METHODS: Retrospective, longitudinal study of 294 consecutive patients, all underwent primary liver resection for colorectal metastasis between January 1993 and December 2001. Clinical, pathological and outcome data were reviewed using a prospectively collected database. Patients who died in hospital were excluded from disease recurrence analysis. Cases were stratified into those with involved and non-involved resection margins. Different non-involved margin widths were analysed against survival, recurrence rate, pattern (hepatic, extra hepatic) and timing (<12 months, >12 months) of recurrence. Univariate and multivariate analysis was carried out to assess which variables influenced patients’ survival. RESULTS: The 1-, 3-, and 10 years actuarial survival rates were 82%, 58%, 43%, 35%, respectively. The median survival was 46 months. Six factors were found to have an effect on survival by univariate analysis: age, primary nodal status, intraoperative blood transfusion, histological liver resection margin involvement, size of largest liver metastasis and presence of multiple satellite nodules. On multivariate analysis only primary tumour nodal status, intraoperative blood transfusion and resection margin involvement remained independent predictors of survival after surgery. Further analysis of survival was then undertaken in patients whose resection margin was free of tumour. 1-, 2-, 3-, and 10-mm resection margin widths were found not to be significant in influencing patients’ survival or recurrence rate. They had no significant correlation to the recurrence pattern and timing of recurrence. CONCLUSION: A positive hepatic resection margin was associated with a higher incidence of postoperative recurrence and lower survival rate. The width of the resection margin did not influence the postoperative recurrence rate, pattern and timing of recurrence.

230 A STAGED OPERATIVE APPROACH FOR PATIENTS WITH SYMPTOMATIC CARCINOID-RELATED CARDIAC AND LIVER DISEASE
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BACKGROUND: In patients with metastatic carcinoid disease, liver resection has been shown to be a useful method of palliation and improves survival. Carcinoid syndrome with significant right heart failure and liver congestion occasionally precludes liver resection due to operative risk. Our aim is to evaluate the outcome of a staged, operative approach of cardiac valve replacement prior to liver resection for symptomatic carcinoid syndrome. METHODS: A retrospective review of all patients from 1976 to 2003 of all patients having staged cardiac valve procedures and liver resection for carcinoid syndrome. RESULTS: A total of 5 patients (3 male) with a mean age of 54 (range 34–70) underwent liver resection for symptomatic metastases after cardiac valve replacement. Preoperatively, all patients had significant symptomatic right heart failure and ‘pulsatile’ liver congestion presenting an operative risk preclusive for liver resection. All patients underwent tricuspid valve replacement with significant clinical improvement and subsequently underwent liver resection after a mean of 3 months (range 2–5). Liver resection included a mean of 3 segments (range 2–4) in addition to subsegmental wedge resections to achieve a gross curative resection or maximal tumor debulking. Morbidity and mortality were 40% and 0% respectively. All patients are alive at follow-up for a mean of 52 (range 28–94) months. All patients had resolution of carcinoid-related symptoms after liver resection. Only two patients developed recurrent symptoms after 11 and 19 months requiring re-institution of octreotide acetate (Sandostatin). These data compare favorably with our institutional controls of patients undergoing liver resection for carcinoid syndrome without significant right heart failure. CONCLUSION: A staged surgical approach for patients with significant carcinoid-related, right heart failure and hepatic metastases is feasible, rendering a subgroup of patients candidates for liver resection to provide optimal palliation and improve survival.

231 HEPATOPANCREATICODUODENECTOMY WITH ZERO MORTALITY FOR ADVANCED BILIARY MALIGNANCIES
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Hepatopancreatoduodenectomy (HPD) is theoretically a most curative en bloc resection for advanced biliary malignancies involving hepatopancreaticoduodenal ligament. However, reported mortality and morbidity after HPD have been inhibitory high, around 20% and 100%, respectively, and HPD has not
been accepted as a routine procedure for biliary cancers. To increase the safety of this aggressive procedure, we have devised three modifications: 1. preoperative portal vein embolization (PVE) to increase remnant liver volume over 40% and thus reducing the risk of postoperative liver failure, 2. omental graft to cover major arteries including common hepatic artery and the stump of gastroduodenal artery, 3. two-staged pancreaticojunostomy following complete external drainage of pancreatic juice. The latter two avoid the fatal outcome associated with pancreaticojejunal anastomotic leakage. The whole procedures of HPD including the above modifications are presented in the video. PATIENTS: From January 1996 to July 2003, 10 cases underwent HPD. There were 6 cases with wide-spread bile duct cancer and 4 cases with gallbladder cancer. Eight cases underwent PVE and subsequent extended right hepatectomy. The %volume of the left liver increased from 36.0 ± 2.5% (mean ± SE) to 45.5 ± 1.9%. Mean operative time was 822 min (range 625–1050) and mean intraoperative blood loss was 1256 ml (500–2060). There was no mortality, and maximal postoperative serum level of total bilirubin was 2.3 mg/dl (0.4–7.9). Morbidity rate was 50%, but most of them were not severe. Postoperative complications were intra-abdominal abscess (1 case), pancreatic leakage (3 cases), pulmonary embolism (1 case), and ileus (1 case). Mean hospital stay was 34.7 days (16–63). The 2nd stage reconstruction was performed 99–160 days (mean 116 days) after HPD. The median follow-up period was 15 months (2–91) and 3 patients died of recurrent disease. CONCLUSION: We have established a safe HPD procedure with 3 modifications listed above. Patient selection for HPD is yet to be determined.

232 PROXIMAL SPLENORENAL SHUNT FOR MASSIVE SYMPTOMATIC SPLENOMEGALY IN NON-CIRRHTIC PORTAL HYPERTENSION
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BACKGROUND: Massive splenomegaly with concomitant hypersplenism is a presenting feature in non-cirrhotic portal hypertension. Splenectomy with proximal splenorenal shunt is an effective solution for this. PATIENTS AND RESULTS: Splenectomy with non-cirrhotic portal hypertension was subjected to proximal splenorenal shunt surgery over the past 18 months for giant splenomegaly (>15 cm) with concomitant hypersplenism (platelets <100,000/mm and WCC <4000/mm) owing to massive variceal bleed (2) nid bleeding tendency due to low platelets (4). Preoperative splenic vein patency was confirmed by Doppler ultrasonography. Mean operating time was 5 h (4–6 h) and blood transfusion requirement 2 units (0–3 units). Median hospital stay was 10 days (7–21 days). There was no mortality. One patient developed central line sepsis and one had transfusion-related multiple organ failure. Shunt patency was confirmed on D-echoreasonography. Three patients completing 6-month follow-up had variceal obliteration confirmed on endoscopy. Postoperative thrombocytopenia is the rule requiring low dose aspirin therapy. CONCLUSIONS: Proximal splenorenal shunt is a safe and effective treatment for massive splenomegaly in non-cirrhotic portal hypertension. Postoperative thrombocytopenia follows.

233 TRANSDUODENAL BILIARY AND PANCREATIC DUCT SPHINCTEROPLASTIES WITH PANCREATOBILIARY SEPTECTOMY FOR CHRONIC RELAPSING PANCREATITIS
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A 40-year-old woman with chronic, recurrent pancreatitis presented with a pancreatic duct stricture just proximal to the ampulla. She underwent endoscopic biliary and pancreatic duct sphincterotomies on two occasions but continued to have persistent relapsing pancreatitis and a persisting distal pancreatic duct stricture. Biliary manometry revealed residual biliary sphincter pressure and an elevated pancreatic duct pressure of 40 mmHg. She underwent open operative transduodenal biliary and pancreatic duct sphincteroplasties along with pancreatic septectomy. This video will discuss the indications, approach, and operative technique of this unusual biliary and pancreatic operation.

234 SURGICAL AMPULLECTOMY FOR PRESUMED BENIGN AMPULLOMAS
Alain Suvanet, Réza Kianmanesh and Jacques Belghiti Beaujon, Clichy, France
Presumed benign ampullomas can be treated by pancreaticoduodenectomy or ampullectomy. This latter can be performed surgically or endoscopically. The aim of this video is to describe surgical ampullectomy (SA) and to underline its advantages. SA is indicated in patients with ampullomas presumed to be benign after duodenoscopy with multiple biopsies and endoscopic ultrasound. High-grade dysplasia on preoperative biopsies is not a contraindication to SA. Previous endoscopic sphincterotomy generally results in absence of bile duct dilatation but does not preclude SA. After Kocher maneuver and cholecystectomy with insertion of transcutaneous drainage, the duodenum is entered through a longitudinal incision on the antimesenteric aspect of D2. The bilio-pancreatic orifice is localized by blue dye injection through the transcutaneous drainage and the ampulla is grasped by a U-shaped stitch. With gentle traction on the tumor, a margin 2–3 mm wide is delimited on the duodenal mucosa. The duodenal wall is incised and all submucosal vessels are ligated with fine absorbable monofilament sutures. Use of electrocaurolisation should be avoided to prevent postoperative hemorrhage. Resection of duodenal musculature proper allows isolation of both biliary and pancreatic ducts at their emergence from pancreatic parenchyma. In case of large tumors, resection of both mucosal and submucosal layers are delineated by the tumor limits but resection of muscular propria should be localized around the Oddi’s sphincter. The ensuing duct is transected and the margin is sent for frozen section. The common bile duct can be further mobilized from the pancreas and is transected. Frozen section is performed on both ductal and duodenal margins, and on enlarged peripancreatic lymph nodes if present. The biliary and pancreatic ducts are sutured together with fine absorbable monofilament sutures, with careful assessment of ductal patency. The duodenotomy is closed longitudinally with running suture and its tightness is tested by injection of air through the transcutaneous drain. This drain is ultimately removed with ligation of the cystic duct. A soft open drainage is left close the duodenal suture. SA allows resection of presumed benign ampullomas with intra-operative assessment of adequate margins. Involvement of lateral margins can be recognized intraoperatively and treated by extension of resection. Pancreaticoduodenectomy can be safely indicated in patients with good general condition either intraoperatively (positive final margins, lymph node metastasis) or postoperatively (if definitive pathological examination shows invasive carcinoma).

235 LAPAROSCOPIC COMMON BILE DUCT EXPLORATION AND CHOLEDOCHOUDENOSTOMY
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Complex biliary procedures such as biliary reconstruction represent a relatively untested frontier in laparoscopic surgery. Our patient is a 70-year-old female who presented with obstructive jaundice secondary to a 1.3-cm primary cholangiocarcinoma. This tumor is to be resected via laparoscopic common bile duct exploration, including a choledochoectomy, common bile duct exploration with cholecystectomy and ultrasound-guided Fogarty balloon stone extraction. A side-to-side choledochooduodenostomy is then performed. Operative time is 360 minutes, estimated blood loss 55 ml. The patient was discharged home on the third postoperative day and was well and complication-free at 22-month follow-up.

236 LAPAROSCOPIC HAND-ASSISTED PANCREATICODUODENECTOMY
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BACKGROUND AND AIMS: The limited world experience with laparoscopic pancreaticoduodenectomy (PD) had, by and large, been unfavourable. More recently, the laparoscopic hand-assisted approach to PD has been promising. We report the first successful UK experience with laparoscopic hand-assisted PD (LHAPD). METHODS: A 62-year-old man presented with painless obstructive jaundice, and was found to have an ampullary tumour at endoscopy. Preoperative biopsies confirmed an adenocarcinoma, and computed tomography showed no evidence of either vascular involvement or metastatic disease. A staging laparoscopy showed no intra-abdominal metastases, and a LHAPD employing a Gelport was performed. RESULT: The intraoperative course was uneventful and two units of blood were transfused. No postoperative blood transfusion was required. The operative time was 11 h (and 30 minutes break). The postoperative recovery was uneventful but for superficial pressure sores over the buttocks and elbows. The patient resumed oral fluid and dietary intake on the 1st and 3rd postoperative days respectively, and was discharged from hospital on the 9th postoperative day. Histology demonstrated an ampullary adenocarcinoma with clear margins and involvement of 2 of 13 lymph nodes examined. At 2 months follow-up, the patient remains well
and is receiving adjuvant chemotherapy. CONCLUSION: The LHAPD may be performed safely in the selected patient and achieves good oncological clearance. The early promising results with this approach will undoubtedly encourage an expansion of experience and are likely to widen the selection criteria for this procedure.

Organ-preserving pancreatic segmentectomies for benign or low grade malignancies

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According to an anatomical pancreatic classification, the pancreas is divided into four segments: proximal, posterior, medial and distal – that is to say the ventral pancreas is renamed the posterior segment, and the dorsal pancreas is composed of the proximal, medial and distal segments. To prevent insufficiency of exocrine and endocrine function of the pancreas, we perform various organ-preserving pancreatic segmentectomies, such as duodenum-preserving pancreatic head resection with preservation of the bile duct or without (DpPHR: both proximal and posterior segmentectomy), dorsal pancreactectomy, medial segmentectomy (MS), medial segment-preserving pancreactectomy, and proximal and medial pancreactectomy for intraductal papillary mucinous tumors (IPMTs) and pancreatic endocrine tumors. In our study of the location, clinical type and histological findings of IPMTs, we have concluded that these segmental pancreatectomies can be applied in the majority of patients with IPMTs. In case of tumor occurrence in the pancreatic head, however, it is necessary to completely resect the head of the pancreas to avoid tumor remnant and pancreatic fistula from the remaining pancreatic rim. Therefore, we modified DpPHR to include a total resection of the pancreatic head and the preservation of both anterior and posterior arterial arcades, due to the unbalanced development of the arterial arcades of the pancreatico-duodenal region. The blood flow in these organs was based on the blood supply from both the preserved arterial arcades, the duodenum retained good color, and the early postoperative results were satisfactory. Gastric emptying and pancreatic exocrine and endocrine function following DpPHR are superior to those following pylorus-preserving pancreato-duodenectomy and pancreato-duodenectomy with gastrctomy. In this video, I present a procedure of the proximal and medial pancreactectomy for IPMTs.

Laparoscopic spleen preserving distal pancreatectomy – technique and series

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INTRODUCTION: Lesions of the distal pancreas are uniquely suited to resection via a laparoscopic approach. Advances in diagnostic technology have improved the preoperative staging and intraoperative decision-making capabilities of the surgeon. Spleen preservation markedly facilitates the procedure. METHODS: We hypothesized that isolated lesions of the distal pancreas may be resected safely and efficaciously by laparoscopic techniques while avoiding splenectomy. To test our hypothesis, laparoscopic, spleen-preserving distal pancreatectomies were performed for isolated disease on 4 patients over a 1 year period by the same surgeon. The oncologic principles of open distal pancreatectomy were observed. Laparoscopic intraoperative pancreatic ultrasound was used to confirm resectability. A video of the technique will be included in the presentation. RESULTS: Four laparoscopic spleen-preserving distal pancreatectomies were performed without complications. The average operative time was 260 minutes (range 197-332), average blood loss was 39 ml (range 10-100 ml). The mean length of stay was 3.5 days (range 2-4 days). All patients were eating a regular diet and returned to routine activity by 7-10 days postoperatively. There were no conversions to open pancreatectomy, and no complications. CONCLUSIONS: Laparoscopic spleen-preserving distal pancreatectomy can be performed safely while continuing to strictly adhere to established surgical oncology principles in the treatment of this disease. A critical adjunct to this technique is the use of laparoscopic intraoperative ultrasound.

Resection of the superior mesenteric-portal vein confluence and celiac axis (Appleby procedure) with partial gastric conservation for body and tail pancreatic cancer

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BACKGROUND: The Appleby procedure permits curative resection of large body and tail pancreatic cancer involving the celiac axis. This method is classically associated with a left upper abdominal evisceration including total gastrectomy. Morbidity and long-term nutritional consequences are strongly correlated to stomach resection. We report a case of Appleby operation for body and tail pancreatic cancer with partial gastric conservation. CASE REPORT: A 55-year-old female was treated in our institution for an initially non-resectable histologically proven adenocarcinoma of the body and tail of the pancreas and received neoadjuvant fluorouracil-based chemoradiation (CRT). 4 months after the end of CRT, clinical examination was normal and a restaging was performed. Helical dual-phase scanning, magnetic resonance imaging and angiography showed a 6-cm pancreatic tumor with stenosis of mesentericoportal confluence and common hepatic artery but normal superior mesenteric artery. Liver vasculization was provided by gastroduodenal artery. General restaging was normal and a resection was planned. The video shows images from helical dual-phase scanning, magnetic resonance imaging, angiography and surgical resection. Per-operative examination did not show peritoneal carcinomatosis. Distal subtotal pancreatectomy was performed with portal vein resection, celiac axis and hepatic artery resection. The portal vein was reconstructed by reapproaching the cut ends of the vein with a growth factor. The gastroduodenal artery permitted liver vasculization. Gastric vascularization was provided by the pyloric and right gastroepiploic arteries. Postoperative Doppler ultrasound shows normal liver and gastric vasculization. The postoperative outcome was uneventful and 4-month staging showed no recurrence. The patient experienced pulmonary metastases 18 months after surgery, underwent gemcitabine-based chemotherapy and died 24 months after diagnosis.

Retropertitoneal necrosectomy for infected pancreatic necrosis: a case report

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BACKGROUND: Infected pancreatic necrosis is an indication for drainage and debridement, which has traditionally been treated by percutaneous drainage or open necrosectomy. However, percutaneous drainage is often unsuccessful because of difficulty in managing the particulate debris through small catheters. Open necrosectomy involves a high morbidity and a high rate of repeated surgery for abdominal sepsis. Recently laparoscopic transmesocolic or transgastric and retroperitoneoscopic approaches have been reported. This case report describes retropertitoneoscopic necrosectomy. METHODS: A 63-year-old male was referred to our department, because of infected pancreatic necrosis after acute severe pancreatitis due to alcohol. His white blood cell count (WBC) was 13650/mm³ and C-reactive protein (CRP) was 23.5 mg/dl. A CT scan revealed a large necrotic abscess in the head and tail. Percutaneous drainage was performed, but his symptoms, WBC, and CRP did not improve. Therefore, retropertitoneoscopic pancreatic necrosectomy was performed. Two 12-mm blunt ports were inserted through the fistulas of percutaneous drainage. A 10-mm video laparoscope was used to visualize the inside of the cavity. The cavity was irrigated, the necrotic tissue was excised, and four sump drains were placed in the retropertitoneal space. RESULTS: Intraoperative blood loss was minimal, and operative time was 205 min. The debrided necrotic tissue weighed 20g and was infected with Proteus mirabilis and Klebsiella pneumoniae. The patient did not require ICU stay and was given imipenem postoperatively. Irrigation via the sump drains was continued for 2 weeks. However, 9 weeks later, the patient was found to have an ascending colon fistula with the retroperitoneal cavity, and ascending colectomy with ileostomy was done. After the second operation, he recovered uneventfully and he was discharged on postoperative day 42. The patient has remained asymptomatic during 2 months of follow-up. CONCLUSION: The retropertitoneoscopic necrosectomy for infected pancreatic necrosis appears to be an effective and useful technique, and would be a minimally invasive alternative to open necrosectomy.