

## Abstracts

### President's Plenary Session and Young Investigator's Awards PPL-01

4/20/07 8:00 to 9:30 am

Abstract Numbers 1–7

1

#### RNA STABILITY REGULATES DIFFERENTIAL EXPRESSION OF THE METASTASIS PROTEIN, OSTEOPONTIN, IN HEPATOCELLULAR CANCER

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**Introduction.** Osteopontin (OPN) is a potential therapeutic target in hepatocellular cancer (HCC) as it is a critical mediator of metastatic function. OPN antibody blocks HCC cell invasion in vitro and inhibits pulmonary metastasis in vivo. However, the molecular mechanisms which determine expression of OPN in HCC are largely unknown. In this study, we examine differential OPN expression in HepG2 (high OPN) and Hep3B (low OPN) HCC cell lines.

**Methods.** OPN protein was measured with Western blots; Northern blots determined steady state OPN mRNA levels. Chromatin immunoprecipitation assays (ChIP) for RNA pol2 at the OPN promoter measured transcription. Actinomycin D (100 mcM) was used to inhibit transcription. Transient transfection analysis used the full length human OPN promoter (2.1 kb) cloned into a luciferase reporter vector. In vitro decay analysis measured OPN mRNA decay relative to the poly (A) tail. The contribution of OPN 3'-UTR (400 bp) or 5'-UTR (170 bp) was determined by transient transfection of luciferase-3'UTR or 5'-UTR-luciferase constructs in pGL3 promoter vector following excision of the SV40 poly (A) signal; luciferase mRNA determined differences in RNA degradation. RNA gelshift assays measured extent and patterns of protein binding to OPN 5'-UTR. (Data are expressed as mean  $\pm$  SEM; analysis was performed with the Students t test.)

**Results.** HepG2 OPN protein in cell lysate and medium was 12-fold higher than Hep3B ( $p < 0.01$  for cell lysate and media). Similarly, OPN mRNA was 7-fold greater in HepG2 cells ( $p < 0.01$  vs Hep3B). However, transfection of the OPN promoter demonstrated equivalent luciferase activities in the two cell lines; the rate of transcription was also equivalent as determined by ChIP. OPN mRNA half life was  $6.3 \pm 0.9$  and  $1.1 \pm 0.3$  hrs in HepG2 and Hep3B, respectively ( $p < 0.02$ ). RNA stability is regulated by the poly (A) tail, 5'-UTR or 3'-UTR. In HepG2 and Hep3B, nucleotide sequence of OPN and its 5'-UTR and 3'-UTR were identical between. The poly (A) tails were also equivalent in length and did not impact OPN mRNA stability. Luciferase mRNA coupled with OPN-5'-UTR was 6-fold higher in the HepG2 cells ( $p < 0.01$  vs Hep3B); 3'UTR did not alter OPN mRNA expression. RNA gelshift assays demonstrate differing protein binding patterns to 5'-UTR between the 2 cell lines.

**Conclusion.** In HepG2 and Hep3B, different repertoires of RNA binding proteins targeting OPN 5'-UTR regulate OPN mRNA stability and alter OPN expression. We conclude that RNA stability is one mechanism which regulates OPN expression in HCC to convey metastatic function. This has not been previously described for OPN regulation in any setting.

2

#### ATTENUATED *LISTERIA* STRAINS DEPLETED OF REGULATORY T CELLS EFFECTIVELY TARGET HEPATIC COLORECTAL METASTASES

Kiyoshi Yoshimura, MD, PhD, Lindsay Sue Laird, None, Kristen Faith Meckel, None, Drew Mark Pardoll, MD, PhD, Richard David Schulick, MD  
Johns Hopkins Medical Institutions, Baltimore, MD

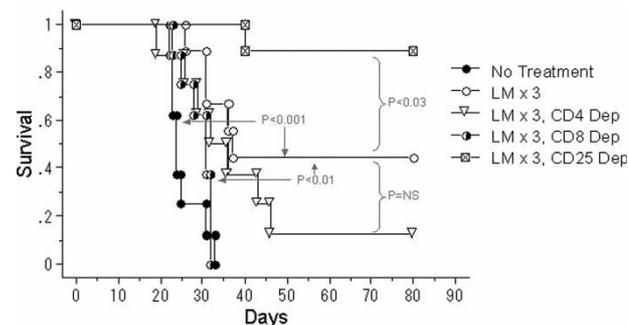
**Background and Objectives.** The liver represents a major and frequently sole site of metastases for many types of cancer, particularly gastrointestinal cancers. Here we demonstrate that administration of multiple doses of an engineered hepatic targeting *Listeria monocytogenes* (LM) generates therapeutic responses against hepatic metastases. LM treatment of mice bearing hepatic metastases induced tumor-specific CD8 responses that were enhanced by depletion of regulatory T cells either by anti-CD25 or Cytoxin treatment. Antitumor activity of LM was dependent on the presence of NK cells but was inhibited by the presence of NKT cells.

**Methods.** BALB/c mice were challenged with  $10^5$  CT26 (syngeneic colorectal cancer cells) in an isolated hepatic metastasis model. Three days after tumor challenge, the mice were initiated on a course of intraperitoneal injections of attenuated strains of LM (at 1/10 of the LD50) for three doses

three days apart. Survival was followed and immune cells were analyzed for phenotype, activation status, and effector function. Depletions of key subsets of immune effectors was performed to analyze effect.

**Results.** LM treatment provided a significant survival advantage which was greatly enhanced by depletion of CD25+ regulatory T cells. (See Figure). Furthermore depletion of CD8+ T cells abrogated the survival advantage of LM and depletion of CD4+ T cells was intermediate in effect.

**Conclusions.** These results demonstrate the utility of LM in the treatment of hepatic metastases and further suggest that blockade of regulatory T cells will enhance anti-tumor activity.



3

#### TREATMENT OF UNRESECTABLE CHOLANGIOCARCINOMA WITH GEMCITABINE-BASED TRANSCATHETER ARTERIAL CHEMOEMBOLIZATION (TACE): SINGLE-INSTITUTION EXPERIENCE

Niraj Gusani, MD, Fady Balaa, MD, Jennifer Steel, MD, David A Geller, MD, Wallis Marsh, MD, Brain Carr, MD, PhD, T. Clark Gamblin  
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**Background.** Survival for patients with unresectable cholangiocarcinoma is reported to be only 5–8 months. Systemic chemotherapy has been disappointing and not shown to significantly improve survival. Transcatheter arterial chemoembolization (TACE) has been shown to prolong survival in hepatocellular carcinoma patients but experience with cholangiocarcinoma is limited. We report our experience with TACE using chemotherapeutic regimens based on the well-tolerated drug gemcitabine.

**Methods.** Forty-two patients with unresectable cholangiocarcinoma were treated with one or more cycles of gemcitabine-based TACE (2001–2006) at our institution. Follow-up imaging was performed on all patients after each TACE procedure. Regimens of TACE included: gemcitabine only (17), gemcitabine followed by cisplatin (2), gemcitabine followed by oxaliplatin (5), gemcitabine and cisplatin (15), and gemcitabine and cisplatin followed by oxaliplatin (3). Actual survival is reported, as 40 of 42 patients have died from disease (95%).

**Results.** Patients were 59.4 years of age (range 36–87) and a median of 4 treatments (range 1–11) were administered. 37 patients (88%) had central cholangiocarcinoma and 5 (12%) had peripheral tumors. Median survival from time of first treatment was 9.7 months overall. Patients receiving gemcitabine followed by cisplatin or oxaliplatin had improved survival (median 16.5 and 11.2 months respectively) when compared to gemcitabine alone (median 6 months). Patients receiving gemcitabine and cisplatin as a combination also had improved survival (median 11.3 months) compared to single agent gemcitabine. Patients who progressed on gemcitabine and cisplatin and then received oxaliplatin also showed improved survival (median 14.3 months) compared to gemcitabine only. Neutropenia, thrombocytopenia and hyperbilirubinemia were the most common toxicities observed. Three patients in the entire series exhibited grade 3 thrombocytopenia while seven patients had grade 3 and one had grade 4 elevation of bilirubin levels.

**Conclusions.** Our report represents the largest series to date regarding hepatic artery directed therapy for unresectable cholangiocarcinoma and provides evidence in favor of TACE rather than historically reported alternatives such as systemic chemotherapy or chemotherapy/RT. Our results suggest that gemcitabine based TACE is well-tolerated and with seemingly better survival when given in combination therapy for patients with unresectable cholangiocarcinoma.

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#### PANCREATIC TRANSECTION MARGIN AT THE TIME OF PANCREATICOUDENECTOMY: CLINICAL IMPLICATIONS OF A POSITIVE MARGIN

Curtis J Wray, MD, Henry F Gomez, MD, Jean Nicholas Vauthey, MD, Eddie K Abdalla, MD, Jeffrey E Lee, MD, Huamin Wang, MD, PhD, Douglas B Evans, MD, Peter Wt Pisters  
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**Introduction.** The pancreatic transection margin (PM) is often submitted for frozen section when performing pancreaticoduodenectomy for adenocarcinoma to allow re-resection if the PM is positive. However, the natural history of patients with an initially positive PM is not well defined and therefore, there are no clear guidelines for the performance of a frozen section or the management of a positive PM.

**Methods.** The pancreatic cancer database was queried for all patients with pancreatic adenocarcinoma who underwent pancreaticoduodenectomy. Patients with cystic neoplasms (including IPMN) were excluded. Pathology and operative reports were re-reviewed to verify margin status. Patients were classified based on the status of the PM as: Group 1: negative initial frozen section; Group 2: negative after re-resection of a positive PM; and Group 3: positive margin.

**Results.** PD was performed on 383 patients with PA from 1990 to 2005, 14 patients were excluded due to follow-up less than 1 year (n=6), post-operative death (n=4) or incomplete records (n=4). Of the remaining 369 patients, the PM was negative on intraoperative frozen section in 309 (84%), positive in 45 (12%) and margin assessment was not performed in 15 (4%). Of the 309 Group 1 patients, permanent pathology review confirmed a negative PM in 308, and 1 was changed to a positive margin. All 45 patients with a positive intraoperative margin underwent re-resection; 40 (89%) were successfully re-resected to a negative PM (Group 2) and re-resection was unsuccessful in achieving clear margins in 5 (11%). Other margins of resection were positive in 7 (18%) of the 40 Grp 2 patients and in 1 (20%) of the 5 Grp 3 patients. Median survival was 24.2 months for the 309 Grp 1 patients, 23.8 months for 40 Grp 2 patients, and 17.5 months for 5 Grp 3 patients.

**Conclusions.** Patients who undergo successful re-resection of an initially positive PM have a survival similar to patients that had a negative PM on initial frozen section. These findings support the practice of intraoperative frozen section assessment of the PM and re-resecting additional pancreatic parenchyma if the initial margin is positive.

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#### SIGNIFICANCE OF THE ANTI-INFLAMMATORY FACTOR HEMOXGENASE-1 (HO-1) FOR THE FUNCTION OF TUMOR INFILTRATING MACROPHAGES IN HUMAN HEPATOCELLULAR CARCINOMA

Christoph Benckert, MD, Armin Thelen, MD, Thorsten Cramer, MD, Anotonino Spinelli, MD, Peter Neuhaus, MD, Sven Jonas, MD, Charité Campus Virchow Klinikum, Universitätsmedizin Berlin, 13353 Berlin, Germany

**Introduction.** The infiltration of various tumours with macrophages as indicated by tumor associated macrophage density (TAMd) is associated with a higher rate of metastasis and a poor prognosis. The underlying mechanisms are widely unknown. Hemoxygenase-1 (HO-1) is expressed in macrophages and acts predominantly anti-inflammatory and anti-oxidative. The significance of HO-1 for the migration of macrophages in human hepatocellular carcinoma (HCC) and the accumulation in surrounding tumor tissue has not been investigated so far.

**Methods.** TAMd was determined by using macrophage specific anti-CD68 antibody and counting immunostained macrophages analogous to the determination of the microvessel density as shown by Weidner. HO-1 was immunostained with a monoclonal antibody. In vitro expression and regulation of HO-1 was measured by western blot and real time PCR in the human monocyte cell line THP-1. Migration was analysed in THP-1 cells in Boyden chamber invasion assays.

**Results.** Determination of TAMd showed a correlation between low TAMd an better survival in HCC patients ( $p \leq 0,05$ ). In vivo Expression of HO-1 was determined in 30/70 human HCCs over tumor associated macrophages and correlated with a better survival ( $p \leq 0,05$ ). In vitro HO-1 protein and RNA could not be detected in THP-1 cells under normal conditions. Stimulation by oxidative stress lead to a highly significant stimulation of the HO-1 RNA and protein expression (150-fold). Induction of the HO-1 activity by haemin resulted in a significant decrease of the migration of THP-1 cells. Otherwise, inhibition of the HO-1 activity by Sn-protoporphyrin resulted in a significantly higher migration rate of THP-1 cells.

**Discussion.** Our results show that TAMd is associated with poorer survival in human HCC and HO-1 expression leads to a survival benefit. For the first time we could demonstrate the exclusive expression of HO-1 in human HCC tissues by macrophages and/or kuper cells and confirm data shown by other groups in animal HCC models. Inhibition of the migration of macrophages by HO-1 activation adverts to a central role of HO-1 for the accumulation of macrophages in human HCC. Further studies should investigate whether HO-1 inhibition may reduce HCC tumour growth.

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#### C-REACTIVE PROTEIN AS A PREDICTOR OF PROGNOSIS FOLLOWING CURATIVE RESECTION FOR COLORECTAL LIVER METASTASES

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**Aim of Study.** To analyze the impact of an elevated C-reactive protein (CRP) on outcome following curative resection for colorectal liver metastases.

**Method.** Retrospective analysis of a prospectively gathered dataset. 170 patients with CRP measurements taken immediately prior to the surgery were included in this study. Patients were followed up at specialist clinics with regular blood tests, including tumor markers carcinoembryonic antigen (CEA) and CA19-9, and liver function tests. In addition, regular chest and abdominal computerized tomography were performed. Patients were followed up a minimum period of 1 year post liver resection at the time of study (range 1–5 years; median 28 months). The data examined included patient demographics; liver resection histology; pre-hepatectomy CEA and CA19-9 tumor marker; pre-hepatectomy CRP; post-operative morbidity/mortality results as well as recurrence and survival figures. A CRP value above 10 mg/l was taken as elevated.

**Results.** Pre-operative CRP was elevated ( $>10$  mg/l) in 54 (31.8%) patients. The median survival of patients with an elevated CRP was 19 months (95% CI 7.5–31.2 months) compared to 42.8 months (95% CI 33.2–52.5 months) for those with a normal CRP,  $p=0.0044$ . The results of a multivariable analysis of the predictors of survival showed that an elevated CRP ( $p=0.032$ ) as well as primary "T" stage ( $p=0.019$ ) both predicted for poorer overall survival.

**Conclusions.** This study showed that an elevated CRP level, measured before surgery, is present in a significant proportion of patients with CLM. This is found to predict for a poor survival outcome in patients who had liver resection performed. The inflammatory response, as reflected by CRP, is the only factor that can be modulated pre-operatively in these patients and this may lead to the use of novel therapies among this group of patients in the future.

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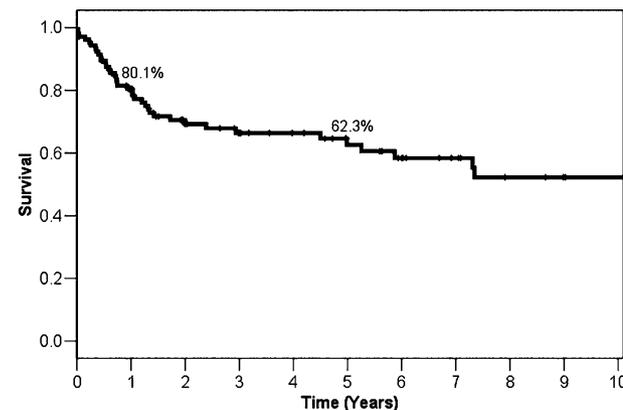
#### LONG-TERM OUTCOMES FOLLOWING LIVER TRANSPLANTATION FOR HEPATIC HEMANGIOENDOTHELIOMA: THE UNOS EXPERIENCE FROM 1987 TO 2005

Joel A Rodriguez, Natasha S. Becker, MD, Neal R. Barshes, MD, Christine A. O'mahony, MD, Thomas A. Aloia, MD, John A. Goss, MD  
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**Introduction.** Hepatic hemangioendothelioma is a vascular neoplasm with intermediate malignant potential that commonly afflicts pediatric and young adult patients. Outcomes following liver transplantation, which is currently reserved for patients with unresectable liver involvement, have only been reported as small, single-institution experiences. The purpose of this study was to evaluate patient and graft survivals following liver transplantation in a large, multi-institutional cohort of patients with hepatic hemangioendothelioma (HEH).

**Methods.** Using the United Network for Organ Sharing (UNOS) database, we identified 105 patients with a diagnosis of HEH who underwent 117 transplants between 1987 and 2005. Demographic information including age, race, and gender were recorded, and 1-year and 5-year patient and graft survivals were calculated using Kaplan-Meier survival curves. Analyses were further stratified by the cause of death.

**Results.** Of the 105 transplanted patients, 71 patients (68%) were female, 77 patients (73%) were Caucasian, and the median age was 36 years (range: 0–70 years). The 30-day post-transplant mortality rate was 1.7%. At a median follow-up interval of 742 days (range: 0–5,497 days), 1-year and 5-year graft



survivals were 71.6% and 54.9%, respectively. Calculated 1-year and 5-year overall survivals were 80.1% and 62.3%, respectively, with 31 actual 5-year survivors. (See figure below.) Nine patients (8.6%) required re-transplantation, including 2 patients who received a third graft. Of the 39 patients who died during follow-up, 14 patients (36.9%) died of recurrent disease.

**Conclusions.** Analysis of the UNOS dataset indicates that survivals following transplantation for hepatic hemangioma (5-yr OS: 62.3%) are favorable, particularly in comparison to the survivals associated with transplantation for other hepatic malignancies. Given the propensity for recurrence following resection, these data support consideration of liver transplantation for all patients with this disease.

#### Oral Posters – Transplantation I OP-01

4/20/07 1:30 to 3:30 pm  
Abstract Numbers 8–17

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#### METABOLIC CHANGES IN THE PIG LIVER DURING WARM ISCHEMIA AND REPERFUSION MEASURED BY MICRODIALYSIS

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**Background and aims.** Portal triad clamping by the Pringle manoeuvre (PM) during liver surgery can cause ischemia-reperfusion (I/R) injury. The aim of the present study was to monitor metabolic changes in the four lobes by microdialysis before, during and after warm ischemia in the pig liver.

**Material and Methods.** Eight landrace pigs (body weight 60 kilos) underwent laparotomy followed by ischemia by the PM. Four microdialysis catheters were placed in the liver, one in each lobe. A reference catheter was placed in a peripheral muscle. Microdialysis samples were collected at intervals of 30 minutes starting two hours before one hour of total ischemia followed by three hours of reperfusion. Glucose, lactate, pyruvate and glycerol concentrations in the liver were measured by microdialysis and blood samples from a peripheral vein were drawn for determination of standard liver parameters.

**Results.** During the first two hours of normal liver perfusion (baseline), glucose, lactate, glycerol and pyruvate remained stable. Immediately after initiating total ischemia lactate and glycerol levels increased significantly ( $P < 0.05$ ), while an insignificant increase was observed for glucose and pyruvate. Lactate levels decreased 30 minutes after reperfusion and did not reach baseline levels. Glycerol levels started to decrease immediately after reperfusion and continued to decrease for the rest of the experiment but did not return to initial values. Glucose levels started to decrease at the start of reperfusion and normalized at the end of reperfusion. From the time of ischemia pyruvate showed a slight increase which lasted for the rest of the experiment. The lactate-pyruvate ratio increased significantly after initiating ischemia ( $P < 0.05$ ) and decreased immediately after reperfusion. An insignificant increase in standard liver parameters was seen after ischemia/reperfusion. The metabolic changes were comparable and similar between the four liver lobes.

**Conclusions.** During and after warm ischemia there were profound metabolic changes in the pig liver measured by microdialysis and there were no difference in the four liver lobes in between. This indicates that one catheter for microdialysis will be sufficient for monitoring metabolic changes in the whole of the liver during warm ischemia and reperfusion induced by the PM.

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#### SYNTHETIC TACE INHIBITOR Y-41654 IMPROVES HEPATIC ISCHEMIA REPERFUSION INJURY

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Ochsner Clinic Foundation, New Orleans, LA

**Aim.** Our previous study has demonstrated that hepatic TACE expression is increased in a pattern similar to the pro-inflammatory cytokine TNF- $\alpha$  and IL-6 expression following ischemia/reperfusion injury to the liver. This implies that TACE plays an important role in liver ischemia-reperfusion injury (*TIMP-3 ameliorates hepatic ischemia/reperfusion injury through inhibition of tumor necrosis factor- $\alpha$ -converting enzyme activity in rats. Transplantation 2006, in press*). In this study, we applied a synthetic TACE inhibitor Y-41654 to our hepatic ischemia-reperfusion injury rat model and found that Y-41654 improves hepatic ischemia-reperfusion injury.

**Methods.** Male Wistar rats received an i.v. injection of Y-41654 at a dosage of 12 mg/Kg body weight (experimental group, n=8) or saline (control group, n=8) at a speed of 1 ml/hour. One hour later, the animals underwent 30 minutes of partial warm ischemia followed by 6 hours of reperfusion. Hepatic TACE and TNF- $\alpha$  were assessed by RT-PCR. Serum TNF- $\alpha$  was measured by ELISA. Liver function (ALT level) was tested.

**Results.** Serum TNF- $\alpha$  levels ( $92.5 \pm 16.34$  vs  $106.16 \pm 8.1$  pg/ml,  $p < 0.05$ ) and ALT levels ( $1900.83 \pm 212.88$  vs  $2153.96 \pm 153.65$  units/L,  $p < 0.05$ ) were significantly reduced in Y-41654 treated group than control group, but

hepatic levels of TACE and TNF- $\alpha$  mRNA were unchanged with Y-41654 treatment.

**Conclusion.** Synthetic TACE inhibitor Y-41654 may improve hepatic ischemia-reperfusion injuries presented as reduction of ALT levels and depression of circulating levels of TNF- $\alpha$ , demonstrating that TACE inhibition may have an important role in preventing liver ischemia/reperfusion injuries. Besides TACE inhibition, Y-41654 may also have effects on some other biomarkers such as MMPs and warrants further study.

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#### GENDER DIFFERENCES INFLUENCE NF- $\kappa$ B-DEPENDENT RESPONSES TO HEPATIC ISCHEMIA-REPERFUSION

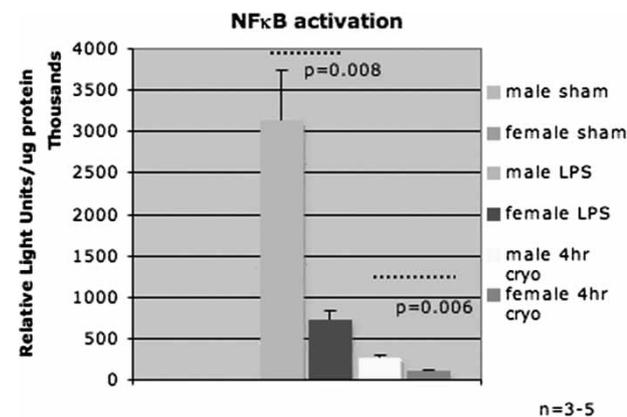
Jane M Liaw, MD, Travis J Pagliara, None, Krista A Csontos, None, Sucharita Das, MS, Sabarinathan Ramachandran, PhD, Thalachallour Mohanakumar, PhD, William C Chapman, MD  
Washington University, St Louis, MO

**Introduction.** Gender differences influence responses to hepatic injury including ischemia-reperfusion (I/R) and alcoholic liver disease. Estrogen is thought to protect the liver through activation of eNOS, improving hepatic circulation. However, mechanisms of hepatic injury and protection are not fully understood.

**Methods.** Male and female transgenic 5'-HIV-LTR-Luciferase (HLL) mice underwent 35% hepatic cryoablation using a recirculating liquid nitrogen probe to simulate liver ischemia. Control mice underwent exploratory laparotomy. Mice were sacrificed 4 hours post-reperfusion, with blood and organs collected for NF  $\kappa$ B analysis and cytokine profiling. Separate male and female HLLs were given a single intraperitoneal injection (250  $\mu$ g) of LPS endotoxin, and sacrificed 3 hours following injection. NF  $\kappa$ B activation was measured by a standard luciferase reporter assay using liver protein homogenates. Serum cytokines were measured using standard luminex techniques. Total RNA was isolated by Trizol extraction, reverse transcribed, 32P-labelled, and hybridized to GEArray Q microarrays containing cDNA sequences of genes mediating inflammation, pro- and anti-apoptosis.

**Results.** At four hours post-reperfusion, NF  $\kappa$ B was significantly activated in male versus female mice,  $p = 0.006$ . In LPS injected males, NF  $\kappa$ B was again significantly elevated versus females,  $p = 0.008$ . This differential activation was associated with an increase in serum cytokines TNF- $\alpha$  ( $1006 \pm 239$  vs  $729 \pm 181$  pg/mL) and IL-1 $\beta$  ( $231 \pm 61$  vs  $178 \pm 40$  pg/mL), although results did not reach significance. There was a significant decrease in serum KC ( $11497 \pm 44$  vs  $12645 \pm 567$  pg/mL) and MIG ( $648 \pm 106$  vs  $1531 \pm 246$  pg/mL),  $p \leq 0.05$  in males versus females.

**Conclusions.** Male mice undergoing hepatic cryoablation ischemia-reperfusion injury show significantly increased NF  $\kappa$ B activation and differential expression of inflammatory cytokines associated with increased morbidity/mortality, compared to female counterparts. Similar patterns were observed with endotoxin challenge. Gender differences can thus significantly influence NF  $\kappa$ B dependent hepatic injury. Identification of pathways to which females appear resistant to hepatic injury will result in the identification of normal targets to ameliorate I/R mediated injury.



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#### A PROLONGED GRAFT COLD ISCHAEMIA TIME IS SIGNIFICANTLY ASSOCIATED WITH INCREASED RECIPIENT MORTALITY IN LIVER TRANSPLANT RECIPIENTS

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University of Cambridge, Cambridge, United Kingdom

**Introduction.** The shortage of donor livers and the increasing need for liver transplantation has led to the use of more marginal donors. The aim of this study is to analyze the impact of various donor and recipient factors on outcome following cadaveric liver transplantation.

**Method.** The analysis included all liver transplants performed over a five year period at Addenbrooke's Hospital, University of Cambridge, UK. A selection of donor and recipient variables were identified and assimilated

from the Addenbrookes transplant donor database, recipient database and the United Kingdom Transplant (UKT) database. Missing data were obtained directly from the case notes. Univariate, multivariate and survival analyses were performed (SPSS v12.0, Inc. Chicago).

**Results.** A total of 373 liver transplants were carried out in 346 patients consecutively during this period. The overall graft failure and recipient mortality rates were 20.64% (77/373) and 14.16% (49/346) respectively. A cold ischaemia time of greater than 16 hours was significantly associated with increased recipient mortality using univariate analysis. Cox's regression analysis revealed that a cold ischaemia time of greater than 16 hours and a secondary warm ischaemia time of greater than 1 hour were significantly related to poor patient survival. A significantly poorer overall patient survival on Kaplan-Meier analysis was shown using donor livers with a cold ischaemia time of greater than 16 hours.

**Conclusion.** A cold ischaemia time of more than 16 hours and a secondary warm ischaemia time of more than 1 hour are associated with reduced patient survival. These factors are therefore important and must be considered when using livers from marginal donors.

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### OUTCOMES OF LIVER ALLOGRAFTS THAT HAVE EXPERIENCED SURGICAL OR TRAUMATIC INJURY

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**Introduction.** Donor allograft injury from trauma or surgical error is a frequent occurrence that can result in organ refusal and potential loss of an opportunity for transplantation.

**Purpose.** To evaluate outcomes of liver allografts that had experienced either traumatic or surgically-induced injury and underwent subsequent repair and transplantation.

**Methods.** Retrospective analysis of 329 liver allografts transplanted between 07/03 and 10/06. This included 289 allografts from adult donors (age > 18yrs) and 40 allografts from pediatric donors (ages: 1 mo–17 yrs). Donor injuries were categorized as vascular (transection of an hepatic artery) or parenchymal (avulsion, >Grade II laceration). All injuries were recognized and repaired as a back-table procedure prior to implantation. Vascular injuries were primarily repaired utilizing microsurgical techniques (7-0 polypropylene, interrupted) from the remnant gastroduodenal or splenic artery origin. Parenchymal injury was repaired utilizing oxidized-cellulose matrix with or without a surgical sealant. Patient and graft survival, and the occurrence of a complication associated with the repair (vascular: stenosis/thrombosis, parenchymal: hemorrhage) were analyzed.

**Results.** Vascular injuries were encountered in 8 allografts (2%). Injuries occurred in 5 pediatric and 4 adult allografts. All vascular injuries were inadvertent transection of a replaced right hepatic artery with no available or insufficient remnant. Parenchymal injuries occurred in 6 adult allografts (2%). Long-term Doppler interrogation revealed 7 of 8 repaired injuries patent at >30days with thrombosis of 1 repair leading to elevated liver function tests and subsequent biliary ischemic injury. Return to the operating room for hemorrhage secondary to parenchymal repair was required in 1 recipient. No allograft was not transplanted as a result of an injury.

**Conclusion.** Back-table repair of vascular and parenchymal injuries from trauma or surgical error yield outcomes that support their utilization.

## 13

### ARE LACERATED LIVERS TRANSPLANTABLE? – A CASE REPORT WITH REVIEW OF THE LITERATURE

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University of Heidelberg, Heidelberg, Germany

To reduce the gap between organ demand and supply transplant centers defined extended donor criteria to use more marginal donors. Using traumatized liver for liver transplantation (LTx) can in part decrease this disparity. Our aim is to present a successful case of LTx using a high grade traumatized liver as well as a review of the literature for reported cases which have shown a promising outcome. For LTx, we used a traumatized liver from a 19 years old brain dead patient suffering from a simultaneous liver and spleen injury. The liver had a grade IV laceration on the right lobe without vascular disruption and a grade II laceration on the left lobe, which were managed by digital compression, sealing of the lacerations by sealants with consecutive stitching and perihepatic packing following the splenectomy. The liver and kidneys were preserved using HTK. The liver was transplanted to a 49 years old male with a hepatitis C induced liver cirrhosis accompanying HCC (cold ischemia time: 4.5h). The 2-month follow up was uneventful with a normal liver function test. All published LTx cases using traumatized livers (n = 17) were analyzed emphasizing the graft and patient survival. The mean donors and recipients age were 24 and 57 years, respectively. The severity of liver injury varied from subcapsular hematoma to deep ruptures leading to liver resection in 4 cases. No hepatic vascular avulsion was reported. About 2/3 of reported lacerations were on right lobe. The intraoperative hemostatic managements were digital compression, electrocautery and perihepatic packing. Mean post-LTx follow-up period was 7.5 months (6–26). The

reported complications were primary non-function (18%) or poor-function (one case), liver abscess (one case), and hematoma (one case). For all reported cases, the 6-month grafts and patients survival rates were 71% and 88%, respectively. With meticulous managements and intact major hepatic vasculatures, traumatized livers can be used for successful LTx. Using this option allows transplant surgeons to expand the donor pool. Due to the complexity of the management of the traumatized livers the harvesting should be done by experienced liver surgeons. Moreover, because of the vulnerability of these organs to develop primary non- or poor-function they should be classified as marginal organs and offered to HCC or elderly patients. Finally for better analyzing and defining a guideline, it is mandatory to start multicentric collaborations to gather and analyze the data of all performed LTx cases using traumatized livers with emphasizing the longterm outcome and quality of life of these patients.

## 14

### DONOR AGE AFFECTS IMMEDIATE BUT NOT LONGTERM SURVIVAL FOLLOWING LIVER TRANSPLANTATION

Markus Selzner, MD, Nazia Selzner, MD, PhD, George Therapondas, MD, Stuart McCluskey, MD, Ian McGilvray, MD, PhD  
Toronto General Hospital, Toronto, ON, Canada

Organ shortage has resulted in an increased use of elderly donors (>60 years) for liver transplantation (OLT). The aim of this study is to re-examine, in a modern era of transplantation, the effect of donor age on outcomes following OLT. In addition, we compared the effect of old donor livers on outcomes following transplantation between young and old recipients.

**Methods.** Data was collected in a prospective clinical database on 479 patients receiving cadaveric liver transplantation between January 1998 and October 2005. Donor and recipient age were analyzed as continuous and categorical variables. Univariate and multivariate regression analysis were performed investigating donor and recipient age, cold and warm ischemia time, recipient gender, hepatitis B & C infection, year of transplantation, MELD score, and acute vs chronic liver failure. Postoperative outcomes were assessed by length of hospital stay, postoperative AST, ALT, creatinin, INR, bilirubin, alk phos, complication score, graft failure, and patient survival.

**Results.** As expected, cold and warm ischemic times were significantly associated with postoperative AST and ALT levels, and postoperative creatinin was predicted by the MELD score and warm ischemia time. When the influence of donor and recipient age was examined, we found that an increased donor age was associated in univariate analysis with the max postoperative, AST, ALT, bilirubin, and INR. This association held true in multivariate analysis for AST, ALT, and bilirubin. Recipient age was associated in univariate analysis only with increased max ALT, an association that did not persist upon multivariate regression analysis. Combining older donor livers with young (≤40 years) or old (≥60 years) recipients resulted in identical peri-operative outcomes. Graft and patient survival as well as the overall complication score were identical between patients receiving livers from old or young donors. Combining old donors and old recipients did not result in worsened long-term survival.

**Conclusion.** The use of old donor livers for liver transplantation is associated with increased indices of reperfusion injury in the immediate postoperative period. However, recipient survival is not affected by the age of the donor, and the age of the recipient receiving the older donor liver does not affect short or long-term results. This study provides evidence for the safety of using older liver grafts.

## 15

### WITHDRAWN

16

**PLASMAPHERESIS IN SEVERE COAGULOPATHY AND SEVERE GRAFT DYSFUNCTION IN LIVER TRANSPLANTATION: IS IT WORTH THE RISK?**

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Medical University of South Carolina, Charleston, SC

The use of plasmapheresis in the setting of liver transplantation (OLTx) remains controversial. The goal of our study was to evaluate our single center experience using plasmapheresis in the setting of severe pre-operative coagulopathy and post-operative severe graft dysfunction (SGD). We have begun to retrospectively review all OLTx's performed in our center, and from 06/99 through 10/01, 22 of 178 total transplant patients received plasmapheresis pre- and/or post-operatively. Data collection included donor and recipient demographics, PT/PTT/INR, factor V, percent steatosis, serum transaminases, MELD scores both before transplant and before intervention, rates of retransplantation, and graft and patient survival. SGD encompassed both delayed graft function and primary nonfunction (PNF) and was defined by peak AST greater than 1000 IU/L, within seven days post-operatively, along with clinical determination of poor liver function. Twenty-two patients (12.3%) received plasmapheresis: 3 for severe coagulopathy pre-operatively, and 19 for SGD. Patients who received pre-operative plasmapheresis saw a significant decrease in INR values from  $3.33 \pm 1.04$  to  $1.74 \pm 0.57$  ( $p = 0.03$ ) and 100% patient and graft survival at one year. Eight of the 19 patients with SGD were retransplanted because of PNF, and one-year survival for the patients with SGD was 45.5% and 37.5% with and without retransplantation respectively. There were no statistically significant differences in patient and donor demographics, ischemia time, MELD scores, or peak serum AST and ALT values between patients experiencing graft survival and failure. Sepsis was the cause of death in almost all patients who expired regardless of recovery of graft function. Our experience suggests a beneficial role of plasmapheresis in the treatment of pre-operative coagulopathy, but not for the treatment of patients experiencing SGD after liver transplantation. Though plasmapheresis shows some temporary benefit in the setting of SGD, the apparent predisposition to sepsis that it imparts on patients warrants caution in its use.

17

**ISLET ISOLATION FROM NON-HEART BEATING DONOR AND EVALUATION OF DONOR FACTORS TO AFFECT ISOLATION RESULTS**

Michihiro Maruyama, MD, PhD, Takashi Kenmochi, MD, PhD, Kenichi Saigo, MD, PhD, Naotake Akutsu, MD, PhD  
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**Background.** Because of recent progression in islet transplantation this therapy has become one of the most important therapies for patients with type 1 diabetes mellitus. However the shortage of cadaveric donor is an obstacle preventing widespread application of islet transplantation. An application of marginal donor is necessary. Pancreatic graft from brain dead donor is generally applied to pancreatic transplantation prior to islet isolation in Japan. Grafts from non-heart beating donor (NHBD) are mainly used for islet isolation. We have experienced islet isolation from 18 NHBDs and evaluate which donor factors affect islet isolation from NHBDs.

**Methods.** In only two cases, life support was withdrawn, and in the other cases death was declared after cardiac asystole without life support withdrawn. The period from death declaration to organ perfusion was defined as warm ischemia time (WIT). Pancreata were harvested after removal of both sides of kidneys. University of Wisconsin Solution or two-layer method was used for preservation and transportation of pancreata. Islets were isolated using the automated two-step digestion method we had originally developed by the same isolation team.

**Results.** Overall; Donor age was averaged 40.0 year old (range, 10–69). WIT was averaged 11.2 min (2–30), and cold ischemic time (CIT) was averaged 316 min (211–540). Total islets number after purification was 145,124 IE (38,560–491,040). The purity after purification was averaged 40.6% (10–80). Islets from 3 out of 18 cases were transplanted immediately. Influence of donor variance; Only long CIT affected the recovery of islets statistically. Islet yield of up to 300 minutes of CIT group were  $219,176 \pm 153,435$  (mean  $\pm$  SD) and that of over 300 minutes group were  $93,288 \pm 60,698$  ( $p < 0.05$ ). The episode of cardiac arrest, hypoxia as cause of death, long (over 240 minutes) anuria before death and no use of two-layer method were tended to affect isolation results.

**Conclusions.** The result of isolation of islets from NHBD was varied with the donor condition. However in some cases, functioning islets were successfully isolated and were successfully transplanted to type 1 diabetes patient. NHBD may be a good source for islet transplantation. However it is necessary to improve the technique of islet isolation from NHBD.

**Oral Posters – Biliary I: Malignant**

**OP-02**

**4/20/07 1:30 to 3:30 pm**

**Abstract Numbers 18–28**

18

**COMPOSITE TUMOR OF THE AMPULLA OF VATER: SIGNET-RING CELL AND NEUROENDOCRINE CARCINOMA – A CASE REPORT**

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Most tumors affecting Vater's ampulla are ordinary adenocarcinoma and other histological variants or mixed forms are less frequent, even rare. We encountered a rare case of composite signet-ring cell carcinoma and well differentiated neuroendocrine carcinoma of the ampulla of Vater in a 72-year-old Korean man with postprandial abdominal discomfort and jaundice for two weeks. Computed tomography and endoscopic retrograde cholangiopancreatography (ERCP) revealed about 2 cm protruding mass with abrupt narrowing of distal common bile duct. Pancreaticoduodenectomy was performed. An ill-defined nodular 2 cm sized mass in the ampulla of Vater invaded the entire duodenal wall and pancreatic parenchyma with duct dilatation of remaining common bile duct and pancreatic duct. Two out of twenty regional lymph nodes were metastatic. Histopathologically, the tumor was composed of mucinous adenocarcinoma with predominant signet-ring cell components (80%) and well differentiated neuroendocrine carcinoma (20%). Intimately intermingled or transitional areas between both elements as well as amphicrine tumor cells with dual differentiation were also present. By immunohistochemistry, the adenocarcinoma with signet-ring cells was positive for CK7 and CEA and neuroendocrine carcinoma was diffusely positive for CK7, synaptophysin, chromogranin but negative for insulin and CEA. Of the two metastatic peripancreatic nodes, one was neuroendocrine carcinoma and the other was adenocarcinoma. The patient is alive and disease-free 13 months since surgery.

19

**INTRAHEPATIC PAPILLARY CHOLANGIOCARCINOMA: A RARE CHOLANGIOCARCINOMA WITH A MORE FAVORABLE PROGNOSIS**

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**Introduction.** Intrahepatic papillary tumors are the most rare form of cholangiocarcinoma. Some studies suggest that this tumor has a more favorable biology and better survival than other types of cholangiocarcinoma; however, there are limited data on outcomes following intrahepatic papillary tumors. Here we report a case and review the available literature on



intrahepatic papillary cholangiocarcinoma (IPC). Case: A 57 year old female with right upper quadrant pain underwent an ultrasound revealing left intrahepatic ductal dilatation with a normal extrahepatic biliary tree. Her bilirubin and transaminases were normal, but she had an elevated CA 19-9 (278). A cholangiogram revealed a left hepatic duct stricture. A subsequent CT angiogram revealed biliary dilatation of segment 2 and 3 with no obvious mass and normal hepatic vasculature. She underwent a left hepatectomy and pathology revealed an intraductal papillary cholangiocarcinoma with negative margins.

**Methods.** The clinical and pathologic features of our case were reported. The English language literature was searched for IPC. Articles which reported papillary pathology, intrahepatic location of tumor, patient age and sex, and therapy provided were selected. Available clinical data were collected from these articles.

**Results.** Twelve articles meeting the stated criteria were located. Cumulatively, there were 194 patients with average age of  $59.8 \pm 12$  years. There was a predominance of female patients (112 female, 73 male) and left lobe tumors (126 left vs 31 right). Resection was carried out in 183 patients with a negative margin reported in 155. Cumulative perioperative mortality was 6.6%. Cumulative survival was incompletely reported, but averaged 37.6 months with the vast majority remaining alive with no evidence of disease at last followup.

**Conclusions.** IPC is a rare form of cholangiocarcinoma. It should be suspected when unilobar or segmental biliary dilation is discovered. The majority of the reported cases occur during the 6th and 7th decade of life with a female predominance. Margin negative resection offers long term survival and this tumor may have a more favorable prognosis than other histological types of intrahepatic cholangiocarcinoma.

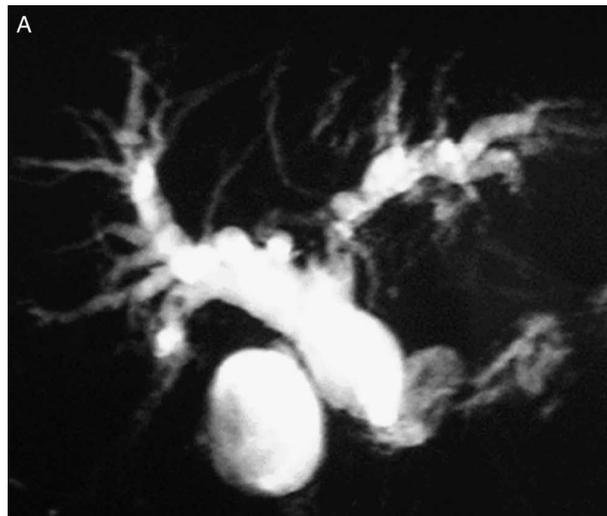
#### 19a SYNCHRONIC CANCER OF THE BILIARY TRACT: CASE REPORT AND REVIEW OF THE LITERATURE

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**Introduction.** The association of two or more cancerous lesions (synchronism, double cancer) limited to biliary tract is uncommon. The literature reports twelve cases. Adenocarcinoma of gallbladder associated to cholangiocarcinoma is a rare presentation of a double cancer.

**Case Report.** A 69 years old male patient was seen in admission for presenting jaundice, choloria and weight loss with an evolution of 6 months. He did not present abdominal pain. In addition, he presented pruritus and fever. Physical examination showed generalized jaundice and non painful hepatomegaly. The laboratory tests were all normal, except for a marked elevation of total bilirubin: 27.19 (N: 0.90), CEA: 2.5 ng/ml, Ca 19-9: 38 U/ml, Ca 125: 30 U/ml, AFP: 10 ng/ml. The preoperative ultrasonography showed dilatation of the intra and extrahepatic biliary tree, and cholelithiasis. Cholangioresonance (MRC) confirmed dilatation of ducts due to obstruction of the biliary tract in its distal segment. Cholecystectomy was practiced plus choledocoduodenostomy. The pathological study reported adenocarcinoma of gallbladder and adenocarcinoma of choledocus. The post surgical evolution was remarkable and received the medical discharge one week later. The patient died five months after the operation.



**Discussion.** Single world-wide literature reports twelve cases of double cancer of gallbladder and biliary ducts, associated mainly to ducts anomalies of the pancreatic-biliary system. The symptomatology is silent and can be confused with other pathologies. The visualization by ultrasonography of expanded intrahepatic or extrahepatic tract demands the complementation of its study with cholangioresonance (MRC) and endoscopic cholangiography (ERCP) mainly and others diagnostic tests if they are considered necessary. Mortality by this type of tumors continues elevated.

#### References.

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#### 20 SURGERY FOR ADVANCED KLATSKIN'S TUMOR WITH VASCULAR INVOLVEMENT

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**Purpose.** Klatskin's tumor today is still a challenge for hepatobiliary surgeon, especially for those advanced cases with extensive bile duct and vascular invasion. Complete resection of tumor is the only way for long-term survival.

**Materials and methods.** We report one case of advanced Klatskin's tumor with main portal vein and extended bile duct involvement. Extended right lobectomy (Right+S<sub>1</sub>+S<sub>4a</sub>), portal vein resection and hepatico-jejunostomy were performed. The main portal vein was resected 2 cm in length. Left and

main portal veins were reconstructed. Portal vein thrombosis was found during operation and thrombectomy was done immediately. Ductal plasty was performed for making S<sub>4</sub> and S<sub>2+3</sub> bile ducts to one hole to simplify hepatico-jejunostomy.

**Results.** The post-operative course was eventful. This patient stayed in the ICU for a long time due to CO<sub>2</sub> retention caused by COPD. Color Doppler sonographies were performed 3 and 10 days after operation. The reconstructed PV blood flow was good. The cholangiography performed two weeks after operation showed good hepatico-jejunostomy anastomosis. Bile leakage was noted from liver stump. The pathology showed tumor-free resection and no lymph node metastasis. This patient was discharged fifty-one days after operation.

**Conclusion.** Advanced Klatskin's tumor is a tough work to overcome. Sufficient pre-operative management (such as PTCD, PTPE) and excellent operation technique can increase the tumor-free resection rate.

## 21

### RECURRENCE-FREE SURVIVAL AND PATTERN OF RECURRENCE FOLLOWING RESECTION OF HILAR CHOLANGIOCARCINOMA

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**Background.** Hilar cholangiocarcinoma is a rare tumor with a poor prognosis. We sought to evaluate recurrence pattern and prognostic factors for recurrence-free survival in surgically resected hilar cholangiocarcinoma.

**Methods.** From 1985 to 2006, patients with hilar cholangiocarcinoma referred to a tertiary surgical clinic were evaluated. Demographic data, tumor characteristics, and outcome were analyzed retrospectively.

**Results.** Thirty-eight patients underwent resection, which included excision of the extrahepatic biliary system and porta-hepatis lymphadenectomy, with (n=20) or without (n=18) hepatic lobectomy. The 30-day operative morbidity and mortality was 32% and 0%. Overall three-year survival was 47%. The median recurrence-free survival was 31 months, with a median time to recurrence of 19 months. Factors predictive of improved disease-free survival on univariate analyses included negative histological margins, concomitant hepatic lobectomy, lack of nodal disease, and an earlier tumor stage (p<0.05). On multivariate analysis the only significant favorable prognostic factor was lack of nodal disease (p=0.02). Of the 20 patients with recurrent disease, the site of first recurrence was porta hepatis lymph nodes (n=6, 30%), liver (n=4, 20%), peritoneal deposits (n=3, 10%), lung (n=1, 5%), and multifocal recurrence (n=6, 25%).

**Conclusions.** Hilar cholangiocarcinoma is an aggressive tumor with a high likelihood for recurrence. Because it is possible to decrease the risk of recurrence by performing concomitant hepatic lobectomy and obtaining a negative margin, aggressive resection including hepatectomy should be the standard treatment. Improvements in adjuvant therapy are essential to improving outcome in patients with hilar cholangiocarcinoma.

## 22

### A CASE OF COMBINED RESECTION FOR SYNCHRONOUS PRIMARY CARCINOMAS OF GALLBLADDER AND DUODENUM

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**Purpose.** The incidence of multiple primary malignant tumor ranged from 0.7% to 11% in the literatures. In digestive system, various organs are the site of multiple primary cancer (MPC). The major sites are large intestine, stomach and liver, and others are esophagus, pancreas, small bowel and gallbladder (GB). MPC may be synchronous or metachronous depending on the interval between their diagnosis. To the best of our knowledge, the resected case of synchronous primary carcinomas developed in GB and duodenum has been reported very rarely.

**Methods.** We present a patient who underwent an operation for synchronous primary carcinomas of GB and duodenum. A 51 year-old-female was admitted for postprandial abdominal discomfort. CT scan and MRI of abdomen showed 3 × 2 cm sized heterogeneously enhancing mass in GB and 3.7 × 2.7 cm sized heterogeneously enhancing mass in duodenal 2nd portion. The laboratory findings including tumor markers were non-specific. Elective operation was done under the impression of combined GB cancer and duodenal 2nd portion cancer. In operative findings, there were 3 × 2.5 cm sized mass in GB and 5 × 4 cm sized duodenal mass with near complete luminal obstruction 3 cm distal from pyloric ring. Radical cholecystectomy with wedge resection of liver bed and Whipple's operation was performed.

**Results.** In microscopic examination, GB mass was well differentiated adenocarcinoma and duodenal mass was moderately differentiated adenocarcinoma, and one lymph node (lymph node along common hepatic artery) among 18 dissected lymph nodes was invaded by tumor cells. In immunohistochemical study, GB mass shows CK7(+), c-erbB2(3+), Topoisomerase

II(+, <10%), p53(+, <5%), E-cadherin(3+), Ki-67(+, 50%), CK20(+) and duodenal mass shows CK7(+), c-erbB2(2+), Topoisomerase II(+, 70%), p53(-), E-cadherin(2+), Ki-67(+, 50%), CK20(-). The microscopic and immunohistochemical findings showed that the GB mass and duodenal mass were synchronous primary carcinomas. The patient had recovered uneventfully and is well lived without evidence of recurrence in 20-month-follow up evaluation.

**Conclusions.** We report a case of combined curative resection for synchronous primary carcinomas of gallbladder and duodenum.

## 23

### PRIMARY NON-HODGKIN'S LYMPHOMA OF THE GALLBLADDER

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Primary non-Hodgkin's lymphoma of the gallbladder is a very rare location of extranodal non-Hodgkin's lymphomas. More common than primary lymphoma of the gallbladder is secondary involvement with adjacent lymph nodes in patients with known malignant lymphoma. A search through the literature demonstrates only 12 cases of reported primary non-Hodgkin's lymphoma of the gallbladder. The origin of gallbladder lymphoma is controversial as lymphoid tissue in normal gallbladder mucosa is sparse. Cholelithiasis usually causes chronic cholecystitis leading to infiltration of the gallbladder mucosa with lymphocytes. A method for preoperative diagnosis has not been established. All cases have been diagnosed after surgery by pathologic examination. Most patients present with signs and symptoms indicating biliary disease. The majority of cases are found incidentally in cholecystectomy specimens performed because of cholecystitis or cholelithiasis. We present a patient without a history of lymphoma who presented with clinical and radiographic signs of cholecystitis. An open cholecystectomy was performed and final pathology demonstrated primary non-Hodgkin's lymphoma (Diffuse Large B-cell lymphoma).

## 24

### A SINGLE-CENTER EXPERIENCE ON THE SURGICAL TREATMENT OF THE GALLBLADDER CARCINOMA

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**Aim.** To optimize surgical treatment of the gallbladder carcinoma, we analysed prognostic factors of these cancer patients based on a single center experience.

**Methods.** The records of 64 patients with the primary gallbladder cancer between October, 1994 and December, 2004 at our department were reviewed retrospectively. Fifty-nine patients of them were performed Surgery in this sample. Data were collected by chart review including review of surgical records, pathological specimens and clinical information.

**Results.** Eight of the patients with surgery were performed only bypass operation. The overall 3, 5-year survival rate of the patients performed resection (51 patients) was 43.8% and 38.9%. Thirty-three patients of the patients with resection were performed macroscopic curative resection. The 3, 5-year survival rate of patients with curative resection was accomplished was 62.7% and 55.7%. No metastatic lymph node status and no biliary invasion were predictors of favorable outcome (p<0.05). For the invasion of the liver cases, the prognosis of patients treated with anatomical liver resection (segment 5 and of the lower part of segment 4) was better than that of patients performed extended cholecystectomy under the condition of curative resection (p<0.05). In the patients with regional lymph node metastasis, the prognosis of patients performed radical lymphadenectomy was better than that of patients not performed radical lymphadenectomy (p<0.05).

**Conclusions.** Our data suggested that lymph node metastasis and biliary invasion were prognostic predictors and patients with gallbladder carcinoma with directly invaded the liver should be performed radical resection including the anatomic resection of the liver segment 5 and of the lower part of segment 4 with radical lymphadenectomy.

## 25

### INCIDENTALLY DETECTED T3/T4 CARCINOMA OF GALLBLADDER: THE RACE AGAINST TIME AND DISEASE TIDE

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Recent literature review on carcinoma of gall bladder (CaGB) suggest that incidental CaGB with T3 or T4 tumor status could also be considered for extended surgeries. We looked into our data retrospectively. During a 20 year period 335 cases of CaGB were operated in the department of GI surgery and liver transplant in the All India Institute of medical Sciences, Delhi, India. 20 of them were incidental. 11 of them had T3 and one had T4 adenocarcinoma. The mean age of the 12 patients was 46.3 years. Two of them were males. Five were following laparoscopic cholecystectomy. 9 of the 12 presented after 2 months (13,9,7,6,4,3,3,3,2.5 months respectively) of

primary surgery, 3 of them presented with recurrence at scar site. All 9 cases had disseminated disease at second surgery. Some form of palliative resection or bypass was done in 5 cases. 4 had laparotomy and closure. One patient died on 16th post operative day due to cholangitis. 6 cases died within 2 to 6 months. Two were lost to follow-up. 3 of the 12 cases presented within 1 to 2 months of primary surgery. Extended cholecystectomy (ECCX) was possible in one case. However the resected specimen did not show any tumor on histopathology. He had no evidence of recurrence at one year follow-up. The second case underwent ECCX with resection of adjacent colonic segment and pylorus. She survived for 6 months. The third patient had disseminated disease. She died after 3 months. Seven of the 20 cases of incidental CaGB presented with T2 disease. Six of them presented within 19 days to 2 months. All 6 underwent ECCX with R0 resections. One patient who presented after 1 year had dissemination. One case of T1 disease had extended ECCX after 2 months of primary surgery. She presented after 30 months with local recurrence and obstructive jaundice. Only a segment III bypass could be possible. Our data suggest that the prognosis of patients presenting with incidentally detected T3 or T4 disease is dismal, especially if they present after 2 months. Further studies are required on the surgical outcome in this subgroup of patients presenting at the earliest. That would possibly answer, whether the disease tide has too less time to be with in the reach of the surgeon.

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### SURGICAL TREATMENT OF GALLBLADDER CANCER: A POPULATION BASED ANALYSIS

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**Introduction.** The primary modality of cure for gallbladder cancer, an uncommon but aggressive neoplasm, remains surgical resection. Multiple single institutional studies have reported that a more aggressive surgical approach results in better survival. A population-based analysis was performed to study the access to and outcomes following radical resection for gallbladder cancer.

**Methods.** From 1988–2002, all patients (ages 18 years and greater) with gallbladder cancer were identified from the Surveillance, Epidemiology, and End Results (SEER) registry. Patients identified initially with metastatic disease or diagnosed by autopsy or death certificate only were eliminated.

**Results.** 3,684 patients were identified. Median age of the population was 71.8 years and 72% of patients were female. Surgical treatments included: 15.1%, no surgical intervention; 4.1%, exploratory surgery without resection; 74.6%, simple cholecystectomy; and 6.2%, radical resection. Depth of invasion included: 7.2% T1a; 13.4% T1b; 21.9% T2; 47.4% T3; 10.1% localized NOS. For all patients, survival was not improved with radical resection. However, on subgroup analysis, there was improved survival with radical surgery for T2 tumors only ( $p=0.0495$ ). Survival analysis of T1a and T1b was limited due to small numbers. In patients with T3 tumors, there was no survival benefit in patients undergoing radical resection compared to cholecystectomy ( $p=0.7746$ ). Only 4.8% of patients with T2 tumors underwent radical resection. The proportion of patients undergoing radical resection varied by SEER region (range 4.1–9.7%). Other predictors for receiving a radical resection included younger age, T3 tumor, and moderately-well differentiated tumors.

**Conclusion.** The benefits of radical resection in T3 tumors that are seen in single institution studies do not seem to be translated to population-based outcomes. However, relatively few patients appear to be selected for radical resection and these criteria cannot be assessed using SEER data. Further detailed studies on the outcomes of gallbladder cancer need to be conducted, including criteria for resection and access to radical resection, where appropriate.

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### EFFECTIVENESS OF THE INTRA-ARTERIAL INFUSION CHEMOTHERAPY FOR THE LIVER METASTASIS OF THE RECURRENCE OF LOWER BILE DUCT CANCER

Hideaki Andoh, MD, PhD, Yoshio Kobayashi, MD, Yuich Tanaka, MD, Manabu Onuki, MD, Koji Fukuda, MD  
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**Introduction.** This study shows the effect of the intra-arterial infusion chemotherapy for the liver metastasis of recurrent bile duct cancer.

**Patients.** Nine patients were treated with the intra-hepatic-arterial infusion chemotherapy for the recurrence of the liver metastasis. Pancreatoduodenectomy were performed for all patient with lower bile duct cancer.

**Method.** The catheter was guided to the common hepatic artery or splenic artery with partial embolization to the splenic artery. The 5-FU was administered 500 mg/day for 7 days continuously. MMC 10 mg once at the first day. After then, 5-FU 500 mg administered once a week. Second line chemotherapy was low dose CDDP (10 mg/w; a.i.) every week.

**Results.** No side effect was occurred in all patients. Average duration period between surgery and liver metastasis was 355 days (0–533 days). Total mean 5-FU dosage for chemotherapy was 14.8g/case (7–25.5g/case). In effect, CR was two case, PR two cases, NC two case and PD three cases. Response ratio was 44%, and median survival time was 330 days. In seven cases, liver

metastasis was controlled with chemotherapy. One case was died for liver metastasis but other eight cases were died for distant metastasis such as brain or lung metastasis.

**Conclusion.** For the liver metastasis of lower bile duct cancer, intra-arterial infusion chemotherapy was effective without side effect nor high invasive treatment. But it was not effective and could not protect the distant metastasis.

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### USEFULNESS OF GEMCITABINE COMBINED WITH 5-FLUOROURACIL AND CISPLATIN (GFP) IN PATIENTS FOR ADVANCED BILIARY TRACT CANCER

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**Background.** Advanced biliary tract cancers have poor prognosis and chemotherapy has been shown to have little impact. To date, effective chemotherapy regimens for this carcinoma have not been established. The effectiveness of CDDP with 5FU therapy is established in several digestive cancers. Furthermore the effectiveness of gemcitabine for biliary tract cancer is indicated recently. Therefore we hypothesized CDDP with 5FU combined with gemcitabine (GFP) therapy is effective, we induced this therapy for biliary tract cancers from 2004. The aim of the present study is conducted to clarify the effectiveness of GFP chemotherapy for advanced biliary tract cancer.

**Patients and methods.** Twenty-seven patients of unresectable cholangiocarcinoma, eleven patients of unresectable gallbladder cancer were enrolled. Of these, five patients of cholangiocarcinoma and six patients of gallbladder cancer with no prior chemotherapy were treated with a 4-week cycle GFP chemotherapy consisting of gemcitabine at 1000 mg/m<sup>2</sup> on days 1,8,15, and 22, and of 5-FU at 250 mg/m<sup>2</sup> and CDDP at 3 mg/m<sup>2</sup> on days 1 to 5, 8 to 12, 15 to 19 and 22 to 26.

**Result.** In six cases with gallbladder cancer, three patients demonstrated partial response (PR) with an additional two patients having stable diseases (SD), as assessed by RECIST. Clinical benefit rate and response rate were 83% and 50% individually. The median survival time was 8.7 months. In efficacy case, multiple liver metastases could be reduced after GFP chemotherapy, we could do radical operation. In five cases with cholangiocarcinoma cases, one patient demonstrated PR with an additional three patients having SD, as assessed by RECIST. Clinical benefit rate and response rate were 80% and 20% individually. The median overall survival time was 10 months. Although response rate was lower than gallbladder cases, survival time prolonged. In efficacy case, Tumor which replace almost liver was reduced after 4 course GFP chemotherapy. Over all survival rates improved significantly compared with cases before induction of GFP chemotherapy in both biliary tract cancers ( $P<0.05$ ).

**Conclusion.** This GFP chemotherapy has promising antitumor activity in patients with advanced biliary tract cancers. This regimen needs to be evaluated in large numbers of patients.

#### Oral Posters – Basic Sciences I

OP-03

4/20/07 1:30 to 3:30 pm

Abstract Numbers 29–40

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### THE DEVELOPMENT OF A SWINE MODEL OF SECONDARY LIVER TUMORS FROM A GENETICALLY INDUCED SWINE FIBROBLASTS CELL LINE

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Swine models of secondary liver tumors may demonstrate to be an ideal model to study the efficacy of surgical and ablative treatment options available for liver tumors. The purpose of the present studies was to develop a secondary liver tumor in a large animal model. Fibroblasts from swine were isolated from ear lobule; cells then were transfected with amphotrophic retroviruses encoded with human genetic (hTERT, p53<sup>00</sup>, cyclinD-1, CDK4<sup>R24C</sup>, Myc<sup>T58A</sup>, RAS<sup>G12V</sup>) material. Transformed cell lines were inoculated into swine under tacrolimus based immunosuppression ( $n=4$ ). Isolates from first pass were cultured and then inoculated as a second pass into 1) nude immunodeficient mice ( $n=5$ ), 2) immune intact wild mice ( $n=2$ ) and, 3) porcine animals without immunosuppression ( $n=2$ ). Tumor growth was evident in 75% of immunosuppressed swines. One animal die with diarrhea and failure to thrive before the completion of experiment (3 weeks). Growth of tumors was slow in two animals while in one animal tumor was larger with a peak growth of 42 mm at three weeks. All growths showed to be malignant on histology. Cell morphology changed from initial cell line as compared with cell isolates after first pass. Tumor growth was evident in 100% of the nude immunodeficient mice with a peak size of 22 mm ( $17 \pm 5$  mm, Mean  $\pm$  SD) at the time of sacrifice (3 weeks). Tumor growth was evident in all wild mice with a peak size of 8.9 mm at the end of

the third week. Tumor growth in swine was characterized for slow growth with a peak size of 8 mm at three weeks. Characterization of new mutations in cell lines after first pass is the matter of current studies. Further changes may produce a more rapid growth of genetically induced tumorigenic cells in the immune-intact swine.

### 30 DENDRITIC CELLS GENERATION FROM PERIPHERAL BLOOD MONONUCLEAR CELLS OBTAINED FROM JAUNDICED PATIENTS WITH PANCREATIC ADENOCARCINOMA

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Pancreatic adenocarcinoma (PAde) is an aggressive malignancy with poor prognosis, urging for improved or new therapeutic strategies. Dendritic cells (DC)-based vaccination is one of such promising approaches. DC are the most potent antigen-presenting cells and central to the induction and maintenance of an immune response. However, in cancer patients DC generation and function may be deficient, imposing an obstacle to the success of their use. Here, we describe the *in vitro* generation of DC from peripheral blood mononuclear cells (PBMC) obtained from jaundiced patients with PAde and, also, the effect of jaundiced plasma (JP) in the phenomenon. PBMC were separated from blood obtained from 10 patients and 10 healthy controls over a density gradient. Adherent cells were cultured with GM-CSF and IL-4 (50 ng/mL) for 7 days. On the 5th day, TNF-Alpha (50 ng/mL) was added for DC activation. Cultures were performed in 10% JP or normal plasma (NP). Non-adherent cells were harvested at day 7, labeled with FITC- or PE-conjugated monoclonal antibodies against CD86, CD80, CD11a, CD11c, CD14, HLA-DR and analyzed by flow cytometry. Patient cells, cultured in 10% JP, compared to healthy donor cells, cultured in 10% NP, had a significantly ( $p < 0.05$ ) lower expression of CD11c, CD80, CD86 and HLA-DR. It is noteworthy that cells generated from patients PBMC did not express CD11c, while 60% of those derived from healthy donor cells did so. The presence of JP in healthy donor cells cultures caused a significant decrease in the percentage of HLA-DR+ ( $66\% \times 89\%$ ), CD11c+ ( $43\% \times 60\%$ ) and CD86+ cells ( $43\% \times 66\%$ ). Finally, when patients PBMC were cultured in NP, a significant increase in HLA-DR ( $87\% \times 75\%$ ) and a tendency ( $p = 0.06$ ) to increase in CD86 ( $43\% \times 30\%$ ) expression occurred. These data indicate a significant alteration in the patients PBMC ability to differentiate into DC *in vitro*, a phenomenon that seems to depend both on soluble factors present in plasma and on the cells, themselves.

### 31 TOLERANCE TO A TUMOR ASSOCIATED ANTIGEN IS DEPENDENT UPON THE SITE OF EXPRESSION AND ANTIGEN LOAD

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**Introduction.** Although hepatoma (HCC) is a leading cause of cancer mortality worldwide, the immune response to this virally-induced tumor has been largely unexplored. Evidence from liver transplant results and elsewhere has suggested that the liver is a tolerogenic organ. To evaluate this possibility, we challenged mice with tumor cells that bear a transforming viral antigen. Such cells have been shown not to grow in an immunocompetent host when injected subcutaneously or intraperitoneally. Hypothesizing that tumors that seed the liver directly might avoid immunologic destruction, we injected varying doses by intrasplenic and intravenous routes into syngeneic immunocompetent hosts and compared the growth kinetics.

**Methods.** C57BL/6 3 month old mice were inoculated with different amounts of tumor cells by intrasplenic injection. The tumor cells used were derived from liver tumors from MTD2 mice. MTD2 mice are syngeneic to C57BL/6 mice and spontaneously develop T antigen (Tag)-expressing hepatomas resulting from transgenic expression of the Tag of the SV40 virus. We have grown these tumor cells in culture and demonstrated Tag and MHC class I expression by flow cytometry. C57BL/6 mice were divided into 3 different groups according to the number of cells injected intrasplenicly: 5 million (5 mice), 1 million (5 mice) and 1/2million (3 mice). Tumor cell growth was evaluated microscopically 30 days after injection. In a separate experiment comparing intrasplenic versus intravenous routes of injection, 1/2 million cells were injected into the tail vein (5 mice) and intrasplenicly (4 mice). Growth in the liver and lung was evaluated grossly at 120 days after the inoculation.

**Results.** The groups inoculated with 5 million and 1 million cells intrasplenicly did not show growth at anytime. Similarly, the group injected IV showed no growth 4 months post injection. Interestingly, the group injected intrasplenicly with 1/2 million cells did grow tumors. In these mice, 30 days after intrasplenic injection, H & E staining showed multiple tumor foci (3 of 3 mice). Immunohistochemistry staining was used to confirm Tag expression. 120 days after injection the same group developed hepatocellular cancer evident macroscopically and with H & E staining (2 of 4 mice). Overall 5 of 7 mice that received 1/2 million cells intrasplenicly developed HCC; none of the other groups developed HCC ( $p < 0.01$ ).

**Conclusion.** The liver has a critical role inducing tolerance to tumor cells, but may also induce an effective immune response depending on the antigen load. To clarify liver specific immunogenicity of tumor antigen, future experiments will explore the Tag-specific immune response in each group.

### 32 FIBROBLASTS PROMOTE PANCREATIC CANCER CELL GROWTH IN VITRO

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Desmoplasia is a common histological finding in ductal pancreatic adenocarcinoma and fibroblasts, the main cellular constituent of tumor stroma, may create a context that promotes tumor progression. The tumor micro-environment is known to effect tumor cell invasion, metastasis, and drug sensitivity. Juxtatumoral stroma has different gene expression from panstromal cells suggesting that direct communication between tumor cells and stromal fibroblasts is important for these effects. However, measurements of tumor growth are difficult in the context of mixed cell types. We developed a contacting co-culture system consisting of red fluorescent protein (RFP)-tagged AsPC-1 pancreatic cancer cells and T31 human fibroblasts that allows direct evaluation of tumor cell growth in a mixed cell culture. In this system, we assessed the dose response of fibroblasts on RFP-AsPC-1 pancreatic cancer cell proliferation (Table). Relative proliferation was determined as the ratio of the mean fluorescence intensity at day 3 divided by the initial mean fluorescence intensity at day 0. The presence of fibroblasts in co-culture conferred a significant growth advantage on RFP-AsPC-1 cells. The effect was fibroblast dose dependent with the highest dose (1:1 ratio) yielding a 34% increase in tumor cell growth relative to controls. Our results suggest that direct mesenchymal-epithelial cell interaction within the tumor micro-environment can contribute to tumor cell proliferation.

Proliferation of Pancreatic Cancer Cells in Fibroblast Co-culture

RFP-AsPC-1/Fibroblast Ratio	Relative Fluorescence (Day3/Day0) $\pm$ SEM
0	2.96 $\pm$ 0.62
20:1	3.19 $\pm$ 0.59*
10:1	3.29 $\pm$ 0.52**
5:1	3.46 $\pm$ 0.51**
2:1	3.68 $\pm$ 0.43**
1:1	3.96 $\pm$ 0.55**

\* $P > 0.05$ , vs. RFP-AsPC-1 cells only, \*\* $P < 0.01$  vs. RFP-AsPC-1 cells only,  $n = 15$ /group, 3 replicates.

### 33 THALIDOMIDE TREATMENT OF DEVELOPING HEPATOCELLULAR CARCINOMA: AN IN-VIVO STUDY IN RAT

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**Objective.** This animal study was to investigate the effect and possible mechanisms of thalidomide therapy for developing HCC.

**Materials and methods.** Adult male LEW/SsN rats were separated into three groups of 50 each, group A the control, groups B and C given diethylnitrosamine (DEN), 5 mg/kg/day for 18 weeks. In addition, Group-C received an intraperitoneal injection of thalidomide, 2.5 mg/kg/day for the following six weeks. Ten in each group were sacrificed at the 6th, 12th, 18th, 20th and 24th weeks. The body weight of the rat, presence/absence of liver tumors, and the number of organs involved with HCC were determined at each stage of observation. Further, at the 24th week, we compared vascular endothelial growth factor (VEGF) mRNA, methionine aminopeptidase-2 (MetAP-2) mRNA, Bcl-2 mRNA, telomerase mRNA, and telomerase activity within the liver of Group-A and within HCC from Group-B and C.

**Results.** No HCC developed deriving from Group A, but tumors were present for some Group-B and -C by the 18th week. At the 20th and 24th weeks, the median liver tumor weight for individuals from Group B was, 0.64g (0.58–0.70 g) and 0.79g (0.70–0.90g;  $P = 0.04$ ), and corresponding weight for Group C was 0.38g (0.35–0.42g) and 0.41g (0.35–0.47 g;  $P = 0.67$ ). The liver weights for Group-C was significantly lower than that for Group-B ( $P < 0.001, 0.001$ ). The metastasis score (number of organ systems involved) were two (20%) and three (80%) at the 20th week, and three (100%) at the 24th week for Group-B rats, and one (80%) and two (20%) at the 20th week and one (70%) and two (30%) at the 24th week for Group-C individuals, significant inter-group (B and C) difference ( $P < 0.001$ , and  $P < 0.001$ ). The levels of MetAP-2 mRNA within the liver of Group-B and -C rats were significantly greater than the corresponding values for Group-A rats ( $P = 0.000$  and  $P = 0.001$ ), although no significant difference between Group-B and Group-C. The level of Bcl-2 mRNA within test animals' livers for both Group-B and Group-C individuals was significantly greater than the corresponding Group-A value ( $P < 0.001$  and  $P < 0.001$ ), whilst no such difference was noted for the comparison between Group B and Group C.

Group-B's and Group-C's liver telomerase mRNA levels were not significantly different.

**Conclusion.** Thalidomide effectively but not completely, inhibits both HCC growth and metastasis formation, when administered to rats during the stage of HCC development. VEGF mRNA may play an essential role in thalidomide-induced inhibition. Changes to hepatic Bcl-2 mRNA level, telomerase mRNA level and telomerase activity, but not Met AP-2 mRNA level, might also make a significant contribution.

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#### IS IT EFFECTIVE TO TREAT HEPATOCELLULAR CARCINOMA IN RATS BY TMPYP4?

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**Background.** This animal study to investigate the effect and possible mechanisms of telomerase inhibition therapy on HCC in the rat.

**Methods.** Adult male LEW/SsN rats were divided into 3 groups of 50 animals each. Group A was the control group. Groups B and C were given diethylnitrosamine, 5 mg/kg/day. In addition, Group C rats received an intraperitoneal injection of TMPyP4 (tetra N-methyl-4-pyridyl-porphyrin chloride), 0.3 mg/kg/day for 14 days. Ten animals in each group were sacrificed 6, 12, 18, 20 and 24 weeks to evaluate for development of HCC and metastasis. The weight of the rat, the liver, liver tumors, and number of organs involved by HCC were measured at each stage. We compared Bcl-2 mRNA, telomerase mRNA, and telomerase activity at 24 weeks in the liver tissue of group A rats and tumor tissue of HCC from group B and C rats.

**Results and Conclusion.** No HCC developed in group A, but tumors were present in group B and C rats by the 18th week. At the 20th and the 24th weeks, the changes of body weight increased without significance. However, the median liver weight in group B was 0.62g (range: 0.55–0.72 g) and 0.81g (range: 0.68–0.94 g) ( $P=0.04$ ), and that in group C was 0.34 g (range: 0.30–0.42 g) and 0.39g (range: 0.31–0.49 g) ( $P=0.43$ ). The group C rats' liver weight was significantly lower than that of group B rats both times ( $P=0.012$  and  $0.007$ ). At the same times, the median metastasis score (number of organ system involved) was 3 (range: 2–3) and 3 (2–3) in group B, and 1

(1–2) and 1 (1–2) in group C, a significant difference between the groups ( $P=0.008$  and  $0.003$ ). Group B's Bcl-2 mRNA was significantly higher than group A's ( $P=0.025$ ), while group C's was lower than group B's, although not significantly so ( $P=0.530$ ). Group B's telomerase mRNA was significantly higher than group A's ( $P=0.033$ ), but group C's was significantly lower than group B's ( $P=0.018$ ). The same intergroup relationship was also true for telomerase activity ( $P=0.001$  and  $0.037$ ). TMPyP4 effectively inhibits both liver tumor progression and metastasis in rats "in vivo". A possible mechanism is TMPyP4-induces inhibition of telomerase and telomere which plays an essential role in HCC cell proliferation and progression.

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#### GENETIC EXPRESSION PROFILE OF SIGNAL TRANSDUCTION (ST) PATHWAYS IN W-3 FATTY ACID TREATED PANCREATIC CANCER CELLS

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This study profiles the effects of n-3 FA, gemcitabine (GEM) and a combination treatment of n-3 FA and GEM on 18 human ST pathways to further the global analysis of n-3 FA treated pancreatic cancer cells.

**Methods.** MIA PaCa-2 cells were treated with DMEM (control), 100  $\mu$ m n-3FA emulsion (95  $\mu$ m EPA and 78  $\mu$ m DHA), 100  $\mu$ m GEM and a combination treatment of 100  $\mu$ m n-3 FA emulsion and 100  $\mu$ m GEM for 12 hours at 37°C and 5% CO<sub>2</sub>. Homogenized cell contents were transferred to Qiagen RNeasy columns, washed and RNA was eluted; spectrophotometry and gel electrophoresis confirmed the quality of material. Microarray analysis used a 60-mer oligonucleotide array (113 genes, 18 human ST pathways, Superarray). Data was analyzed with minimal value background subtraction and normalized with an interquartile normalization technique. Spots were considered absent if signal intensity was less than  $1.5 \times$  the average intensity of the lower 75th percentile of all non-bleeding spots. Significance was determined as a 1.5-fold difference in expression compared to control, DMEM.

Table 1. Significant Differential Expression Profile for Each Treatment.

100 $\mu$ m n-3 FA			100 $\mu$ m GEM			Combination Treatment		
Gene symbol	Pathway(s)	Fold change	Gene symbol	Pathway(s)	Fold change	Gene symbol	Pathway(s)	Fold change
WSB1	Hedgehog	2.161	FOXA2**	Hedgehog	13.066	CYP19A1	CREB	2.337
IL2RA	Calcium/PKC	1.959	CDKN1A	Androgen	1.867	CDKN1A	TGFB	2.093
				TGFB			p53	
				p53	1.840		Androgen	
TFRS	Calcium/PKC	1.760	TNFRSF10B	p53	1.840	CDKN2A**	TGFB	2.045
TNFRSF10B	p53	1.759	CDK2	Androgen	1.640	CDKN2B**	TGFB	2.022
TMEPAI	Androgen	1.548	STRA6	Retinoic Acid	0.658	TP53	Stress	1.620
CTSD	Retinoic Acid	0.663	MYC	Wnt	0.657	IL2	NFKB	1.594
	Estrogen			PI3K/AKT			NFAT	
				Stress			Calcium/PKC	
EGRI	PLC	0.651	CDKN1B	TGFB	0.651	FN1"	PI3/AKT	1.593
	Mitogenic							
	CREB							
FOS	Calcium/PKC	0.630	GYS1	Insulin	0.605	IRF1	Jak-STAT	1.591
	PLC							
	Mitogenic							
	CREB							
	Stress							
BCL2L1	Jak/Src	0.614	NAB2	Mitogenic	0.529	CDKN1B	TGFB	0.659
BRCA1	Estrogen	0.574	FOS	Calcium/PKC	0.502	BIRC5	Wnt	0.618
				PLC				
				Mitogenic				
				CREB				
				Stress				
STRA6	Retinoic Acid	0.415	EGRI	PLC	0.489	NFKBIA	NFKB	0.577
				Mitogenic				
				CREB				
						FOS	Calcium/PKC	0.520
							PLC	
							Mitogenic	
							CREB	
							Stress	
						TMEPAI	Androgen	0.506
						STRA6	Retinoic Acid	0.438

\*Fold Change was calculated relative to cells treated with DMEM for 12 hours (control). Significance was defined as a 1.5-fold change in expression relative to control after minimum value background subtraction. \*\*Gene in control treatment considered absent (less than  $1.5 \times$  average intensity of lower 75th percentile of non-bleeding spots).

**Results.** n-3 FA had significant differential expression in 11 genes (Table 1). Of these, 7 genes were differentially expressed in only n-3 FA treatment: IL2RA, TFRC, TMEPAI, WSB1, BCL2L1, BRCA1 and CTSD. GEM treatment had 11 genes differentially expressed, representing 13 pathways (Table 1). Of these, 5 genes were differentially expressed in only GEM treatment: CDK2, FOXA2, GYS1, MYC and NAB2. Combination treatment had differential expression in 14 genes, representing 14 pathways (Table 1). Of these, 10 are differentially expressed in only combination treatment: CDKN2A, CDKN2B, CYP19A1, FN1, IL2, IRF1, TP53, BIRC5, NFKBIA and TMEPAI. TMEPAI was found up-regulated in n-3 FA and down regulated in combination treatment and is considered unique to each treatment because its regulation was different for each.

**Conclusion.** The anti-neoplastic effects associated with n-3 FA are associated with differentially expressed genes or combinations of genes not present and/or differentially expressed in the genetic profile of GEM; for which there is poor evidence of anti-neoplastic activity. The pathways and genes highlighted herein will serve as a template for future pathway-focused studies for n-3 FA and combination strategies to examine genetic-level mechanisms that may potentially increase pancreatic cancer cell chemosensitization.

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### TUMOR GENETICS AND SIGNALING RESPONSE TO GEMCITABINE CORRELATE WITH TREATMENT EFFECT OF GEMCITABINE-BASED MOLECULAR TARGETING STRATEGIES

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**Introduction.** Pancreatic cancer is a deadly cancer with 5-year survival rates of <5%. Gemcitabine is standard chemotherapy but has minimal efficacy. Molecular targeting of critical signaling pathways in combination with gemcitabine may improve responses. Pancreatic cancers may have differential responses according to their molecular genetics and signaling response to treatment.

**Purpose.** To determine if pancreatic cancer cells with different genetic profiles will respond differently to various molecular-targeted agents.

**Methods.** PANC-1, PaCa-2, and BxPC-3 cells were treated with curcumin (0.5–25µM), LY294002 (5–50µM), or PD325901 (0.1–1µM) alone or in combination with gemcitabine (0.005–10µM). Proliferation was measured with cell counts. Enzyme activity was measured with Western, EMSA and ELISA.

**Results.** All cells had concentration-dependent decreased proliferation with each agent. BxPC-3 was sensitive to low doses of each agent, but gemcitabine or PD325901 were most effective agents for Kras-mutated PANC-1 or PaCa-2. All cells decreased NF-κB activity with curcumin (24hr) and MEK activity with PD325901 (24hr). Pi3Kinase activity decreased early (3hr) but rebounded to (PaCa-2) or above (Panc-1, BxPC-3) basal in LY294002-treated cells (24hr). Combination of molecular-targeted agents with gemcitabine resulted in at least additive effects on inhibition of proliferation in all cells. For PANC-1, curcumin+gemcitabine was nearly synergistic. Correspondingly, PANC-1 demonstrated an increase in gemcitabine-induced NF-κB activity. For PaCa-2, LY294002+gemcitabine was synergistic. Correspondingly, long term (24hr) PaCa-2 Pi3Kinase activity was not induced by LY294002. Finally, gemcitabine+PD325901 was only effective in Kras-wildtype BxPC-3. Correspondingly, BxPC-3 demonstrated the greatest increase in gemcitabine-induced MEK activity.

**Conclusions.** These results demonstrate differences in treatment effects, which correlate with tumor genetics and signaling response to treatment. Genetic and signaling profiles of each tumor may be necessary to determine an optimal treatment strategy for pancreatic cancer.

Table 1: Drug effect on pancreatic cancer cell growth alone or in combination with gemcitabine

	Gemcitabine	PD325901	LY294002	Curcumin
Panc-1 IC-50	0.02	0.75	35	17
Panc-1 combination with gemcitabine		LA	A	HA
PaCa-2 IC-50	0.01	0.1	10	8
PaCa-2 combination with gemcitabine		LA	S	A
BxPC-3 IC-50	0.005	0.4	15	1
BxPC-3 combination with gemcitabine		HA	A	A

Concentrations are micromolar. S=synergism, HA=highly additive, A=additive, LA=weakly additive.

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### A NOVEL CONDITIONALLY REPLICATIVE ADENOVIRUS GENE THERAPY TARGETING OVEREXPRESSION OF CHEMOKINE RECEPTOR CXCR4 IN A PANCREATIC CANCER CELL LINE

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**Background.** Overexpression of the chemokine receptor CXCR4 has been demonstrated in a variety of solid tumors including pancreatic cancer, and is believed to play a pivotal role in cancer metastasis by facilitation of cell migration. In vitro and animal studies designed to block CXCR4 have reduced tumor cell migration and abrogated metastatic development. Use of a conditionally replicating adenovirus (CRAD) gene therapy may represent a useful modality to exploit CXCR4 overexpression. CRADs utilize the expression of a gene product specific to cancer cells as a promoter for production of cytotoxic gene products. In this study, we investigated the in vitro activity of a CRAD based gene therapy targeting CXCR4 against the human pancreatic cancer cell line CRL-1918.

**Methods.** CXCR4 overexpression was assessed by western blot analysis. The pancreatic cancer cell line was cultured and divided into three groups. Each group was treated with a different adenovirus vector. Group 1, the negative control, was infected with a non-replicative adenovirus expressing green fluorescent protein. Group 2, the positive control group, was treated with a CRAD containing no upstream promoter. Group 3 utilized a CRAD with a CXCR4 promoter. Each group was infected with a logarithmic cell to adenovirus ratio beginning at 1:1 and ending at 1:10,000. Crystal-violet staining was used to assess cell viability.

**Results.** Western blot analysis confirmed overexpression of CXCR4 in this human pancreatic cell line. Marked cell cytotoxicity was noted in Group 3. This group achieved 100% cell death at an infection ratio of 1:100 and 1:1000. There was no appreciable cytotoxicity noted in the negative control group.

**Conclusion.** The human pancreatic cell line CRL-1918 was found to overexpress CXCR4. By targeting CXCR4, conditionally replicating adenovirus therapy was able to successfully achieve E1A-mediated cytotoxicity at concentration similar to positive controls. CXCR4 targeted CRAD gene therapy demonstrates in vitro efficacy against the human pancreatic cell line CRL-1918. This novel CRAD may serve as a tumor-specific target for the treatment of pancreatic cancer.

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### PEPTIDE YY (PYY) AND INOSITOL HEXAPHOSPHATE (IP6): EVALUATION OF NATURAL AND NOVEL COMPOUNDS FOR THE TREATMENT OF PANCREATIC CANCER

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**Background.** We have reported that both PYY and IP6 inhibit cell growth in the PANC1 pancreatic cancer cell line *in vitro* when applied as single and combined therapies. To confirm the additive effects of combined therapy with PYY and IP6, we evaluated their effects in regards to cellular proliferation, apoptotic activity and VEGF production in both the PANC1 and MIAPACA cell lines.

**Materials and methods.** The MIAPACA and PANC-1 human pancreatic cancer cell lines were cultured using standard techniques and treated with IP6 (0.8mM/well), PYY (500pMol/ml) and the combination of the two. Cell viability was measured by MTT at 24, 48 and 72 hours. VEGF production was measured in the cell supernatants by ELISA. Apoptosis was evaluated by Annexin V-FITC and results calculated using FACS analysis. Statistical analysis was performed by ANOVA.

**Results.** Significant reductions ( $p < 0.01$ ) in cellular proliferation were observed with IP6 in both cell lines at 24, 48, and 72 hours (Range 12.7–75.3%). The combination of PYY and IP6 displayed additive effects on cellular proliferation when compared to that of each alone in both cell lines tested at 48 hours. In MIAPACA cells, IP6 decreased cell proliferation by 40.6% and PYY by 14.1%; however when combined, the response increased to 63.7%. The anti-proliferative response was increased to 46.5% by combined treatment in the PANC1 cells; compared to 25.9% with IP6 and 9.6% with PYY alone. No changes in apoptotic or necrotic activity were observed in either cell line tested with PYY, IP6 or when combined. IP6 reduced VEGF by 37.2% in the PANC1 cells ( $p = 0.04$ ) and by 68.3% in MIAPACA cells compared to control ( $p < 0.001$ ).

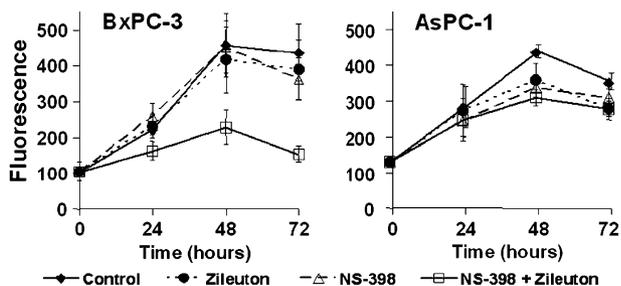
**Conclusions.** These findings support that combination therapy with IP6 and PYY has the potential to become an effective adjunct for pancreatic cancer treatment. The reduction in VEGF in both cell lines suggests that IP6 may act as an anti-angiogenic agent. Further *in vivo* and human studies are planned to evaluate the safety and clinical utility of these agents in patients with pancreatic cancer.

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**SYNERGISTIC EFFECT OF SIMULTANEOUS 5-LOX AND COX-2 INHIBITION ON PANCREAS CANCER CELL GROWTH IN VITRO**

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Inflammatory mediators produced by arachidonic acid (AA) metabolism via the COX-2 and 5-LOX pathways are thought to play a role in the development of cancer. The use of non-steroidal anti-inflammatory drugs (NSAIDs), including COX-2 inhibitors, has been consistently associated with reduced risk in multiple cancers. In pancreatic cancer, however, the association of NSAID use and cancer risk is not clearly defined. Pancreatic cancers frequently over-express both COX-2 and 5-LOX. Specific inhibition of COX-2 alone may result in a shift of AA towards the 5-LOX pathway leading to increased production of proinflammatory leukotrienes. We examined the effect of the COX-2 inhibitor, NS-398, and the 5-LOX inhibitor, zileuton, on the growth of human pancreatic cancer cell lines, BxPC-3 and AsPC-1. Proliferation was monitored over 72 hours of exposure to the drugs individually or in combination. For combination treatments, minimally effective doses that individually produced 10–20% inhibition in each cell line were selected. Potential synergy between drugs, defined as greater than additive growth effects, were tested in a linear mixed effects model fit using a restricted maximum likelihood procedure. In BxPC-3 cells, which express both COX-2 and 5-LOX, individual drugs inhibited proliferation by 15.9% for NS-398 (100 microM) and 12.2% for zileuton (250 microM). When the drugs were combined, statistically significant synergy was seen with inhibition increased to 63.7% ( $p=0.0025$ ). In AsPC-1 cells,



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**INHIBITION OF PANCREATIC CANCER CELL PROLIFERATION BY A COMBINATION TREATMENT STRATEGY EMPLOYING N-3 FATTY ACIDS AND GEMCITABINE**

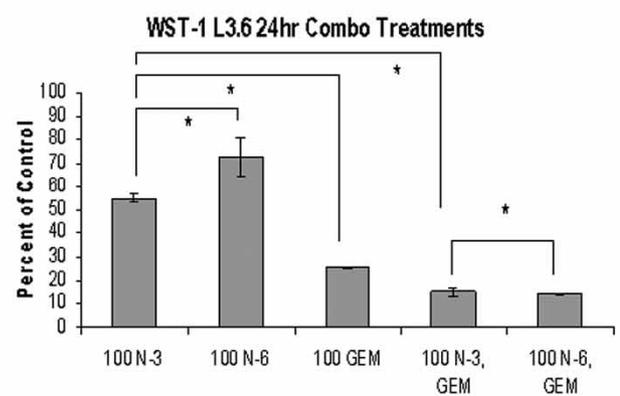
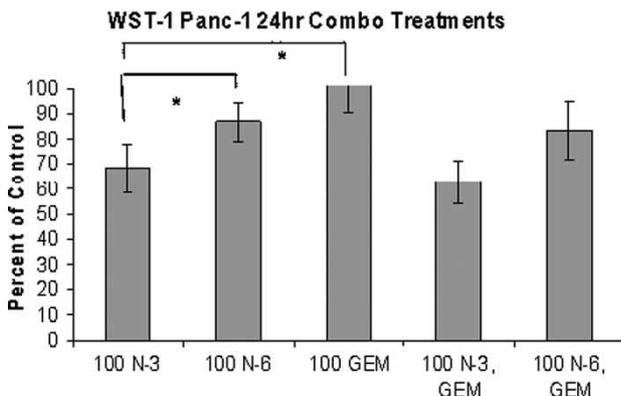
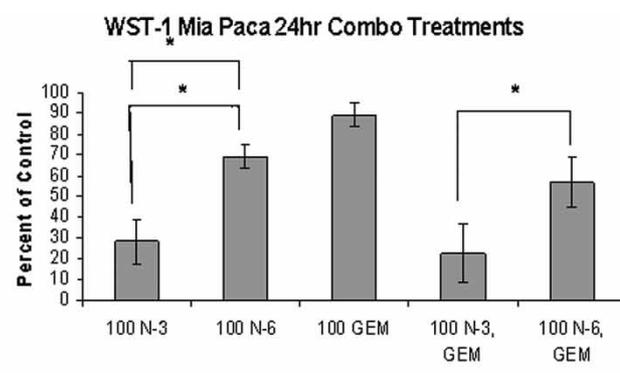
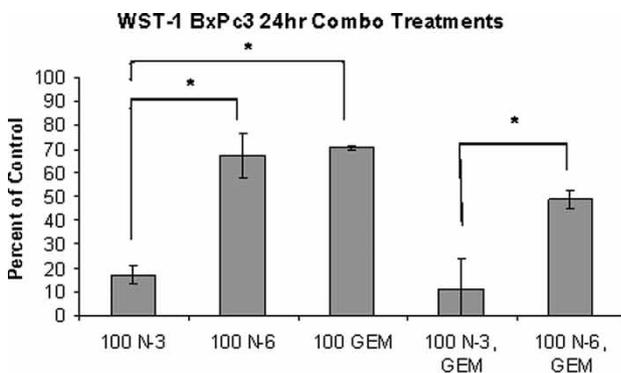
Justin Hering, MD, Anthony Razzak, Sean Garrean, MD, Babcock Tricia, Jose Trevino, MD, Ws Helton, MD, N Espot, MD  
UIC, Chicago, IL

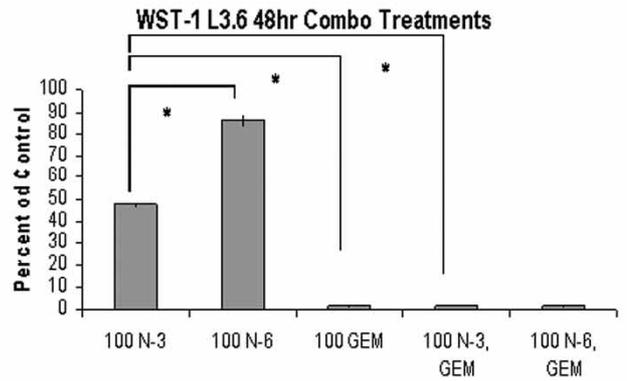
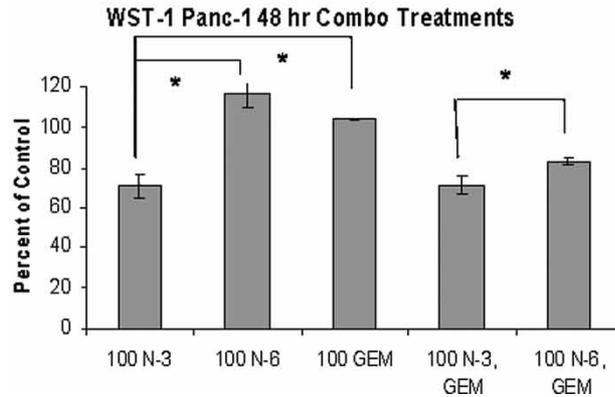
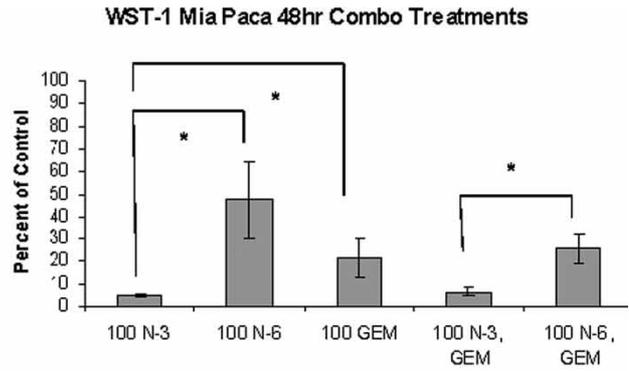
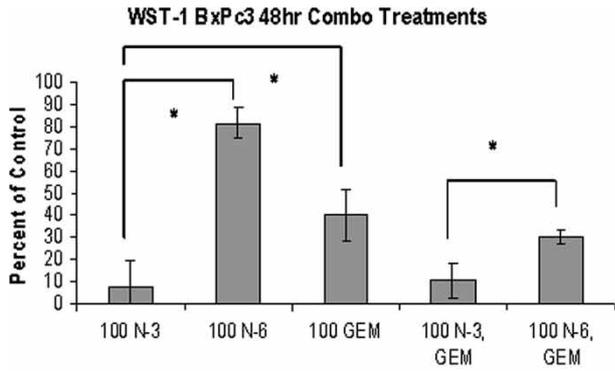
Gemcitabine (GEM) is the standard treatment for pancreatic cancer. Pancreatic cancer has been demonstrated to have significant chemoresistance to GEM attributable to increased NF- $\kappa$ B activation. Several models have demonstrated that n-3 fatty acids (n-3FA) can significantly decrease proliferation of several pancreatic cell lines and in MIA Paca2 cells this decrease has been demonstrated to occur through G2/M arrest leading to increased apoptosis. These experiments were designed to evaluate combination n-3FA with GEM as inhibitors of proliferation and evaluate the potential to overcome the known chemoresistance. In this study, the effects of n-3FA alone and in combination with GEM on proliferation in 4 distinct in-vitro models are examined.

**Methods.** MIA PaCa2 & L3.6 (GEM sensitive[S]) and BXPc3 & Panc1 (GEM resistance [R]) pancreatic CA cell lines were treated with 100 mM of n-3FA or GEM alone or in combination for 24 and 48 hrs; (n-6 FA were used as control). Non-lipid control used media alone, for a percent of control calculation. Proliferation was measured by WST-1 assay. Experiments were run in triplicate and statistics were done by Chi<sup>2</sup> analysis, significance at  $p < 0.05^*$  (Table).

**Results.** n-3FA were found to significantly reduce cellular proliferation as compared to n-6FA and GEM treated cells at 24&48hr time points. GEM combined with 100 mM n-3FA was not demonstrated to be any more effective at inhibiting proliferation than n-3 FA treatment alone except in the highly sensitive L3.6. n-3FA/GEM did significantly decrease proliferation compared to n-6FA/GEM. However, n-6FA/GEM treatment was statistically decreased compared to n-6FA treatment alone in all groups except L3.6.

**Conclusion.** Based on the individual cell line, underlying GEM R or S; differential n-3FA effects were observed. For GEM resistant cell lines, n-3 FA with GEM contributed to increased cell death versus control. In addition, the





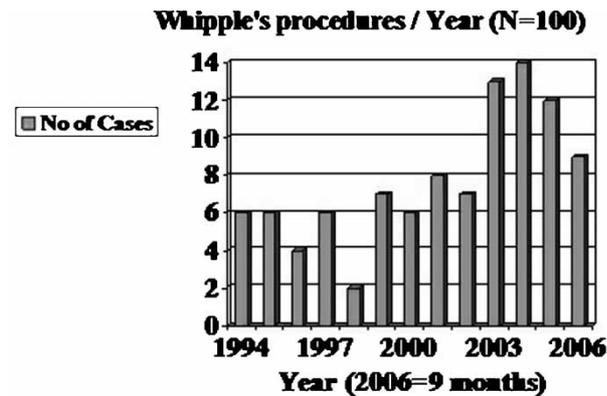
more GEM resistant a cell type was the greater the observed effects of n-3 FA/GEM. These observations have interesting implications for future treatment design.

**Oral Posters – Pancreas I: Outcomes**  
 OP-04  
 4/20/07 1:30 to 3:30 pm  
 Abstract Numbers 41–52

**41**  
**MORTALITY RATES FOR PANCREATICODUODENECTOMY (WHIPPLE'S PROCEDURE) IN A MEDIUM VOLUME, PUBLIC FUNDED SYSTEM**

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**Background.** There is general agreement that regionalization of low volume, high risk surgical procedures such as a Whipple's procedure results in lower mortality rates and may improve survival. The Winnipeg Regional Health Authority audited Whipple's procedures performed at the 6 regional hospitals from 1999–2001. 34 cases had Whipple's at 3 hospitals. The Health Sciences Center (HSC) performed half the cases with a 0% mortality, and the other 2 hospitals had a 6% mortality (NS). Following this audit, all Whipples procedures in the region are performed at HSC. This paper evaluates whether this medium volume, public funded, tertiary care institution with a feeding population of 1.2 million meets the designated standards of performance for Canada, and those published in the United States.



**Method.** A retrospective review of Whipple's procedures at one hospital (HSC) was undertaken from January 1994 to December 2000. A prospective audit was instituted in 2001, and is ongoing. The database was examined to establish volume of procedures and mortality rates.

**Results.** A total of 100 pancreaticoduodenectomies were performed from 1994–Oct 2006. Annual hospital volumes increased after consolidation of services at one site (table1). The in hospital mortality was 1%, and the 30 day mortality was 2%. The in hospital death apparently occurred from hemorrhage after reinstitution of long term anticoagulation. The other death occurred in a patient with long standing cardiac disease who presented to another emergency room in cardiogenic or septic shock one week after discharge.

**Conclusion.** The mortality rate for a Whipple's procedure at the Health Sciences Centre in Winnipeg is below that reported in Ontario, and compares favorably with that reported from higher volume institutions in the United States. Current volumes are adequate to maintain a regional hepatobiliary service, avoiding the need to transport patients over 1000 miles to the nearest larger Canadian center.

**42**  
**THE OUTCOME OF SURGICAL MANAGEMENT OF PANCREATIC AND NON PANCREATIC PERIAMPULLARY TUMORS**

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**Background & Aims.** Surgery remains the curative option for patients with either pancreatic or periampullary tumors. The outcome of surgical management of patients with these tumors by evaluating the prognostic factors influencing survival and recurrence is reported here.

**Methods.** The current study examines the outcome of surgical therapy either with curative or palliative intention in patients with pancreatic and non pancreatic periampullary tumors. One hundred and forty patients with these tumors underwent surgery from January 1990 to December 2004. Survival and disease-free survival were evaluated. Univariate and multivariate analyses were performed to determine factors affecting survival and recurrence.

**Results.** The overall median survival time was 6 months after by-pass operations (n=28) and 20 months after resection (n=112). In patients who underwent resection, the 5 year actuarial survival rate was 14.2% whereas the 5 year disease-free survival rate was 9.8%. Among these patients pancreatic adenocarcinoma accounted for 55% of resections, with a median survival of 17 months and an actuarial 5 year survival of 6% whereas patients with non pancreatic periampullary adenocarcinoma had median survival of 31 months and an actuarial 5 year survival of 24%. In the former subgroup, multivariate analysis identified an advanced UICC stage (p=.01) as a significant predictor of shorter disease-free survival. However, in the latter subgroup postoperative sepsis (p=.008) and the presence of four or more lymph nodes

were found to be associated with worse survival rates ( $p = .009$ ) whereas a poor tumor differentiation ( $p = .03$ ) was found to be significantly related to shorter disease-free survival.

**Conclusions.** Patients who had non pancreatic periampullary tumors had a better prognosis and survival than those with pancreatic tumor. Factors influencing survival and recurrence included stage of disease, number of lymph nodes, postoperative sepsis, and tumor grading.

#### 43 FEASIBILITY AND SAFETY OF PANCREATODUODENECTOMY (THE WHIPPLE PROCEDURE) IN A HIGH VOLUME COMMUNITY HOSPITAL

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**Purpose.** The purpose of current study is to evaluate whether pancreaticoduodenectomy (PD) can be safely performed in a high volume community center with results comparable to a high volume university setting.

**Method.** Retrospective review of 45 consecutive pancreaticoduodenectomies performed by a single surgeon in a community center over 13 months. Morbidity, mortality, final pathology, margin and lymph node status were analyzed.

**Results.** five PDs were performed for benign preoperative diagnoses. There was one postoperative death (2.2%). There were 18 periampullary cancers, 12 intrapapillary mucinous neoplasms (IPMN), 4 benign adenoma of ampulla or duodenum, 1 neuroendocrine tumor, one solid pseudopapillary tumor and 2 cystadenoma/cystadenocarcinoma. 8 patient had a positive margin (17.7%) and 14 patient had a positive nodal status (31.1%).

**Conclusion.** Volume-outcome relation has been reported previously and regionalization of PD has resulted mostly in academic settings. Here we report the safety and feasibility of performing PD in a high volume community center with outcomes comparable to high academic centers. We propose that such a center can be safely assigned as a regional center for PDs. The experience of the surgeon and familiarity of hospital team members with the disease process play a key role in achieving these outcomes.

#### 44 SAFETY OF PANCREATIC RESECTION IN THE ELDERLY

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**Aim.** In recent years, pancreatic resection has come to be indicated mainly in the elderly. However, risk increases with age, therefore, indication of the operation as well as pre- and post-operative management are important. The safety of pancreatectomy was investigated retrospectively in elderly patients over 75 years in this department.

**Materials and methods.** From May 1996 and December 2005, 243 patients underwent pancreatic resection. The operative procedure was pancreaticoduodenectomy (PD) in 180 cases and distal pancreatectomy (DP) in 63 cases, and combined resection of portal vein was performed 36 cases. The subjects were divided into two groups by the aged 75 and above (aged group,  $n = 41$ ,  $77.1 \pm 3.2$  yr) and the aged 74 and below (control,  $n = 202$ ,  $61.2 \pm 8.8$  yr). Fifteen preoperative factors and 4 operative factors were compared between these two groups.

**Results.** Postoperative complications were seen in 86 cases (35.4%), and death during hospital stay occurred in 10 cases (4.1%). In the term of 15 preoperative factors, the incidence of cardiovascular failure and urea level were significantly higher in the aged group than in the control. In the 4 operative factors, the operative time was significantly lower in the aged group than in the control. There were no difference between the groups for post-operative complication (16/41, 70/202) and hospital death (2/41, 8/202).

**Conclusion.** Pancreatic resection can be performed safely even in elderly patients.

#### Results

	Aged group (Over 75 yrs)	Control (Less than 74 yrs)	P value	Significance
Jaundice (yes)	17/41 (41%)	78/202 (39%)	0.733	(-)
Respiratory failure (yes)	5/41 (12%)	11/202 (5%)	0.213	(-)
Cardiovascular failure (yes)	12/41 (29%)	18/202 (9%)	<0.001	**
Diabetes mellitus (yes)	10/41 (24%)	54/202 (27%)	0.756	(-)
Prothrombin time (%)	92.6+12.9	92.8+16.0	0.949	(-)
Cholinesterase (U/ml)	244+83	262+70	0.137	(-)
Urea (mg/dl)	15.0+5.5	13.3+4.6	0.032	*
Blood loss (ml)	660+451	870+708	0.069	(-)
Operation time (min)	398+102	451+118	0.007	**

#### 45 COMMUNITY HOSPITAL OUTCOMES OF WHIPPLE PROCEDURE - FOR REGIONALIZATION OF CARE

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Because the outcome of Pancreaticoduodenectomy (PD) has been shown to depend on surgeon and hospital volume we have examined our results for PD at a regional nonprofit HMO Medical Center that is part of a regional network of hospitals. The study focus is operative and oncologic outcome. A detailed analysis of the PD volume at all other network hospitals was performed. All PD cases from 1999 to 2006 were retrospectively reviewed. On average 13 PD were performed per year. The Kaplan Meier method was used for survival analysis. Of 92 patients undergoing PD, 25 had benign neoplasm's or non-AdenoCA malignancies. 67 patients with AdenoCa (AC) of the pancreas or the ampulla were entered in the survival analysis. The majority of patients had stage 2B. The rate of positive margins was 6%. Adjuvant therapy was given to 71% of Head AC and 20% of Ampuller AC patients. For the whole series 30 day hospital mortality was 3%, major morbidity was 15%, average LOS was 11 days, and mean operating time and blood loss was 4 hrs and 450 ml respectively. Mortality occurred only after PV or SMV resection with reconstruction. Mean overall survival was 35 months for head AC and 82 months for ampullary AC. Liver metastases were the major cause of death. The resection rate for all patients explored for AC of the pancreas was 74%. Median survival in unresected patients was 10 months. Our results show that PD can be performed safely in a high volume managed care community hospital with outcomes equivalent to those published in modern series. Analysis at all other network hospitals shows a great disparity in PD volume. Only 2 network hospitals fulfill "high volume" criteria. This underscores the value of regionalization for high risk, low volume cancer surgery and supports the creation of a limited number of regional subspecialty centers for pancreato-biliary disease within an HMO hospital network.

#### 46 OUTCOME FOLLOWING RESECTION FOR PANCREATIC CANCER BASED ON SURGEON EXPERIENCE: THE LONG AND SHORT OF IT

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**Introduction.** The Medicare database has proven invaluable in correlating hospital and surgeon volume with short term outcome following major abdominal surgery. Long term outcome (i.e. survival) is more difficult to ascertain due to inherent limitations of this database but is arguably the most important of all outcome variables in patients with cancer. Herein we report short and long term outcomes following pancreaticoduodenectomy for adenocarcinoma performed by low and high volume surgeons at the same institution.

**Methods.** A pancreatic cancer database begun in 2001 consisting of over 400 patients was queried to identify patients more than 48 months from undergoing pancreaticoduodenectomy for adenocarcinoma by low (<7/year) and high (>7/year) volume surgeons. Kaplan-Meier survival curves were generated for each group and compared using the log rank test. Short term outcomes were tabulated for low and high volume surgeons and compared using the student's t-test. Data are presented as mean  $\pm$  standard deviation.

**Results.** Patients operated on by low and high volume surgeons were similar in terms of age, gender and disease stage on final pathologic exam but inexperienced surgeons operated on patients with significantly higher comorbidities. Adjuvant chemoradiation therapy was applied with similar frequency for each group. Surgeon experience significantly impacted most intraoperative variables such as blood loss, operative time and transfusion requirement while length of stay, complications and short and long term survival were not impacted. (Table).

Surgeon experience	Outcome following resection for pancreatic cancer based on surgeon experience		
	Low (n=13)	High (n=38)	p value
Length of Stay (days)	13.2 $\pm$ 5.18	15.3 $\pm$ 10.25	n.s.
Estimated Blood Loss (ml)	1323.1 $\pm$ 1036.54	562.2 $\pm$ 312.81	0.0029
Operative Time (hrs)	7.9 $\pm$ 1.23	5.0 $\pm$ 1.03	<0.0001
Intraoperative Transfusion (units)	2.4 $\pm$ 2.87	0.3 $\pm$ 0.69	0.0017
Postoperative Transfusion (units)	1.2 $\pm$ 3.05	1.4 $\pm$ 4.48	n.s.
Major complications (%)	46.2	36.8	n.s.
30 day mortality (%)	7.7	5.3	n.s.
Comorbidities per patient	2.5 $\pm$ 2.40	1.2 $\pm$ 1.05	0.0318
Overall Survival (months)	12.1 $\pm$ 9.42	16.1 $\pm$ 12.53	n.s.

Data presented as mean  $\pm$  SD, (n.s. = p value not statistically significant).

**Conclusions.** Surgeon experience, while critical in determining perioperative factors does not impact long term outcome following pancreaticoduodenectomy for cancer. This observation may reflect the futility of surgical management for pancreatic cancer, patient selection or the requisite low number of patients necessary to define inexperienced surgeons for such comparisons.

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#### PANCREATIC CANCER SCREENING PROGRAM: TRANSCUTANEOUS ULTRASOUND, MAGNETIC RESONANCE IMAGING, AND PSYCHOSOCIAL MEASURES

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Mount Sinai Hospital, Toronto, ON, Canada; University Health Network, Toronto, ON, Canada; Women's College Hospital, Toronto, ON, Canada; Toronto Sunnybrook Regional Cancer Centre, Toronto, ON, Canada; University of Toronto, Toronto, ON, Canada

The poor prognosis associated with pancreatic adenocarcinoma is primarily due to late detection. Currently, there are no clinical screening guidelines available for this cancer, particularly for individuals who are at higher risk. We implemented a pancreatic cancer screening protocol including annual transcatheter abdominal ultrasound, magnetic resonance imaging (MRI), and blood collection (for future biomarker studies) for individuals at increased risk for this disease. Participants were also asked to complete pre- and post-test psychosocial questionnaires to measure pancreatic cancer worry, pancreatic cancer specific anxiety, perceived risk, and satisfaction with the screening/genetic counselling program. To date, 176 participants have been enrolled since 2003, with 57 subjects having undergone at least three sets of screening studies. The majority of participants are individuals with familial pancreatic cancer (56.8%), BRCA2 carriers (29.5%), and p16 carriers (5.7%). Thirty three (18.8%) individuals have required further investigation based on ultrasound or MRI findings. No cases of pancreatic adenocarcinoma have been identified. Incidental findings include a 3.5 cm neuroendocrine tumour of the pancreas in an individual with familial pancreatic cancer (FPC); a suspected intraductal papillary mucinous neoplasm (IPMN) in another FPC case; and a gastrointestinal stromal tumour (GIST) of the stomach in a p16 carrier. Following screening/counselling, the FPC group had reductions in perceived risk for pancreatic cancer while levels of cancer-related worry and anxiety for both the FPC and BRCA2 groups remained stable from pre to post counselling. Overall satisfaction with the screening/counselling program has been high. Recruitment and surveillance will continue for at least 5 years for each subject.

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#### TREATMENT OF PANCREATIC CANCER IN A SINGLE PAYER NETWORK

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**Background.** The incidence of pancreatic continues to increase. It remains the 4th leading causes of cancer death in the United States. The purpose of this study was to characterize multimodality treatment of pancreatic cancer over several decades. We analyzed the records of 4640 patients diagnosed with adenocarcinoma of pancreas during this study period.

**Methods.** A retrospective review was undertaken to identify patients with adenocarcinoma of pancreas treated at all the Northern California Kaiser Permanente facilities. The large cohort of patients included all stages of disease. All patients received their treatment between January 1970 and January 2006. Univariate and multivariate analyses of predictive factors were evaluated with the log-rank test and Cox regression. In addition chi-square test of relevant clinicopathologic factors determined which factors were predictive of overall survival (OS).

**Results.** Mean age was 68 years (range 13–102). Mean follow-up was 9 months (range 1–292) and 52% were male. By univariate and multivariate analysis age, sex, stage, surgery, chemotherapy and radiation were predictive of OS ( $p < .05$ ). The strongest determinant of survival was surgery. Surgery patients had an OS of 42 months versus 8 months in those patients who did not undergo any surgical intervention. Chemotherapy and radiation both increase survival by 4 months and 7 months, respectively ( $p < .05$ ). However OS did not change through the various decades ( $p > .05$ ).

**Conclusion.** Despite the various advances in technology and chemotherapeutic agents in the past several decades pancreatic cancer remains lethal. Complete surgical resection continues to be the strongest predictor of survival.

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#### PRACTICE VARIATION AND OUTCOMES OF PANCREATICO-DUODENECTOMY: A POPULATION-BASED STUDY

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Although surgical resection is the only curative modality for pancreatic cancer, there is ongoing debate on how the technique and extent of surgery impacts outcomes. This population-based study examines variations in current surgical practice and outcomes in this group of patients. All patients 18–85 years old diagnosed with non-metastatic adenocarcinoma of the pancreatic head from 1998–2003 were identified from the Surveillance, Epidemiology and End Results (SEER) registry. Tumors with extension to organs other than the duodenum were excluded. Patients were stratified by the extent of organ resection and lymphadenectomy. Logistic regression was used to elucidate independent factors associated with the type of surgery. Early mortality and cancer-specific mortality were derived from Kaplan-Meier methods and Cox models. A total of 3467 patients were identified, of whom 1607 had surgery. Subtotal pancreatectomy (SP) was performed in 1428 patients (89%), total pancreatectomy (TP) in 124 (7.7%) and extended pancreaticoduodenectomy in 55 (3.4%). Among patients who had SP, pylorus-preserving pancreaticoduodenectomy (PPPD) was performed in 118 patients (8.3%), standard Whipple (SW) in 1225 (85.8%) and the extent of gastric resection was unspecified in 85 (6.0%). There were no significant differences in age, sex, race, tumor size or extent, nodal status or use of radiotherapy between patients who received PPPD, SW or TP. There was marked regional variation in the rates of TP (range 0–15%,  $p < .001$ ) and PPPD (range 0–35.7%,  $p < .001$ ). TP was associated with a significantly higher 30- and 60-day mortality (HR at 30 and 60 days: 2.2), but long term survival did not differ significantly between TP, PPPD and SW ( $p = .44$ ). Although the extent of organ resection was not associated with differences in lymphadenectomy, significant regional variation was found with rates of extended lymphadenectomy ranging from 0% to 9.8% across SEER regions ( $p = .02$ ) and the mean number of LN retrieved ranging from 7.7 to 13.5 ( $p < .001$ ). Importantly, increased LN retrieval independently resulted in improved long term survival ( $p = .0001$ ). In this large, population-based study, we found marked regional variation in the surgical treatment of adenocarcinoma of the pancreatic head. Significant variation in extent of organ resection was found but there were no associated differences in number of LN retrieved or long term outcomes. However, extent of lymphadenectomy was found to have significant regional variation and was associated with long term outcomes. Future improvements in surgical therapy for adenocarcinoma of the pancreatic head may be best focused on performance of adequate lymphadenectomy.

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#### OUTCOME OF DISTAL PANCREATECTOMY FOR PANCREATIC ADENOCARCINOMA

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**Introduction.** Due to the late presentation, adenocarcinoma of the distal pancreas is often irresectable. However in recent times, investigators are reporting increasing numbers of patients undergoing distal pancreatectomy (DP) for adenocarcinoma of the pancreas of which a significant proportion would require an extended resection. The aims of this study were to determine the outcome of patients undergoing DP for adenocarcinoma of the pancreas and to compare extended (portal vein or adjacent organ resection) versus standard resection. The secondary aims were to determine factors correlating with survival for ductal adenocarcinoma and to compare the outcome of DP for ductal carcinoma versus malignant mucin-producing neoplasms.

**Methods.** Retrospective review of 29 consecutive patients who underwent DP for an adenocarcinoma over 15 years.

**Results.** Twenty-one patients underwent DP for ductal adenocarcinoma, 5 for malignant intraductal papillary mucinous neoplasm and 3 for mucinous cystadenocarcinoma. Seven patients required an extended resection. An extended resection was associated with a longer operating time compared to a standard resection [280 (150–355) vs 160 (75–250 min,  $P = .004$ ) but there was no significant difference in terms of surgical morbidity or mortality, blood transfusions, length of hospitalization, positive margins or long-term survival. For ductal adenocarcinoma, age  $> 65$  yrs, platelet count  $< 200 \times 10^9$  and lymph node involvement correlated with survival on univariate analysis. A mucin-producing cystic neoplasm was less likely to have an elevated CA 19-9, less likely to demonstrate perineural involvement, more likely to have a well-differentiated cancer and had a longer median disease-specific survival [42 (3–144) vs 14 (12–16) months,  $P = .002$ ] compared to ductal adenocarcinoma. Four patients (50%) with a mucin-producing cystic neoplasm were actual 3-year survivors compared to 3 (14%) with ductal adenocarcinoma.

**Conclusions.** Extended DP can be performed safely with similar long and short-term outcomes compared with standard resection. Age, platelet count and lymph node involvement are predictors of survival in ductal adenocarcinoma. Patients with malignant mucin-producing neoplasms have markedly improved long-term survival compared to ductal adenocarcinoma.

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#### TRENDS IN THE EPIDEMIOLOGY AND TREATMENT OF PANCREATIC CANCER

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**Introduction.** Cancer of the pancreas usually develops insidiously and presents late resulting in poor prognosis.

**Methods and Materials.** We evaluate pancreatic cancers identified over a 12-year period (1992–2003) using the Surveillance, Epidemiology and End Results (SEER) Program of the National Cancer Institute (NCI). SEER\*Stat 2.6.4 software was used to search the SEER 13 registry for our analysis.

**Results.** Our analysis included 44,941 cases of pancreatic cancer. The majority (49.6%) occurred in the head of the pancreas, and the tail (9.3%) and body (7.5%). Histology was mainly adenocarcinomas (58.8%) and carcinomas (23.7%). Endocrinomas made up 1.1% and carcinoid tumours 1.5%. Adenocarcinoma was the prevalent at all sites except the islets of Langerhans where endocrinomas (66.1%) and carcinoids (23.7%) were the most prevalent.

The incidence (I) of pancreatic cancer in 2003 is 10.9 per 100,000 and has not changed significantly in the past 12 years (Percentage Change, PC = -3.13; Annual Percentage Change, APC = -0.11; P=0.37). Adenocarcinomas (I=6.34; PC = -5.83; APC = -0.11; P=0.63) and cystadenocarcinomas (I=0.09; PC = -31.59; APC = -0.24; P=0.91) have not changed in incidence. Carcinomas (I=2.15; PC = -27.15; APC = -3.27; P<0.05) and endocrinomas (I=0.1; PC = -39.65; APC = -3.42; P<0.05) are declining whereas duct carcinomas (I=0.8; PC = +94.86; APC = +7.09; P<0.05) and carcinoid tumours (I=0.22; PC = +185.1; APC = +9.44; P<0.05) are on the increase.

The majority of pancreatic cancers diagnosed have distant (49.6%), regional (24.2%) or localised (7.4%) spread; 0.2% are in situ. The observed 5-year survival rates are better in situ (75.3%) and with localised spread (14.2%) compared with regional (6.4%) and distant spread (1.6%). Most (62.6%) have unknown histological staging, or are poorly (16.6%) or moderately (14.2%) differentiated. The majority of pancreatic tumours (31.4%) are diagnosed with distant spread and unknown histological grade (5-yr survival=1.8%). In 1992, 83.7% were offered no surgery other than biopsy and explorative surgery, and this hasn't changed significantly over the 12 years analysed (2003=83.3%). Prognosis following surgery has improved over the last 12 years, where the 5-year survival rate in 1998–2003 is 20.06%, compared to 1992–1997 where it is just 16.27%. Without surgery, the 5-year survival for 1992–1997 and 1998–2003 is just 1.62% and 1.65% respectively.

**Discussion.** Pancreatic cancer remains a disease of poor prognosis. Its incidence remains the same over the past 12 years and the failure to diagnose it early has meant most patients are not offered surgery. The same proportion receives surgery but the prognosis has improved only slightly.

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### THE NATURAL HISTORY OF RESECTED PANCREATIC CANCER WITHOUT ADJUVANT TREATMENT

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**Introduction.** A recently completed prospective double-blinded placebo-controlled adjuvant therapy trial provides a unique opportunity to study and establish the natural history of resected pancreatic cancer. Five years after completion of this trial, we report survival outcomes and patterns of recurrence in patients undergoing resection for pancreatic cancer without adjuvant therapy until disease recurrence.

**Methods.** Records of patients randomized to receive placebo in a double-blinded placebo-controlled adjuvant therapy trial were reviewed noting tumor-related factors (AJCC stage, nodal and margin status, CA 19-9, Karnofsky Performance Score (KPS) at baseline and recurrence) and patterns of recurrence prior to initiation of salvage chemoradiotherapy. Multiple regression analysis was utilized to determine which factors impacted disease-free and overall survival. Recurrence categories were classified as: liver only, local, distant, multiple, or "clinical" (defined by absence of radiological recurrence in the presence of unexplained weight loss, intractable pain, jaundice or ascites). Follow up was 100% at 60 months.

**Results.** 98 patients receiving placebo as adjuvant therapy until disease progression were identified. Patients with negative margins (67%) experienced longer (21 mo ± 14.4) overall survival than those with positive margins (33%) (15 mo ± 13.7, p=0.02 Log-rank test) and longer disease-free survival (16 mo ± 14.4 vs. 10 mo ± 11.7, p=0.01 Log-rank test). Multiple regression analysis documented that only stage significantly correlated with disease-free survival (p=0.01) while only KPS at recurrence significantly predicted overall survival (p<0.05). Patterns of recurrence and their impact on survival are noted (Table):

Site of Recurrence	Disease Free Survival (months)	Overall Survival (months)	p-Value Compared to Clinical Recurrence
Multiple (n=13)	7 ± 9.7	8 ± 10.0	<0.0001
Distant (n=9)	7 ± 5.7	10 ± 8.3	<0.0001
Liver only (n=22)	8 ± 9.9	13 ± 12.0	0.0001
Local (n=20)	10 ± 11.2	13 ± 10.4	0.0002
Clinical (n=34)	24 ± 15.1	29 ± 14.8	N/A

**Conclusions.** Stage at the time of resection and performance status at the time of recurrence are the best predictors of survival following resections of curative intent for pancreatic adenocarcinoma. Anatomical evidence of recurrent disease leads to particularly short survival. Patients surviving longest before succumbing to recurrent cancer had initially no identifiable anatomic site of recurrence and died after a prolonged interval of systemic manifestations of recurrent pancreatic cancer.

## Oral Posters – Liver I: Malignant

### OP-05

4/20/07 1:30 to 3:30 pm

Abstract Numbers 53–64

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### ACCURACY OF 3 DIMENSIONAL LIVER IMAGES RECONSTRUCTED FROM CT SCANS USING COMPUTER SOFTWARE: PROSPECTIVE NON-RANDOMISED STUDY

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**Introduction.** The ability to construct a 3D model of the liver and its structures before hepatic resection could be useful in determining the extent and nature of resection. Accurate assessment of Liver and tumour volume dictates functional liver volume and predicts postoperative liver failure in patients undergoing resection.

**Methods.** A prospective non-randomized study was conducted on patients scheduled for liver resection following discussion at multi-disciplinary meeting. 3D models were constructed from CT images using computer software. From these 3D models, total LV, functional LV, and tumor volume were calculated. The resected Liver volume was also calculated and was compared to the resected liver weight.

**Results.** A total of 37 patients of mean age 63 (31–78), and male to female ratio 2:1 were scheduled for liver resection, mean height was (162.4 ± 9.08 cm) and mean weight was (73.87 ± 12.39). Of these patients; 28 had Colorectal Metastasis, 5 had Hepatocellular Carcinoma, 3 had cholangiocarcinoma, and 1 presented with metastatic leiomyosarcoma of the round ligament. Pre-operatively; 9 patients went for volume enhancing embolization, 2 had a non-resectional approach, and 1 patient was subjected to further imaging due to proximity of the tumour to the vessels. 8 patients underwent right hemihepatectomy, 5 underwent extended right hemihepatectomy, 3 had extended left hemihepatectomy, 5 were operated using Habib resection, 4 had right trisectionectomy, and 1 had left medial sectionectomy, 1 had trisegmentectomy, 4 patients were managed by local resection, 1 by central resection, 2 by wedge resection, and atypical resection was used in 3 patients. Postoperative blood tests showed mean bilirubin level (17.3 ± 23.9), Albumin (35.1 ± 4.32), PT (11.06 ± 1.18), and serum creatinine level (86.4 ± 15.22). Incidence of postoperative liver failure was 0%. The mean total liver volume calculated based on 3D-CT model was (1565 ± 404 ml), mean functional liver volume was (1404 ± 358 ml), and mean tumour volume was (104 ± 142 ml). computer prediction of resected LV using 3D reconstructed CT images correlated well with resected liver weight, mean of resected liver volumes predicted was (578.46 ± 307 ml) and the mean specimens weights was (415.6 ± 200.68 g) (P > 0.05).

**Conclusion.** 3D-CT reconstructed images can accurately predict resected liver volume and future liver remnant volume during liver resection surgeries. It aids the decision on the need for pre-operative portal vein embolization to induce liver hypertrophy.

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### TRANS-ARTERIAL CHEMOEMBOLIZATION FOR HEPATOCELLULAR CARCINOMA – INSTITUTIONAL EXPERIENCE

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**Introduction.** Lipiodol chemoembolization is a widely used method of treatment for patients with unresectable hepatocellular carcinoma (HCC), but its efficacy remains debated. The aim of this study was to assess the outcome of trans-arterial chemoembolisation (TACE) in the management of unresectable hepatocellular carcinoma.

**Methods.** Between January 2002 and May 2006, patients with unresectable hepatocellular carcinoma who had lipiodol chemoembolization (lipiodol plus doxorubicin) were reviewed. Both patient, and tumour characteristics, results of chemoembolization including complications and survival were collected for analysis.

**Results.** A total of 28 patients received 61 TACE procedures with a mean number of treatment of 2 per patient. Tumours were large and multifocal, Okuda score was II and III in 50% of patients. Twenty patients had a repeat TACE (71%), 4 three times (14%) and one five times respectively (4%). All patients tolerated the procedure well. Post TACE, one patient developed liver abscess which was treated with percutaneous drainage and one patient developed acute renal failure treated with dialysis. Mild abdominal pain and fever were common and occurred in 40% of the patients. The mean follow-up time was 17 months (range, 1–56 months). Seven patients die of tumour

progression (25%), one of acute gastrointestinal haemorrhage from varices.(3.6%) Partial Response achieved in 50% of the patients. The 3-year survival was 68%.

**Conclusion.** TACE is an effective therapeutic option for cirrhotic patients with unresectable HCC.

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#### LIVER RESECTION FOR HEPATOCELLULAR CARCINOMA IN CIRRHOTIC PATIENTS – HOW DYSFUNCTIONING LIVER IS NOT BENEFICIAL?

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**Purpose.** The risk of liver resection for hepatocellular carcinoma (HCC) in cirrhotic patients was higher than in non-cirrhotic patients. The risk will be higher in those with poor liver function. Moreover, liver cirrhosis was considered as a pre-cancerous state, even 100% 5-year recurrent rate after HCC resection in cirrhotic patients has been reported. Liver transplantation is another option in cirrhotic patients with HCC meeting Milan criteria, but insufficient cadaver donor or inappropriate living donor remains problematic.

**Methods.** A retrospective review of 816 cirrhotic patients with HCC who underwent a curative liver resection from 1990 to 2004 was made. All HCC patients who were admitted for liver resection required liver images, liver function test and indocyanine-green (ICG) clearance test. The extent of liver resection was based on the tumor extension and ICG 15-min retention rate (ICG). According to ICG 15 value, these patients were divided into 3 groups, group 1: 563 patients, whose ICG was <20%, group 2: 175 patient, whose ICG R15 was between 20–29.9%, and group 3: 59 patients whose ICG R15 was ≥30% and <50%. The patient background, early and long term results after liver resection were compared among the groups.

**Results.** Because of different patient selection criteria among the groups, the tumor size was significantly larger, the extent of liver resection was significantly greater, and tumor stage (TNM staging) was significantly more advanced in group1. Liver tumor of group 3 was smaller than the other two groups. The extent of liver resection was significantly. The blood transfusion rate, postoperative morbidity and mortality were comparable among the 3 groups. The 6 year–disease free and actuarial survival rates of the 3 groups were 43.6%, 35.9%, 41.3% (p=0.4652) and 45.9%, 38.9%, and 42.5% (p=0.3637), respectively.

**Conclusion.** Under careful patient selection, cirrhotic patients whose ICG R15 <50% will be beneficial for HCC resection. Liver transplantation may be indicated in patients with poorer dysfunctioning liver. ICG >50% and tumor condition meeting Milan criteria.

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#### A PERIOPERATIVE COMPLICATION-FREE COURSE WITHOUT A HIGH SERUM HYALURONATE LEVEL ENSURES PROLONGED DISEASE-FREE SURVIVAL AND OVERALL SURVIVAL AFTER HEPATECTOMY FOR HEPATOCELLULAR CARCINOMA

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comparisons by the log-rank test and Cox proportional hazards regression model, respectively.

**Results.** Among clinical laboratory data, the ICGR15 and serum hyaluronate (HA) level in GI were significantly higher than in GII. Furthermore, values for operative variables such as operative time, bleeding and blood transfusion in GI were significantly higher than in GII. On follow-up, 18 patients in GI and 16 patients in GII died of either liver failure or cancer recurrence. The log-rank test revealed that the overall survival rate in GII was significantly longer than in GI, although there was no significant difference in disease-free survival. Multivariate analysis showed that HA in GII was the only independent factor to predict long-term survival. Therefore, we divided GII into two groups. In the high HA group (n=24) the HA level was 150 mg/dl or more. In the low HA group (n=44) it was less than 150 mg/dl. The log-rank test results for three-year overall survival and disease-free survival rates in the low HA group showed that they were significantly longer than in the high HA group (87.3% vs. 42.2%: p<0.001 and 45.1% vs. 16.4%: p<0.001, respectively).

**Conclusions.** Perioperative complications could be a predictive factor for overall survival. Even in patients without complications, a low HA level could predict both long-term disease-free survival and overall survival in hepatocellular carcinoma patients who received initial hepatectomy.

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#### PROGNOSTIC SIGNIFICANCE OF P53, BETA-CATENIN, AND ALPHA-FETOPROTEIN EXPRESSION IN PATIENTS WITH SURGICALLY RESECTED HEPATOCELLULAR CARCINOMA

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Several molecular pathways have been implicated in the carcinogenesis of hepatocellular carcinoma (HCC), marked by key mutations in the b-catenin or p53 gene, as well as aberrant expression of alpha-fetoprotein (AFP). The purpose of this study was to determine the prognostic value of immunohistochemical determination of these molecular markers in sequential sections from patients with resected HCC. Thirty informative patients with complete (R0) liver resection were evaluated. Univariate and multivariate analyses were performed using clinical, pathologic and molecular expression parameters. 35% of tumors were positive for AFP, 22% for p53, and 16% for b-catenin, with 13% positive for more than one molecular marker. Follow-up information was collected to determine survival and the prognostic value of each parameter. On univariate analysis, AFP was associated with worse prognosis, while beta-catenin was associated with better prognosis. p53 expression had no independent association with prognosis. When both beta-catenin and AFP were included in a multivariate model (table, along with nuclear differentiation), the estimated prognostic information remained nearly the same, although the expression of beta-catenin was no longer significant. When nuclear grade, beta-catenin and AFP were combined in a prognostic score, patients with favorable prognosis had 3- and 5-year survival rates of 91% and 78% respectively, compared with 42% and 17% in patients with two or more unfavorable factors (p<0.001). In conclusion, utilization of histologic grade combined with assessment of b-catenin and AFP immunohistochemical expression has independent prognostic significance. Determination of these biomarkers may permit more accurate prediction of survival after resection of HCC.

	Sig.	Crude HR	95,0% CI for Exp (B)		Sig.	Corrected HR	95,0% CI for Exp (B)	
			Lower	Upper			Lower	Upper
Nuclear Differentiation								
Well		1.00				1.00		
Moderate	.073	3.34	0.89	12.50	.119	2.94	0.75	11.47
Poor	.041	6.65	1.08	41.08	.040	7.29	1.09	48.67
b-Catenin Expression	.149	0.40	0.11	1.39	.353	0.53	0.14	2.00
AFP Expression	.007	3.82	1.43	10.21	.085	3.33	0.84	13.15

**Background.** Assessment of liver functions before hepatectomy is important to avoid complications after the operation. However, it is not clear that a history of perioperative complications is associated with the long-term prognosis. Therefore, we prospectively surveyed patients who received hepatectomy in our institute with and without perioperative complications.

**Methods.** Between January 2001 and December 2005, 100 hepatocellular carcinoma patients who underwent initial hepatectomy were enrolled. The complication group (GI) consisted of 32 patients, including four patients who died during the hospital stay. The non-complication group (GII) consisted of 68 patients who were discharged without any adverse events. The times to recurrence and death were recorded after hepatectomy for as long as possible. Factors determining disease-free survival and overall survival were assessed by univariate and multivariate analyses using the Kaplan-Meier method with

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#### SURGICAL TREATMENT OF HEPATOCELLULAR CARCINOMA: WHICH FACTORS PREDICT RECURRENCE?

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**Background.** Effective treatment of hepatocellular carcinoma (HCC) remains a challenge despite multimodality therapies. We sought to evaluate predictors and patterns of recurrence in patients undergoing surgical treatment of HCC with resection and/or ablation.

**Methods.** Patients with HCC treated with surgical resection or ablation from 1990–2006 were identified from a prospective hepatobiliary database and hospital records. Demographic data, clinicopathological characteristics, and outcome were analyzed.

**Results.** All patients treated with surgical exploration with curative intent were identified. This included 66 patients undergoing hepatic resection and 20 ablation; 13 patients who eventually underwent transplantation were excluded from our long-term analysis. The 30-day mortality was 7% (5/73), and the overall 5-year survival was 37%. The median disease-free survival was 20 months with a median time to recurrence of 10 months. Preoperative factors predictive of improved disease-free survival include: absence of positive margins ( $p=0.006$ ), AFP value  $<100$  ng/mL ( $p=0.04$ ), and low Model for End-Stage Liver Disease (MELD) score ( $p=0.03$ ). On multivariate analysis, only increasing AFP value and positive margins predicted recurrence. Notably, none of the following factors were found to be statistically significant predictors of disease-free survival: tumor number or size of largest initial lesion, vascular invasion, tumor grade, or hepatitis status. The sites of first recurrence included liver (76%), distant (50%), or both (21%). Patients initially undergoing ablation versus resection were equally likely to develop a recurrence. Following recurrence, the median survival was 37 months; 26% of these patients were treated with resection or ablation, while 41% received medical treatment. None of the following parameters predicted increased survival after recurrence: site or number of recurrent lesions, or type of treatment rendered after recurrence.

**Conclusions.** Treatment of patients with hepatocellular carcinoma remains a challenging problem. Careful consideration of both tumor characteristics and preoperative liver function as reflected by the MELD score are important in predicting recurrence after initial operation. The site of first recurrence is the liver in the majority of patients; thus, novel adjuvant treatment regimens should focus on this regional recurrence pattern.

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#### RESULTS OF TREATMENT IN 245 MEXICAN PATIENTS WITH HEPATOCELLULAR CARCINOMA

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**Background.** The incidence of hepatocellular carcinoma HCC in Mexico is 1.4% with increasing tendency, it is diagnosed at late clinical stages with poor treatment alternatives.

**Aim.** To detect risk factors for HCC and its opportune management based on an observational analysis of 245 patients with HCC in Mexico.

**Patients/Methods.** Retrospective review from 245 patients with HCC performed at the Instituto Nacional de Cancerología and Centro Médico ISSEMyM from January 1990 to September 2006. Data analyzed from clinical records includes epidemiological data, presentation forms, treatment and survival.

**Results.** One hundred twenty six males 51%, 119 females 49%. Mean age: 59 years old (range 12–90), mean time at the beginning of symptoms was 4 months, most common presentation was stage II. Clinical manifestations: abdominal pain 83.1%, weight loss 58%, liver enlargement 45% and anorexia 29.9%. Alpha-fetoprotein (AFP) was found  $>400$  ng/dL in 97 patients 39.5%. Diagnosis performed with computed tomography (CT) in 202 patients 82.4%, ultrasonography (USG) in 172 patients 70.2%, and magnetic resonance images (MRI) in 19 patients 7.7%. One hundred and thirty one 54.1% had liver cirrhosis, 58 (23.7%) hepatitis C (HCV), 33 (13.5%) alcohol abuse history, 13 (5.3%) hepatitis B (HBV), and ten patients (4%) with not determined cause. Sixty seven patients 27% only had biopsy and 49 received chemotherapy and radiotherapy 20%, liver resection (LR) was performed in 26 cases 11%, 25 patients 10% received tamoxifen-talidomida (TMX-TLD), 22 were not treated 9%, 18 patients 7% received Tamoxifen (TMX), 18 patients 7% received percutaneous ethanol injection (PEI), radiofrequency ablation (RFA) in 16 cases 6%, two cases 0.8% were submitted to LR and TMX-TLD and one case 0.4% received RFA-TMX-TLD and liver transplant (LT). Median survival for LR was 20.4 months, for RFA was 10 months, for PEI was 8 months, for chemotherapy and radiotherapy was 4.1 months, for LR-TMX-TLD was 3.6 months, for those who did not receive treatment was 2.5 months, for TMX-TLD was 2.3 months, for RFA-TMX-TLD was 1.5 months, for TMX was 1 month and for the case of LT+RFA-TMX-TLD was 10 months of survival.

**Conclusions.** HCC is usually diagnosed at late clinical stages therefore the alternatives of management are far away from success. Bad prognosis factors are age  $<55$  years, AFP  $>400$  ng/ml, HCV, tumor size  $>5$  cm, vascular invasion, and poor differentiation. LR is the best option for earlier stages. RFA and PEI are also excellent alternatives for those not elective for resection. For unresectable lesions TMX-TLD is the best option in our cases.

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#### FLUORINE-18-FDG-PET COULD BE AN EFFECTIVE SURVEILLANCE MODALITY FOR DETECTION OF DISTANT METASTASIS IN HEPATOCELLULAR CARCINOMA

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**Aim.** To evaluate the role of FDG-PET in the surveillance of hepatocellular carcinoma after surgery, we compared the sensitivity and specificity of FDG-PET with that of the ordinary follow-up system.

**Method.** From November 1999 to December 2003, the total number of seventy-five post-operative HCC patients (44 cases were received hepatectomy and 31 were living-donor liver transplantation cases.) received FDG-PET at the Hokkaido University Hospital and were included in this study. Patients usually underwent serial measurement of tumor markers, US, CT and/or MRI scans every 3 months. "Post-operative Recurrence" was determined, when the positive sign for recurrence were detected by two or more different these modalities.

**Result.** Thirty-seven cases and total 47 recurrence sites were diagnosed as "post-operative recurrence" by the ordinary follow-up system. Twenty-six cases of 28 FDG-PET-positive cases, post-operative recurrence was confirmed by ordinary follow-up study, and remained two cases were diagnosed pancreatic cancer by additional examination. Thirty-six of 47 negative cases had no post-operative recurrence. The sensitivity of FDG-PET was 41.0, 66.7, 100, 100%, and specificity was 100, 98.4, 100, 100% in intrahepatic, lung, lymph node, adrenal gland respectively.

**Conclusion.** FDG-PET was not always useful in HCC surveillance after surgery, because conventional modalities were enough to detect recurrence, but in extrahepatic lesions, FDG-PET could be useful for detection of metastatic lesions. FDG-PET also had an additional effect to find unexpected malignancies.

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#### RESULTS OF YTTRIUM-90 MICROSPHERE TREATMENT IN THE MANAGEMENT OF UNRESECTABLE LIVER CANCER

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**Introduction.** Selective internal radiation therapy (SIRT) is emerging as a new therapeutic modality in recent years for management of non-resectable hepatic metastases. Our initial experience in clinical application of this treatment is reported here.

**Material and methods.** From November 2004, patients whose liver tumour was no longer amenable for any conventional treatment with either chemotherapy or surgery were considered for yttrium-90 microspheres treatment after discussion at our multidisciplinary meeting. None of the patients had extrahepatic disease. A pre treatment planning was carried out with visceral angiography and technetium-99m macroaggregated albumin (MAA) for assessment of both tumour volume and extrahepatic shunting in addition to a baseline PET and CT scan respectively. Two weeks later, a second visceral angiography was performed to deliver the calculated dosage of microsphere into the arterial system supplying the tumour. Patients were then followed up with repeat PET and CT scans of abdomen at 6 weeks, and 3 monthly thereafter.

**Result.** A total of 19 patients with a mean age of 59 years received yttrium-microspheres treatment, consisting of cholangiocarcinoma ( $n=3$ ) and liver metastases from colorectal carcinoma ( $n=10$ ), pancreas ( $n=2$ ), GIST ( $n=1$ ), breast ( $n=1$ ), squamous cell carcinoma of anus ( $n=1$ ) and adenocarcinoma of an unknown primary ( $n=1$ ) respectively. The average dosage of microspheres delivered was  $1.9 \pm 0.3$  GBq. Injection of microspheres had no immediate effect on either clinical haematology or liver function tests. At follow up, 17% of patients showed a radiological response of a reduction in the size of tumour measured on CT scan at 3 months and 33% of a decreased PET activity on PET scan at 6 weeks. For patients with colorectal liver metastases, there was no significant reduction in CEA level ( $127 \pm 115$  vs  $75 \pm 72$ ,  $p=0.39$ ). Four patients died at follow up of pancreatic ( $n=1$ ) and colorectal primaries ( $n=3$ ). Others remained alive with a stable disease. The total cost of this procedure was £11,000/patient.

**Conclusion.** Microspheres treatment should be considered as a last option for patients with liver cancer. Its use should be balanced against its cost/effectiveness.

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#### Y-90 RESIN MICROSPHERE SELECTIVE INTERNAL RADIATION TREATMENT IN PRIMARY AND METASTATIC LIVER CANCER: OBJECTIVE RESPONSE AND THERAPEUTIC RATIO ANALYSIS

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**Introduction.** Yttrium-90 (Y-90) microsphere therapy via hepatic arterial administration is emerging as a mainstream treatment modality in the management of patients with primary and metastatic liver cancer. The selective nature of microsphere distribution allows the delivery of high doses of radiation to tumors while keeping the exposure of the un-involved liver at a minimum.

**Methods.** Treatment records and follow-up data on 37 patients (21 M, 16 F, and ages 44–86) with primary and metastatic liver cancer who underwent a selective internal radiation treatment (SIRT) with Y-90 resin microspheres (SIR-Spheres™ Sirtex Medical, Lake Forest, IL) were retrospectively reviewed. Liver and tumor radiation doses were determined using the

medical internal radiation dosimetry (MIRD) technique. Liver toxicity was assessed clinically and by liver function tests. Response to treatment was evaluated by tumor markers and PET-CT in all patients.

**Results.** Of the 37 patients, 10 had primary liver cancer (8 hepatocellular carcinoma (HCC), 2 cholangiocarcinoma (CC)), and 27 had metastatic liver tumors (16 colorectal cancer, 5 neuroendocrine tumors, 2 breast cancer, 1 endometrial cancer, 1 lung cancer, 1 gastric, 1 GIST). Tumor volumes ranged from 10.0 cc to 1,187.3 cc (mean: 300.2). 9 patients (24%) were treated for down-staging/bridge to surgery. 28 patients (76%) were treated in a salvage setting. 8 patients with CRCLM received SIRT concomitantly with first or second line chemotherapy (6 FOLFOX-6, 2 FOLFIRI). Median follow-up was 17 weeks (2 to 82 week). 31 patients had at least had a 4-week response-to-therapy assessment. Mean administered activity was 1.9 GBq (0.7 to 3.2 GBq). Liver absorbed doses ranged from 5.2 Gy to 173.9 Gy (mean: 40.4 Gy). Tumor absorbed doses ranged from 45.6 Gy to 699.3 Gy (mean: 221.2 Gy). An objective tumor response was seen in 21/31 (68%). 5/8 CRC patients who received chemo-SIRT had complete, 3/8 had more than 75% FDG-PET response at 4 weeks. There were two complete responses in HCC/CC patient group who were treated in a segmental fashion. None of the patients had clinical radiation hepatitis or therapy-induced liver failure.

**Conclusions.** SIRT with Y-90 microspheres is an effective cytoreduction modality with a relatively wide margin of safety. Complete objective tumor responses are possible with appropriate patient selection, conjunctive interventions, and treatment planning. The response rate and scale were markedly better in those who were treated front-line with chemo-SIRT combination.

### 63 IDENTIFICATION OF NOVEL SINGLE NUCLEOTIDE POLYMORPHISM IN THE PROMOTER REGION OF HUMAN ALPHA-FETOPROTEIN (AFP) GENE IN HEPATOCELLULAR CARCINOMA (HCC)

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Variations of serum AFP levels found in patients with HCC and HCC cell lines are likely due to the differential activity of enhancer/silencer elements that control AFP expression. To understand the potential mechanism underlying the differential expression of AFP, we have examined the sequence of the AFP promoter in HCC. Three novel SNPs in the promoter region of the human AFP gene, which have not been previously reported, were found at positions -330, -401 and -692 in relation to the transcriptional start site. The level of serum AFP was significantly higher in HCC patients with the CT genotype of 330 SNP or the CG genotype of the 401 SNP. The genotype of CG in 692 SNP was also associated with a significant elevated level of serum AFP, and further this genotype appeared to be associated with the high risk of HCC development. Bioinformatics analysis revealed that 401 SNP and 692 SNP were located at the positions of known binding sites for the transcription factors, HNF1 and the RNA pol III TFIII, which have a role in the production of AFP and the growth of tumors. Therefore, our study suggests that the polymorphism identified in the promoter region of the human AFP gene may be pathologically significant in HCC.

### 64 ONCOLYTIC MUTANT HERPES VIRUS KILLS HEPATOMA CELLS THROUGH A MITOGEN ACTIVATED PROTEIN KINASE (MAPK)-DEPENDENT PATHWAY

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**Introduction.** Mutant herpes simplex type 1 (HSV) oncolytic viruses are a promising anticancer therapy. The cellular determinants of oncolytic HSV therapy are not completely elucidated. The MAPK signal transduction pathway is important for cellular proliferation and apoptosis, both important factors for viral proliferation. We seek to determine if MAPK pathways, specifically MAPK/extracellular-regulated kinase kinase (MEK) inhibitors, mediate viral proliferation.

**Methods.** The human hepatoma cell line PLC5 was infected with the oncolytic HSV G207, at MOI (multiplicity of infection; number of viral particles per cell) of 0.1. The MEK inhibitor U0126 (30 micromolar) or control was added to each well simultaneously. Cytotoxicity was assessed by LDH release assay and viral growth by viral plaque assay on sensitive Vero cells.

**Results.** PLC5 cells exhibited less cell death in the combination G207/U0126 group compared to virus alone. Viral growth was lower in the combination groups. Nine days after treatment, G207 alone yielded 70% cell kill compared to 21% in the combination G207/U0126 group ( $p < 0.01$ ). The MEK inhibitor decreased viral proliferation from 27 fold increase in virus alone group to 1.3 fold in the U0126 treated cells ( $p < 0.01$ ).

**Conclusion.** The MAPK pathway is involved in both viral proliferation and tumor cell kill. Though MAPK inhibition is a potentially useful therapy for hepatoma, they should not be used in combination with oncolytic viral therapy. In fact, MAPK inhibitors could potentially be used as treatment for unchecked viral proliferation during oncolytic therapy.

## Oral Posters – Liver II: Benign and Education / Outcomes

OP-06

4/20/07 1:30 to 3:30 pm

Abstract Numbers 65–76

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### LIVER, PANCREAS AND BILIARY SURGERY, WHAT IS THE RIGHT FELLOWSHIP FOR THE RIGHT TRAINING?

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**Purpose.** To determine if a non-transplant, non-surgical oncology fellowship can appropriately train the general surgery resident in organ specific diseases of upper gastrointestinal tract, based on a personal experience.

**Background.** General surgery residency training has undergone significant changes over the last few years including reduced work hours. Subsequently, exposure to cases in each field of surgery has reduced especially in HPB (hepatobiliary) and upper gastrointestinal (GI) surgery. This will, in turn, motivate more residents to pursue further training in a fellowship training program.

**Method.** Based on a personal experience we propose a surgical training model in benign as well as malignant diseases of upper gastrointestinal tract. This fellowship will be focused on organ specific approach to disease processes.

**Results.** Over the first 3.5 months of a hepatobiliary/upper GI fellowship training program in a relatively high volume community center case logs of the fellow are as follows: 15 pancreaticoduodenectomy, 8 other pancreatic procedures (including total and distal pancreatectomy), 10 esophageal, 8 complex biliary, 6 liver and 12 other major foregut procedures. Many of the procedures were approached laparoscopically when possible including distal pancreatectomy and esophagectomy. During a year of fellowship there would also be a block in transplant service and a dedicated hepatobiliary GI rotation performing endoscopic retrograde cholangiopancreatography (ERCPs) and Endoscopic ultrasound (EUS). There are also weekly multidisciplinary conferences with oncology and non oncology services. Also, the fellowship is designed so that there are no deleterious effects on general surgery residency program.

**Conclusion.** Based on a personal experience, we propose that an organ specific fellowship program in both benign and malignant diseases of upper gastrointestinal tract provides a practical and focused training in this surgical field. This model is a non-transplant, non surgical oncology fellowship aiming to train the general surgery resident in all aspects of HPB/upper GI disease processes.

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### OUTCOMES OF HEPATOBILIARY SURGERY IN A COMMUNITY HOSPITAL

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This is a retrospective analysis of open and laparoscopic hepato-biliary surgeries performed at the Walnut Creek Kaiser Medical Center. We started performing hepato-biliary surgery in 1999. In 2003 we established a multimodality clinic for hepato-biliary surgery to serve as a regional referral center for the network of Northern California Kaiser Medical Centers. A total of 168 hepato-biliary cases were performed at our institution since 1999, of which 51 were for primary liver cancer, 96 for metastatic liver cancer and 21 for benign disease. The majority consisted of 77 metastatic colorectal cancer (CRC) and 40 hepatomas. Clinical data including length of stay, blood loss and transfusion requirements, stage, adjuvant chemotherapy rates, recurrence rate and morbidity were analyzed. Overall 90 day surgical mortality was 0%. Mean survival was 28 months for hepatomas, 34 months for gallbladder/bile duct cancers, 36 months for CRC and 55 months for other cancer metastases. Radiofrequency ablation (RFA) was used in 51% of CRC metastases, 50% of hepatomas, 60% of other cancer metastases and 14% of benign lesions. RFA was not used in biliary cancer cases. One half of the RFA were performed by laparoscopy. Open hepatectomies included 48 segmentectomies, 30 lobectomies, and five extended lobectomies. In 3 cases preoperative portal vein embolization was used. This analysis demonstrates that with appropriate interventional radiology, gastroenterology and medical oncology support hepato-biliary surgery can be performed safely and with appropriate surgical and oncologic outcomes in a community hospital setting.

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### OUTCOMES IN PATIENTS UNDERGOING HEPATIC RESECTION IN THE CALGARY HEALTH REGION BEFORE AND AFTER THE CREATION OF A REGIONAL HPB PROGRAM

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**Introduction.** There has been a profusion of information published in support of the relationship between outcomes (improved) with increasing

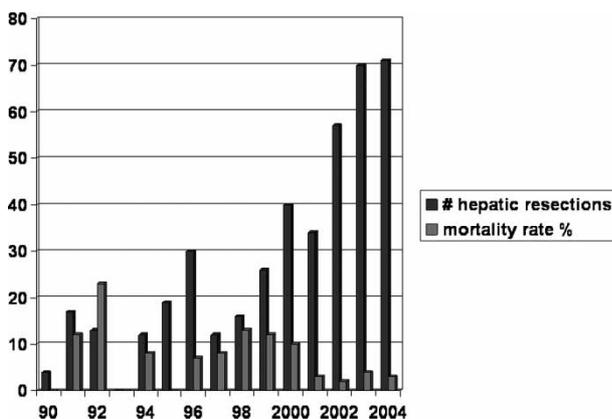
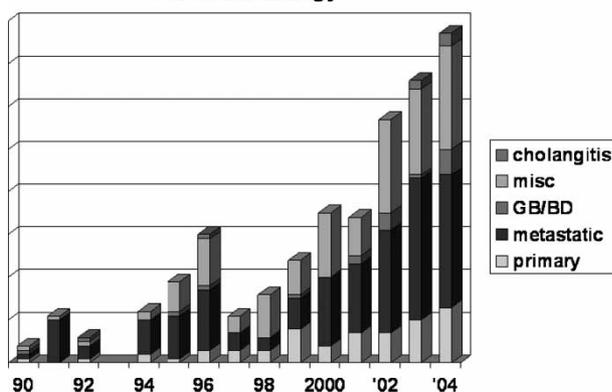
volume of procedures performed for certain complex surgical procedures. The Calgary Health Region provides care to the residents of Calgary, Alberta (pop. 1 million), as well as a large portion of the southern half of the province of Alberta, Canada. Very few studies have examined what effect at a population level the creation of a regional program (multidisciplinary HPB) has had on outcomes.

**Methods.** Using administration discharge data from all hospitals in the Calgary Health Region, we reviewed all hepatic resections performed. Hepatic resections were identified using procedure codes for hepatic resection (ICD - 9 prior to April 2002, and ICD - 10 and CCI after April 2002). All patient encounters from 1990 to 2004 were identified. The creation of a multidisciplinary HPB program occurred in 2002/3.

**Results.** From January 1990 to December 2004 there were a total of 421 hepatic resections performed. The average was 55 (95% CI, 19-91). The majority of the hepatic resections were performed for metastatic disease, hepatocellular carcinoma, and miscellaneous diseases (Figure 1). Fifty-five percent of the patients were male. Comorbidity of the patients as measured by the Charlson score did not change significantly over time. The average length of stay was 14.5 days (median is 10, 1-183 range). Overall there were 25 deaths, for a mortality of 6%. Figure 2 illustrates the annual change in volume of hepatic resections along with the annual mortality rates.

**Conclusions.** The creation of a multidisciplinary hepatobiliary and pancreatic surgery program has resulted in both increasing volumes of hepatic resections, and concomitantly improved outcomes (mortality).

Disease Etiology



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**LAPAROSCOPIC HEPATIC CYST MARSUPIALIZATION: A REVIEW OF OUR INSTITUTIONAL EXPERIENCE**

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**Introduction.** In an era of increased use of computed tomography for work-up of abdominal pain, the incidence of hepatic cysts is increasing. While most of these cysts are incidental findings and asymptomatic, in some patients, these cysts become relatively large and manifest as a painful abdominal mass with obstructive symptoms due to compression of adjacent viscera. Previous studies have demonstrated cyst resection to have a lower recurrence rate than cyst aspiration, though patients must be subjected to the morbidity associated with an open procedure. We reviewed our institution's experience of both laparoscopic hepatic cystectomy and open cystectomy, comparing recurrence rates and complications.

**Methods.** We performed a retrospective review of patients that underwent hepatic cyst excision with marsupialization at two institutions. Radiographic studies and indications for operation were reviewed and complications were noted, including conversion to an open procedure. Statistical analysis was performed using Chi-square.

**Results.** During 1998-2005, 17 patients underwent treatment for hepatic cysts. Age range was 43-83 with a mean of 60 years. Cyst size ranged from 5-22 cm with a mean size of 11.5 cm. The most common presenting symptoms were pain (13/17 [76%]) and nausea/vomiting (7/17 [41%]). Twelve patients underwent laparoscopic hepatic cystectomy with cyst marsupialization, five underwent an open procedure, and one had percutaneous aspiration. There was an overall cyst recurrence rate of 12% (2/17); one of these was in the patient who had undergone a previous percutaneous aspiration and the second was in a patient who had a laparoscopic procedure (1/12, [8%]). None of the patients who underwent open procedure had a recurrence. Overall complication rate was 24% (4/17); three were in patients who underwent open resection (3/5, [60%]) (2 MI, 1 bile leak requiring IR guided drain placement), and the fourth was a bile leak in a patient who had undergone laparoscopic resection (1/12, [8%]). There was no significant difference in recurrence between the laparoscopic and open procedures. More complications occurred in the patients that underwent an open procedure and this was statistically significant (P=0.02).

**Discussion.** From these data, we conclude that laparoscopic hepatic cyst resection with cyst marsupialization is as effective as open cyst resection in preventing recurrence and also results in fewer complications.

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**SURGICAL TREATMENT OF HYDATID LIVER DISEASE**

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**Background.** Surgery remains the main treatment modality of hydatid liver disease. There still debate about the best approach, conservative surgery (marsupialization, drainage, partial cystectomy) has opposed to radical surgery in which the cyst is totally removed including the pericyst by total pericystectomy or partial hepatectomy.

**Aim.** This study aims to show that radical surgery resection of the hepatic hydatid cysts is a safe and effective technique.

**Patients and Methods.** A series of 49 consecutive patients operated on for liver hydatid disease between January 2001 and December 2005 was analyzed. The most common complaint were pain (62%), hepatomegaly and abdominal mass (39%). Diagnostic assessment was obtained with serology (ELISA) and radiology (US and CT scan). Surgery comprised conservative methods like partial cystopericystectomy with intracavitary placed drainage and omentoplasty of residual cavity (21 pts.), and radical surgical methods like total cystopericystectomy (5 pts.) and liver resection (segmentectomy, lobectomy, hemihepatectomy) (23 pts.).

**Results.** In the entire series, morbidity was 19% of which 28% was seen with conservative surgery and 11% with radical methods (p < 0.05). Biliary fistula was more frequent complication in both groups: 15.9% vs. 4.2% (p < 0.01) in patients that underwent conservative methods and radical methods, respectively. There was no operative and postoperative mortality in our studied group. Long-term follow-up showed that hydatid disease relapsed frequently in patients who underwent conservative treatment than in those who underwent radical surgical approach: 4 pts. Vs. 0 pts.

**Conclusion.** According to our results, radical surgery of the hydatid liver disease represents the method of choice over others such as partial pericystectomy.

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**RESECTION OF HEPATIC ADENOMA IN PATIENTS WITH GLYCOGEN STORAGE DISEASE TYPE IA**

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**Introduction.** Hepatic adenomas occur in 50-75% of adults with glycogen storage disease type Ia (GSD Ia). Because better metabolic control has enabled long-term survival, the incidence of malignant adenoma transformation is increasing. While limited organ availability makes hepatic resection an attractive option for dominant adenomas, the metabolic dysfunction, hepatomegaly, and renal insufficiency common in GSD Ia patients raises doubts about the safety of resection. The objective of this retrospective study is to assess the safety of hepatic adenoma resection in GSD Ia patients.

**Methods.** Clinicopathologic, peri-operative, and long-term data were reviewed from patients who underwent hepatic adenoma resection from one center. Peri-operative management of GSD Ia patients included aggressive treatment of metabolic acidosis, dextrose infusions, and vigilant blood glucose control. Comparisons were made with Fisher's exact and Mann-Whitney tests; survival was estimated with Kaplan-Meier analysis.

**Results.** From 1998-2006, 37 patients underwent resection of hepatic adenomas. Seven (19%) had GSD Ia. Three of seven (43%) with GSD Ia and 16/30 (53%) without GSD Ia underwent major hepatectomy (≥3 segments), p=NS. The number of resected adenomas was higher among GSD Ia patients (median 3 vs. 1, p=0.01), with no difference in size of largest

resected adenoma (median 8 cm for both groups). One GSD Ia patient had post-operative mortality. GSD Ia patients were more likely to have major post-operative complications (5/7, 71% vs. 6/30, 20%,  $p=0.02$ ). Complications among GSD Ia patients included liver failure (2), multisystem organ failure (2), fascial dehiscence (1), intra-abdominal abscess (1), bleeding from the liver resection bed requiring re-operation (2), and unstable blood glucose levels with persistent lactic acidosis (2). Six of seven patients recovered from resection with no additional long-term morbidity. One patient had HCC and died of disseminated disease three months after resection. All GSD Ia patients with benign disease had adenoma progression after resection; median time to progression was 23 months (range 19–71 months). Of five living patients, three have undergone successful liver transplantation 77, 32, and 23 months after resection and one is being evaluated for transplantation 20 months after partial hepatectomy.

**Conclusion.** Despite frequent post-operative morbidity, partial hepatectomy is feasible in GSD Ia patients. Given uncertainties on timing of liver transplantation, waning enthusiasm for adult live-donation, and lack of priority for cadaveric grafts, resection can be considered for GSD Ia patients with large adenomas or those with associated symptoms.

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### INDICATION AND LONG-TERM OUTCOME OF TREATMENT FOR FOCAL NODULAR HYPERPLASIA

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**Background.** Unlike malignant liver tumours, the indications for hepatic resection for benign disease are not as well defined. This is particularly true for FNH, where the indications for surgery include progressive disease, increasing pain and lesions where malignancy can not be excluded. Here we summarise a single-centre experience of the diagnosis and management of Focal Nodular Hyperplasia.

**Methods.** Using a prospectively collected database, a retrospective analysis of consecutive patients who were managed at our centre for Focal Nodular Hyperplasia between January 1997 and Dec 2006 was performed.

**Results.** The cohort was divided into two groups; surgically ( $n=15$ ) and conservatively managed ( $n=37$ ) patients. There was no correlation between tumour size and no. of lesions with oral contraceptive use ( $p=0.07$  and  $0.90$  respectively) and pregnancy ( $0.45$  AND  $0.60$  respectively). However, tumour size ( $p=0.006$ ) and no of lesions ( $p=0.02$ ) were associated with the occurrence of pain in these patients. Pain was the commonest symptom of patients (13/15) who were managed surgically. All patients underwent radiological imaging prior to diagnosis. The sensitivities of Ultrasound, CT scanning and MRI scanning at characterising these lesions were 30%, 70% and 87% respectively. The surgical procedures performed on these patients include 3 trisegmentectomies, 3 lobectomies and 8 segmentectomies. On histopathological analysis other neoplasms were found incidentally with the FNH lesions. These included adenomas ( $n=5$ ) and HCC ( $n=1$ ). There were no post-operative deaths and three post-operative complications that were successfully managed non-operatively. With a median follow-up of 22 months in the surgically treated group, two patients have developed recurrence of FNH, one with minor symptoms of pain. 5 patients in the conservatively managed group continue to complain of atypical pain and are currently under investigations for this prior to consideration of resection.

**Conclusion.** FNH is a benign lesion of the liver that can cause pain that is associated with the increase in size and number of the lesions. Surgical resection is usually performed in persistent pain and for suspicious lesions on radiological investigations. In this series, there has been no mortality directly due to the surgical procedure and a modest morbidity, justifying surgical resections in selected patients.

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### SPONTANEOUS RUPTURE AND HEMORRHAGE OF FOCAL NODULAR HYPERPLASIA: A CASE REPORT AND REVIEW OF LITERATURE

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A 50 year-old female presented to an outside emergency room for evaluation of abdominal pain. She was a healthy without significant medical history other than several back surgeries and hypertension. Emergency room evaluation included a CT scan showing fluid within her abdomen. The patient was felt to have an acute abdomen and was taken urgently to the operating room and was found to have a large volume hemoperitoneum. The source of the bleeding was felt to be a right-sided liver lesion. The bleeding was controlled with packing and cautery and biopsies of the lesion were performed. Original biopsies showed areas of dysplastic hepatocytes with inflammatory changes. Postoperatively the patient did well. She was referred for evaluation of her liver mass. This was visible on computerized tomography. All tumor markers were negative. The patient was allowed to recover from her original surgery but ultimately had operative resection of this liver lesion. Preoperatively she was presumed to have an adenoma or HCC. A partial hepatectomy of segment 7 was performed without complication. The final pathology was returned as focal nodular hyperplasia.

Focal nodular hyperplasia is a lesion most commonly found in women of child-bearing age and is associated with use of oral contraceptive pills. It has been classified as a benign, highly vascularized pseudotumor with a low risk of complications. In the surgical literature, FNH is very rarely described to have hemorrhagic complications. Due to this fact, as well as the benign nature of the lesion, the literature supports non-operative management of FNH unless the lesion is significantly growing, or causing progressively worsening symptoms. In the patient that is managed expectantly, the provider must be aware of this rare but potentially lethal complication.

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### SPONTANEOUS HEPATIC RUPTURE

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**Purpose.** Spontaneous hepatic rupture is a rare condition with multiple reported aetiologies. Many case reports and series are published in the literature, however, a comprehensive review of this condition has not previously been undertaken. The aim of the study was therefore to review the literature with emphasis on the incidence of each respective aetiology and risk factors for rupture.

**Method.** A systematic review of the English literature from 1966 to 2005 was performed using an Ovid Medline search. Keywords included "spontaneous", "hepatic" and "rupture". All papers were cross-referenced yielding 242 papers. Exclusion criteria included a history of traumatic rupture and contained intra-hepatic or sub-capsular haematomas. Series of patients were checked to ensure that they had not been previously reported.

**Results.** Spontaneous hepatic rupture occurs more commonly in non-European countries like Taiwan, China and Japan. The overall incidence of rupture over the 40 year study period was 49.28 per year ( $n=1971$ ). The most common cause of rupture was hepatocellular carcinoma (HCC) followed by pregnancy related conditions. Ninety seven and a half percent of paediatric ruptures were secondary to neoplasms with the exception of a rupture following organophosphate poisoning. Miscellaneous conditions included polyarteritis nodosa, amyloidosis and an amoebic liver abscess. These conditions generally disrupt the vascular integrity of the liver, or soften liver parenchyma thus predisposing to rupture. Risk factors for rupture include tumor hypervascularity, tumor size and location, the use of steroid hormones and clotting diathesis. Risk factors specific to pregnancy include multiparity, age and the stage of pregnancy. Pre-eclampsia is also a common risk factor for rupture.

**Conclusions.** Spontaneous hepatic rupture is a rare and catastrophic condition with significant morbidity and mortality. There are various underlying aetiologies including HCC, which was the most common by far, followed by pregnancy. In children, almost all ruptures were related to neoplasms. Risk factors for rupture universally included the size or severity of the lesion, the location of the tumour in the liver and associated coagulopathy.

Incidence of Spontaneous Hepatic Rupture by Aetiology

Condition	n	Incidence (per population)	Reported Incidence of Rupture (per year)
Hepatocellular Carcinoma (HCC)	1694	150/100 000	42.35
Pregnancy	76	66/1000	1.90
Hepatic Adenoma	71	3/100 000	1.78
Metastases	26	Variable	0.65
Paediatric	40	1/1 000 000	100
Miscellaneous	64	Variable	1.60

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### A NEW TECHNIQUE FOR A SUCCESSFUL MANAGEMENT OF SUPRAHEPATIC COMPLETE CAVAL TRANSECTION

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A vena cava injury should be always suspected if a retroperitoneal hematoma is present. Exploring the hematoma blindly is a life threatening technical error. In fact, it is mandatory to clearly visualize the injury, and to keep blood loss to a minimum to prevent hemorrhagic shock and to avoid irreversible coagulopathy, acidosis, hypothermia, multi-organ failure and death. Various operative strategies have been used to decrease the mortality rate such as atriocaval surgical shunting, vascular clamping, hepatic resection and perihepatic packing.

**Patient and Method.** A 17-year-old female, involved in a high-speed motorcycle crash, was taken to a local hospital where multiple, actively

bleeding lacerations of the spleen and of the right lobe of the liver were found. A splenectomy was performed and silk sutures were placed between the liver and the diaphragm to provide a tamponade effect. Possibly, the sutures had created a watertight compartment able to tamponade the bleeding and to support the systemic venous return and filling pressure. Hemostasis was unsuccessful and after packing, the patient was transported to our operating room by helicopter. After removing the packing when mobilization of the right lobe was attempted the blood pressure dropped to a critical level. For this reason, an injury of the suprahepatic inferior vena cava was suspected. It was then decided to attempt a direct approach to the juxta-diaphragmatic segment of the inferior vena cava by placing the patient on an atrial-caval venous-venous bypass. A complete suprahepatic inferior vena cava (IVC) transaction was demonstrated and the IVC was reconstructed performing an end-to-end anastomosis with 3-0 polypropylene running suture, using the same technique as in orthotopic liver transplantation.

**Results.** The patient, in spite of her fixed mydriasis at the time of the surgery, woke up 8 hours after it and on postoperative day 25, an angiogram of the IVC demonstrated no leak and no IVC stenosis. On postoperative day 28 the patient was discharged and after 4 years is in excellent health with normal liver function.

**Conclusions.** A new technique of caval-atrial venous-venous bypass is proposed. This technique allows, by working in a bloodless field, anatomical control and a direct approach of the traumatic injury of the most inaccessible portion of the inferior vena cava, which historically has always led to a 100% mortality rate.

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#### INTRAHEPATIC PORTAL VENOUS VARIATIONS: DEMONSTRATIONS BY 64-CHANNEL MULTIDETECTOR CT

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**Purpose.** We assessed the prevalence and types of intrahepatic portal venous variations by 64-MDCT.

**Methods.** In 101 patients without vascular invasion or distortion, 3-dimensional images of portal vein were gained and studied prospectively to identify portal venous variations.

**Results.** Of the 101 patients examined, 82 (82%) had classical pattern, 8(8%) had trifurcation, 10 (10%) had a right anterior sectional branch arising from left portal vein and 1(1%) had a right portal vein arising from left umbilical portion. The branching pattern of right portal vein was showed eight different patterns. Sixty patients (60%) had a right anterior sectional branch feeding upper portion of segment 7,5 and 8 and a right posterior sectional branch feeding lower portion of segment 7 and 6. Ten (10%) had a right anterior sectional branch feeding segment 5,7,8 and a right posterior sectional branch supplying only segment 6. Another small portions of variations were a right anterior branch supplying segment 7,8 and a right posterior branch feeding segment 5,6,7.

**Conclusion.** Sectionectomy or segmentectomy of right liver using Glisson's approach will be inaccurate because of many variations of portal vein. Therefore, the branching pattern of portal vein will be elucidated before hepatectomy.

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#### EXTRAHEPATIC PORTAL VEIN ANEURYSM - REPORT OF SIX CASES AND REVIEW OF LITERATURE

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**Introduction.** Extrahepatic portal vein aneurysm is a rare condition. We report six cases of extrahepatic portal vein aneurysm, of which four were treated surgically. Review of literature was performed to clarify the natural history, management and outcomes.

**Method.** Records of patients with extrahepatic portal vein aneurysm greater than two centimeters in diameter were reviewed (1998 to 2006). There were 5 females, and median age was 66.5 (30-77). CT scan was utilized for diagnosis in all cases. The median diameter of the aneurysm was 4.7 centimeters (2.7-6.0). The aneurysm was located at the confluence of SMV and splenic vein in 3 cases, at the main portal vein in two cases, and at the extrahepatic left portal vein in one case. Indications for surgery included choledocholithiasis with biliary pancreatitis, compression of the duodenum and common bile duct by the aneurysm, radiologically nonspecific peripancreatic mass, and end stage liver disease.

**Result.** Three patients underwent aneurysm resection and one patient had an orthotopic liver transplant due to advanced cirrhosis and an associated portal vein aneurysm. Two patients were managed conservatively with observation. The median follow-up from the time of first presentation and from surgery was 41.5 months (9-180 months) and 4 months (1-73) respectively. Five patients are alive without symptoms attributable to the extrahepatic portal vein aneurysm and demonstrate portal vein patency on surveillance ultrasonography. One patient died two months following liver transplantation. There was no case of aneurysm rupture. One patient had intramural thrombus at presentation that resolved on a subsequent CT scan.

**Conclusion.** This is the largest case series of patients with extrahepatic portal vein aneurysm who were surgically treated. It provides evidence that symptomatic aneurysms can be safely resected with acceptable patency.

#### Oral Posters - Liver III: Techniques

OP-07

4/20/07 1:30 to 3:30 pm

Abstract Numbers 77-88

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#### EPIDURAL USE IS ASSOCIATED WITH INCREASED RISK OF BLOOD TRANSFUSION FOLLOWING HEPATIC RESECTION

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**Purpose.** We examined the influence of epidural pain management on perioperative outcome for hepatic resection with respect to transfusions, complications, and length of hospital stay.

**Methods.** Perioperative outcome of patients undergoing partial hepatectomy from 2000 to 2004 was analyzed according to route of perioperative pain management: epidural (EPI) vs. intravenous (IV). Patient factors: age, body mass index (BMI), ASA classification, and cancer diagnosis and operative factors: time (OP time), blood loss, use of low CVP anesthesia, extent of resection, and route of pain management use were analyzed for associations with blood transfusions, morbidity, and length of stay (LOS). Univariate (Fisher's exact) and multivariate (binomial logistic regression) analyses were performed for those patients who received  $\leq 2$  units, as blood transfusion may potentially be avoided in this group.

**Results.** 295 patients were identified. Major resections ( $\geq 3$  Couinaud segments) were performed in 171 (58%), median LOS was 9 days (range 2-57), and analgesia was delivered by EPI in 200 (67.8%) patients. Complications were observed in 93 (31.5%) patients. 113 (38.3%) received blood, and 72 (24.4% of all, or 63.7% of transfused patients) received  $\leq 2$  units. Excluding patients who received  $> 2$  units, 56 of 172 (32.6%) EPI patients vs. 16 of 82 (19.5%) IV patients received blood ( $p=0.03$ , Chi square), despite having similar operative blood loss ( $744 \pm 488$  cc (EPI) vs.  $872 \pm 530$  cc (IV),  $p=NS$ , Student's T test). Factors associated with receiving any blood transfusion on univariate analysis were age  $> 65$ , ASA  $> 2$ , OP time  $> 300$  min., blood loss  $> 1L$ , and EPI use. By multivariate analysis, using the variables approaching significance on univariate analysis, all 5 factors maintained independent association with perioperative blood transfusion (EPI use,  $p=0.04$ , RR=2.1, 95% CI=1.02-4.50). Complication rate and LOS, however, were not statistically tied to route of pain management.

**Conclusions.** In comparison to intravenous pain control, epidural pain management was associated with a greater likelihood of perioperative blood transfusion, despite similar operative blood loss. The only adjustable variable associated with transfusion practices was EPI use. EPI anesthesia should not be routine in patients undergoing partial hepatectomy.

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#### COMPARISON OF INTRAOPERATIVE BLOOD SALVAGE VERSUS CONVENTIONAL METHODS TO LOWER CENTRAL VENOUS PRESSURE IN PATIENTS UNDERGOING LIVER RESECTION FOR PRIMARY AND SECONDARY HEPATIC MALIGNANCIES

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**Introduction.** Hepatic resection for primary and secondary malignancies of the liver has become safer partly due to less perioperative blood loss. Low central venous pressure (CVP) during surgery has been shown to decrease back bleeding from hepatic veins during parenchymal transaction. The optimal method to achieve low CVP has not been determined.

**Methods.** One hundred ten patients who underwent hepatic resection between 2000 and 2006 were retrospectively examined. Patients who had intraoperative blood salvage (IOBS) to help achieve low CVP with autologous transfusion after the resection was finished, were compared to patients who had low CVP achieved with either fluid restriction or pharmacologic agents alone. Patients were matched according to number of segments resected, histology of cancer, and liver function rating (0-3 severity range). Statistical analyses took into account the matched pairs using Wilcoxon signed-rank or Sign tests.

**Results.** Ten patients who underwent IOBS were successfully matched to 10 patients achieving low CVP by other methods. Matched pairs were similar in age, gender, and race. All patients in both groups had a liver function rating of "0", while 1 patient in the IOBS group had cirrhosis. The median volume of blood withdrawn in the IOBS group was 500 cc (range, 250-500). Median CVP achieved during parenchymal transaction was 5.75 mmHG (range, 3-12) for the IOBS group and 5.25 mmHG (range, 4-9) for the non-IOBS group. The mean number of segments resected in both the IOBS and non-IOBS group was 2 (range, 1-4) with an average vascular inflow occlusion time of 25 minutes (range, 10-60). The median operative time was 380.5 minutes (range, 214-695) and 350 minutes (range, 173-720) for the IOBS and non-IOBS group, respectively. The mean operative blood loss was

766.7 cc (range, 100–3000) in the IOBS compared to 541.7 cc (range, 125–1050) in the non-IOBS group ( $p = .406$ ). The mean perioperative transfusion (PRBC + FFP) was 0.8 units (range, 0–6) in the IOBS group versus 0.5 units (range, 0–4) in the non-IOBS group ( $p = 0.907$ ). Using a complication rating scale of 0–5, the IOBS and non-IOBS group had a mean rating of 1.3 (sd = 1.70) and 0.89 (sd = 1.36), respectively ( $p = .800$ ). There was no post-operative mortality in either group.

**Conclusion.** There was not a significant difference in perioperative clinical outcomes using IOBS versus other methods to achieve low CVP. Until further research proves otherwise, low CVP for hepatic resection can be achieved using various methods with equal effectiveness.

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#### CURRENT PRACTICE OF US HEPATIC SURGEONS – RESULTS OF A SURVEY OF SURGICAL TECHNIQUE

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**Introduction.** Despite the plethora of equipment available to surgeons for parenchymal transection during liver resection, the optimal technique remains undefined. Whether the method of transection affects the incidence of complications such as biliary fistula is difficult to determine because of low overall rates and use of multiple techniques. The aim of the study was to examine the techniques employed by US hepatic surgeons performing major hepatic resections.

**Methods.** A questionnaire was sent to all 440 active members of the AHBPA via mail. Details of each surgeon's preference for methods of liver parenchymal transection in both normal and cirrhotic livers, as well as anatomical and non anatomical resection were requested. Use of drains, hemostatic agents and methods (if any), to check for bile leak from the cut surface of the liver was queried. Details of the surgeon volume and perceived complication rates for all types of liver resection, liver transplants and living donor resection were also requested.

**Results.** 149 responses were returned (34% response rate). 10 of these were from AHBPA members who do not practice hepatic surgery and were not included in the analysis. 139 responses were analyzed. 39 respondents were transplant surgeons also performing hepatic resections and 31 had living donor surgery experience. The most popular technique among non-transplant surgeons was fracture with clips/sutures or the Cavitron Ultrasonic Surgical Aspirator (CUSA). The ligasure and gyrus were the least utilized. Transplant surgeons however, use the waterjet dissector and linear staplers more commonly than non-transplant surgeons ( $p < 0.005$ ). Sealants were used selectively by 55%, always by 30% and never by 15% of surgeons and the most popular ones were Avitine, Surgicel and Tisseal. 51% of surgeons always use drains for anatomical resection and 19% for non-anatomic resections. Perceived biliary fistula rate was 5%. Endoscopic intervention was performed most commonly for persistent fistula, while acute surgical intervention was reserved only for uncontrolled sepsis.

**Conclusions.** Optimal parenchymal transection technique is not known. Despite the availability of many technologically advanced instruments, use of the simple fracture and ligate method still predominates. It is unknown whether transection methods affect complication rates or outcome.

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#### FACTORS PREDICTING OUTCOMES FOLLOWING HEPATIC RESECTION IN LIVERS WITH ABNORMAL PARENCHYMA

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**Background.** Liver resection in patient with steatosis, fibrosis and cirrhosis is associated with a high morbidity and mortality rate. Belghiti et al described the "50–50" criteria in predicting outcome following liver resections. Such criteria will help in post-operative management, allocation of scarce Intensive Care resources and prognostication of disease.

**Methods.** Using a prospectively collected database, a retrospective analysis of consecutive patients who underwent liver resection surgery with underlying liver pathology of steatosis and fibrosis between 1999 and 2005 were studied. The impact of preoperative liver and kidney function, American Society Anaesthesiologists (ASA) grade, Model of End Stage Liver Disease

(MELD) score, extent of resection, day 5 Bilirubin, day 5 Prothrombin Time (PT) and "50–50 criteria" (day 5 Bilirubin  $> 50 \mu\text{mol/l}$  and day 5 PT  $< 50\%$ ) on morbidity and mortality was analysed.

**Results.** 236 patients underwent liver resection surgery for colorectal metastases ( $n = 198$ ) and Hepatocellular Carcinoma ( $n = 38$ ) with abnormal liver parenchyma of steatosis ( $n = 203$ ) and fibrosis ( $n = 33$ ). The median patient age was 65 years (range: 30–86) with 44% of patients classed as ASA grade 1, 41% ASA grade 2, 15% ASA grade 3 and median MELD of 5.2. The median hospital stay was 8 days (range: 3–62), Intensive Care was required in 35 (14.8%) of patients. On multivariate analysis, ASA grade, Day 5 PT  $< 50\%$  and "50–50 criteria" independently predicted the need for Intensive Care ( $p = 0.04$ ,  $< 0.001$  and  $0.017$  respectively). The post-operative complication and mortality rate was 46.2% and 3.8% respectively. PT  $< 50\%$  on day 5 was the only independent predictor of morbidity and mortality on multivariate analysis.

**Conclusion.** ASA status and "50–50" criteria predicted ICU stay but not mortality in liver resection surgery on livers with abnormal parenchyma. Only PT  $< 50\%$  on day 5 predicts ICU stay, morbidity and mortality. In this cohort, adding Bilirubin of  $> 50 \mu\text{mol/l}$  at day 5 to this PT result did not contribute to predicting surgical outcome.

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#### THE RISK OF GAS EMBOLISM DURING LAPAROSCOPIC LIVER RESECTION IS RELATED TO PARENCHYMAL TRANSECTION TECHNIQUE

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The risk of gas embolism during laparoscopic liver resection has been previously shown. However, whether parenchymal transection technique affects the risk of gas embolism has not been previously studied. The purpose of this study was to evaluate whether staple transection of the liver reduced the risk of gas embolism compared to thermal energy techniques in a porcine model.

**Methods.** Fifteen female pigs underwent laparoscopic left lateral hepatectomy. For transection technique, pigs were randomized into 3 groups: Ultrasonic Coagulation Shears (UCS) ( $n = 5$ ), Electrothermal Bipolar Vessel Sealer (EBVS) ( $n = 5$ ), or Endostapler ( $n = 5$ ). CO<sub>2</sub> pneumoperitoneum was established at 12 mm Hg, and a transesophageal echo (TEE) probe was positioned to detect gas emboli. A reviewer blinded to the transection technique measured the frequency, duration, and grade of gas emboli events. Grade of gas emboli ranged from 0 (no emboli) to 4 (total vessel opacification with emboli). Blood loss was measured with a laparoscopic suction device, and operative time was measured from the start of liver marking for transection to the completion of resection. Proper TEE sampling was confirmed at the end of each case. Data are presented as median [IQR] and were compared using the Kruskal-Wallis Test. A  $p$ -value of  $< 0.05$  was considered statistically significant.

**Results.** Proper TEE sampling was confirmed in 14/15 pigs. Gas emboli occurred in 5/5 cases with the UCS, 4/4 cases with the EBVS, and in 4/5 cases with the Endostapler. However, there was a significant difference between groups for grade of gas emboli, operative time, and blood loss favoring the Endostapler (Table).

	UCS	EBVS	Endostapler	P-Value
Grade of gas emboli	4 [2.5–4]	3 [2.25–3.75]	1 [0.5–2.5]	0.040
Frequency of gas emboli events	3 [2–9]	4.5 [1.75–5.75]	3 [1–5]	0.491
Duration of gas emboli events (seconds)	388 [149–659]	163.5 [81.5–439]	11 [1–196]	0.110
Operative time (minutes)	25 [22–48]	52 [33.5–71.5]	22 [19.5–24]	0.018
Operative Blood loss (mL)	120 [100–150]	70 [32.5–100]	50 [27.5–85]	0.021

**Conclusions.** Gas emboli occurred during laparoscopic left lateral hepatectomy with all transection techniques used in this study. However, the endostapler device was associated with the lowest grade and duration of gas emboli events, as well as the shortest operative time and least operative blood loss.

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#### A COMPARISON OF STAPLED TRANSECTION VERSUS LIGASURE IN LAPAROSCOPIC LIVER RESECTION

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**Background.** Advancements in technology have allowed laparoscopic surgery to expand into advanced procedures such as liver resection; however, the transection method is debatable. This study was designed to evaluate the

feasibility and outcome of laparoscopic liver resection comparing the Ligasure device versus endomechanical stapling devices for parenchymal transection in a swine model.

**Methods.** Laparoscopic left hepatectomy was performed in 2 groups (n = 5 in each group) comparing the stapler device with the Ligasure device. The cut surfaces of the liver were evaluated for bleeding and biliary leakage at the time of the operation and one week later. The animals were euthanized one week after the operation to determine hemorrhage, bile leakage, and to allow for histological evaluation of the liver. Serum liver enzymes were checked before, after, and one week postoperatively.

**Results.** No evidence of biliary leakage or hemorrhage was noted at the time of the operation and one week later for both groups. There was a trend toward an increase in blood loss in the stapled group compared to Ligasure (40 ± 16.4 cc vs. 17 ± 3.7 cc, p > 0.05). There was also a trend toward shorter transection time in the stapled group compared to the ligasure group (15 ± 4.1 min vs. 21.8 ± 5.3, p > 0.05). The instrument cost was significantly higher in the stapled group (720 ± 110 vs. 400 ± 50; p < 0.05). There was no difference in serial liver enzymes and liver histopathology in either group.

**Conclusions.** The Ligasure device and endomechanical stapler can be safely and effectively used for parenchymal transection during laparoscopic liver resection. However, using endomechanical staplers is associated with an increase in cost.

### 83 LESSONS LEARNED FROM 130 LAPAROSCOPIC LIVER RESECTIONS

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Laparoscopic liver resection is steadily increasing worldwide. This paper examines the first 130 lap liver resections performed at our institution. Patient selection and surgical technique have evolved considerably over 10 years. 128 patients (2 had successful iterative resections). 91 female, mean age 51 (21–86). Operations: 19 rights, 5 lefts, 61 left laterals, 29 segmentals and 26 subsegmental resections. Six operations were hand assisted. Conversions of 10% are not considered failure. Most were for blood loss (mean 400 mls in whole group, 250 mls in nonconverted cases; range 0–2500 mls). Mortality of 1 liver failure after left lateral in cirrhotic. Bile leak rate of 4%; overall morbidity of 11%. Over the first 8 years, most patients had benign conditions. Over the last 2 years 26 of 45 resections were for malignancy. 'Chemo-naive' livers are preferred and this is influencing our adjuvant therapy decisions. Positive margins appear more common in subsegmental resections. Laparoscopic ultrasound is essential and Ligasure, harmonic shears and linear staplers are used for parenchymal resection. As experience grows more challenging cases are attempted with an accepted rise in conversion rates, either to hand assist or full laparotomy. Video of current techniques and problems will be demonstrated.

### 84 MESOHEPATECTOMY AS A SAFE ALTERNATIVE TO EXTENDED HEMIHEPATECTOMY IN CENTRAL LIVER TUMORS

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Despite significant improvement of perioperative management in extended right and left hemihepatectomy, as the curative option for treatment of central liver tumors, the high morbidity and mortality rate is still an important obstacle. Mesohepatectomy, as a sectoral but not a segment-oriented resection, preserves up to 35% more functional liver tissue than either extended left or right hepatectomy. However, mesohepatectomy has not been generally applied, which might be partially due to the difficulty of this procedure as a complex resection method. The aim of this study is to present our experience using mesohepatectomy for central liver tumors. At our department, thirty nine consecutive patients (m/f = 27/12) with centrally

located liver tumors underwent mesohepatectomy. The peri- and post-operative data were prospectively evaluated and analyzed regarding the morbidity and mortality rate. The mean age of the patients was 63.9 years. The indication of mesohepatectomy was liver metastasis (n = 19), HCC (n = 8), gallbladder carcinoma (n = 5), cholangiocellular carcinoma (n = 3), and others (n = 4). Mean operative time was 239 min (range: 65–480 min) and mean intra-operative blood loss was 1285 ml (range: 150–5000 ml). For the moment, mean intra-operative RBC and FFPs transfusion was 3.9 units (range: 0–12 unit) and 4.5 units (range: 0–14 unit), respectively. Mean postoperative hospitalization was 17.4 days (range: 6–104 days). Post-operative surgical complications were seen in 11 patients (28.2%) including; intra-abdominal abscess, bilioma or bile leakage, hemorrhage and hematoma, peritonitis due to intestinal perforation, and wound infection. Two patients (5.1%) died in the early postoperative phase. The causes of death were portal vein bleeding with severe coagulopathy due to liver failure in one patient and septic multiorgan failure in the another one. Compared to the traditional extended liver resection the mesohepatectomy accompanies with a clearly smaller parenchymal loss. Although it is a technically difficult operation and requires special attention to prevent surgical complications it is justified in selected patients, with centrally located tumors, as a safe alternative to extended liver resection. However, further prospective multicentric investigation about advantages and disadvantages of this technique is demanding.

### 85 PROLIFERATIVE ACTIVITY OF LIVER TUMOURS FOLLOWING EMBOLIZATION OF THE PORTAL VEIN

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**Introduction.** Although Portal Vein Embolization (PVE) proved to be effective in extending the indications for liver resection in patients previously considered with non-resectable liver tumours, the effects of this procedure on tumor growth remain controversial.

**Methods.** 12 patients with liver tumours of mean age 63 year and male to female ratio 4:3, underwent preoperative PVE between 2001 and 2006 (PVE group). Of these patients 8 had Colorectal Liver Metastasis, 1 had Neuroendocrine Tumour, 1 had metastatic GIST, and 1 had GB carcinoma. 9 patients who underwent major hepatic resection without PVE served as control (non-PVE group) 4 of which had Colorectal metastasis, 1 had Hepatocellular Carcinoma, and, 1 had Cholangiocarcinoma, 1 had Neuroendocrine Tumour, 1 had metastatic GIST, and 1 had Pancreatic cancer. The resected livers were examined using immunohistochemical staining of tumour cells. Cell proliferation was determined by over or under-expression of Ki-67, Vascular Endothelial Growth Factor (VEGF), Hepatocyte Growth Factor (HGF), Hypoxia Induced Factor (HIF), CAIX and CD34.

**Results.** Ki67 was overexpressed in 50% of patients who underwent PVE and in 42.9% of patients who did not have PVE (p < 0.05). Again VEGF was overexpressed in the PVE group (63.6%) (p < 0.05). No significant over-expression difference was noted in the other markers (HIF, CAIX and CD34). Correlation with clinical findings and radiological progression was made.

**Conclusion.** We conclude that PVE increases tumor proliferation and overgrowth. Although PVE is effective in extending indications for surgery, this potential effect on tumour growth should be taken into consideration.

### 86 MORBIDITY AND MORTALITY FOLLOWING MULTI-VISCERAL RESECTIONS IN COMPLEX HEPATIC AND PANCREATIC SURGERY

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**Introduction.** Complex multi-visceral resections in major hepatic and pancreatic surgery are relatively infrequent, and evidence regarding the

Pathologies of Patients Undergoing Multivisceral Resection According to Primary Operation Performed

Pathology	Number of Patients (N)	Liver Resections Performed (n)	Pancreaticoduodenectomies Performed (n)	Distal Pancreatectomies Performed (n)	Total Gastrectomies Performed (n)
Neuroendocrine Tumor	5	2	1	2	
Pancreatic Adenocarcinoma	3		1	2	
Gastric Adenocarcinoma	3				3
Sarcoma*	4	1	2	1	
Colorectal Adenocarcinoma	2	2			
Renal Cell Carcinoma	2	2			
Inflammatory Mass Mimicking Cholangiocarcinoma	2	2			
Gall Bladder Carcinoma	1	1			
Melanoma	1		1		

\* Includes 1 GIST, and 1 sarcoma of bile duct.

associated morbidity and mortality is scant. The purpose of this paper was to describe the outcomes following such aggressive surgical treatment.

**Methods.** A retrospective review of the outcomes following multi-organ resection in the setting of major liver or pancreatic resection was conducted from 2002 until July 2006. The primary outcome measures analyzed were postoperative morbidity and mortality. Secondary outcomes were recurrence rates and survival.

**Results.** 23 patients underwent multivisceral resections in that time period. There were 13 males and 10 females, with a mean age of 62.2 years. The various pathologies and the principle operations performed are listed in Table 1. A median of 4 organs were resected (range 2 to 6). Median operating time was 398 minutes (range 191 to 683) and median blood loss was 1500 ml (range 300 to 5000). Ten patients received a peri-operative blood transfusion, with a median of 2 units transfused. Median length of stay was 23 days (range 7 to 60). Three patients (13%) were admitted to ICU for a median of 3.5 days. There was one operative mortality (4.3%) in a patient who underwent a pancreaticoduodenectomy, right trisegmentectomy, and bile duct resection for what was thought to be a cholangiocarcinoma, but proved to be a bile duct sarcoma. In the remaining patients, minor and major morbidity occurred in 6 (27%) and 8 (36%) patients, respectively. One patient suffered a leak from a biliary anastomosis after a pancreaticoduodenectomy and two patients suffered pancreatic fistulas following distal pancreatectomies. After a median follow-up of 5.7 months (range 1.2 to 46.3), 5 patients (23%) suffered disease recurrences, and 5 have died. Median disease-free and overall survivals have not been reached.

**Conclusions.** The morbidity following such multivisceral resections is significant. However, with careful patient selection, acceptable results may be achieved. The requirement to remove multiple organs should not be a contraindication to tumor resection in complex hepatobiliary and pancreatic surgery.

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#### LIVER AUTOTRANSPLANTATION ACCORDING TO A "MODIFIED ORTHOTOPIC PIGGY-BACK" TECHNIQUE

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We performed OLT in the treatment of diffused liver mets from colorectal cancer by Boron Neutron Capture Therapy (BNCT) in 2 patients; the method includes neutron irradiation of ex situ liver inside a nuclear reactor. Reconnection of the liver after BNCT resulted to be rather difficult, total ECC set up was required, the VC reconstruction was performed by the interposition of a dacron prosthesis, required a long time and several post operative complications were registered. To simplify the procedure and to shorten the operating time as well as the time of total ECC we propose a modified orthotopic piggy back technique for OLT. The method was developed in the swine model (25 kg). After hepatectomy the VC flow was preserved by interposing a goretex prosthesis by 2 end to end anastomosis. The vascular reconnection of the liver was then performed by a side to side VC prosthesis anastomosis with lateral clamping of the prosthesis so that the VC flow was uninterrupted also during the reconnection. The mean time for VC reconstruction was 54 ( $\pm 8$ ) min. and the mean time for side to side VC prosthesis anastomosis was 13 ( $\pm 4$ ) min. In our previous experiences the main difficulty in the reimplant of the liver was represented by the reconstruction of suprahepatic VC and the interposition of a prosthesis ( $\emptyset$  20 mm) was required in the reconstruction of infrahepatic VC; on the whole 3 end to end sutures were performed and the mean time of total ECC, was 5.30 hrs including portal vein reconstruction (15 min.). The time required to treat the liver in the nuclear reactor was 45 minutes. In the postoperative period we registered not inconsiderable morbidity. The modified piggy back technique that we propose could shorten the times of liver reconnection and of total ECC as VC reconstruction by interposition of a prosthesis could be carried out during the anhepatic phase, when the liver is away for neutron irradiation, then the VC flow could be immediately restored. Nonetheless, this is not a reason to completely forget a veno venous bypass, to avoid the inevitable congestion of the splanchnic system in situations without poorly developed porto systemic collateral circulation. Finally to perform a side to side VC prosthesis anastomosis by lateral clamping of VC is obviously easier and faster than to perform end to end anastomoses with the liver in situ. All this should decrease the risk of afterbleeding and owing to the reduced time of total ECC, furthermore potential haemodynamic disruption and circulatory instability should be reduced.

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#### TRANSCATHETER ARTERIAL CHEMOEMBOLIZATION (TACE) FOR BREAST CANCER LIVER METASTASIS: SINGLE INSTITUTION EXPERIENCE

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**Introduction.** More than half of patients with breast cancer develop liver metastasis in their lifetime. Recent data suggests hepatic resection may

prolong survival in carefully selected patients. Currently there is a paucity of data on the role of TACE as a locoregional therapy for hepatic metastasis.

**Method.** From a prospectively established database ten patients treated with TACE for liver metastasis from breast primary were reviewed (1998–2006). Median age was 46.5 (29 to 60). Nine patients had multiple bilobar liver metastases and one had a single large right lobe lesion. The liver was the only site of metastasis in five patients. The remaining five patients also had bone metastasis, which were treated with external beam radiation. Adriamycin was chosen as the TACE agent for 6, cisplatin for 3 and oxaliplatin for one adriamycin-failure patient. TACE agents were chosen based on prior systemic therapy administered. Median number of TACE cycles was 3 (1 to 5).

**Result.** Median time interval from the primary breast cancer to diagnosis of liver metastasis was 16 months (0 to 95). Surveillance CT scans showed that liver metastasis progressed in 6 patients, regressed in 2 patients and stabilized in 2 patients. Tumor markers (CA15.3 or CA125) decreased in 5 patients during TACE therapy. Median time interval from diagnosis of liver metastasis to death ( $n=7$ ) or last follow-up ( $n=3$ ) was 24 months (1 to 65). 6 patients developed new or progressive extrahepatic metastasis during TACE therapy. Toxicity of TACE included: 7 patients with post-embolization syndrome (mild nausea, vomiting or abdominal pain) and 3 patients needed neupogen for transient neutropenia. One patient died of upper GI bleeding and hepatic failure.

**Conclusion.** Hepatic artery directed therapy offers a feasible locoregional palliative therapy which is generally well tolerated. This is the largest case series of patients with metastatic breast cancer to the liver who were treated with chemoembolization. TACE for metastatic breast cancer may aid in controlling progression of hepatic metastasis, however prognosis of patients is generally poor.

#### Videos

##### Competitive Videos Liver

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#### LIVER HYDATID CYST: LAPAROSCOPIC TREATMENT

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**Background.** Hydatidosis is an endemic disease in South America. The gold standard treatment for the liver hydatid cyst is surgery. The classical approach was laparotomy. In the last 10 years, minimally invasive techniques emerged as alternative treatments. The laparoscopic approach still remains controversial and with few cases reported in literature.

**Objective.** To show the laparoscopic resection of a hepatic hydatid cyst.

**Methods.** Sixty-five year-old male patient, referred to our Unit with a hepatic cystic mass in segment IV. CT Scan showed a cystic image with internal septums. Serology (Arc 5) was positive. Previous the surgery, the patient received pharmacological treatment with albendazole.

**Results.** Previous to the resection, the cyst was evacuated with a fine needle aspiration. A laparoscopic cystectomy was performed. For the transection, we used monopolar electrocautery. A cholecystectomy was associated due to gallbladder lithiasis. The patient was discharged at day 2 without post-operative complications.

**Conclusions.** Laparoscopic treatment for liver hydatid cysts is feasible in selective cases and in high volume centers. It provides the benefits of minimally invasive approach.

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#### SMALL DIAMETER PROSTHETIC H-GRAFT PORTACAVAL SHUNT

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The small diameter prosthetic H-graft portacaval shunt decompresses the portal system directly and provides partial portal decompression. This video presents our technique of small diameter prosthetic H-graft portacaval shunt. The operation is undertaken through a transverse abdominal incision. A limited Kocher maneuver is used to expose the inferior vena cava and ultimately the portal vein. About 50% of the circumference of the inferior vena cava needs to be freed, and, similarly, about 70% of the circumference of the portal vein needs to be freed to undertake shunting. An 8 mm PTFE graft is utilized. The graft is 3 cm from toe-to-toe, and 1.5 cm from heel-to-heel, with the bevels cut at 90° to each other to accommodate the orientation of the portal vein to the inferior vena cava. The cava-graft anastomosis is completed first, followed by the portal vein-graft anastomosis. Pressures in the portal system and the inferior vena cava are measured before and after shunting. Shunting should lead to a decrease in the portal vein pressure of >10 mmHg, a decrease in the portal vein-inferior vena cava pressure gradient of >10 mmHg, a gradient of <10 mmHg between the portal vein and the inferior vena cava, and a thrill in the inferior cava just cephalad to the cava-graft anastomosis. Outcomes after small diameter H-graft portacaval

shunt promote its application. Small diameter prosthetic H-graft portacaval shunts optimally palliate portal hypertension, prevent variceal rehemorrhage, and promote long-term survival.

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#### VIDEO: BLOODLESS OPEN RIGHT HEPATIC LOBECTOMY FOR METASTATIC COLORECTAL CANCER WITH THE STAPLE TECHNIQUE

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**Purpose.** A 5-minute video will be presented showing a rapid technique for open right hepatic lobectomy (hemihepatectomy) for metastatic colon cancer facilitated by linear stapling devices.

**Results.** After liver mobilization and ligation of the short hepatic veins from the IVC, the right hepatic vein is divided with endoGIA stapler. The right hepatic artery is doubly ligated. The right portal vein, and right hilar plate with right hepatic duct(s) are sequentially divided with the endoGIA stapler. Intra-operative U/S is then used to delineate the transection plane for clearance of the tumor margin and identification of the crossing middle hepatic vein branches. The liver parenchymal slice is then accomplished under Pringle inflow occlusion using a one-handed crushing endoGIA stapler. The entire right lobe parenchymal slice takes 3–4 minutes, and EBL is typically <100 ml. For this case, pathology showed a solitary 4 cm tumor adjacent to the right portal vein. Margins were negative. The patient is NED 2 yrs after the resection. We have performed more than 200 hemihepatectomies with this technique. Overall transfusion rate is ~5%, and bile leak rate is <2%.

**Conclusion.** Use of endovascular staplers for vascular and parenchymal transection in major hepatic resection is a safe and rapid technique.

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#### HEPATIC METASTECTOMY USING A FOUR-PRONG RADIO-FREQUENCY COAGULATION DEVICE (HABIB 4X, RITA MEDICAL)

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**Background.** Advances in surgical technique and perioperative care have reduced mortality from liver resection over recent years. A significant focus has been on the reduction of blood loss during parenchymal division. Intraoperative hemorrhage during parenchymal transection and need for transfusion remain a predictor of perioperative morbidity.

**Methods.** The video details a segmental resection of segments 3 and 4. The patient is a 30-year-old female with a history of adenoid cystic carcinoma of the left lacrimal gland. She was treated by an orbital resection and adjuvant radiation. She was found to have liver-only metastases two years after treatment of her primary. From August 2005 to October 2006, 29 patients with hepatic lesions underwent resection using a four-prong radiofrequency (RF) device. The use of bipolar RF energy and multiple prongs rapidly creates a zone of necrosis within the liver substance approximately 1 cm wide and nearly as deep as the needles are placed. Intraoperative ultrasound was performed to delineate the tumor location and assess for other lesions. The selected line of transection is thermoablated using the device. The parenchyma is then cut using a scalpel or parenchymal fracture (clamp or finger fracture). Surgical clips are selectively used to ensure vessel and bile duct ligation.

**Results.** No drains were used. There were 5 right hepatic lobectomies, 4 left hepatic lobectomies, and 20 segmental resections. A synchronous colonic resection was performed on three patients having segmentectomies. Mean operative blood loss was 354 ml (Range = 100–1500). Mean procedural time was 244 minutes (Range = 97–557). Average LOS was 8 days (Range = 4–18). The duration of the case presented was 153 minutes. The estimated blood loss was 100 ml. The largest tumor size was 13 cm. She was discharged on postoperative day 6.

**Conclusions.** Use of the four-prong radiofrequency dissecting device for liver resection is safe. This novel device offers a new tool for near bloodless hepatic parenchymal transection.

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#### EN BLOC RESECTION OF THE LEFT COLON, DISTAL PANCREAS, SPLEEN AND SIMULTANEOUS RIGHT HEPATECTOMY FOR METASTATIC COLON CARCINOMA BY THE LAPAROSCOPIC APPROACH

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**Introduction.** The preferred treatment approach for patients presenting with colon carcinoma and hepatic metastasis (Stage IV) is induction chemotherapy. In the presence of impending symptoms an immediate operative intervention is warranted to address the primary. In a select group of patients, it is sometimes possible to resect the hepatic tumours also simultaneously. The ability to perform this via the laparoscopic approach may

facilitate recovery. We present a case of en bloc resection of left colon, distal pancreas, spleen and simultaneous right hepatectomy for metastatic colon carcinoma by the laparoscopic approach.

**Material.** A 57 year old male patient that presented with abdominal pain, anorexia and weight loss. Colonoscopy revealed an apple-core at the splenic flexure which on biopsy revealed adenocarcinoma. A CT scan and MRI scan of the abdomen showed a lesion of the splenic flexure involving the distal pancreas and spleen in addition to a metastatic lesion involving segment VI, VII and VIII of the liver. Due to the obstructive nature of the lesion and the inability to place a colonic stent, it was decided to proceed with operative intervention.

**Result.** The patient underwent en bloc left hemicolectomy, distal pancreatectomy, splenectomy and simultaneous right hepatectomy via the laparoscopic approach. The splenic flexure carcinoma was initially approached with en bloc resection of the left colon, distal pancreas and spleen, following which an stapled anastomosis was performed between the transverse colon and the distal sigmoid colon. A right hepatectomy was performed with extra-hepatic division of the hepatic artery and portal vein. The bile duct and the right hepatic vein were encountered during parenchymal transection and divided. The estimated blood loss was 500 ml (100 ml for colectomy and 400 ml for hepatectomy) and the operative time was 330 minutes. (120 minutes for colectomy and 210 minutes for hepatectomy) Histo-pathology revealed T3 N0 (of 25 nodes) M1 (stage IV) colon carcinoma with negative margins for the colon (4.5 cms) and the liver (2 cms). Post operatively, the patient developed a bile leak which was managed conservatively. The patient tolerated diet on the 5th and was discharged home on the 20th post operative day respectively.

**Conclusion.** We present a case of en bloc resection of left colon, distal pancreas, spleen and simultaneous right hepatectomy via the laparoscopic approach

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#### LAPAROSCOPIC HEPATIC AND DIAPHRAGMATIC RESECTION FOR THE TREATMENT OF AN OVARIAN TUMOR IMPLANT

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**Background.** Laparoscopic resection is a possibility for the treatment of an ovarian cancer implant. There are few publications describing this approach.

**Objective.** to show a laparoscopic resection of a hepatic and diaphragmatic ovarian cancer implant.

**Population.** A 64 year-old patient with a bilateral oophorectomy, hysterectomy and omentectomy because of an ovarian cancer. During the follow-up, the patient presented an increasing level of tumoral markers and appeared a hepatic nodule in segment VII.

**Methods.** The patient was placed in left lateral position. Four trocars were needed (10 mm, 5 mm × 3). There was no carcinomatosis. There was a hepatic nodule, compromising the adjacent diaphragm. The invaded diaphragm was resected with endo-scissor and pneumothorax was created. The diaphragmatic orifice was closed with separated stitches, without pleural drainage. The hepatic parenchyma was resected with monopolar electrocautery. The implant was packed and removed through the umbilical access.

**Results.** The patient was discharged at day 2, without postoperative complications. In the 6th month follow-up there are no evidences of tumoral recurrence.

**Conclusions.** Hepatic lesions with limited diaphragmatic extension can be safely resected by laparoscopic approach, in selected cases.

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#### RIGHT HEPATECTOMY WITH CHOLECYSTECTOMY FOR METASTATIC COLORECTAL CANCER

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This operation typifies an optimal approach for hepatic resection for metastatic cancer to the liver. Hepatectomy begins with an incision that allows for adequate exposure. An upper abdominal transverse incision was utilized and extended to the xiphoid process after documenting no metastatic cancer beyond the liver. The liver was mobilized and the retro-hepatic vena cava was exposed with numerous branches between the liver and the inferior vena cava being divided. The inflow to the right side of the liver was controlled. The right hepatic duct was identified, doubly ligated, and divided. After demarcation, the dissection was carried into the left side of the liver to obtain an adequate margin about the lesion in Segment 5. During the dissection through the parenchyma of the liver, the right branch of the portal vein was divided near the porta hepatis. The right hepatic vein was clamped, divided, and sutured. The incision was closed after omentum was placed over the cut edge of the liver. The wound was closed with monofilament suture and the skin was approximated with paper strips. Hepatic function remained intact with minimal blood loss. Hepatectomy can be undertaken without notable difficulty and with wide exposure.

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**VIDEO: LAPAROSCOPIC LEFT HEPATIC LOBECTOMY FOR 12 CM HCC**

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UPMC Liver Cancer Center, University of Pittsburgh, Pittsburgh, PA

**Purpose.** A 8-minute video will be presented showing laparoscopic left hepatic lobectomy (Left Hemihepatectomy) for a large 12 cm HCC arising in a non-cirrhotic liver.

**Results.** A low midline handport is placed along with 3 LUQ (2–12 mm, 1–5 mm) and 1 RUQ (12 mm) trocars. After dividing omental adhesions, the round, falciform, and left triangular ligaments are divided. The left hepatic vein is exposed. The left hepatic artery is divided. The left portal vein is dissected and clamped with an intra-corporeal bulldog. Laparoscopic liver U/S delineates the transection plane through segment 4, and confirms contralateral inflow through the right portal vein. The liver parenchyma is divided with combination of harmonic scalpel, tissuelink, and endoGIA vascular staplers. The left hepatic vein is divided flush with the IVC using a stapler. The left portal vein is divided last with the stapler. The left hepatic lobe is removed intact through the handport incision. The margins were widely negative, and pathology showed a large HCC. EBL was 125 ml, and blood transfusion was not required. The patient was discharged home on the 2nd postoperative day.

**Conclusion.** Laparoscopic liver resection is safe and technically feasible, even in the setting of anatomic hepatic lobectomy for malignancy. It requires training in both MIS skills and open hepatic surgery.

**Videos****Competitive Videos Pancreas / Biliary**

VD-02

4/20/07 7:00 to 9:15 pm

Abstract Numbers 97–104

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**MIRIZZI'S SYNDROME: LAPAROSCOPIC TREATMENT**

Martín Palavecino, MD, Mariano Bregante, MD, Victoria Ardiles, MD, Diego Fernández, MD, Eduardo De Santibañes, Juan Pekolj, MD, PhD  
Hospital Italiano, Buenos Aires, Argentina

**Background.** Mirizzi's Syndrome is a rare complication of a long standing cholelithiasis. Many surgical approaches of varying complexity have been advocated for treatment. Minimally invasive surgery has been used for many other procedures and it could be feasible to resolve different types of this syndrome.

**Objective.** to show two Mirizzi's Syndrome type II cases resolved by laparoscopic approach.

**Population and Methods.** Case one is a female 73 year-old patient with abdominal pain and jaundice; Ultrasound showed a cholecystitis with a gallstone impacted at the infundibulum and intrahepatic duct dilatation. Case 2 is a male 82 year-old with abdominal pain and jaundice; the CT scan and MRI showed gallbladder dilatation with a gallstone and intrahepatic duct dilatation.

**Results.** Both patients were approached by laparoscopy, first case was resolved doing a subtotal cholecistectomy and laparoscopic closure; second case II was resolved performing a laparoscopic hepaticojejunostomy; Both patients were discharged at 3 and 4 day respectively without postoperative complications.

**Conclusion.** Mirizzi's syndrome sometimes can be anticipated on the basis of preoperative staging, and often is diagnosed or confirmed during the procedure. Subtotal cholecystectomy and simple closure with secure intraperitoneal drain appears to be a safe option for these patients, also a hepaticojejunostomy could be performed when the closure is not safe because the local conditions.

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**INTRAHEPATIC SEGMENT III HEPATICOJEJUNOSTOMY FOR BILIARY OBSTRUCTION AFTER RIGHT HEPATECTOMY**

Richard A Mackey, MD, Conrad H Simpfendorfer, MD, J. Michael Henderson, MD  
Cleveland Clinic Foundation, Cleveland, OH

Extrahepatic duct obstruction requires decompression by surgical bypass or biliary stenting to relieve jaundice, pruritus and prevent secondary biliary cirrhosis. Unresectable hilar obstruction lead to a modification in biliary bypass procedures for palliation. Left sided, intra-hepatic segment III hepaticojejunostomy has been described for malignant obstruction. We report a case of an intra-hepatic segment III hepaticojejunostomy for obstructive jaundice following right hepatic lobectomy for metastatic colon carcinoma. A benign post-operative stricture developed 6 months following lobectomy. Following a prior failed attempt at an extrahepatic hilar reconstruction, the patient had long term decompression with a percutaneous transhepatic catheter. Re-exploration and a successful segment III hepaticojejunostomy, through the umbilical fissure, was performed. The patients post-operative course was unremarkable. Segment III hepaticojejunostomy

can provide adequate internal biliary decompression and effectively palliate selected patients with an unapproachable hilus.

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**LAPAROSCOPIC TREATMENT OF CHOLEDOCHAL CYST**

Sergio E Bustos (Maac), MD, Jorge Nefa (Maac), MD, Pablo Omelanczuk, MD, Walther Minatti (Maac), Mario Masrur, MD, Mariana Debé, MD  
Italian Hospital of Mendoza, Mendoza, Argentina

**Purpose.** To present our experience with the technical aspects of the laparoscopic resection of a type Ic Choledochal-Cyst.

**Methods.** 22 years-old woman complaining of abdominal pain. Abdominal ultrasound, Computerized Axial Tomography and Cholangio Magnetic Resonance were performed showing the presence of a choledochal cyst. Exploratory laparoscopy was performed and the cyst was identified. The presence of a Todani type-Ic Cyst was confirmed by cholangiography. The hepatic duct and the neck of the cyst were isolated from the portal vein. A cholangioscopy of the cyst was performed. The hepatic duct was transected and the cyst removed. A Roux-en-Y anastomosis was performed. The jejunojunctionostomy was completed in an open fashion extending the umbilical port incision. The hepatojejunostomy was performed laparoscopically.

**Results.** Operative time was 210 minutes and the hospital stay 5 days. No complications were observed.

**Conclusion.** Type-Ic Choledochal-cyst can be treated by laparoscopy in a safe manner as in open surgery.

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**LAPAROSCOPIC BILIODIGESTIVE ANASTOMOSIS**

Mariano Bregante, MD, Martín Palavecino, MD, Diego Fernández, MD, Rodrigo Sánchez Clariá, MD, Eduardo De Santibañes, Juan Pekolj, MD  
Hospital Italiano, Buenos Aires, Argentina

**Background.** Bilio-enteric anastomosis have historically been performed using an open technique. We describe here a single experience with this procedure using laparoscopic techniques in 3 consecutive patients.

**Materials and methods.** During a 2 year period between July 2002 and July 2004, the authors attempted 3 bilio-enteric reconstruction by a total laparoscopic approach. Indications included benign primary intrahepatic lithiasis in one patient, benign stricture in one patient with a previous open choledochoduodenostomy and one patient with choledochal cyst. Operations performed included choledochoduodenostomy, hepaticojejunostomy and choledochal cyst excision with hepaticojejunostomy and extraabdominal Roux-en-Y anastomosis.

**Results.** The mean operation time was 180 minutes (r 140–310). There was no intraoperative complications and no major complications associated with anastomosis leakage or obstruction. No operative or post-operative transfusion was required. Oral food intake was started within 2 days and tolerated well, the average length of hospital stay was 5 days. Median follow up was 15 months, all patients are symptom free with no signs of stricture or recurrent biliary obstruction.

**Conclusion.** Total laparoscopic biliary reconstruction is feasible for a select group of patients, but requires advanced laparoscopic skills, including intracorporeal suturing. It must be attempted only in centers well versed in advanced laparoscopic surgery.

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**ORGAN-PRESERVING PANCREATIC HEAD RESECTION IN CHRONIC PANCREATITIS**

Gyula Farkas, MD, PhD, László Leindler, MD, Gyula Farkas Jr., MD  
Department of Surgery, Faculty of Medicine, University of Szeged, Szeged, Hungary

**Introduction.** Twenty to thirty per cent of patients with chronic pancreatitis (CP) develop enlargement of the head of the pancreas in consequence of inflammatory alterations, which leads to complications such as obstruction of the pancreatic duct, common bile duct stenosis and duodenal compression. A safe procedure has been developed for organ-preserving pancreatic head resection.

**Patients and Methods.** The surgical procedure consists in a wide local resection 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 applied one-layer Vicryl® suture. In icteric cases or in patients with stenosis of the common bile duct, prepyloric bile duct anastomosis is also performed with the jejunal loop.

**Results.** This procedure was performed in 142 patients with no mortality. The mean operative time was 150 min (range 120 to 180). In the postoperative period, only one reoperation was required in consequence of anastomosis bleeding, another gastrointestinal bleeding was treated conservatively and one patient had pneumonia. The duration of hospitalisation ranged between 7 and 12 days, with a median of 8.5 days. In the median follow-up period of 4.0 years (range 3 months to 7 years), 90% of the patients became complaint-free, and the weight increased by a mean of 11.3 kg (range 4–28).

**Conclusion.** This organ-preserving pancreatic head resection is a safe and effective procedure for definitive control of the complications following the inflammatory alterations of CP and should be regarded as a recommended procedure in the treatment of CP.

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### BILIARY PERITONITIS: LAPAROSCOPIC TREATMENT

Diego Fernández, MD, Martín Palavecino, MD, Mariano Bregante, MD, Rodrigo Sánchez Clariá, MD, Eduardo De Santibañes, Juan Pekolj, MD Hospital Italiano, Buenos Aires, Argentina

**Background.** Biliary peritonitis is one of the troublesome complications after laparoscopic biliary surgery. Relaparoscopy allows drainage of bile collection and direct control of the site of leakage in selected situations.

**Objetives.** To show 4 cases of biliary peritonitis treated by laparoscopic approach.

**Methods.** We present 4 patients with biliary peritonitis: Case 1: Patient referred to our Unit with a bile duct injury after a laparoscopic cholecystectomy. Case 2: Patient with abdominal pain in the postoperative time after a laparoscopic cholecystectomy. The laparoscopy demonstrated the migration of the Endoloop. Case 3: Patient with abdominal pain after the removal of a T-Tube. The exploration showed a biliary peritonitis secondary to a leakage in the T-Tube fistula. Case 4: Patient with pain after a needlescopic cholecystectomy. The laparoscopy demonstrated a leakage from an aberrant biliary duct in the gallbladder bed.

**Results.** All patients were solved with relaparoscopy without postoperative complications. Mean operative time was 75 minutes (r: 55–120). Mean length of stay after relaparoscopy was 3 days (r: 1–7). Case 1: We performed a drainage of the peritonitis. Case 2: After a cholangiogram demonstrating the absence of associated bile duct injuries, a new Endoloop was placed. Case 3: A cholangiogram through the T-Tube fistula showed no leakage in the common bile duct. The fistula was sutured. Case 4: After a normal cholangiogram, the aberrant duct was sutured.

**Conclusions.** Relaparoscopy is useful in the management of biliary peritonitis. Minimally invasive technique can be applied to these complications safely and effectively in selected cases and performed by experienced surgeons.

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### LAPAROSCOPIC DISTAL PANCREATECTOMY AND SPLENECTOMY FOR INSULINOMA

Maki Yamamoto, MD, Michael S Hayashi, MD, Blanding U Jones, MD, Peter Lin, MD, Kaylene Anne Barrera, John G Lee, MD, Thang D Nguyen, MD, Ninh Nguyen, MD, David K Imagawa, MD, PhD UC Irvine Medical Center, Orange, CA

Minimally invasive surgery is becoming more widespread in its usage for cases that had previously been treated with open procedures. Prior to the advent of laparoscopy, pancreatic neoplasms were treated with laparotomy. Currently, laparoscopic distal pancreatectomy (LDP) has only been published in small series of patients. In this video, we show our technique with

**Population and Methods.** A 59 year-old female patient referred to our Unit with an E5 (in Strasberg Classification) bile duct injury. The laparoscopic cholecystectomy was carried out 6 months before. The patient developed colangitis and was successfully managed with ERCP and a stent was placed in the biliary tract. The patient was admitted to our Hospital for elective surgery. A CT Scan showed a right lobe atrophy, MRI showed a E5 Strasberg BDI and angiography showed an associated right hepatic artery injury. The surgery was done without complications.

**Results.** We performed right hepatectomy, due to the atrophy of this lobe. We used an ultrasonic dissector for transection. The biliary reconstruction was made with a Roux-en-Y hepaticojejunostomy. The patient developed right pleural effusion that required a percutaneous drainage and she was discharged at day 14 postoperative.

**Conclusions.** In selected cases, a major hepatectomy is needed to treat complex bile duct injuries. These cases must be treated in HPB centers by a trained team.

### Free Papers

#### Pancreas Benign

FP-01

4/21/07 8:00 to 9:55 am

Abstract Numbers 105–112

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### SYSTEMATIC APPRAISAL OF BIOCHEMICAL MARKERS FOR ASSESSMENT OF DISEASE SEVERITY IN ACUTE PANCREATITIS: GUIDANCE FOR EVIDENCE-BASED PRACTICE IN 2007

Benoy I Babu, MBBS, Ajith K Siriwardena, MD HPB Unit, Dept of Surgery, Manchester Royal Infirmary, Manchester, United Kingdom

**Introduction.** Early detection of patients with severe acute pancreatitis is pertinent as it allows treatment to be delivered in an appropriate “high-dependency” environment with invasive monitoring. Although a host of biochemical markers have been evaluated as markers of severity there are no current selection guidelines. This study undertakes a structured, systematic appraisal of the available evidence in an attempt to identify optimal markers.

**Methods.** A 56-year search from 1950 to 2006 on EMBASE and MEDLINE using keywords “acute pancreatitis, markers and severity” was performed. Articles were excluded if they were: experimental data, non-english medium, case reports, reviews or letters to produce a total of 384 studies. Further restriction to report markers which were prospectively analysed and where there was evidence from more than one study resulted in a reduction to 82 publications reporting 5390 patients. Data for sensitivity, specificity and ROC curve (where available) are presented.

#### Results.

**Conclusion.** Interpretation of these data must accept that data-pooling for systematic review has inherent limitations in sensitivity of analysis. Although the findings favour urinary trypsinogen and serum elastase, there is strong support for the continued use of admission haematocrit and C-reactive protein at 48 hours as widely available and inexpensive markers of severity with results that translate readily across health-care systems.

Marker	Number of studies	Number of patients	ROC for severity Median	Median sensitivity (%) (range)	Median Specificity (%) (range)
Serum Amyloid A	5	300	0.65	76 (67–77)	69 (69–70)
CAPAP	6	140	n/a	(67–89)	(81–96)
Procalcitonin	13	478	0.61	94 (92–100)	84 (73–84)
Hematocrit	5	797	0.73 on admission	na	na
c-reactive protein	37	2130	0.69	78 (6–93)	83 (9–93)
Urinary Trypsinogen	11	1147	0.96	93 (90–96)	91 (86–92)
Serum Elastase	6	496	0.956	92	91

this relatively new procedure. To date we have performed 20 LDP. In our series of patients, LDP with or without splenectomy has been shown to be feasible with minimum morbidity.

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### COMPLEX BILE DUCT INJURY TREATMENT WITH A RIGHT HEPATECTOMY AND HEPATICOJEJUNOSTOMY

Eduardo De Santibañes, MD, PhD, Martín Palavecino, MD, Diego Fernández, MD, Mariano Bregante, MD, Juan Pekolj, MD, PhD Hospital Italiano, Buenos Aires, Argentina

**Background.** Laparoscopic cholecystectomy is the treatment of choice for symptomatic gallstones. This approach is associated with a higher incidence of biliary injuries. Complex injuries could lead to major hepatic resections.

**Objective.** To show a case of a complex bile duct injury that required right hepatectomy.

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### THE LOGISTIC ORGAN DYSFUNCTION SCORE-MODIFIED ATLANTA CATEGORIZATION PERMITS PRECISE PROGNOSTICATION AND ALLOCATION OF SEVERITY IN ACUTE PANCREATITIS

Srinivasan Balachandra, MBBS, James M Mason, PhD, Anil Bagul, MBBS, Ajith K Siriwardena HPB Unit, Dept of Surgery, Manchester Royal Infirmary, Manchester, United Kingdom; School for Health, University of Durham, Stockton-on-tees, United Kingdom

**Introduction.** The 1992 Atlanta consensus conference defined two categories of acute pancreatitis – severe and mild – according to the presence or absence, respectively, of organ failure (OF). However OF can be transient. This study tests the hypothesis that application of a contemporary, well-validated organ dysfunction scoring system such as the Logistic Organ Dysfunction Score (LODS) will provide greater precision in categorization.

**Methods.** A prospective single-centre study was undertaken in a consecutive series of 181 patients with a clinical diagnosis of acute pancreatitis (AP) presenting to a University Teaching Hospital from June 2001 through November 2004. Patients with known chronic pancreatitis and those transferred for tertiary care were excluded. In addition to demographic detail, data were collected on critical care occupancy, in-patient stay and in-hospital mortality. Charts were reviewed at end-of-episode for allocation of conventional Atlanta category (blind to other scoring). Variables required for calculation of LODS (omitting hepatic score component) were collected on admission and at 24 hours. Data were analyzed by receiver operator curves (ROC). The principal end-points were selected as utility of categorization system in prediction of in-patient stay and critical care unit occupancy as these translate across health-care systems. The study was approved by institutional review board.

**Results.** For critical care occupancy, the ROC for conventional Atlanta was 0.62 (95% confidence interval [c.i.] 0.56–0.68). LODS  $>2$  at 24h as a descriptor of severe disease generated a ROC of 0.63 (95% c.i. 0.51–0.74) which was further improved to ROC 0.75 by modelling cut-offs as  $\text{LODS} >2$  at 24h or  $\text{LODS} >0$  at 48h for selection of severe disease. For in-patient stay, ROC for conventional Atlanta was 0.69 compared to 0.76 for LODS-categorized Atlanta.

**Conclusion.** Calculation of a one-off logistic dysfunction score on the day of admission in patients with acute pancreatitis permits precise assessment of prognosis with a cut-off of LODS  $>2$  at 24h identifying severe disease. Calculation of the LODS score on admission in acute pancreatitis should replace prognostic testing and combines the value of admission predictive tests with improved disease categorization.

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### PANCREATIC PSEUDOCYSTS: IS DELAYED SURGICAL INTERVENTION ASSOCIATED WITH ADVERSE OUTCOMES?

Kaori Ito, MD, Michael Abramson, MD, Alexander Perez, MD, Hiromichi Ito, MD, Amarsanaa Jazag, MD, PhD, Jill Van Der Zee, MD, Edward E Whang, MD

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**Background.** Non-surgical interventions are increasingly applied for pancreatic pseudocysts. We hypothesized that surgical therapy applied after failure of percutaneous or endoscopic therapies for pseudocysts are associated with poorer outcomes than cases in which surgery is the initial intervention.

**Methods.** Medical records of all 284 patients diagnosed with pancreatic pseudocysts at our institution from January 1990 through September 2005 were analyzed. 46 patients underwent surgery as the initial interventional therapy (group A). Among 162 patients who underwent percutaneous or endoscopic drainage as the initial intervention, 75 patients required subsequent surgery after failure of non-surgical intervention (group B).

**Results.** Groups were comparable in demographic variables and with respect to location, number, and size of pseudocysts. 42% of group B patients developed infection within their pseudocysts after their non-surgical interventions. Compared to group A patients, group B patients had a higher overall perioperative morbidity rate (44.0% v.s. 72.4%,  $p=0.01$ ), a higher postoperative readmission rate (24.0% v.s. 44.7%,  $p=0.04$ ), and a higher pseudocyst recurrence rate (16.0% v.s. 35.5%,  $p=0.04$ ). Five (6.7%) group B patients died in the perioperative period; there were no perioperative deaths among group A patients.

**Conclusion.** Delayed surgical intervention for pancreatic pseudocysts are associated with higher incidences of recurrence, readmission, morbidity and mortality. The increasing application of non-surgical interventions needs to be re-evaluated.

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### LONG-TERM FOLLOW-UP AFTER ORGAN-PRESERVING PANCREATIC HEAD RESECTION IN PATIENTS WITH CHRONIC PANCREATITIS

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Department of Surgery, Faculty of Medicine, University of Szeged, Szeged, Hungary

**Introduction.** In chronic pancreatitis (CP), enlargement of the pancreatic head develops as a result of inflammatory alterations. An organ-preserving pancreatic head resection (OPHR) technique has been developed, and this report is concerned with the results attained with this operation in a 7-year period.

**Patients and Methods.** In 135 patients (m: 103, f: 32; mean age: 49.5 yr.), an organ-preserving procedure was performed. The preoperative morbidity comprised frequent abdominal pain, a weight loss in all patients, jaundice in 10 patients, and latent and insulin-dependent diabetes mellitus (IDDM) in 16 and 21 patients, respectively. The surgical procedure consists in 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 10 icteric cases and in 15 patients with stenosis of the common bile duct, prepapillary

bile duct anastomosis was also performed with the jejunal loop. The quality of life was measured during the follow-up using our simplified ESPAC Quality-of-Life Questionnaire (QoL).

**Results.** Only one reoperation was required in consequence of anastomosis bleeding, but no mortality was noted in the postoperative period. The duration of hospitalisation ranged between 7 and 12 days. The mean follow-up period was 4.1 years (range 0.5 to 7.0). The late mortality rate was 3.7% (4 and 1 patients died after a cardiovascular attack and accident, respectively). The QoL improved in 88% of the patients. 116 patients became complaint-free, 14 patients had moderate symptoms and the weight increased by a median of 11.3 kg (range 4–28). One or two years after the operation, bilio-digestive anastomosis was performed in 5 patients because of bile duct stenosis. No change was noted in the preoperative endocrine function of 125 patients, but 10 patients with latent diabetes mellitus acquired IDDM.

**Conclusion.** The 7-year experience clearly reveals that this OPHR technique is a safe and effective procedure for definitive control of the complications following the inflammatory alterations of CP and should be regarded as a recommended procedure in the treatment of CP.

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### SURGICAL TREATMENT OF ALCOHOL-INDUCED CHRONIC PANCREATITIS: THE CHALLENGES AND PITFALLS

Thomas Schnelldorfer, MD, David B. Adams, MD  
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**Introduction.** Long-term excessive alcohol consumption is the most common risk factor for development of chronic pancreatitis. Management of patients with alcohol-induced chronic pancreatitis can differ because of problems associated with dependency, psychosocial burden, and physical changes like malnutrition and hepatic insufficiency.

**Methods.** The records of 171 consecutive patients who underwent lateral pancreaticojejunostomy (LPJ,  $n=102$ ), pancreaticoduodenectomy (PD,  $n=38$ ), or distal pancreatectomy (DP,  $n=31$ ) for alcohol-induced chronic pancreatitis between 1995 and 2003 were retrospectively reviewed and analyzed. Long-term outcome was assessed by patient survey with a median follow-up of  $5.8 \pm 0.3$  years.

**Results.** According to patient questioning, the prevalence of alcohol cessation prior to operation was 81%. Co-existing addictions were found frequently with 78% of patients admitting to tobacco use and 61% of patients using narcotic analgesics on a regular basis. Forty-one percent of patients were at least moderately or severely malnourished and 2% had hepatic insufficiency due to alcohol abuse. Peri-operative morbidity was 20%, 50%, and 26% after LPJ, PD, and DP respectively with an overall peri-operative mortality rate of 2%. Average hospital length of stay was  $9 \pm 1.3$  days. During hospital stay, patients were treated for early symptoms of alcohol withdrawal using a standardized protocol. None of the patients developed delirium tremens. The presence of continued alcohol abuse prior to operation did not affect peri-operative morbidity ( $p > 0.05$ ). Follow-up was available for 95 patients, out of which 37 patients (39%) had died. Out of the remaining 58 patients, 13 (22%) were pain free, 13 (22%) had good pain control, and 32 (55%) had poor pain control. The median weight loss was  $2 \pm 2.5$  kg. Alcohol cessation occurred in 91% of patients by the time of follow-up, while relapse of alcohol use was found in 3% of patients. Continuation of alcohol abuse after operative intervention did not affect success for pain control at follow-up ( $p > 0.05$ ).

**Conclusion.** Surgical treatment of alcohol-induced chronic pancreatitis can be performed with similar morbidity and mortality compared to other forms of chronic pancreatitis. Alcohol cessation is preferred but not mandated in order to achieve good operative long-term outcome. Caution needs to be taken to prevent postoperative alcohol withdrawal. Long-term follow-up with psychosocial support and management of co-existing addictions is important.

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### PREDICTIVE RISK FACTORS FOR DEVELOPMENT OF PANCREATIC FISTULA UTILIZING THE ISGPF CLASSIFICATION SCHEME

Wande Pratt, Mark Callery, MD, Charles Vollmer, MD  
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**Background.** The ISGPF classification scheme has become a useful system for characterizing the clinical impact of pancreatic fistulae. However, it is unclear what factors predispose patients to clinically relevant fistulae, and whether these features are equivalent between proximal and distal resections. We sought to identify predictive factors for pancreatic fistulae, and to describe the clinical and economic significance of risk stratification within this framework.

**Methods.** 287 consecutive pancreatic resections occurred from 10/01 to 9/06 – 209 pancreatoduodenectomies (PD) and 78 distal pancreatectomies (DP). Pancreatic fistula is defined as either biochemical (amylase-rich effluent on or after POD 3) or clinically relevant (therapeutic intervention required) according to ISGPF criteria. Logistic regression analysis was performed to identify risk factors for pancreatic fistula development. These features were compared across resection types, and then analyzed to determine whether additive risk equates to worsening clinical and economic impact.

**Results.** Overall, pancreatic fistula occurred in 86 patients; yet only 42 (14%) were clinically relevant. There are *no* identifiable risk factors for biochemical fistulas. For PD, univariate analysis shows that age, diabetes, and patient acuity (POSSUM) are associated with clinically relevant fistulae, as are those factors that are also significant by multivariate analysis – small pancreatic duct size (<3 mm); soft gland texture; ampullary, duodenal, cystic, or islet cell pathology; and operative blood loss >500 ml. An additive effect is illustrated using these 4 parameters (risk profile) in which clinical and economic outcomes progressively worsen as the number of risk factors increases (Table). For DP, increased body mass index is the only significant variable; overweight patients (>25 kg/m<sup>2</sup>) develop fistulae twice as often (48% vs. 24% *p* = .028).

**Conclusion.** For PD, small duct, soft gland texture, ampullary, duodenal, cystic, or islet cell pathology, and increased operative blood loss are convincing risk factors for developing clinically relevant fistulae as judged by ISGPF classification. As risk profile accrues, patients suffer more severe clinical and economic outcomes. However, predictive factors for proximal and distal pancreatic resections differ, further demonstrating the inherent differences in these operations.

**Methods.** A retrospective cohort study was performed with 64 patients undergoing pancreas resection. Bioglu sealant was applied to the pancreatic anastomosis (Whipple) or resection margin (distal pancreatectomy) in 32 cases. Factors that could affect the rate of postoperative pancreatic fistula were recorded. Pancreatic fistula was defined as >50 cc of drain output with amylase content >3 times normal serum value after postoperative day 10. To improve the sensitivity of our study, we also examined pancreatic fistula with a strict definition of any drain output on or after postoperative day 3 with a high amylase content and graded the fistulas in terms of clinical severity. Grade A leaks were defined as subclinical. Grade B leaks required some response such as making the patient N.P.O., T.P.N., octreotide, antibiotics, or a prolonged hospital stay. Grade C leaks were defined as serious and life threatening. They were associated with hemorrhage, sepsis, resulted in deterioration of other organ systems and mandated intensive care. Comparisons between the 2 groups were made using the chi-square test or Fisher's exact test for categorical variables and by the Wilcoxon rank-sum test for continuous variables. P-values of 0.05 or less were deemed statistically significant.

**Results.** There were no differences between the patients who received Bioglu and the control cohort in terms of comorbid conditions, tumor

Clinical and Economic Impact of Risk Factors for Pancreatic Fistula in Pancreaticoduodenectomy

Risk Profile (# Risk Factors) <sup>†</sup>	None N=33	1 Risk Factor N=75	2 Risk Factors N=68	3 Risk Factors N=24	4 Risk Factors N=9	p-value
Pancreatic Fistula (%)						
Overall	6 (18)	13 (17)	25 (37)	12 (50)	4 (44)	.004
Biochemical (Grade A)	5 (15)	7 (9)	12 (18)	3 (13)	1 (11)	.692
Clinically Relevant (Grade B/C)	1 (3)	6 (8)	13 (19)	9 (37)	3 (33)	<.001
Non-fistula Complications (%)	13 (39)	36 (48)	32 (47)	15 (63)	6 (67)	.382
LOS (mean, days)	8.6	9.7	11.3	12.1	15.3	.007
Hospital Costs (mean)	\$20,429	\$23,093	\$27,166	\$30,882	\$39,137	.161

<sup>†</sup> Risk factors: (a) small pancreatic duct <3 mm; (b) soft gland texture; (c) ampullary, duodenal, cystic, or islet cell pathology; (d) intraoperative blood loss >500 ml.

## 111 PANCREATIC LEAK RATES AFTER DISTAL PANCREATECTOMY USING THE INTERNATIONAL GRADING SYSTEM (ISGPF)

Thien Khai Nguyen, MD, L. William Traverso, MD  
Virginia Mason Medical Center, Seattle, WA

**Objective.** To assess usefulness of the ISGPF and calculate the leak and clinical severity rates after distal pancreatectomy.

**Method.** From May 1998 to February 2006, 125 distal pancreatectomies (DP) were performed by one surgeon. One surgical drain was used, the duct was ligated, and the stump was fish-mouthed. Cases were divided into 4 groups – No leak, Grade A (chemical leak only, drain amylase >3x upper limit of normal serum, ≥postoperative day 3), Grade B (leak that alters postoperative management, i.e. percutaneous drainage, prolonged drain use, prolonged length of stay, readmission), and Grade C (severe clinical sequelae, i.e. sepsis, ICU, reoperation). We compared the predictability of ISGPF chemical leak to the Sarr definition (J Am Coll Surg 2003;196:556–565, drain amylase >5x upper limit of normal serum, >30 ml/day, ≥postoperative day 5).

**Results.** The overall ISGPF leak rate was 36% (45/125) – Grade A = 26%, B = 8%, C = 2.4%. The ISGPF system missed 2 patients without chemical leak but were readmitted for symptoms of peripancreatic fluid collections. The chemical leak criteria had a positive predictive value (PPV) of 23%, negative predictive value (NPV) 95%, Accuracy 57%. Using the Sarr definition, PPV was 100%, NPV 89%, Accuracy 90%.

**Conclusion.** The clinical course after distal pancreatectomy in our patients was altered in 10% due to pancreatic leak. The NPV using either definition was similar but the Sarr definition was more accurate, and hence, more useful at predicting clinical outcomes after distal pancreatectomy.

## 112 EFFECT OF BIOGLUE ON THE INCIDENCE OF PANCREATIC FISTULA FOLLOWING PANCREAS RESECTION

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**Background.** Despite numerous modifications of surgical technique, pancreatic fistula remains a serious problem and occurs in about 10% of patients following pancreas resection. Bioglu is a new sealant that creates a flexible mechanical seal within minutes independent of the body's clotting mechanism.

**Hypothesis.** Application of Bioglu sealant will reduce the incidence of pancreatic fistula following pancreas resection.

location and stage, texture of the pancreas, size of the pancreatic duct, or surgical technique. By the common definition, pancreatic fistula occurred in 19.0% (Bioglu) vs. 10.7% (Control). By the strict definition, a subclinical leak (Grade A) occurred in 37.5% (Bioglu) vs. 50% (Control), and a clinical leak (Grade B) occurred in 25.0% (Bioglu) vs. 11.5% (Control). There were no severe (Grade C) leaks. There were no statistically significant differences in the incidence or severity grades of postoperative pancreatic fistulas between the two groups. Patients who did experience a pancreatic fistula were more likely to experience additional complications.

**Conclusion.** Application of Bioglu sealant does not reduce the incidence of pancreatic fistula following pancreas resection.

**Free Papers**  
**Biliary I**  
**FP-02**  
**4/21/07 8:00 to 9:55 am**  
**Abstract Numbers 113–120**

## 113 PANCREATICOBILIARY MALJUNCTION WITH NON-DILATED BILE DUCT IS AN EXTREME HIGH RISK GROUP OF BILIARY TRACT CANCERS: ANALYSIS OF A NATION WIDE REGISTRY OF PANCREATICO-BILIARY MALJUNCTION IN JAPAN

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Japanese Study group on Pancreaticobiliary Maljunction, The University of Tokushima, Tokushima, Japan; Committee for Registration of the Japanese Study group on Pancreaticobiliary Maljunction, Tokushima, Japan

**Introduction.** Pancreaticobiliary maljunction (PBM) is a congenital anomaly which can be defined as a union of the pancreatic and biliary ducts that is located outside off the duodenal wall. Pancreatic juice regurgitates in the biliary tract continuously, and this eventually causes the cancer to occur in the biliary mucosa. Regarding the PBM patients without bile duct (BD) dilatation, it remains controversial whether or not BD should be removed in the treatment. We herein investigate characteristics of PBM with non-dilated BD focusing on coexistence of biliary tract cancers.

**Patients and Methods.** During 15 years (from January 1, 1990 to December 31, 2004), a nationwide survey was conducted and 2,237 patients were registered as patients with PBM at 141 medical institutions in Japan. Among them eligible patients (n=2,222) were divided into two groups according to bile duct (BD) dilatation (Dilated BD group: n=1712; Non-dilated BD group: n=510). Comparison of clinical variables, especially coexistence of biliary tract cancers was performed between the two groups.

**Results.** (Tables 1 and 2): Characterisitits of PBM patients with non-dilated CBD are as follows: adult dominant, male dominant, PBM type B dominant, and higher incidence of biliary tract cancers than those with dilated CBD (non-dilated CBD 39% vs dilated CBD 11.3%). Incidence of biliary tract cancers in patients with PBM is extreme high, when compared with epidemiologic prevalence of biliary tract cancers in Japan (around 0.002%). Analysis according to time period showed increased incidence of bile duct cancer instead of gallbladder cancer.

**Conclusions.** PBM is an extreme high-risk group of biliary tract cancers. Furthermore, PBM patients with non-dilated CBD has a higher risk than those with dilated BD, and has increasing tendency of bile duct cancer. Surgeons, therefore, should take it into account to perform not only cholecystectomy but also resect extrahepatic BD with hepatico-jejunostomy.

Table 1. Comparison of clinical variables in PBM (Non-dilated BD vs. Dilated BD)

Variables	Dilated BD (n = 1712)	Non-dilated BD (n = 510)	p-value
Child : Adult	812:891	56:453	p < 0.001
Male : Female	436:1575	143:375	p < 0.005
PBM type			
A : B : C	981:551:97	153:299:30	p < 0.001
Biliary tract cancer			
Total	194 (11.3%)	199(39.0%)	
GB	123 (7.2%)	167(32.7%)	p < 0.001
BD	62 (3.6%)	23 (4.5%)	
GB + BD	9 (0.5%)	9 (1.8%)	

Pancreaticobiliary maljunction (PBM): n = 2237 (data unknown: n = 15).

GB: gallbladder, BD: bile duct.

BD dilation was defined as diameter of more than 10 mm.

PBM type: according to Ohi's classification.

Table 2. Comparison according to time period

Biliary tract cancers	Dilated BD		Non-dilated BD	
	1990 ~ 97 (n = 1025)	98 ~ 2004 (n = 687)	1990 ~ 97 (n = 310)	98 ~ 2004 (n = 200)
Total	101 (9.8%)	93 (13.5%)	117 (37.7%)	82 (41.0%)
GB	70 (6.8%)	53 (7.7%)	104 (33.5%)	63 (31.5%)
BD	30 (2.9%)	32 (4.6%)	8 (2.6%)*	15 (7.5%)*
GB + BD	1 (0.1%)	8 (1.2%)	5 (1.6%)	4 (2.0%)

\*: p < 0.01.

Prevalence in Japan : GB cancer and BD cancer Male 11.5/100,000 (0.0115%) Female 13.2/100,000 (0.0132%).

## 114

### LOSS OF FHIT EXPRESSION IN PANCREATOBILIARY CANCERS

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**Background.** Chromosome 3p is one of the most commonly deleted chromosomal regions in human tumors. The *Fragile Histidine Triad Gene (FHIT)* is a tumor suppressor gene which encompasses the *FRA3B* fragile site. Genomic alterations at the *FHIT* locus have been described in several solid tumors, including pancreatic cancer. Little is known, however, regarding *FHIT* loss in other pancreaticobiliary cancers. We sought to determine *FHIT* expression patterns in cancers of the pancreas, ampulla of Vater, and gall bladder and to investigate whether loss of *FHIT* correlates with tumor characteristics or survival.

**Methods.** Tissue microarrays (TMAs) were created in duplicate from formalin fixed paraffin-embedded resected specimens retrieved from archival files for pancreatic cancer (N = 98), gall bladder cancer (N = 23), ampullary cancer (N = 49), normal pancreas (N = 11), chronic pancreatitis (N = 35), and benign gall bladder (N = 15). Immunohistochemistry for *FHIT* was undertaken on all TMAs and compared between malignant and benign tissue. Staining of at least 5% of cells was considered positive. *FHIT* expression was correlated with tumor grade, nodal status, and stage as well as survival.

**Results.** *FHIT* was expressed in all normal pancreas and gall bladder cases and in 97% of chronic pancreatitis cases. *FHIT* expression was significantly reduced in pancreatic cancers (49%) and ampullary cancers (20%) relative to normal pancreas and chronic pancreatitis (p < 0.00001, Fisher's exact test). Similarly, *FHIT* expression was decreased in gall bladder cancers compared to benign gall bladders (57% vs. 100%, p = 0.003). *FHIT* expression was significantly lower in ampullary cancer compared to pancreatic cancer (20% vs. 49%, p = 0.02) and gall bladder cancer (20% vs. 57%, p = 0.007) and was

similar between pancreatic cancer and gall bladder cancer (p = 0.64). *FHIT* expression did not correlate with the tumor characteristics measured nor was it predictive of survival.

**Conclusions.** *FHIT* expression does not predict tumor progression and subsequent patient survival. Loss of *FHIT* expression, however, appears to be important in the pathogenesis of cancers of the gall bladder, pancreas, and ampulla, supporting its role as a tumor suppressor in pancreaticobiliary malignancies.

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### THE ROLE OF THYMIDYLATE SYNTHASE (TS) AND DIHYDRO-PYRIMIDINE DEHYDROGENASE (DPD) EXPRESSION IN BILIARY TRACT CARCINOMA

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**Introduction.** Thymidylate synthase (TS) and dihydropyrimidine dehydrogenase (DPD) are important enzymes to metabolize 5-fluorouracil and have been indicated as possible predictive markers for epithelial malignancies. However no reports have examined the expression of these enzymes in biliary tract carcinoma. This study was conducted to clarify a role of TS and DPD gene expressions and a prognostic factor for biliary tract carcinomas according to TS and DPD gene expressions.

**Patients and Methods.** Twenty-eight patients with intrahepatic cholangiocarcinoma (IHCC) and forty-four patients with gallbladder carcinoma (GBC) who underwent surgical resection were included in this study. Intratumoral DPD mRNA expressions were examined by using the Danenberg tumor profile method consisted of laser microdissection of tumor cells on FFPE specimens, RNA extraction and cDNA synthesis and quantification of mRNA expression by real-time PCR. The expression of TS and DPD was classified into 2 groups according to median values: high and low groups, individually. The impact of gene expression was evaluated and significant prognostic factors were determined using the clinicopathological variables including TS and DPD mRNA expression.

**Results.** Median values of TS and DPD were 1.15 and 0.88 in IHCC, 2.28 and 1.44 in GBC, individually. In IHCC, DPD expression was higher than median values of all gastrointestinal malignancies (total number: 1977 cases) reported from TAIHO pharmaceutical co., LTD. (TS: 1.99, DPD: 0.67). Furthermore, in GBC, TS and DPD expression were higher than ita<sup>TM</sup>s values. In the correlation to clinicopathological variables, difference of macroscopic type was observed between high and low DPD expression groups in IHCC, while no correlation was observed between both genes expression (high and low groups) and any clinicopathological variables in GBC. Postoperative survival rate in low DPD expression group was significantly lower than that in high DPD expression group in IHCC. However, in GBC, there was no significant difference according to expression of both genes in postoperative survival rate.

**Conclusion.** In biliary tract carcinoma, the tolerance of 5-FU based chemotherapy seems to be occurred by high expression of TS and DPD. Furthermore, DPD mRNA expression in tumor cells is suggested to be a new prognostic indicator in IHCC.

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### INTRAHEPATIC CHOLANGIOCARCINOMAS: TREATMENT CHARACTERISTICS AND RESULTS

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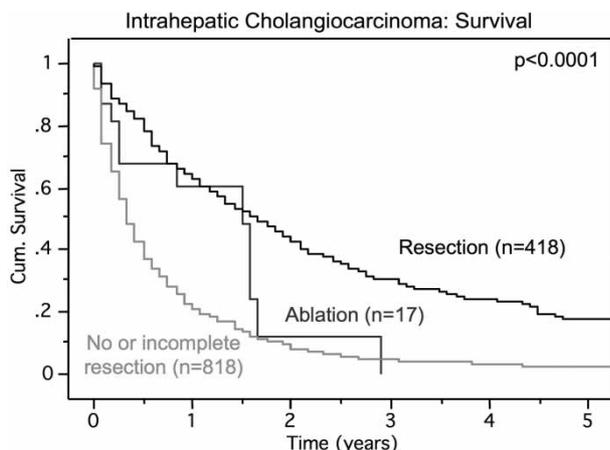
**Background.** Intrahepatic cholangiocarcinoma (ICC) frequently poses challenges to proper diagnosis and treatment. We investigated prognostic information and survival outcomes for ICC in U.S. patients.

**Methods.** A clinical ICC dataset was created from the SEER 1970–2003 database. Prognostic factors with survival impact, and relationships between treatment modality and overall survival (OS) were analyzed.

**Results.** A total of 5397 patients classified with an ICC diagnosis were identified. The median age was 72 (range: 19–102), and 52% of patients were male. The median primary tumor size was 5.0 cm (0.4–30). The disease extent included single lesions (29%), multiple intrahepatic lesions (15%), and extrahepatic metastatic disease (56%). Two multivariate survival analyses were conducted, based on the status of clinicopathologic information. In the first model including all patients, treatment modality, stage, grade, age, marital status (all at p < 0.0001), vascular invasion (p = 0.0004), total LN count (p = 0.0006), radiation (p = 0.0012), race (p = 0.0013), and gender (p = 0.03) were prognostic variables. In the second model based only on individuals with complete pathologic information, disease extent, LN involvement, age, and local therapy mode remained significant (all at p < 0.0001). Median survival after resection (20 m) exceeded that after ablation (18) and no or incomplete local treatment (4, p < 0.0001). Long-term survival, while not evaluable after ablation, was only observed after resection (see graph). Interestingly, the number of negative LNs examined had significant survival implications, both for N0 (p < 0.0001) and N+ stage categories (p = 0.03). Cancer as cause of death differed between anatomic

resection (62%), ablation (53%), segmental/wedge resection (75%), incomplete resection (92%), and no resection (90%,  $p < 0.0001$ ).

**Conclusions.** Despite some limitations within the dataset, the importance of complete local treatment is obvious. Aside from disease extent and stage, the local treatment mode strongly influences ICC survival. Although the data do not allow for a specific comparison to transplantation or ablation, complete anatomic resection of localized disease appears to be linked to best long-term survival results.



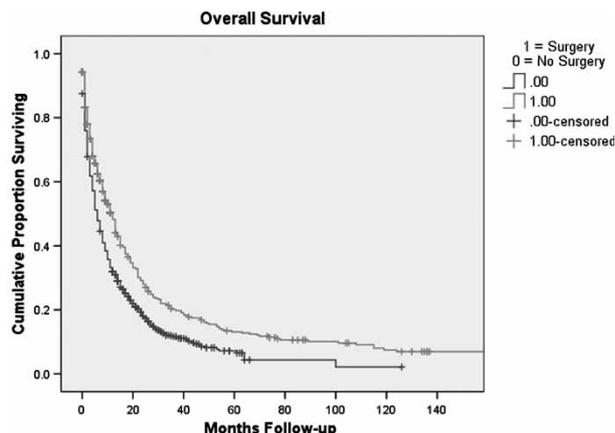
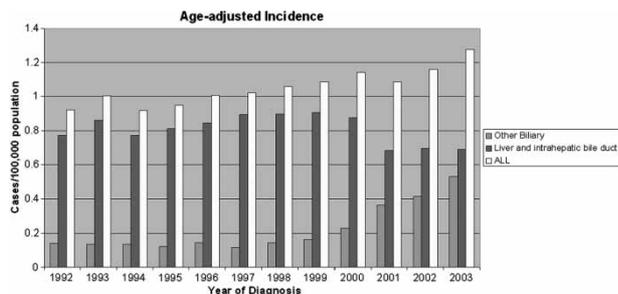
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**EVOLVING INCIDENCE AND OUTCOMES FOR CHOLANGIOCARCINOMA IN THE U.S.: ANALYSIS OF 7,410 CASES**

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**Purpose.** Analyze the changes in incidence, treatment patterns, and outcomes in patients with cholangiocarcinoma (CCA).

**Methods.** Analysis of all CCA reports in the SEER registry from 1973–2003.

**Results.** Overall, 7410 cases of CCA were identified. The age-adjusted incidence of CCA increased in from 0.92/100,000 in 1992 to 1.27/100,000 in 2003. Incidence of extra-hepatic biliary CCA increased significantly from 1992 to 2003 (0.14 v. 0.53/100,000, APC 16%), while for liver and intra-hepatic CCA it did not (0.77 v. 0.69/100,000, APC -1.2%). Median age at



diagnosis was 70, with a slight male predominance (53%). Ethnic distribution was 68% Caucasian, 12% Hispanic, 7% Black, and 13% Asian/Native American. There were 5220 (70%) intra-hepatic tumors, 2190 (30%) extra-hepatic tumors, and 10% were Klatskin tumors. Histologically, 18% were well-differentiated, 39% moderately-differentiated, 40% poorly differentiated, 3% anaplastic, and 5% were combined CCA and hepatocellular carcinoma. Regarding stage, 1480 (20%) patients presented with localized tumors, 1775 (24%) with regional, and 1959 (26%) with distant disease. Since 1997 statistically more patients have presented with local and regional as opposed to distant disease ( $p < 0.02$ ). In 2406 (32%) patients surgery was a component of the treatment, and in 1189 (16%) radiation was used. Mean survival was 13 months with 24%, 12%, and 4%, 1, 2, and 5-year survival, respectively. Patients with localized tumors doubled their mean (16 v. 35 months) and median (6 v. 12 months,  $p < .0001$ ) survival with surgery.

**Conclusions.** The overall incidence and incidence of extra-hepatic CCA has increased in the United States. Contrary to analysis of previous years, the incidence of intra-hepatic and liver CCA has not increased. While there has been little improvement in overall survival, detection while still localized with prompt surgical intervention remains the best chance for cure.

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**GERMLINE APC AND MYH MUTATIONS DO NOT ACCOUNT FOR A SIGNIFICANT FRACTION OF SPORADIC AMPULLARY CANCER**

George Zogopoulos, MD, PhD, Zane Gallinger, Robin Kim, MD, Ian D. Mcgilvray, MD, PhD, Alice Wei, MD, Bryce Taylor, MD, Bernard Langer, MD, Paul Greig, MD, Richard Hart, MD, Runjan Runjan Chetty, MD, Steven Gallinger, MD  
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Adenocarcinoma of the ampulla of Vater is uncommon in the general population and usually presents after the fifth decade of life. However, in patients with familial adenomatous polyposis (FAP) or MYH Associated Polyposis (MAP), ampullary neoplasia presents earlier and is a major cause of morbidity and mortality. Both FAP and MAP are caused by germline mutations of tumor suppressor genes, dominantly inherited mutations of APC in the case of FAP, whereas biallelic recessively inherited MYH mutations cause MAP. Since individuals with FAP and MAP are at increased risk for periampullary and ampullary cancer, and since variable expression of these syndromes is well known, we hypothesized that a fraction of apparently sporadic ampullary cancer patients may have germline APC or MYH mutations as a predisposing cause of their malignancy. A retrospective review of pathology department databases and hepatobiliary/pancreatic surgeon practices at the University of Toronto identified 61 cases, treated between August 1994 and August 2005, with a diagnosis of ampullary adenoma or ampullary cancer. A death clearance was performed by the Ontario Cancer Registry, and with the approval of the treating surgeon, living subjects were approached by mail for participation in this study. Screening for germ-line APC and MYH mutations was performed using the protein truncation test and denaturing high performance liquid chromatography analysis, respectively. We did not identify truncating germline APC mutations or pathogenic biallelic MYH mutations in the 33 subjects tested. One subject was found to have a monoallelic G382R MYH mutation, although this unlikely contributed to her ampullary cancer, since heterozygous MYH mutations do not seem to be a strong predisposing factor to colorectal or periampullary neoplasia. These data suggest that germline APC and MYH mutations are likely not causative in sporadic ampullary cancer.

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**ESTROGEN RECEPTOR  $\alpha$ , ESTROGEN RECEPTOR  $\beta$  AND PROGESTERON RECEPTOR AS A POSSIBLE PROGNOSTIC FACTOR IN RADICALLY RESECTED PRIMARY GALLBLADDER CARCINOMA**

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Yonsei University Medical College, Seoul, Republic of Korea

**Background.** Gallbladder carcinoma is a relatively rare malignancy with an extremely poor prognosis. The pathologic staging of gallbladder carcinoma is a key determinant of the patient's prognosis and the treatment options. However, we have often encountered patients in whom the course of their disease differed substantially from what would be predicted based on their clinical staging, which highlights the needs to consider additional predictive factors. Gallbladder carcinoma occurs more frequently in women than men, yet expression of the estrogen receptor (ER) family and progesterone (PR) have not been studied. We applied an immunohistochemical technique to examine the expression of ER $\alpha$ , ER $\beta$  and PR in radically resected gallbladder carcinoma tissues and then compared their expression status with several clinicopathological factors.

**Methods.** We immunohistochemically investigated 30 formalin-fixed, paraffin-embedded specimens of gallbladder adenocarcinoma tissues using ER $\alpha$ , ER $\beta$  and PR antibodies. The expression of ER $\alpha$ , ER $\beta$  and PR were compared using the Chi-square test. Survival was analyzed using the Kaplan-Meier method, verified by the Log-Rank test.

**Results.** The results indicated that adenocarcinoma of gallbladder are both negative for ER $\alpha$  and PR, irrespective of histologic grade, TNM stage and

sex. However, twenty-two of 30 cases (73.3%) were confirmed positive for ER $\beta$ , which was significantly correlated with poor differentiated tumor grade. Overall survival rates of ER $\beta$ -positive and negative patients were 77.3% and 37.5%, respectively ( $p=0.034$ ). In multivariate analysis, only ER $\beta$  was statistically significant ( $p=0.033$ ).

**Conclusions.** Evaluation of ER $\beta$  expression in gallbladder carcinoma may be an important factor in identifying a poor prognostic group of gallbladder carcinoma.

**Key Words.** gallbladder, carcinoma, estrogen receptor( $\alpha$ ), estrogen receptor( $\beta$ ), progesterone receptor.

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### LONG TERM FOLLOW-UP OF MEXICAN PATIENTS WITH GALLBLADDER CANCER

Ricardo Joaquin Mondragón-sánchez 80, MD, PhD, Elvira Gómez-gómez 2003, MD, Alicia Ivette López-estrada 2006, Ofelia Arias-arias 2005, Rodrigo Jasso-barranco 2006, MD, Brenda Elena Aguilar-álvarez 5006, MD Issemym, Toluca, Mexico

**Background.** Gallbladder carcinoma (GC) is a rare neoplasm with a poor prognosis because of its rapidly tumor growth and early dissemination. At the time of diagnosis, only 10% of these tumors are candidates for resection.

**Aim.** To analyze epidemiological and prognostic factors in Mexican patients with GC.

**Patients and Methods.** A retrospective review of the clinical files of patients with gallbladder carcinoma diagnosed and treated in two hospitals in Mexico between January 1987 and November 2005 was performed. Epidemiologic data, clinical presentation, forms of diagnosis and treatment were analyzed. Actuarial survival of these patients was also performed.

**Results.** 170 patients with diagnosis of gallbladder carcinoma were registered in this period in both institutions. 149 (87%) patients were women and 21 (12%) were men. The median age at the time of diagnosis was 56 years (range 19 to 86 years). The most common symptoms were abdominal pain in 161 patients (94%), weight loss in 51 (30%), palpable mass in 44 (25%), jaundice in 44 (25%), nausea and vomiting in 17 (10%). 78 patients had abdominal CT Scan, and 48 (28%) had ultrasound. Seven patients (4%) were diagnosed at stage I, 19 (11%) Stage II, 31 (18%) Stage III, 13 A (7%) stage III B, 78 (45%) stage IV and 22 (12%) patients were not classified. 110 (64%) were operated, of whom 17 (10%) had a palliative intent, 30 (17%) radical cholecystectomy and lymphadenectomy, 22 (12%) biopsies of the lesion only and the rest 40 (23%) were treated with simple cholecystectomy and 1 (5%) had a radical cholecystectomy, lymphadenectomy and Whipple procedure. 37 (21%) patients received adjuvant radiotherapy, 10 (6%) patients received chemotherapy alone, 9 (5%) received chemotherapy plus radiotherapy. The most common histology type was Adenocarcinoma in 119 (70%) patients. Global survival was 15.1 months (range from 6 days to 117 months). For the patients in stage I the mean survival was 50.3 months (range from 1 to 99 months), 33.2 months for stage II (range 3 months to 129 months), 21.5 months for stage IIIA (range 1 to 117 months), 5.3 months for stage IIIB (range 6 days to 24 months), 3.8 months for stage IV (range 15 days to 30 months) and 17.3 months (range 1 to 88 months) for those patients that were not classified. Patients that were treated were radical resection had the best survival.

**Conclusions.** Gallbladder cancer is a rare neoplasm with a poor prognosis. Radical resection is the better option for patients with stage II and III of the disease. For more advanced stages none of the treatments used in this study modified the natural history of the disease.

## Free Papers

### Pancreas Malignant

FP-03

4/21/07 8:00 to 9:55 am

Abstract Numbers 121–128

## 121

### DIAGNOSTIC LAPAROSCOPY FOR PATIENTS WITH POTENTIALLY RESECTABLE PANCREATIC ADENOCARCINOMA: IS IT COST EFFECTIVE IN THE CURRENT ERA?

C. Kristian Enestvedt, MD, Skye C Mayo, MD, MPH, Brian Diggs, PhD, Tomi Mori, PhD, Donald Austin, MD, MPH, Donald K Shipley, MS, Brett Sheppard, MD, Kevin G Billingsley, MD  
Oregon Health and Science University, Portland, OR; Johns Hopkins Hospital, Baltimore, MD; Oregon State Cancer Registry, Portland, OR

**Introduction.** Diagnostic laparoscopy (DL) identifies small-volume liver and peritoneal disease in a subset of patients with potentially resectable pancreatic cancer (PAC), sparing them a nonresectional laparotomy. The aim of this study is to retrospectively assess the cost effectiveness of laparoscopy using population-based data.

**Methods.** Data from a state cancer registry was linked with primary medical record data for years 1996–2003, identifying surgically treated patients with PAC using ICD-9 diagnosis and CPT procedural codes. Operative notes and pathology reports were reviewed to determine the role and findings of laparoscopic exploration. Average hospital and physician charges for laparotomy, biliary bypass, pancreaticoduodenectomy, and DL were determined by review of billing data from our institution and Medicare data for fiscal-

years 2005–6. The cost of DL as an adjunct procedure was based on physician fees, cost per minute of operative time, and equipment charges. Cost effectiveness was determined by comparing three methods of utilization of DL: 1) in all patients, 2) selectively, and 3) no utilization.

**Results.** During this study period surgeons used laparoscopy selectively in a subset of patients with PAC. Of 298 patients, 86 underwent laparoscopy. Periampullary tumors were present in 238 patients (79.9%). The prevalence of unresectable disease was 14.1% diagnosed at either laparotomy or DL. Metastatic disease or vascular invasion precluded resection. Cost analysis revealed similar average cost per patient in each of the groups. Selective use proved to be the least expensive, with \$1058 and \$2247 saved per patient versus incorporating DL with all or none of the patients, respectively. The per patient cost based on DRG coding, physician fees, and the addition of DL is shown for each method in the accompanying table.

**Discussion.** The use of DL is not cost-prohibitive. In fact, we found that selective or routine use of DL in pancreatic cancer was effectively cost neutral when compared to non-utilization of DL. These data support the liberal use of DL in potentially resectable PAC in patients for whom there is a high index of suspicion for metastatic disease.

### Average cost per patient for three methods of applying diagnostic laparoscopy

Approach to DL	Mean Cost Per Patient (\$)
All Patients	94,505
Selective	93,447
Not Used	95,694

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### HOW USEFUL ARE CLINICAL, BIOCHEMICAL AND CROSS-SECTIONAL IMAGING FEATURES IN PREDICTING PREMALIGNANT OR MALIGNANT CYSTIC LESIONS OF THE PANCREAS?

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**Introduction.** Presently, the management of cystic lesions of the pancreas (CLP) remains controversial as the natural history of pancreatic cystic neoplasms is not fully understood and the preoperative characterization of CLP is unreliable and often impossible. The aim of the present study is to determine if preoperative clinical, biochemical and cross-sectional imaging features are useful in predicting a potentially malignant or malignant CLP.

**Methods.** Between 1990 and 2006, 153 consecutive patients underwent surgical treatment for a suspected pancreatic cystic neoplasm at a single institution. The patients' clinical, radiology and pathology reports were reviewed retrospectively. The predictive effect of clinical, biochemical and radiologic factors on the malignant potential of a CLP was evaluated with both univariate and multivariate analysis.

**Results.** The median age of the patients was 52 years (range, 14–82 years) and there were 101 females. 60 patients had CLP discovered incidentally of which 63 were benign, 46 potentially malignant and 44 malignant lesions. The presence of symptoms, elevation of serum carcinoembryonic antigen (CEA) or carbohydrate antigen 19–9 levels (CA 19–9), cyst size >3 cm and presence of 1 or more of 3 morphologic features on cross-sectional imaging such as solid component, peripheral calcification and dilatation of the main pancreatic duct were predictors of a potentially malignant or malignant CLP on univariate analysis. On multivariate analysis, elevation of serum CEA or CA 19–9, cyst size >3 cm and the presence of 1 or more of the 3 morphologic features on cross-sectional imaging were independent predictors. The logistic regression model had a sensitivity, specificity, positive predictive value and negative predictive value of 82%, 75%, 82% and 75% in predicting a potentially malignant or malignant CLP.

**Conclusion.** Elevation of serum CEA or CA 19–9, cyst size >3 cm and the presence of morphologic features on cross-sectional imaging such as solid component, peripheral calcification or main pancreatic duct dilatation are independent predictors of a potentially malignant or malignant CLP. Patients with a high likelihood of harboring a potentially malignant or malignant lesion based on this model should undergo resection without further investigations.

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### CHARACTERISTICS OF MALIGNANCY IN INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS

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**Objective.** To evaluate the clinical, radiographic, and pathologic features of resected intraductal papillary mucinous neoplasms (IPMN's) of the pancreas at a single institution.

**Methods.** All patients undergoing pancreatic resection for IPMN between January 1998 and August 2006 were evaluated. Charts were retrospectively

reviewed using a set of prospectively defined criteria. Imaging studies (CT and MRI) were independently, retrospectively reviewed by two blinded radiologists. Pathology slides were reviewed by a single pathologist. IPMN's were categorized pathologically as Benign (Adenoma or Borderline) or Malignant (Carcinoma In Situ or Invasive) and radiographically as Main Duct (MD), Side Branch (SB) or Combined (CB). Adverse radiographic features (mural nodules, papillary projections, or septations) were noted.

**Results.** Twenty-six pancreatic resections for IPMN were performed. The median age of patients with malignant and benign disease was 64.9 and 69 years, respectively ( $p=NS$ ). Demographics were similar in both groups. The presence of two or more symptoms (new/change in diabetes, jaundice, abdominal pain, weight loss, nausea/vomiting, acute pancreatitis, GI bleed) was significantly more common in the malignant group (71% vs 25%,  $p < 0.05$ ). Malignant lesions ( $n=14$ ) were significantly larger than benign lesions ( $n=12$ ) (10.87 vs. 3.21 cm,  $p < 0.05$ ), were more likely to contain adverse radiographic features (81.8% vs. 14.3%,  $p < 0.01$ ), and were associated with greater main pancreatic duct diameter (13.6 vs. 3.77 mm,  $p < 0.05$ ). Benign IPMN's were more likely to occur in the tail (71% vs 18%,  $p < 0.05$ ). All malignant MD/CB lesions were greater than 4.0 cm in size (only one tumor smaller than 11 cm) and had main duct diameters  $>6.5$  mm. All benign MD/CB lesions were smaller than 5 cm in size had main duct diameters  $< 5.5$  mm. Two of the malignant SB IPMN's in this series were less than 2.5 cm with main duct diameters less than 5 mm, but contained adverse radiographic features.

**Conclusions.** Some main duct IPMN's may not require resection and they may be distinguishable by lesion, main duct size, and adverse radiographic features. MRI detection of mural nodules or papillary projections is important in detecting malignant side branch IPMN's. Further evaluation of IPMN's is needed in order to optimize consensus recommendations for resection.

	Malignant (n = 14)	Benign (n = 12)	p-value
Mean Age	63.85 ( $\pm 9.77$ )	69 ( $\pm 9.5$ )	NS
Median Age	64.5	69	N/A
% Male	5 (35.7%)	5 (41.67%)	NS
Caucasian	13 (92.3%)	12 (100%)	NS
Smoking Hx	9 (64.3%)	8 (66.67%)	NS
Presence of symptom	12 (85.7%)	9 (75%)	NS
Presence of >1 symptom	10 (71.4%)	3 (25%)	0.0236
Hx of DM	4 (28.6%)	4 (33.3%)	NS
New/Change in DM	2 (14.3%)	1 (8.3%)	NS
Obs. Jaundice	2 (14.3%)	1 (8.3%)	NS
Abdominal Pain	10 (71.4%)	5 (41.67%)	NS
Wt. Loss	6 (42.9%)	4 (33.3%)	NS
Nausea/Vomiting	3 (21.4%)	1 (8.3%)	NS
Acute Pancreatitis	2 (14.3%)	2 (16.7%)	NS
GI Bleed	0 (0%)	0 (0%)	N/A
Fevers/Chills	0 (0%)	1 (8.3%)	NS
Extra pancreatic Malignancy	3 (21.4%)	2 (16.7%)	NS
Incidental Finding	4 (28.6%)	4 (33.3%)	NS
Size of Lesion (cm)	10.87 ( $\pm 6.59$ )	3.21 ( $\pm 1.92$ )	0.006
Main Duct Diameter (mean)	13.61 ( $\pm 8.97$ )	3.77 ( $\pm 1.68$ )	0.0118
Uncinate	27.30%	28.60%	NS
Tail	18.10%	71.40%	0.0387
Diffuse	45.50%	14.30%	NS
Pts w/ any adverse radiographic feature	81.80%	14.30%	0.009
Mural Nodules	63.60%	14.30%	NS
Papillary projections	18.2%	0%	NS
Septations	18.2%	0%	NS

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**PANCREATIC ADENOCARCINOMA: THE ACTUAL 5YR SURVIVORS**

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**Background.** Less than 15% of patients diagnosed with pancreatic adenocarcinoma will undergo resection. Most reports on patients undergoing resection report estimated (actuarial) 5-year survival rates. Actual five-year survival is rarely described, and factors associated with this long-term survival are not well known.

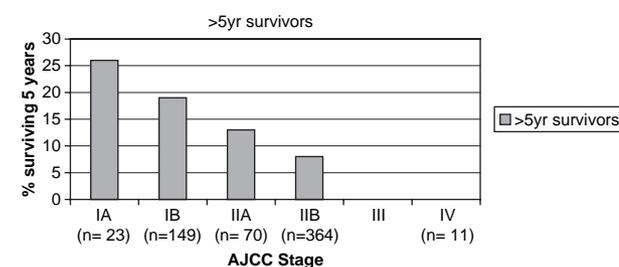
**Methods.** Review of a prospectively maintained database of patients undergoing resection for periampullary neoplasms identified 616 patients who underwent resection for pancreatic adenocarcinoma between 1/1983-1/2001. Patient, tumor, and treatment related variables were assessed for their

association with 5yr survival. This includes the 125 yr survivors previously reported by Conlon et al.

**Results.** There were 73 patients who survived  $>5$  yrs after resection (73/616, 12%), and 18 patients who survived  $>10$  yrs (18/352, 5%). Our actual survival may be lower than published actuarial survival since 6.5% (35/543) died of another cause and 2.9% (16/543) were lost to follow up. Patient age (median 67y vs 68y,  $p=0.8$ ), gender (female 56% vs 49%,  $p=0.4$ ), and tumor location (head 84% vs 85%,  $p=0.3$ ) were not different between those who survived 5 yrs and those who did not. Early AJCC stage (figure 1,  $p < 0.001$ ), and the presence of a negative margin ( $p=0.001$ ) were associated with 5yr survival. Within the sub-group of patients who survived 5 yrs ( $n=73$ ) median follow-up was 108 mos, with 43 patients (59%) developing disease recurrence and succumbing to their disease at the time of last follow-up. No factor (AJCC stage, margin status, tumor differentiation, perineural/perivascular invasion, or the use of adjuvant therapy) was found to predict death after the 5th post operative year. In the group of 5 yr survivors tumors were moderately differentiated in 58% (42/73), perineural invasion in 55% (40/73), lymphovascular invasion in 19%, positive margins in 9.6% (7/73), median size of 2.8 cm (0.8-13 cm), and adjuvant therapy was received by 22% (16/73).

**Conclusions.** In this group of patients with pancreatic adenocarcinoma actual 5and 10-year survival rates were 12% and 5%, respectively. Patients with Stage IA disease ( $<2$  cm, lymph node negative tumors) had an actual 5yr survival of 26%. Early detection and intervention for patients with pancreatic cancer is crucial.

**Figure 1.** Percent of patients who survived more than five years.



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**ADJUVANT CHEMOTHERAPY IS ASSOCIATED TO GOOD SURVIVAL IN PATIENTS UNDERWENT EXTENDED PANCREATICO-DUODENECTOMY FOR PANCREATIC CANCER**

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**Backgrounds.** In pancreatic cancer after surgery several types of adjuvant treatments have been proposed to improve survival. Aims: The present study aims to evaluate whether survival is increased in patients undergoing adjuvant chemotherapy (ADJCT) with respect to patients undergoing surgery alone. The rationale for this treatment is to combine local control of the disease, achieved by Extended Pancreaticoduodenectomy (EPD), with control of distant metastases, achieved by ADJCT.

**Patients and Methods.** From January 1994 to October 2005, 84 patients underwent EPD, 54 patients with ductal pancreatic carcinoma were included in this study. Twenty patients received ADJCT while 34 receive surgery alone. Fifteen of 20 patients received intra-arterial chemotherapy employing FLEC regimen (5-fluorouracil 750 mg  $\text{sqm}^{-1}$ , leucovorin 75 mg  $\text{sqm}^{-1}$ , epirubicin 45 mg  $\text{sqm}^{-1}$ , carboplatin 225 mg  $\text{sqm}^{-1}$  administered every three weeks in to coeliac axis for three cycles), in 7 cases followed by systemic gemcitabine (at the dosage of 1 g  $\text{sqm}^{-1}$  on days 1, 8, 15 every 4 weeks for three months); five of 20 patients received others type of adjuvant treatments.

**Results.** The two group were comparable for gender, age, grading, tumor size, stage, N status, R0 or R1 resection. Median follow up time was 17.5 months. The overall mean and median survival was 43 months and 18 months (range 4-144), respectively, with actuarial 1, 3 and 5-year survival rates of 77.8, 36.4 and 19.3%, respectively. ADJCT was well tolerated, with only one case of grade 3 nausea/vomiting, one patient had grade 3 anemia and leukopenia, and two patients had grade 3 thrombocytopenia. Significant difference in mean survival (50 vs 31 months,  $p < 0.05$ ) and actuarial 5-year survival rates (50 vs 10%,  $p < 0.05$ ) was seen in those who received ADJCT. ADJCT significantly influenced distant recurrence rate (60% vs 85%,  $p < 0.05$ ) but it did not reduced local recurrence rate (35% vs 35%,  $p=0.2$ ).

**Conclusions.** ADJCT is associated with long-term survival and decreased distant recurrence rates in patients with pancreatic cancers who have undergone EPD. Intra-arterial chemotherapy employing FLEC regimen combined with gemcitabine seem to be the better adjuvant therapy after surgery.

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### NEOADJUVANT CHEMOTHERAPY AND RADIATION FOR PATIENTS WITH LOCALLY UNRESECTABLE PANCREATIC ADENOCARCINOMA: SAFETY, EFFICACY AND SURVIVAL

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**Purpose.** We evaluated the safety and efficacy of neoadjuvant chemotherapy and radiation for patients with locally unresectable pancreatic cancer.

**Methods.** From October 2000 to August 2006, 245 patients with pancreatic adenocarcinoma underwent surgical exploration at our institution. Of these, 78 patients (32%) had undergone neoadjuvant therapy for initially unresectable disease, while the remaining patients (serving as the control group) were explored at presentation (n=167). All neoadjuvant patients received gemcitabine based chemotherapy, often in conjunction with docetaxel and capecitabine (81%). 75% of neoadjuvant patients also received preoperative abdominal radiation (4500 rads).

**Results.** Neoadjuvant patients were younger than control group patients (60.8 vs 66.2 years,  $p < 0.002$ ). 76% of neoadjuvant patients were resected with curative intent as compared to 83% of control patients (NS). Concomitant vascular resection was required in 76% of neoadjuvant patients, but only 20% of control patients ( $p < 0.01$ ). Complications were more frequent in the neoadjuvant group (44.1% vs 30.9%,  $p < 0.05$ ), and mortality was higher (10.2% vs 2.9%,  $p < 0.03$ ). Among the neoadjuvant patients, all but one of the deaths were in patients that underwent arterial reconstruction. Mortality for patients undergoing a standard pancreatectomy was 0.8% in this series. Of patients resected, negative margins were achieved in 84.7% of neoadjuvant patients and 72.7% of control group patients (NS). Within the cohort of neoadjuvant patients, radiation significantly increased the complication rate (13.3% vs 54.6%,  $p < 0.006$ ), but did not affect median survival (512 vs 729 days, NS). Using intention to treat analysis, median survival for neoadjuvant patients (503 days) was higher than control group patients that were found to be unresectable (192 days,  $p < 0.001$ ) and equivalent to control group patients that were resected (498 days).

**Conclusions.** Resection rate, margin rate, and median survival were equivalent when neoadjuvant patients were compared to patients considered resectable by traditional criteria, demonstrating efficacy. Surgical resection following neoadjuvant therapy for patients with locally advanced pancreatic cancer can be performed with acceptable morbidity and mortality. This approach extended the boundaries of surgical resection and greatly increased median survival for the "inoperable" patient.

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### MANAGEMENT OF DELAYED ARTERIAL HAEMORRHAGE AFTER PANCREATICOUDENECTOMY – A META-ANALYSIS

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**Background & Aims.** Controversy exists regarding the best management of delayed haemorrhage after pancreaticoduodenectomy. We reviewed extensively the published articles describing this complication and reported our own series among 180 pancreaticoduodenectomy to examine both the role of diagnostic and interventional radiology and laparotomy in management of this serious condition.

**Methods.** A literature search of all reported cases in the last 15 years on delayed haemorrhage after pancreaticoduodenectomy together with identification and review of cases among 180 pancreaticoduodenectomy from our unit between 1993 and 2003. For meta-analysis, the end points evaluated were of operative and functional outcomes and adverse events. A random-effect model was used for analysis and sensitivity analysis was performed to examine the bias in patient selection.

**Results.** One hundred cases of delayed arterial haemorrhage were described among a total of 2503 pancreaticoduodenectomy (3.9%). Analysis revealed that recurrent bleeding occurred in 42.2% of patients undergoing laparotomy in comparison with 23.6% of embolised patients. The mortality rate was 28.8% in laparotomised patients (as compared to 14.6% in radiologically embolised patients). Four cases of delayed arterial haemorrhage were identified among 180 pancreaticoduodenectomy performed in our unit (2.2%). All cases had urgent diagnostic visceral angiography. Two patients were successfully managed with transcatheter arterial embolisation of bleeding vessels. But two patients who were operated on died in the postoperative period from multiorgan failure.

**Conclusions.** Delayed arterial haemorrhage after pancreaticoduodenectomy carries significant mortality. Radiological management with transarterial embolisation would seem to be a better treatment option than laparotomy.

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### RESECTION FOR METASTATIC PANCREATIC CARCINOID TUMORS IMPROVES SURVIVAL

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**Introduction.** Surgery is the recommended therapy for carcinoid tumor of the pancreas, but is often not performed due to advanced disease at presentation. We examined a population based cancer registry to examine the rates and impact on survival of pancreatic resection in the setting of metastatic disease.

**Methods.** Patients over 18 years with histologically confirmed carcinoid tumor of the pancreas were identified from the Surveillance, Epidemiology and End Results (SEER) Program from 1998 to 2003. Overall survival (OS) was evaluated using Kaplan-Meier and Cox proportional hazards modeling. Logistic regression was used to determine independent predictors for pancreatic resection.

**Results.** A total of 607 patients were identified. Distribution of tumors within the pancreas were 37% head; 11% body; 22% tail; and 30% not otherwise specified. At diagnosis, 65% of patients had metastatic, 20% regional and 15% localized disease. While 64% patients were not treated with surgery, 2% had a local excision, 14% had a partial pancreatectomy (including distal pancreatectomy), and 13% had a pancreatoduodenectomy. In total, 28% of the 215 pancreatic resections were performed in patients with metastatic disease. Overall, surgical resection was significantly associated with an improved OS compared to no resection (5 year OS = 63% versus 12% respectively,  $p < 0.0001$ ). In the final model, performance of surgery was independently associated with improved OS (HR 0.3 [0.2–0.4]). Decreased OS was associated with age over 60 years (HR 2.0 [1.6–2.6]) and black race (HR 2.1 [1.4–3.0]). Metastatic disease, tumors extending beyond the pancreas, tumor site and SEER region were not independently associated with survival. When stratified by metastatic disease, surgery was associated with a significant improvement in OS in both groups (HR 0.3 [0.2–0.6] and 0.2 [0.1–0.4] for metastatic and non-metastatic, respectively). Independent factors associated with pancreatic resection included lesions in the body ( $p = 0.03$ ), tail ( $p < 0.001$ ), and localized disease only ( $p = 0.001$ ). Metastatic disease ( $p < 0.0001$ ) and age over 60 years ( $p < 0.0001$ ) were associated with not receiving pancreatic resection. There was no regional or racial variation associated with the performance of surgery.

**Conclusion.** This study confirms that many patients with pancreatic carcinoid tumors present with metastases. It appears that these patients may benefit from surgical resection, however this is often not performed, perhaps due to the burden of disease at presentation. Studies must be conducted to identify patients for whom an aggressive surgical approach is warranted.

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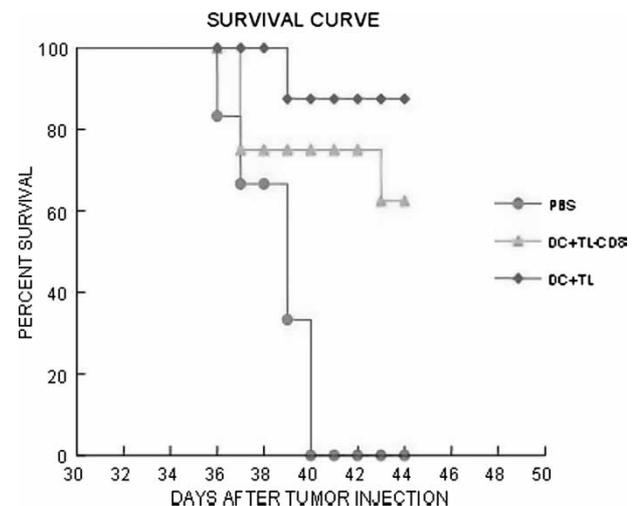
Abstract Numbers 129–139

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### TUMOR LYSATE-PULSED DENDRITIC CELLS CONFER PROTECTIVE IMMUNITY IN A MURINE PANCREATIC CANCER MODEL

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**Purpose.** Use of dendritic cell (DC) based immunotherapy has shown promise in the treatment of solid tumors by inducing anti-tumor immunity. PANC02 is a murine pancreatic adenocarcinoma (PCA) that is resistant to traditional forms of treatment. By using this model of PCA in immunocompetent mice, we attempt to study mechanisms that lead to anti-tumor immunity with the ultimate goal of improving the efficacy of dendritic cell based vaccines.



**Methods.** To measure PANC02 specific killing by CD8<sup>+</sup> T cells, mice were vaccinated subcutaneously three times at seven-day intervals with whole PANC02 tumor lysate-pulsed DC. One week after the final vaccine, splenocytes were collected, restimulated *in vitro* for five days, and used as effector cells in a standard chromium release assay. To measure vaccine efficacy, mice were immunized three times at seven-day intervals with DC pulsed with whole PANC02 tumor lysate or PBS. One week after final vaccination, mice were challenged subcutaneously with  $3 \times 10^5$  PANC02 cells. To determine the effects of CD8<sup>+</sup> T cells on tumor rejection, CD8<sup>+</sup> T cell depletion was undertaken using a monoclonal antibody one day prior to tumor challenge and continued through the end of the experiment. Tumor size measurements were recorded and survival was measured.

**Results.** Splenocytes isolated from mice vaccinated three times with PANC02 lysate-pulsed DC demonstrated PANC02 specific killing in a cytotoxic assay. Negative control cells, GL26 and Yac-1, were not lysed. Mice receiving tumor lysate-pulsed DC displayed the smallest tumors and the most delay in tumor growth, CD8 depleted mice had intermediate size tumors and PBS treated mice grew the largest tumors. Tumor suppression and survival were significantly enhanced in immunized mice as compared to non-immunized controls (Figure).

**Conclusions.** Suppression of tumor growth in vaccinated mice indicates a tumor specific immune response. CD8<sup>+</sup> T cells demonstrate tumor specific cytotoxic activity. The presence of intermediate size tumors in CD8 depleted mice shows that CD8<sup>+</sup> T cells are important in inducing anti-tumor immunity but are not the only effector mechanism.

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#### LIVER SPECIFIC TOLERANCE TO A TUMOR ASSOCIATED ANTIGEN

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**Introduction.** The MTD2 mouse line expresses the oncogenic SV40 T antigen (Tag) transgene under the major urinary protein (MUP) promoter effecting the progression of Tag-expressing hepatocellular cancers (HCC). The 501 mouse strain expresses this oncogenic Tag transgene under the  $\alpha$ -amylase promoter leading to Tag-expressing osteosarcomas. Hypothesizing that tumor location might lead to differences in antigen presentation that will induce different CD8 T cell responses, we compared and contrasted the fate of naïve Tag-specific CD8 T cells after exposure to tumor antigen in these spontaneous tumor models.

**Methods.** Naïve, T antigen epitope I-specific CD8 T cells from T-cell-receptor-transgenic mice (TCR-I cells) were transferred into HCC-bearing MTD2 mice, osteosarcoma-bearing 501 mice, or syngeneic C57BL/6 mice that do not express tumor antigen. Six and seven days after transfer, T cells were isolated from spleens, tumors, and tumor draining lymph nodes. Fluorescent staining quantified epitope I-specific CD8 T cells, and T-cell function was assessed through epitope I-specific  $\gamma$ -interferon production.

**Results.** In osteosarcoma-bearing mice, tumor antigen-specific TCR-I cells underwent a robust, ten-fold, proliferative expansion in spleens and tumor draining nodes. In addition, these cells acquired effector function as demonstrated by their ability to produce epitope I-specific  $\gamma$ -interferon. In HCC-bearing mice, tumor antigen-specific CD8 T cells underwent a very transient, 1–2 fold expansion and were unable to produce epitope I-specific  $\gamma$ -interferon. Accordingly, tumor antigen-specific cells were found to infiltrate osteosarcomas but not hepatomas: staining revealed the presence of significant amounts of TCR-I cells infiltrating the osteosarcomas in 501 mice; however, no site I-specific cells could be detected in the HCC tumors of MTD2 mice. Assessed by intracellular cytokine staining, approximately 10% of TCR-I isolated from mice with osteosarcomas produced epitope I-specific  $\gamma$ -interferon, a slightly diminished number compared to TCR-I isolated from spleens and lymph nodes. While the vast majority of CD8 T cells infiltrating osteosarcomas were tumor antigen specific, there were many CD8 T cells isolated from HCC tumors with unknown specificity.

**Conclusions.** The dichotomous fate of naïve, tumor antigen-specific T cells in the two models points to an important role for tumor location and antigen presentation at the interface of tolerance and immunity to cancer. Liver specific tolerance may impose a significant burden to be overcome by successful vaccine strategies. This model represents a powerful tool for the assessment of strategies to break this tolerance of HCC antigens.

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#### ENHANCING GEMCITABINE-MEDIATED EFFECTS AGAINST EXPERIMENTAL PANCREATIC CANCER VIA TWO ANTIANGIOGENIC STRATEGIES

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**Background.** Systemic treatment options against pancreatic ductal adenocarcinoma (PDAC) remain sparse. We tested an approach to enhance gemcitabine (Gem) mediated effects through antiangiogenic therapy.

**Methods.** Human ASPC PDAC cells were injected into nude mice ( $1 \times 10^6$  per animal s.c., n = 7 per group), and treatment was initiated at an average tumor volume of 50 mm<sup>3</sup>. Anti-VEGF-A bevacizumab (50  $\mu$ g), and Gem

(100 mg/kg) were injected i.p. twice weekly. Antiendothelial human recombinant endothelial monocyte-activating polypeptide II (EMAP-II) was administered through daily i.p. injections at 80  $\mu$ g/kg. Group comparisons were undertaken with ANOVA and Kruskal-Wallis tests.

**Results.** After 14 days of therapy, net tumor growth showed significant differences based on treatment group (p = 0.003). net tumor growth (in mm<sup>3</sup>) after EMAP (81, p = 0.05), Bev (116, p = NS), or Gem (115, p = NS) monotherapy showed only mild effects compared to controls (194). Dual combinations reduced tumor growth more effectively: EB (64, p = 0.01), EG (62, p = 0.008), and BG (59, p = 0.006). The triple combination EBG demonstrated the smallest net growth (7, p = 0.0006). Addition to Gem of EMAP (p = 0.05), Bev (p = 0.04), or of both (EB, p = 0.0007) resulted in significantly enhanced benefits. Tolerance of combination therapy, as measured by weight loss during treatment (in gm, vs. controls), was better in all combination groups (EB: 0.88, EG: 0.79, BG: 0.52, EBG: 0.83), than after Gem alone (1.23, p = 0.0008). Group comparisons of mean microvessel counts (MVC) per HPF and TUNEL-positive apoptotic index showed significantly enhanced activities in all treatment groups over controls, but no further effects in combination. The proliferative index, however, was significantly reduced only in the EMAP containing groups: Gem vs. EG (p = 0.004), Gem vs. BG (p = NS), BG vs. EBG (p = 0.0002). Mechanistic *in vitro* studies of EMAP II demonstrated specific binding affinity to  $\alpha$ 5-beta1 integrin, interference with fibronectin/integrin mediated cell adhesion, endothelial cell cytotoxicity, and decreased PDAC cell migration.

**Conclusions.** Both antiangiogenic agents EMAP II and bevacizumab significantly enhanced the gemcitabine-mediated antitumor effects against a PDAC *in vivo* xenograft. As the EMAP and Bev mechanisms appear to be different, the triple combination therapy was most effective, and offers a promising direction for clinical PDAC therapy.

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#### A NOVEL SUICIDE GENE THERAPY REGIMEN TARGETING THE OVEREXPRESSION OF EUKARYOTIC INITIATION FACTOR 4E IN A PANCREATIC CANCER CELL LINE

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**Background.** Eukaryotic initiation factor 4E (eIF4E) is a 25 kDa cap-binding protein involved in the initiation of protein synthesis. A number of solid tumors have demonstrated overexpression of eIF4E. To exploit this dysfunction, the 619 base pair 5'UTR of FGF-2 was spliced upstream of the herpes simplex virus thymidine kinase gene in an adenovirus vector (Ad-HSV-UTK), with the expectation that the gene product thymidine kinase will be expressed in cells which overexpress eIF4E, and thus yield these cells susceptible to ganciclovir. In this study, we investigated the *in vitro* activity of this suicide gene therapy regimen against the human pancreatic cancer cell line (CRL-1918).

**Methods.** eIF4E overexpression was assessed by Western blot. The pancreatic cancer cell line (CRL-1918) was cultured and divided into 3 groups. Group one was infected with the Ad-HSV-TK vector (no additional 5' UTR) while group two was infected with the Ad-HSV-UTK vector (with the additional 5' UTR), the third group (the control arm) was not infected. 24 hours after infection each group was further divided into 5 groups, each receiving a progressive dose of ganciclovir: group 1 = 0, group 2 = 10mcg/ml, group 3 = 50 mcg/ml, 4 = 100 mcg/ml, 5 = 1000 mcg/ml. Successful infection of the cell line was determined by Western blot analysis for the gene product thymidine kinase. Crystal violet staining assessed cell viability.

**Results.** Western Blot analysis confirmed the overexpression of eIF4E in this human pancreatic cancer cell line. Successful infection of the cell lines was demonstrated by measurable expression of the gene product thymidine kinase by both groups one and two. Marked cytotoxicity was noted in both the Ad-HSV-TK and Ad-HSV-UTK infected groups with a 100-fold less concentration of ganciclovir as compared to the control groups, which received ganciclovir alone.

**Conclusion.** The human pancreatic cancer cell line (CRL-1918) was found to overexpress eIF4E. By splicing a 5'UTR upstream of HSV-TK, this overexpression of eIF4E resulted in the expression of thymidine kinase and subsequently rendered these cells susceptible to treatment with ganciclovir. Marked cytotoxicity was evident in the treatment groups, even at a much lower concentration of ganciclovir. Suicide gene therapy selectively targeting malignant cells by exploiting the overexpression of eIF4E appears effective against the CRL-1918 human pancreatic cancer cell line.

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#### PROLIFERATIVE BILIARY EPITHELIA ARE THE MAJOR CONTRIBUTOR TO HIGH LEVELS OF HEPATIC CD44 EXPRESSED BY CHOLESTATIC LIVERS

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**Objective.** In previous study we demonstrated in a rat model that cholestatic livers induced by bile duct ligation (BDL) expressed high levels of CD44. The current study was carried out to further investigate the cellular source of CD44 expression.

**Methods.** Cholestatic cirrhotic livers were induced in rats by BDL and compared with sham-operated livers. Total non-parenchymal liver cells (NPLC) were obtained via a standard procedure consisting sequential liver perfusion, collagenase digestion and gradient centrifugation. Biliary epithelial cells (BEC) and hepatic stellate cell (HSC) were isolated by gradient centrifugation with isotonic Percoll. CD31+ hepatic endothelial cells (HEC) and ED2+ Kupffer cells (KC) were isolated through flow cytometric cell sorting. Expression of CD44 standard (s) and variant (v) isoforms by different types of NPLC was examined by quantitative real time PCR. Histological distribution of the cells expressing CD44 proteins was examined in cryostat sections of the livers with immunofluorescent technique. Deposition of extracellular hyaluronic acid (HA) was studied by histochemical staining of the liver sections with a hyaluronan binding protein (HABP).

**Results.** CD44 mRNA levels in the BDL livers were significantly increased when compared to sham controls ( $p < 0.001$ ). The levels of CD44 E5 mRNA expressed by BEC isolated from the cholestatic livers were as high as 20-, 8- and 6-fold as that expressed by HSC ( $p < 0.01$ ), Kupffer cells ( $p < 0.01$ ) and HEC ( $p < 0.01$ ), respectively. Immunofluorescent staining of the liver sections showed increased expression of cell surface CD44 proteins, mainly by the proliferative biliary epithelial cells. Metamorphic analysis of the liver sections stained with HABP demonstrated a striking increase in HA synthesis in the portal triads of the BDL livers when compared with that of sham operated controls.

**Conclusion.** In cholestatic livers bile duct proliferation was accompanied by remarkable upregulation of CD44 expression by the biliary epithelial cells and an increase in synthesis of extracellular matrix HA in the portal triads. CD44 species expressed in the cholestatic livers were exclusively variant isoforms. Though the biological implication of CD44v gene up-regulation on biliary epithelial cells in the development of cholestatic cirrhosis is unclear, detection of this CD44 may have a diagnostic value in clinical monitoring of hepatobiliary diseases.

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#### DISRUPTION OF TRANSFORMING GROWTH FACTOR- $\beta$ SIGNALING THROUGH $\beta$ -SPECTRIN ELF LEADS TO EARLY HEPATOCARCINOGENESIS THROUGH OVEREXPRESSION OF CYCLIN D1

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Recent studies in human hepatocellular carcinoma (HCC) have revealed the importance of the transforming growth factor- $\beta$  (TGF- $\beta$ ) signaling pathway in suppressing tumorigenesis through Smads and adaptor proteins such as embryonic liver fodrin (ELF). TGF- $\beta$  signaling induces antiproliferative gene responses by inhibiting cell cycle progression in the G<sub>1</sub> phase. Our laboratory has demonstrated that up to 40% of *elf+/-* mice (16/40) spontaneously develop HCC within 15 months. We now demonstrate that immunohistologic studies of HCC specimens taken from *elf+/-* mice show increased nuclear cyclin D1 expression, which is a major G<sub>1</sub> cell cycle regulatory protein. To investigate the correlation between TGF- $\beta$  inactivation and hepatocarcinogenesis, we examine the expression of TGF- $\beta$  signaling proteins in four human HCC cell lines, SNU-182, SNU-398, SNU-449, and SNU-475. ELF expression is significantly reduced in one cell line, SNU-398, and moderately decreased in SNU-182, SNU-449, and SNU-475. TGF- $\beta$  receptor II (TBR2) expression was significantly reduced in three cell lines, SNU-182, SNU-398, and SNU-475. Restoration of ELF results in a moderate decrease in cyclin D1 expression in SNU-182 and SNU-475 and 8-fold decrease in SNU-398. More importantly, under TGF- $\beta$  stimulation, ectopic expression of ELF together with TBR2 demonstrates an additive decrease in cyclin D1 expression compared to the non-TGF- $\beta$  stimulated naïve SNU-398 cell line. The decrease in cyclin D1 is accompanied by a decrease in hyperphosphorylated-retinoblastoma (pRb-P) expression. Restoration of ELF and TBR2 in SNU-398 results in an additive decrease of pRb-P. Further analysis of the role of TGF- $\beta$  signaling in human HCC confirmed reduced ELF expression by immunohistochemical staining in 7 out of 9 human HCCs ( $p < 0.039$ ). These human HCCs displays increased nuclear cyclin D1 expression as in the *elf+/-* mouse HCCs. Furthermore, immunohistochemical analysis also demonstrates abnormal cytoplasmic localization of TBR2 and decreased expression of Smad4 in HCCs, although the changes do not achieve statistical significance. Thus, we show for the first time that disruption of TGF- $\beta$  signaling by the adaptor ELF plays an important role in human hepatocarcinogenesis, possibly through cyclin D1 deregulation. Loss of ELF could serve as a primary event in hepatocarcinogenesis, further studies on the mechanisms underlying the inactivation of the TGF- $\beta$  signaling pathway could hold promise for new therapeutic approaches in human HCCs.

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#### THE EMERGING ROLE OF NF- $\kappa$ B IN HEPATITIS C-ASSOCIATED HEPATOCELLULAR TUMORIGENESIS

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**Purpose.** With over 4 million Americans infected with hepatitis C, the number of cases of hepatocellular carcinoma (HCC) continues to rise, with no significant improvement in targeted therapies. The transcription factor nuclear factor- $\kappa$ B (NF- $\kappa$ B) promotes the production of angiogenic, anti-apoptotic, and pro-metastatic factors that are involved in carcinogenesis. In addition, NF- $\kappa$ B has been linked to inflammation-associated cancers. This study addresses the applicability of NF- $\kappa$ B-targeted therapy in hepatitis C-associated hepatocellular carcinoma.

**Methods.** Electrophoretic mobility gel shift assays (EMSA) were used to evaluate NF- $\kappa$ B DNA binding *in vitro*. NF- $\kappa$ B activity in two immortalized cell lines (Hep 3B and HepG2) was compared to normal hepatocytes (CL48). The clinical relevance of NF- $\kappa$ B was evaluated using Western blot analysis of NF- $\kappa$ B subunits/heterodimers (p65/p50) in 12 cases of hepatocellular carcinoma taken from explanted livers in patients with hepatitis C undergoing transplantation. NF- $\kappa$ B activity in tumor versus adjacent liver was also analyzed.

**Results.** NF- $\kappa$ B was constitutively active in both the immortalized cancer cell lines and normal hepatocytes. The degree of p65 DNA binding activity appeared to be highest in Hep 3B cells and lowest in normal hepatocytes (CL48). NF- $\kappa$ B also appeared to be constitutively active in all HCC patient samples analyzed, with greater activity noted in the tumor versus adjacent liver tissue. In addition, the p50 subunit of the NF- $\kappa$ B complex was also constitutively active *in vitro* and *in vivo* compared to expression of its precursor protein p105. In hepatocellular carcinoma, the precursor inhibitory protein p105 was negligible compared to the active subunit p50 in all samples.

**Conclusion.** Constitutively active NF- $\kappa$ B is apparent in both immortalized *in vitro* cell lines and human hepatocellular carcinoma samples. Attempts to inhibit NF- $\kappa$ B in liver cancer makes clinical sense and warrants further study.

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#### INCREASED ENDOTOXIN TRANSLOCATION IN OBESITY: A CAUSE OF STEATOTIC LIVER DAMAGE

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In human transplantation, endotoxin (LPS) is thought to be a major contributing factor to the pathogenesis of ischemia/reperfusion (I/R) injury. Upon portal occlusion, bowel congestion causes bacterial and endotoxin translocation and the LPS is introduced into the portal circulation. Upon LPS exposure and recognition by toll-like receptor 4 (TLR4), there is a large release of proinflammatory cytokines, including TNF and IL-1 $\beta$ , which cause inflammation, necrosis, and apoptosis of the hepatocytes. It is well known that steatotic livers are highly sensitive to the effects of endotoxin as compared to their lean counterparts post-I/R. Blockade of endotoxin signaling with a specific monoclonal antibody significantly ameliorates injury and improves animal survival from 14.4% to 83.3%. Therefore, we propose the novel hypothesis that differential injury is due to a higher exposure to endotoxin rather than an increased sensitivity to endotoxin. To test these hypotheses, we subjected male 10-week-old C57BL/6 (lean) and ob/ob mice to 15 minutes of total hepatic ischemia and collected portal blood at baseline (pre-ischemia) and immediately post-reperfusion and measured endotoxin levels ( $n = 5$ /group). We observed significantly increased portal levels of endotoxin at baseline in ob/ob animals ( $0.231 \pm 0.013$  EU/mL vs.  $0.208 \pm 0.005$  EU/mL in lean,  $p < 0.05$ ). In addition, we saw significantly increased levels immediately post-reperfusion ( $0.297 \pm 0.03$  EU/mL in lean vs.  $0.383 \pm 0.008$  EU/mL,  $p < 0.001$ ). Our prior experience with this model has shown drastically increased ALT levels and necrosis in the ob/ob animals, correlating well with the endotoxin bolus. In addition, we have seen no differences in levels of TLR4 mRNA ( $0.288 \pm 0.049$  relative density units in lean vs.  $0.233 \pm 0.11$  in ob/ob) in these animals. Similarly, CD14 protein levels are not significantly elevated between lean and ob/ob animals. Due to the apparent constancy in the receptor complex proteins, we propose the increased endotoxin translocation in obese animals as a cause of increased damage in steatotic livers after I/R and transplantation. We hypothesize that this difference in translocation is caused by an increased permeability in the intestines of the obese animals. This has extremely important implications in the clinic. Should human livers behave similarly, this is a possible cause for liver damage after any abdominal surgery, especially transplantation, as any manipulation of the bowel or bowel ischemia causes this translocation.

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#### REMOTE ISCHEMIC PRECONDITIONING MODULATES HEPATIC MICROCIRCULATION THROUGH THE HEMEOXYGENASE PATHWAY IN A RAT MODEL OF WARM ISCHEMIA REPERFUSION INJURY OF THE LIVER

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**Introduction.** Liver resection and transplantation surgery involve a period of ischemia reperfusion injury (IRI) which initiates an inflammatory cascade resulting in hepatic and remote organ injury. IRI leads to nonfunction or dysfunction of liver grafts in clinical transplant settings. Davidson's group

have shown that remote ischemic preconditioning (RIPC) protects liver function. However the mechanism of protection has not been studied. This is the first study to investigate the effect of RIPC upon hepatic microcirculation by intravital microscopy and to study the role of hemoxygenase pathways (HO-1) as a candidate mechanism. Aim-To study the role of HO-1 pathways in RIPC as the candidate mechanism in the modulation of hepatic microcirculation in a rat model of hepatic IRI.

**Material and methods.** The effect of RIPC was studied in a rat model of ischemia reperfusion injury with 45 minutes of partial liver ischemia (70%) followed by 3 hours of reperfusion. Five groups of animals namely Sham, IRI, RIPC+IRI, RIPC+Sham, pyrrolidine dithiocarbamate (PDTC)+IRI, Zinc protoporphyrin (ZnPP)+RIPC+IRI were studied with six animals in each group. PDTC is a HO-1 inducer while ZnPP is a HO-1 inhibitor. Hepatic microcirculation was assessed by studying velocity of blood flow, sinusoidal perfusion, sinusoidal flow, sinusoidal diameter and neutrophil adhesion. Apoptosis was assessed by propidium iodide staining under intravital microscopy. Liver functions were assessed in all groups. Liver histology and immunohistochemistry for HO-1 expression were also done.

**Results.** The velocity of blood flow was significantly better in the RIPC group at the end of three hours of reperfusion compared to IRI group ( $P < 0.05$ ) but no difference was found between RIPC and Sham. Sinusoidal perfusion and flow was better in the RIPC group. The number of apoptotic cells in the RIPC group was significantly less as compared to IRI only ( $P < 0.05$ ). The PDTC group (HO-1 inducer) showed significantly improved liver functions compared to IRI and ZnPP groups. ZnPP (HO-1 inhibitor) significantly blocked the effects of RIPC on the microcirculation at about two hours of reperfusion and significantly increased apoptosis strongly suggesting the role of HO-1 pathways in RIPC mediated amelioration of hepatic IR injury.

**Conclusion.** This is the first study by intravital microscopy to demonstrate that RIPC modulates hepatic microcirculation in order to ameliorate IRI and hemoxygenase pathways maybe one of the key pathways in the mechanism of RIPC.

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#### INCREASED ACTIVATION OF PROAPOPTOTIC GENES IN OLD VS YOUNG LIVERS FOLLOWING ISCHEMIA AND REPERFUSION: A NEW MECHANISM OF INJURY

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Ischemia/reperfusion injury (IRI) is exacerbated in old livers when compared to young livers. We investigated whether the higher susceptibility of old livers to ischemic injury is associated with differences at the level of the cellular molecular response.

**Methods.** C57BL/6 mice at the age of 6 weeks (young) and 12 months (old) underwent 60 minutes of hepatic ischemia and 0 min, 1hr and 3hr of reperfusion. Hepatocyte injury was investigated with ALT levels and degree of necrosis. Caspase 3 activation was determined after 3hr of reperfusion. Using a 15K murine cDNA array, we compared gene expression levels after 60 minutes of ischemia and 1hr of reperfusion to sham-operated livers in both young and old mice ( $n=5$  per group). Genes with at least 1.5-fold up- or down regulation with a  $p$ -value of 0.05 were considered of interest. Real-time PCR was used for verification of array results.

**Results.** Although comparable indices of liver injury were seen after 60 minutes ischemia and 1 hr of reperfusion, older livers manifested progressively worse injury at later time points. Comparing old to young livers, ALT after 60 minutes of ischemia and 1hr of reperfusion was 1000 U/L vs 1100 U/L ( $p=0.01$ ) but 6200 U/L vs 3900 U/L ( $p=0.045$ ) after 3 hours reperfusion. After 3hr reperfusion older mice had significantly more liver necrosis than young mice (35% vs 10%  $p=0.03$ ). Applying gene expression analysis to the earlier time point, there was hepatic up-regulation of pro-apoptotic genes such as caspase 6, Annexin A3 and TNFR following 60 minutes of ischemia and 1hr of reperfusion in the younger mice. In contrast, anti-apoptotic genes such as heat shock protein 25, 86, 105, Bcl2-associated athanogene 3 and early growth response 3 were significantly down regulated. Comparing young and old mice following reperfusion injury, there was a more pronounced up-regulation of proapoptotic genes, such as FADD and growth arrest specific 6, in the older mice, while levels of antiapoptotic genes, such as Bcl-2 and heatshock protein 70 & 105, were even more reduced in older livers. Caspase 3 activation, as a second endpoint of apoptosis, was significantly increased in old mice compared to young animals following 3hr of reperfusion.

**Conclusion.** Ischemia/ reperfusion injury is associated with increased expression of pro-apoptotic genes, reduced expression of anti-apoptotic genes, and activation of intracellular mediators of apoptosis. This difference is more prominent in older than in younger livers, which might explain in part the decreased tolerance of old livers to reperfusion injury.

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#### UNCOUPLING PROTEIN-2 PROMOTES HEPATOCYTE DEATH IN A MODEL OF IN VITRO STEATOSIS AND HEPOXIA/REOX- YGENATION

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Liver steatosis is associated with severe complications following liver surgeries, which include periods of ischemia. We have shown that the up regulation of mitochondrial uncoupling protein-2 (UCP2) correlates with steatotic liver sensitivity to ischemia/reperfusion. UCP2 is an intermembrane bound protein, which uncouples the mitochondria from oxidative phosphorylation in the effort to decrease the cell's exposure to reactive oxygen species at the expense of efficient ATP production. We propose the hypothesis that fat induced UCP2 expression sensitizes steatotic hepatocytes to injury following hypoxia and reoxygenation (H/R). To test this we employed both WT and UCP2 knockout 8-week old C57BL6 mice ( $n=5$ /group). Hepatocytes were harvested by collagenase perfusion and purified via density gradient, then plated in control or 6% intralipid (emulsified fatty acids) supplemented media. After 24 hours, hepatocyte phenotypes were determined by GCMS and Oil Red O. For all measured fatty acids, significant increases were observed in the intralipid treated groups over control, and ORO staining showed significant intracellular fat accumulation. There were no differences between the WT and UCP2 KO groups. Next, we subjected the same groups to H/R in the effort to mimic ischemia/reperfusion. After 24-hour culture, media was replaced with unsupplemented (serum free) media. Experimental plates were placed in an anaerobic chamber for 4 hours then removed and allowed 24-hours for reoxygenation. Following reoxygenation, hepatocytes were harvested and assessed for viability by trypan blue exclusion. Groups not receiving hypoxia, serving as baseline, displayed the following percentages of cell death: WT control ( $9.0 \pm .09\%$ ), UCP2 KO control ( $7.6 \pm 1.9\%$ ), WT intralipid ( $7.8 \pm .07\%$ ), UCP2 KO intralipid ( $9.1 \pm 2.3\%$ ). For the groups receiving H/R, percent cell death was: WT control ( $20.0 \pm 3.3\%$ ), UCP2 KO control ( $19.6 \pm 1.8\%$ ), WT intralipid ( $31.6 \pm 3.2\%$ ), UCP2 KO intralipid ( $23.7 \pm 2.9\%$ ). Cell death for all groups after hypoxia was significantly higher than baseline. After H/R, death was significantly different between the WT groups (control vs intralipid) and for the intralipid groups (WT vs KO) ( $p < 0.05$ ). Although compensatory at baseline, UCP2 expression in the steatotic hepatocyte promotes death following the stress of H/R. Down regulation of UCP2 through global decrease of hepatic steatosis, or targeted down regulation prior to transplantation may enhance hepatocyte function, decreasing the probability of primary nonfunction. In addition, we have established a model of in vitro steatosis and H/R in hepatocytes. Both may be useful for other areas of research.

#### Free Papers

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Abstract Numbers 140-149

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#### ROLE OF PRIMARY RESECTION FOR HCC UNDER THE ERA OF LIVER TRANSPLANTATION

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**Objective.** To evaluate the advantage and disadvantage of hepatic resection (Hx) for hepatocellular carcinoma (HCC) when patients with HCC were classified according to Milan criteria under the era of liver transplantation.

**Methods.** Between 1990 and 2006, consecutive 501 HCC patients underwent curative primary Hx, in whom 321 (Group1) met Milan criteria and 180 (Group2) did not. The median follow-up period was 53.6 months (range, 5-184).

**Results.** In 114 death cases of Group 1, 81 (71.1%) died of tumor recurrence, 9 (7.9%) of liver failure, 2 (1.8%) of operative complications, 17 (14.9%) of unrelated medical conditions. In 96 death cases of Group 2, 77 (80.2%) died of tumor recurrence, 8 (8.3%) of liver failure, 3 (3.1%) of operative complications, 7 (7.3%) of unrelated medical conditions, 1 (1.0%) of unknown. Patients survival (PS) and disease free survival (DFS) of Group1 were 73.6% and 40.6% at 5years, and 55.8% and 25.0% at 10years. Of the 145 Group1 patients who recurred, only 60(18.7%) exceeded Milan criteria. One hundred forty-five (45.2%) had no recurrence to date. PS and DFS of Group2 were 52.2% and 23.2% at 5years, and 33.7% and 17.4% at 10years. While 116 patients developed recurrence, 39 (21.7%) were within Milan criteria. Fifty-five (30.6%) had no recurrence to date. ICGR15, Anatomical resection, and tumor number were significant preoperative predictors of survival and recurrence for HCC within Milan criteria by multivariate analysis. Preoperative prognostic scoring system was established by three risk factors as ICGR15 >15%, Non anatomical resection, and multiple tumor. Patients who corresponded to no factor were assigned a score 0, patients with any one factor were a score 1, patients with any two factors were a score 2, and patients with all three factors were a score 3. While the selected patients within Milan criteria who had a score 1 or a score 2 were survived 78.5% and 64.9% at 10 years after hepatectomy, the patients who had a score had no 5 years-survivors.

**Conclusion.** After Hx, 18.7% within Milan criteria at the initial hepatectomy lost the chance of liver transplantation (LTx). Hx made 30.6% without

Milan criteria which was not transplantable at the first time alive without recurrence and 21.7% without Milan criteria recurrent within Milan criteria and transplantable, who may be rescued by receiving salvage LTx. Thus, Hx remains as an important strategy for the treatment of HCC even under an era of LTx.

**141 IMPROVED SURVIVAL IN HEPATOCELLULAR CARCINOMA: RESULTS OF A SINGLE CENTER ANALYSIS OF 501 PATIENTS**

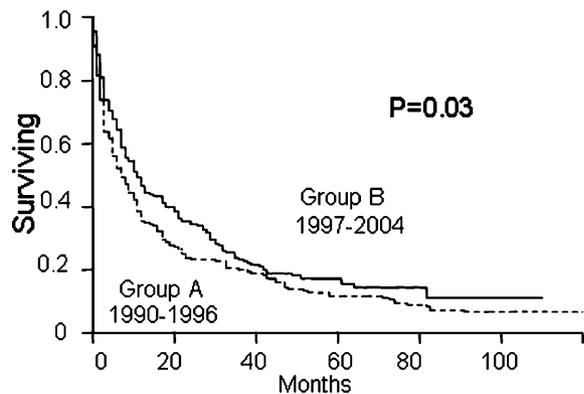
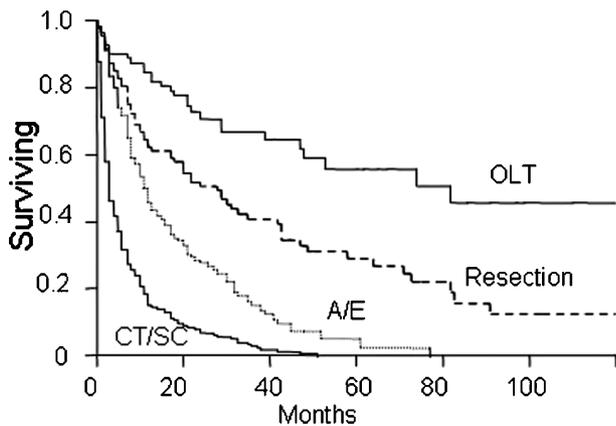
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**Purpose.** Incidence of hepatocellular carcinoma (HCC) is increasing. An analysis of patients treated at a single center was performed to identify outcome changes, as management has evolved.

**Methods.** Three databases (structured query language, tumor registry, and pathology) were queried for HCC patients treated at our institution from 1990–2004. Records were reviewed to confirm diagnosis, and to obtain treatment and outcome data. As criteria for orthotopic liver transplantation (OLT) were established in 1996, patients treated from 1990–1996 (group A) were compared to those treated from 1997–2004 (group B) for outcome differences. Survival was calculated from date of first visit, to permit comparison with patients receiving supportive care.

**Results.** Between 1990–2004, 501 patients were identified, 172 (34%) in group A and 329 (66%) in group B. Median age was 60 (range, 19–89), 361 (72%) were men and 392 (78%) had cirrhosis. 73 (14%) underwent OLT, 99 (20%) were resected, 135 (27%) had ablative/embolic therapy (A/E), and 194 (39%) had chemotherapy or supportive care (CT/SC). Median survival for all patients was 10 months, and by therapy: OLT, 82 months; resection, 28 months; A/E, 12 months; and CT/SC, 6 months ( $p < 0.001$ , Fig. 1). On multivariate analysis, factors associated with reduced survival were cirrhosis, vascular invasion, non-surgical therapy, and treatment prior to 1997. By time interval, survival was better in group B as compared with group A (11 vs. 7 mos,  $p = 0.03$ , Fig. 2). When all OLT patients were excluded from the analysis, this survival benefit was no longer present (8 vs. 6 mos,  $p = 0.17$ ). This effect was not observed by subtracting any other method of treatment from the analysis.

**Conclusions.** HCC referrals to our hospital have increased over time in keeping with rising rates. Surgery is associated with better outcome. In this series, treatment post-1996 is associated with improved survival, likely due to improved criteria for OLT.



**142 TUMOR SIZE AND MELD SCORE PREDICT MICROVASCULAR INVASION IN CIRRHOTIC PATIENTS WITH HEPATOCELLULAR CARCINOMA**

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**Introduction.** Microvascular invasion is a poor prognostic indicator for hepatocellular carcinoma (HCC) in patients with and without cirrhosis, regardless of treatment modality. The status of microvascular invasion is usually unknown prior to surgical intervention. The aim of this study is to determine whether pre-intervention Model of End Stage Liver Disease (MELD) score alone and in combination with other tumor characteristics, can serve as a surrogate marker for tumor microvascular invasion in patients with cirrhosis undergoing hepatic resection.

**Methods.** All consecutive patients with cirrhosis that had undergone hepatic resection for HCC between Jan 1993 to Jan 2005 from Oregon Health & Science University, Portland VAMC and Mayo Clinic, Rochester were retrospectively reviewed.

**Results.** One hundred fourteen cirrhotic patients (27 F: 87 M) with a mean age of 63 years underwent hepatic resection for HCC. The etiology of cirrhosis was viral hepatitis B and/or C in 61 (53.5%), alcohol in 21 (18.3%), cryptogenic in 17 (15%) and other in 15 (13.2%) patients. The mean MELD score was 9 (range 6 to 17) and tumor size was 5 cm (range 1 to 16 cm). Microvascular invasion was present in 36 patients (32%) based on resection specimen histology. Clinical variables that predicted microvascular invasion were tumor size (0.005), MELD score (0.05), and high AFP (0.04), but not tumor multifocality. Tumor size of  $\leq 3$  cm, 3.1 to 5 cm and 5.1 to 7 cm and  $> 7.1$  cm had the respective incidence of microvascular invasion of 9%, 31%, 47% and 65%. MELD score  $\leq 9$  and  $\geq 10$  had the respective incidence of microvascular invasion of 26% and 40%. The incidence of microvascular invasion when these two predictors were combined is shown in the table 1. The 1, 3 and 5 year overall survival for patients with and without vascular invasion was (60% vs. 72%), (30% vs. 51%) and (18% vs. 40%), respectively ( $p = 0.018$ ).

**Conclusions.** Microvascular invasion reflects the biologic aggressiveness of HCC in patients with cirrhosis. Objective clinical criteria, based on tumor size and MELD score, can be used as a guideline to stratify treatment modalities and to predict outcomes. Patients with cirrhosis who have tumors  $> 5$  cm and MELD score  $\geq 10$  may not benefit from aggressive hepatic resection and alternate therapy should therefore be considered.

	Group A (n = 47)	Group B (n = 28)	Group C (n = 22)	Group D (n = 17)	p-value
Tumor Size (cm)	$< 5$	$< 5$	$> 5$	$> 5$	
MELD Score	$\leq 9$	$\leq 10$	$\leq 9$	$\geq 10$	
Microvascular Invasion (%)	14%	25%	50%	64%	0.0003
Median Survival (years)	4.5	2.2	2.4	0.2	$< 0.0001$

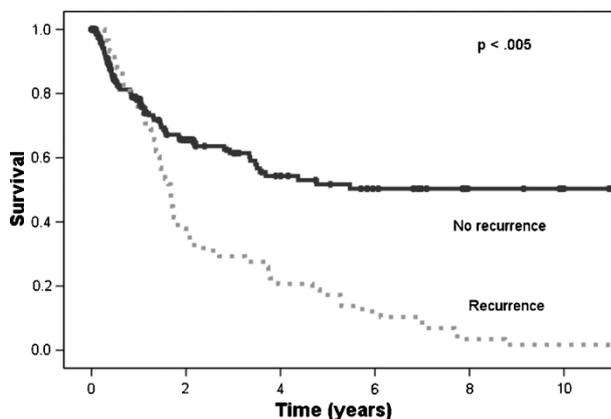
**143 OUTCOMES ANALYSIS FOR 280 PATIENTS WITH CHOLANGIOCARCINOMA TREATED WITH LIVER TRANSPLANTATION OVER AN 18-YEAR PERIOD**

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**Introduction.** Cholangiocarcinoma is an aggressive malignancy associated with a 5-year survival of less than 15%. Based largely on single institution data, liver transplantation is now being considered as a primary treatment option. The purpose of this study was to evaluate a large, multi-institution experience with liver transplantation for patients with this malignancy.

**Methods.** The United Network for Organ Sharing (UNOS) database for the years 1987–2005 was used to identify 280 patients with cholangiocarcinoma who underwent a total of 302 liver transplants. Study variables, including age, race, gender, and date of transplant, were recorded. Survivals were calculated using Kaplan-Meier curves and compared with log-rank tests.

**Results.** The study cohort included 63.6% male patients and 86.8% Caucasian patients with a median age of 48 years (range: 18–73 years). 59 of the 280 study patients (21%) carried a primary diagnosis of primary sclerosing cholangitis. The 30-day post-operative mortality rate was 4.0% (12 patients). At a median follow-up interval of 452 days (range: 0–6166 days), the 1 and 5-year patient survivals were 74.1% and 38.4%, respectively, with 49 actual 5-year survivors and 21 actual 10-year survivors. Twenty patients required re-transplantation, including 2 patients who received a third graft, yielding 1 and 5-year graft survivals of 68.9% and 35.5%, respectively. Survival analysis determined that patients transplanted after 1998 ( $n = 142$ ) experienced improved survivals (5-yr OS: 44.6%) compared to patients



transplanted in the previous era ( $n=138$ , 5-yr OS: 32.9%)( $p=0.005$ ). In addition, recurrent cholangiocarcinoma was associated with a significantly lower 5-year survival rate (52.4% vs. 17.2%.  $p < 0.001$ ) (Figure 1).

**Discussion.** Analysis of the UNOS dataset indicates that selected patients undergoing liver transplantation experience a survival benefit (5-yr OS: 38.4%). Outcomes have improved over time, likely due to advances in perioperative care and adjuvant therapies. Freedom from recurrence was found to be a significant factor related to long-term survival, providing further support for the inclusion of liver transplantation in cholangiocarcinoma multimodality therapy protocols.

#### 144 UTILIZATION OF HTLV POSITIVE DONOR LIVERS FOR TRANSPLANTATION

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**Introduction.** A positive serologic test for Human T-Cell Lymphotropic Virus (HTLV) has been considered a contraindication to organ donation. Potential complications of HTLV-I viral transmission including tropical spastic paraparesis (TSP) and adult T cell leukemia. HTLV-II transmission is associated with more benign symptoms. We hypothesize that there is a high false positive rate of serologic testing and that underutilization of organs from HTLV seropositive donors may be inappropriate.

**Patients and Methods.** This prospective IRB approved study (IRB-AAAC1797) was conducted from 11/03 through 08/06 (median follow-up: 8.3mos). 15 deceased donor liver allografts from HTLV positive donors documented by ELISA were evaluated and 12 OLT performed. All ELISA positive results were confirmed by Western Blot or Immunoblot analysis (typically available 7–10d post-OLT). Predictors of HTLV infection in donors were assessed including gender, ethnicity, age, cause of death, serologies, CDC high-risk behavior, country of birth, transfusion and travel history. Complete recipient demographic and physiologic data were collected including pre-transplant HTLV serology. Serologic surveillance for viral infection post-OLT was performed at 1, 3, 6 and 12 months.

**Results.** All recipients were HTLV negative pre-OLT. Seven of 15 HTLV ELISA positive donors had negative confirmatory testing and 4 donors were indeterminant by repeat testing. Only 4/15 (26.6%) HTLV ELISA positive donors were confirmed HTLV positive by Western blot or Immunoblot. Three were HTLV-II and 1 was HTLV-I positive. Of these, 3 (all HTLV-II positive) allografts were utilized. One recipient died 8 d post-OLT without seroconversion. The remaining two patients are both clinically asymptomatic. One has seroconverted at 1 month and the other remains seronegative 6 months post-OLT.

**Conclusions.** Utilization of HTLV seropositive donors can increase the potential organ pool. Confirmatory testing shows that the majority of these donors are indeterminant or false positive. Even when the donor was a true positive seroconversion has been inconsistent. Medical need, detailed elective discussion, informed consent and intensive risk assessment are essential in determining proper allocation of these grafts.

#### 145 LIVER TRANSPLANTATION IN LATIN AMERICA

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**Background.** Since liver transplantation became the gold standard treatment of end-stage liver disease, Latin America adopted this procedure. After the first successful surgery in Brazil (1987), the number of transplants increased with similar morbidity-mortality rates compared with those published in international literature.

**Objective.** To show the Latin American experience in liver transplantation.

**Methods.** Data was obtained retrospectively from the Transplantation Society of Latin America and the Caribbean's database, the National Registries of each country, Institutional Databases of the principal Transplantation Centers in each country and also contacting Chairmen of the principal groups. The analysis was performed in the 2000–2005 period (when possible).

**Results.** In 12 countries liver transplantation is performed. Brazil, Argentina, Chile, Mexico and Colombia carried out the largest number of procedures. Despite Brazil has more than 5200 transplants, Argentina performs more surgeries per habitants. Mean cost of the procedure is 25000 US\$ ( $r$  21000–30000). Principal indication in HCV cirrhosis in adult recipients and fulminant hepatitis (HAV) in pediatric recipients. Organ shortage determined the use of living related donors. Mean survival rate is 85% at 1 year ( $r$  77–91.7).

**Conclusions.** Despite organ shortage, costs, difficulties of most patients to arrive to specialized centers, results in liver transplantation in Latin America are encouraging.

Liver Transplantation in Latin America

Country	Transplants	Transplantation Units	Population (millions)	Transplants/ Million Habitants
Brazil	5258	62	186	4.5
Argentina	1969	14	37	5.4
Mexico	546	20	97	07
Chile	471	7	15	4.1
Cuba	59	2	10	1.6
Costa Rica	22	1	4	2.5
Peru	20	1	24	0.2
Venezuela	19	1	23	0.1
Uruguay	13	1	4	1.0
Bolivia	6	1	8	0.3
Ecuador	1	1	12	0

#### 146 HOW TO BALANCE THE RISK FOR A LIVING LIVER DONOR – OR IS DEATH ALWAYS PREVENTABLE?

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Expanding the organ pool has become a major goal in transplantation, and living donation is an essential part of this evolution. Concerns have always been the safety and risk for the donor, and one of the important questions is – where are the limits? In a consecutive series of 40 living liver donors we have analyzed preoperative risk factors, and compared to postoperative complications, graded by the classification of Dindo (2004). Donor age was 19–69 years (median 41 years). Types of surgery were 30 right lobe, 1 left lobe, and 7 left lateral lobe resections; the donor operation was aborted in two cases. In 6/40 donors (15%) no preoperative risk could be identified. The majority had one (9), two (13), and three or more risk factors (12), including overweight/obesity in 25 (median BMI of all 40 donors was 26 kg/m<sup>2</sup>), smoking in 15, hypercholesterolemia in 9, steatosis hepatis (5–30%) in 9, history of alcohol and/or illicit drugs in 8, heterozygous factor V Leiden mutation in 4, s/p cholecystectomy in 4, and hypothyroidism in 4 cases, respectively. Postoperative surgical complications occurred in 24/40 (60%) patients. 15 were grade I (wound infections, pleural effusion, ileus), 3 grade II (venous thrombosis, duodenal ulcer), 5 grade III a (biliary leakage/stricture, hematoma), and 5 grade III b (incisional hernia repair). One donor died 57 days after surgery from illicit drug overdose. Preoperative risks correlated to some extent with postoperative complications: except two, all other 10 patients with wound infection and/or incisional hernia were overweight or obese. 1/4 donors with factor V Leiden mutation developed deep vein thrombosis, and one donor died from cocaine use known before surgery. All III a complications occurred in right lobe donors. On the other hand, only 2/6 patients without risk factors were free of complications, as compared to 14/34 patients with different risk factors before surgery who had no postoperative complication. Hepatic steatosis did not contribute to an increase of liver dysfunction after surgery. Ideally, living donors should be completely healthy without any significant preoperative risk. In our experience, 85% of liver donors that were accepted and went into surgery had at least one or more risk factors which may have contributed to postoperative complications to some degree. Except one, the outcome of our donors has been very good, obviously justifying our decision to move along. However, more caution seems to be advocated under certain psychosocial circumstances.

#### 147 LAPAROSCOPICALLY-ASSISTED RIGHT LOBE DONOR HEPATECTOMY: RESULTS AND COMPARISON WITH OPEN LOBE DONOR HEPATECTOMY

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**Objectives.** Recent technical innovations for laparoscopic hepatectomy have suggested its potential application to donation of the liver in living donor liver transplantation (LDLT). However, the technical nuances, efficacy and safety of such a laparoscopic procedure has yet to be assessed. We describe our technique and outcomes of laparoscopically assisted donor hepatectomy (LADH) for adult to adult LDLT.

**Methods.** Right lobe donor hepatectomy was performed on 20 donors through our laparoscopically assisted method. Surgical manipulation via 2 ports and a 5–7 cm subxiphoid incision was used, and parenchymal transection achieved using saline-enhanced electrocautery (TissueLink). Case-controlled contemporaneous living liver donors and recipients, who donated through the traditional open procedure, were selected as controls.

**Results.** Laparoscopic assisted right lobe donor hepatectomy was completed in 20 donors with a mean operative time of  $179.9 \pm 24.0$  minutes and a mean blood loss of  $270 \pm 130.4$  mL; Mean operative time and blood loss for open liver donors were  $307.8 \pm 64.8$  minutes and  $483.3 \pm 299.4$  mL. Open conversion was not required, we experienced no donor biliary complications in any laparoscopic patients, and laparoscopically-harvested grafts had comparable function. The length of post-operative hospital stays was  $2.2 \pm 0.8$  days and  $4.1 \pm 1.1$  days in the laparoscopic and open donors respectively. Currently, all donors and recipients are healthy and have returned to normal activities.

**Conclusion.** We have demonstrated a novel, less invasive method for live-donor hepatectomy. The procedure resulted in favorable donor outcomes and successful transplants in the recipients, suggesting its feasibility as an alternative to the traditional open donor hepatectomy.

**TABLE.** Comparison between lap-assisted and open procedures: Donors' Perioperative characteristics

Variable	Lap-Assisted (n=20)	Open (n=24)	P value
<b>Pre- and intraoperative variables</b>			
Male/Female	8/12	7/17	
Age (y, mean $\pm$ SD)	$31.9 \pm 6.5$	$38.4 \pm 11.4$	NS
BMI (mean $\pm$ SD)	$26.1 \pm 3.5$	$25.8 \pm 4.0$	NS
Operative time (min, mean $\pm$ SD)	$179 \pm 24.0$	$307.8 \pm 64.8$	NS
Blood loss (mL, mean $\pm$ SD)	$270 \pm 130.4$	$483.3 \pm 299.4$	NS
Graft Volume (mL, mean $\pm$ SD)	$948.1 \pm 156.4$	$1003.3 \pm 243.1$	NS
<b>Perioperative variables (peaks)</b>			
AST (UL <sup>-1</sup> , mean $\pm$ SD)	$295.1 \pm 66.3$	$288.84 \pm 116.3$	NS
ALT (UL <sup>-1</sup> , mean $\pm$ SD)	$290.6 \pm 77.9$	$236.84 \pm 125.8$	NS
Total Bilirubin (mg/dL, mean $\pm$ SD)	$2.6 \pm 1.1$	$3.2 \pm 1.9$	NS
AP (mean $\pm$ SD)	$103.7 \pm 37.3$	$168.3 \pm 148.9$	NS
Length of hospital stay (d, mean $\pm$ SD)	$2.2 \pm 0.8$	$4.1 \pm 1.1$	NS
Biliary Leaks	0	2	NS

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## VENOUS RECONSTRUCTION IN LIVING-DONOR HEPATECTOMY

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With wide spread experiences in living-donor liver transplantation, issues of venous outflow have been well recognized and are often discussed with regard to graft function especially using the right lobe. Preservation of the main middle hepatic vein (MHV) and its tributaries is crucial to avoid outflow blockage in the anterior sector of the right lobe. To date remnant liver function in the donor, however, has not been fully addressed assuming that the donor has adequate liver function and therefore can tolerate the procedure. In order to maintain remnant liver function and ensure donor safety, we have reconstructed hepatic veins or inferior vena cava (IVC) during donor hepatectomy when congestion of the remnant liver is of concern. The aim of this presentation is to describe our techniques for venous reconstruction in the donor. From May 2001 to August 2006, 94 adult-to-pediatric living-donor liver transplantations were successfully performed in our institution. Donor surgery consisted of 16 extended left lobectomies, 24 left lobectomies and 54 left lateral segmentectomies. Of these, venous reconstructions were performed in 22 donor hepatectomies including (1) direct anastomoses of MHV tributaries to IVC in 7 cases and (2) interposition grafts between MHV branches to IVC in 12 cases, and (3) venous patches over IVC or MHV in 8 cases. Reconstruction of MHV or its tributaries was indicated when intraoperative doppler ultrasonography disclosed regurgitated portal flow in the right anterior sector after clamping. Umbilical vein, ovarian vein or inferior mesenteric vein were used as autologous vein grafts. With reconstruction, antegrade portal flow as well as adequate hepatic venous flow were confirmed in all reconstructed cases. In conclusion, by reconstructing

hepatic veins or IVC, we have successfully maintained the remnant liver function of the living donor without compromising safety.

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## THE EFFECTS OF PHYSICAL QUALITY OF LIFE, TIME, AND GENDER ON CHANGE IN SYMPTOMS OF ANXIETY AND DEPRESSION AFTER LIVER TRANSPLANTATION

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**Introduction.** Previous research demonstrated that functional performance and health-related quality of life (HRQOL) improve following liver transplantation, but the extent to which improvement in symptoms of anxiety and depression is related to post-transplant physical HRQOL has not been characterized. The aim of this study was to test the effects of physical HRQOL, time post transplant, and gender on pre- to post-transplant change in symptoms of anxiety and depression.

**Methods.** Longitudinal HRQOL data were prospectively collected at specific times before and after liver transplantation using the SF-36<sup>®</sup> Health Survey (SF-36), Center for Epidemiologic Studies Depression Scale (CES-D), and Beck Anxiety Inventory (BAI). Within-subject change scores were computed to represent the longest follow-up for each patient. Multiple regression was used to test the effects of time post transplant, gender, and post-transplant SF-36 physical component summary (PCS) scores on change in BAI and CES-D scores. Baseline scores on outcome measures were modeled to account for and quantify their expected effects. A complementary model of change in PCS was also developed. Summary data are reported as mean  $\pm$  SD.

**Results.** 107 patients (74% male; 51% HCV+; age =  $54 \pm 8$  years) reported 474 survey points over 43 months. Time post-transplant ranged 1 to 39 months (mean =  $9 \pm 8$ ). Patients with the poorest pre-transplant HRQOL showed the greatest improvement on every model. Change in CES-D and PCS scores continued with time post transplant. Reduced post-transplant physical quality of life was associated with less improvement in symptoms of anxiety (model 1) and depression (model 2). This relationship is also reflected in model 3, which quantifies the negative effect of post-transplant anxiety on change in PCS. Gender did not affect these outcomes (table).

**Conclusions.** Despite improvement on all HRQOL measures, there was less improvement in symptoms of anxiety and depression in those patients with reduced physical HRQOL after liver transplantation. Awareness of the significant relationships between physical and mental quality of life indicators in both men and women suggests the importance of early recognition and intervention strategies to promote continued improvement in mental and physical quality of life following liver transplantation.

Multivariate models of pre- to post-transplant change ( $\Delta$ ) in mental and physical HRQOL

Effect/Parameter	(Model 1) $\Delta$ BAI	(Model 2) $\Delta$ CES-D	(Model 3) $\Delta$ PCS
Model outcome <sup>a</sup>	$-7 \pm 11$ **	$-9 \pm 12$ **	$8 \pm 11$ **
Baseline score	$-0.85$ **	$-0.63$ **	$-0.44$ **
Time post txp	$-0.02$	$0.22$ *	$0.26$ *
Gender	0.06	0.09	$-0.05$
Post-tpx PCS	$-0.24$ **	$-0.31$ **	
Post-tpx CES-D			$-0.04$
Post-tpx BAI			$-0.38$ *
Model R <sup>2</sup>	0.71 **	0.53 **	0.40 **

Unless noted entries are standardized regression coefficients. a = Mean change  $\pm$  SD. R<sup>2</sup> = squared multiple correlation coefficient. \* p < 0.05, \*\* p  $\leq$  0.001.

## Free Papers

### Liver I

#### FP-06

4/21/07 2:00–4:10 pm

Abstract Numbers 150–157

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## IMPACT OF LOCAL THERAPY FOR HEPATOCELLULAR CARCINOMA ON SURVIVAL OUTCOMES IN THE U.S. POPULATION

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**Background.** Hepatocellular cancer (HCC) frequently presents with clinical limitations to resection. We investigated survival outcomes after various local HCC therapies in U.S. patients.

**Methods.** A surgical HCC data set was created from the SEER 1970–2003 database. Prognostic factors with survival impact, and relationships between local therapy modality and overall survival (OS) were analyzed.

**Results.** Out of a cohort of 46,065 patients with primary hepatobiliary malignancy, 5,317 individuals with HCC were selected based on complete data. The median age was 62 (range: 0–97), and 68% of patients were male. The median tumor size was 5.2 cm (0.2–30). There were single lesions (52%), multiple lesions (28%), and extrahepatic disease (20%). A multivariate OS analysis yielded these prognostic variables: tumor size, extrahepatic disease extent, grade, gender, age, and local treatment modality (all at  $p < 0.0001$ ), stage (regional or distant disease,  $p = 0.0018$ ), race ( $p = 0.0033$ ), total LN count ( $p = 0.0064$ ), and year of diagnosis ( $p = 0.0087$ ). Compared to segmental/wedge resections, other modalities had the following risk ratios (95% CI): transplantation (LTX) 0.44 (0.38–0.51), anatomic resection 0.89 (0.81–0.97), ablation 1.13 (1.02–1.24), no or incomplete local therapy 2.5 (2.34–2.7). At a median follow up of 12 months (23 for survivors, range: 0–190), the 5-year OS (in %) was 67 for LTX, 38 for resections, 19 for ablation, and 3 for no local therapy ( $p < 0.0001$ ). Among ablation techniques, 5-year OS was 26% (RFA), 22% (cryo), 20% (PEL), 20% (fulguration, laser), or 0% (PDT). 30-day mortality (%) was 6.7 (resection), 3.4 (LTX), 3.0 (ablation), or 21 (no local therapy,  $p < 0.0001$ ). Cirrhosis and HCC differed as causes of death between ablation (6.6 and 70.4%), resection (2.9 and 68.7%), and LTX (7.0 and 37.2%,  $p < 0.0001$ ).

**Conclusions.** Aside from well-established prognostic parameters, the local treatment mode strongly influences HCC survival. Superior outcomes after transplantation and resection are likely biased through confounding patient selection variables, but both treatment options should be considered primary therapy choices in the therapeutic evaluation of HCC patients.

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#### A COMPARATIVE ANALYSIS OF SELECTIVE INTERNAL RADIATION THERAPY (SIRT) AND TRANSCATHETER ARTERIAL CHEMOEMBOLIZATION (TACE) IN TREATMENT OF UNRESECTABLE HEPATOCELLULAR CARCINOMA

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**Purpose.** Regional therapy of unresectable hepatocellular carcinoma (HCC) with transcatheter arterial chemoembolization (TACE) versus Selective Internal Radiation Therapy (SIRT) using SIR-Spheres (NSW, Australia) was evaluated for efficacy and complications.

**Methods.** A prospective database of SIRT patients (2003–present) was analyzed in comparison to a retrospective cohort treated with TACE (1990–present, mixed agents). All patients had liver-only HCC deemed unresectable by surgical consultation and received no other therapy. Chi square and Student's T tests were used to analyze categorical and continuous variables respectively. Univariate (UVA; log rank) and multivariate (MVA; Cox regression) were performed for survival.

**Result.** 73 patients were treated, of which, 47 (64.4%) received TACE and 26 (35.6%) had SIRT. Average ages were  $59.8 \pm 11.4$  vs.  $58.6 \pm 10.5$  ( $p = \text{NS}$ ), AFP scores were  $722 \pm 1005$  vs.  $680 \pm 937$  ( $p = \text{NS}$ ), and MELD scores were  $10.5 \pm 4.2$  vs.  $9.8 \pm 3.1$  ( $p = \text{NS}$ ) for TACE and SIRT patients respectively. VI was present in 12 (26%) TACE and 11 (42%) of SIRT patients ( $p = \text{NS}$ ). At a follow up of  $11.5 \pm 13.9$  months (survivors), mean survival was  $7.9 \pm 11.3$  (TACE) and  $6.9 \pm 7.7$  (SIRT,  $p = \text{NS}$ ). On MVA, including age  $> 60$ , VI positive, MELD  $> 10$ , AFP  $> 400$  and TACE vs. SIRT, only VI and AFP were independently associated with poor survival. Complications of therapy were noted in 19 (40%) of TACE and 10 (38%) of SIRT patients ( $p = \text{NS}$ ).

**Conclusion.** In this study population, TACE and SIRT provided similar survival and complication profiles. Both methods of regional therapy for unresectable HCC are appropriate, and the comparison merits prospective evaluation.

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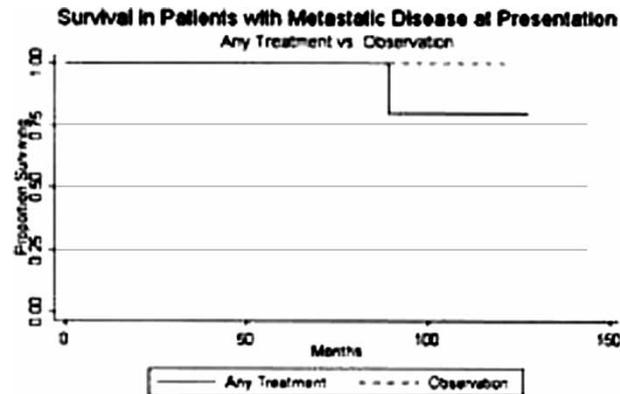
#### HEPATIC EPITHELIOID HEMANGIOENDOTHELIOMA: A MULTI-INSTITUTIONAL STUDY OF TREATMENT AND LONG TERM OUTCOME

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**Background.** Hepatic epithelioid hemangioendothelioma (HEHE) is a rare malignant neoplasm of vascular origin. The natural history is poorly understood, and treatment recommendations vary widely. HEHE may be an indolent disease for which disease evolution over time may better direct selection of treatments, including observation.

**Methods.** We performed a retrospective review of thirty-four (34) patients with HEHE who were identified from tumor registries (1989 to 2004) at two academic centers. Presentation, treatments and outcomes were analyzed.

**Results.** The median patient age was 42 years (range, 18 to 72 years); 22 (65%) were women and 12 (35%) were men. The most common presenting



symptoms were abdominal pain (50%), fatigue (18%), and weight loss (15%). Twenty-seven patients presented with diffuse liver disease with ( $n = 13$ ) or without metastatic disease ( $n = 14$ ); seven (7) patients presented with localized liver disease. Treatments included A: surgery (liver resection or transplantation, 44%), B: non-surgical treatment (systemic or liver-directed chemotherapy, embolization, or tumor injection, 32%) or C: observation (no treatment or COX-2 inhibitor, 24%). There was no treatment-related mortality for surgery or transplantation; 2 of 12 patients in group B died from complications of treatment. Survivals for Groups A, B and C (mean  $\pm$  SD) were  $168 \pm 307$ ,  $49 \pm 38$ , and  $180 \pm 422$  months, respectively (median follow-up, 52 months, median survival has not been reached). Among all patients, overall survival (OS) was not different after surgery vs. all other therapies ( $p = 0.13$ ) or treatment vs. observation ( $p = 0.95$ ). In the subgroup with diffuse liver disease, OS was similar whether patients were treated or observed ( $p = 0.93$ ). Survival was similar in patients with metastatic disease who were treated or observed ( $p = 0.53$ , figure).

**Conclusion.** Hepatic resection and transplantation are safe, effective treatments for HEHE. However, all treatment modalities, including observation, are associated with long-term survival. Therefore, selection for treatment must be highly individualized and a period of watchful waiting with delayed intervention might be considered for patients who present with asymptomatic HEHE.

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#### BENEFICIAL EFFECT OF ELASPOL (SIVELESTAT SODIUM HYDRATE) AFTER MAJOR HEPATECTOMY USING INTERMITTENT PRINGLE MANEUVER IN SWINE

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**Objective.** Ischemia-reperfusion (I/R) injury is widely accepted as a significant source of morbidity and mortality in the liver surgery. However, the mechanism of the I/R is still unclear and it is problem how to protect liver against I/R after major hepatectomy. We investigated the effect of selective neutrophil elastase inhibitor; Elaspol (ONO-5046) on hepatic I/R injury in a swine liver resection reperfusion model to evaluate its possible therapeutic effects on hepatic I/R injury.

**Methods.** Swines ( $n = 12$ ) were divided into two groups (Elaspol group: Group I and saline group: Group II). A left hemihepatectomy was performed using IPM (cycles of 15-min ischemia and 5-min reperfusion) in all swines. In the group I, Elaspol was injected intravenously during operation (10 mg/kg/hr), in group II, same dose of saline was also injected during operation. Hemodynamic change and plasma concentrations of aspartate aminotransferase (AST), lactate dehydrogenase (LDH), lactic acid (LA) and hyaluronic acid (HA) were measured at each observation period (60, 120, 180 minutes). Apoptotic findings (TUNEL staining and electron microscope), plasma tumor necrosis factor-alpha (TNF-alpha) and NO<sub>2</sub>-/NO<sub>3</sub>- were evaluated after hepatectomy for 180 min. We evaluated effect of Elaspol on nitrite production in LPS and INF $\gamma$  stimulated in J774 cells.

**Results.** There were no significant differences in the body weight, blood loss, resected liver weight, Pringle time and hemodynamic change between the two groups. In Group I plasma NO<sub>2</sub>-/NO<sub>3</sub>- levels, AST and TNF-alpha levels were significantly reduced after hepatectomy for 180 min (AST;  $114.6 \pm 30.1$  vs  $223.8 \pm 54.6$  (IU/l);  $P = 0.0045$ , NO<sub>x</sub>;  $9.0 \pm 3.5$  vs  $27.8 \pm 11.9$  ( $\mu\text{mol/l}$ );  $P = 0.0098$ , TNF-alpha;  $257.4 \pm 181.3$  vs  $830.8 \pm 496.5$  (pg/ml);  $P = 0.041$ ). Apoptotic cells were significantly fewer in the group I than in the groups II. Elaspol caused significant reductions of nitrate in vitro.

**Conclusions.** Intermittent Pringle maneuver with Elaspol resulted in less hepatic injury and apoptotic cell death, compared with control. Elaspol with intermittent hepatic pedicle clamping has a possibility to reduce I/R in clinical settings.

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**EVALUATION OF AN AUTOLOGOUS FIBRIN SEALANT IN PATIENTS UNDERGOING LIVER RESECTIONS: A MULTICENTER RANDOMIZED CLINICAL TRIAL**

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**Introduction.** The CryoSeal® FS System consists of a medical device (the CS-1 instrument) and a proprietary plasma processing disposable that work in concert to rapidly (approximately 60 minutes) prepare both components of a fibrin sealant (FS), (cryoprecipitate and thrombin), from a single unit of autologous blood. Existing fibrin sealants are derived from pooled human plasma with bovine additives. Use of such sealants carries recognized risks of viral contamination, e.g. HBV and HIV, and of immunological reaction to bovine products. Alternatively, sealants generated from the CryoSeal® FS System using autologous blood do not carry the same concerns. The primary objective of this study was to investigate the safety and efficacy of the fibrin sealant prepared by the CryoSeal® FS System, in terminating bleeding of the raw liver resection margin following hepatectomy.

**Materials and methods.** The study compared the use of fibrin sealant produced by the CryoSeal® System versus a currently approved adjunct to hemostasis, a collagen absorbable hemostat (Instat, Ethicon, Inc.). The trial reported here was a randomized clinical study in 153 patients undergoing elective hepatectomy, and enrolled at 10 study sites. The primary efficacy endpoint was the time to hemostasis (time between application of the study product and when hemostasis was obtained). Secondary endpoints included: success rate of achieving hemostasis within 10 minutes of application of the product, intraoperative blood loss, use of blood products, and adverse events. Safety evaluation included a 30-day ( $\pm 3$  days) follow-up post surgery.

**Results.** The median time to reach hemostasis was 3.43 minutes in the FS group compared to 8.65 minutes in the control group. Percentage of patients that achieved hemostasis within 10 minutes was 94.0% for the FS group and 60.4% for the control group. This difference was statistically significant ( $p < 0.001$ ) and satisfied the non-inferiority criterion. The FS also satisfied the superiority criterion ( $p < 0.001$ ). The groups were not different in regards to operative blood loss, operative time, postoperative hospital stay or complications.

**Conclusions.** The results of this trial demonstrate that the autologous Fibrin Sealant produced by the CryoSeal® FS System is safe, effective, well tolerated, and superior to the collagen absorbable standard of care in this patient population and indication.

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**GUIDELINES FOR POWER AND TIME VARIABLES FOR MICROWAVE ABLATION IN A PORCINE LIVER**

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Microwave ablation is an emerging thermal ablation technique for primary and metastatic liver tumors. The purpose of our study was to evaluate two variables, power and time, and their influence on diameter in microwave ablations in a porcine liver. We propose guidelines and recommend optimal time and power variables for use. Microwave ablations using a 3.7 cm active tip antenna and VivaWave™ Microwave Ablation System (Valleylab, Boulder, Co, USA) were performed in-vivo in a porcine liver. Independent variables were power (20,30,40,45,50,60 watts) and time (2,4,6,8,10,15,20 minutes). The outcome variable was diameter of ablations measured in millimeters. Ten ablations were performed for each power and time period. Livers were procured following ablations and the ablation zones were measured. Representative samples were sectioned and examined for histology, nicotinamide adenine dinucleotide (NADH) and hematoxylin and eosin (H&E) staining. Based on NADH staining, inner ablation diameter was used representing the minimum ablation diameter correlating with uniform cell death by coagulation necrosis. Analyses of Variance (ANOVA) was performed followed by Tukey tests when appropriate. A p-value of  $< 0.05$  was considered statistically significant. Our study consisted of 420 total ablations. The outcome variable, ablation diameter, was affected significantly by time, power, and time/power interaction ( $p < 0.0001$ ). For each time point, a 1-way ANOVA revealed an overall significant difference in ablation size X wattage ( $p < 0.0001$ ). Tukey tests revealed that at each time point, ablation sizes at 45, 50, and 60 watts were not significantly different. Once it was determined that 45 watts was optimal, a 1-way ANOVA was performed and revealed an overall significant difference in ablation sizes for time points at 45 watts ( $p < 0.0001$ ). Tukey tests revealed that at 45 watts, ablation sizes at 10, 15, and 20 minutes were not statistically different. Our study shows that time, power, and time/power interaction have a significant effect on diameter in microwave ablations. We propose guidelines for diameters based on different time and power variables and recommend usage at 45 watts for 10 minutes to achieve optimal diameters at the shortest time period and lowest wattage.

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**RIGHT HEPATIC TRISECTIONECTOMY – ANALYSIS OF A SINGLE CENTRE EXPERIENCE OF TWO HUNDRED AND SEVENTY FIVE CASES**

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**Objective.** To assess the use of right trisectionectomy for treatment of malignant and benign hepatic disease in a single centre. Summary Background Data: Right trisectionectomy is considered one of the most aggressive liver resections and is traditionally associated with poor outcome. No large studies exist which assess the long term outcome of this type of resection. This study therefore represents the largest study worldwide and provides the longest follow up for patients undergoing such resections.

**Methods.** Retrospective analysis of a prospectively gathered dataset. Patient population included 275 patients.

**Results.** Of the 275 patients, 14 had resections prior to auxiliary liver transplantation and were excluded. 91% of patients had resections for malignant disease. One, three, five and ten year survivals were 74%, 54%, 43% and 36% respectively. Overall morbidity was 41%, and post operative mortality was 8%. Survivals for individual tumour types were acceptable, with 5 year survivals for colorectal metastasis and cholangiocarcinoma (the most common malignancies) being 38% and 32% respectively. Multivariate analysis disclosed the amount of intraoperative blood transfusion to be the sole independent predictor for the development of morbidity. Age, pre-operative bilirubin levels and the development of post operative renal failure were found to be independent predictors of long term survival.

**Conclusion.** Right trisectionectomy can safely be used in patients with aggressive malignant liver disease and provides good long term survival in such patients. Caution must be taken when considering patients above 70 years of age for such resections.

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**RIGHT PORTAL VEIN LIGATION IS AS EFFICIENT AS PORTAL VEIN EMBOLIZATION TO INDUCE HYPERTROPHY OF THE LEFT LIVER REMNANT**

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**Background and Aim.** Right Portal Vein (PV) obstruction induces hypertrophy of the future left liver remnant. Right Portal Vein Ligation (PVL), which is supposed to result in an incomplete and transient occlusion, has been considered to be less efficient than right Portal Vein Embolization (PVE) before a right hepatectomy. The aim of this study was to compare PVL and PVE before right hepatectomy in terms of efficacy for induction of left liver hypertrophy.

**Methods.** Between 1998 and 2003, 35 patients with liver metastases underwent a right portal branch obstruction before "high risk" right hepatectomy because of a future remnant liver volume less than 30% of the total liver volume or because of a postchemotherapy liver parenchyma. PVE was performed percutaneously in 18 patients, while 17 patients underwent a PVL during a first stage laparotomy for resection of the primary tumor ( $n = 10$ ) and/or resection of left liver metastases ( $n = 6$ ).

**Results.** Right portal vein occlusion was complete in all the cases in both groups except for one patient in group PVE. Interval time between portal vein occlusion and liver resection was similar in both groups ( $7 \pm 3$  weeks after PVE vs.  $8 \pm 3$  weeks after PVL,  $p = 0.6$ ) There was no complication following PVE and postoperative hospital stay was  $2 \pm 1$  days. In group PVL, 6 patients had postoperative complications which were related to primary tumor resection and postoperative hospital stay was  $13 \pm 6$  days. The left liver volume increased from  $509 \pm 222$  ml to  $641 \pm 220$  ml after PVE ( $p < 0.001$ ), and from  $477 \pm 179$  ml to  $638 \pm 192$  ml after PVL ( $p < 0.001$ ). After PV occlusion, the increase of the left liver volume was not significantly different between the two groups ( $35 \pm 38\%$  after PVE vs.  $38 \pm 26\%$  after PVL,  $p = 0.7$ ). After PVE, 6 patients were not eligible for right hepatectomy because of insufficient hypertrophy of the left liver ( $n = 2$ ) or tumor progression ( $n = 4$ ). After PVL, 3 patients were not eligible for resection because of tumor progression ( $n = 2$ ) or death ( $n = 1$ ). Prior to resection, CT-scan showed a portal cavernoma in 3 patients of each group. Technical difficulties during surgical procedure were similar in both groups according to duration of procedure ( $6.4 \pm 1$  hours vs.  $6.7 \pm 1$  hours,  $p = 0.7$ ) and transfusion rates ( $33\%$  vs.  $28\%$ ,  $p = 0.7$ ) after PVE and PVL, respectively. Pathologic examination showed an amount of tumor necrosis of  $47 \pm 29\%$  in group PVE and  $43 \pm 43\%$  in group PVL ( $p = 0.6$ ).

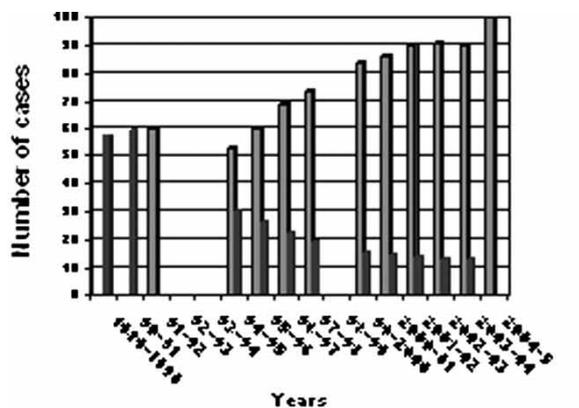
**Conclusion.** Right PVL and PVE result in a comparable hypertrophy of the left liver. During the first laparotomy of a two-step liver resection, PVL can be efficiently and safely performed.

**Free Papers****Education / Outcomes****FP-07****4/21/07 2:00–4:10 pm****Abstract Numbers 158–167**

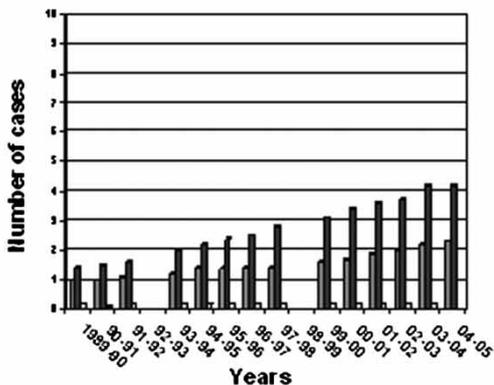
**THE CHALLENGES OF RESIDENT TRAINING IN COMPLEX HEPATIC, PANCREATIC, AND BILIARY PROCEDURES**

Thomas S Helling, MD, Anjay K Khandelwal, MD  
Conemaugh Memorial Medical Center, Johnstown, PA

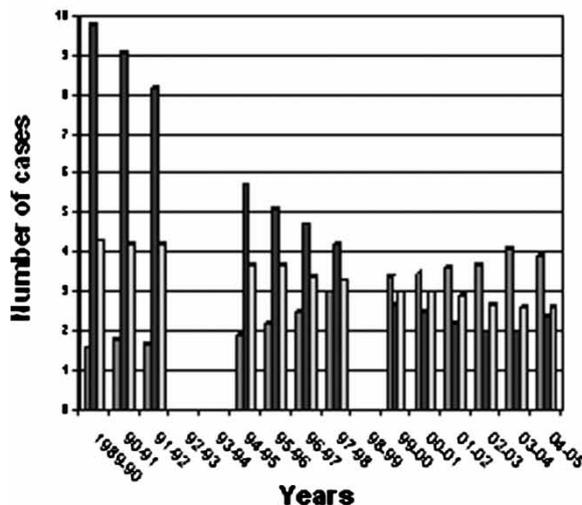
Operations on the liver and pancreas have fallen within the domain of the general surgeon and have been part of general surgery training. The more



Legend: ■ Laparoscopic Cholecystectomy, ■ Open Cholecystectomy



Legend: ■ Distal Pancreatectomy, ■ Total Pancreatectomy, ■ Pancreaticoduodenectomy



Legend: ■ Lobectomy or Segmentectomy, ■ CBDE (open), □ Choledochocenteric Anastomosis

complex procedures involving these structures are limited in number in most general surgery residencies and do not afford an opportunity for vast experience. Moreover, fellowship programs in hepato-bilio-pancreatic (HPB) surgery, and the development of laparoscopic techniques have further limited the familiarity of general surgery residents with these areas. It was our hypothesis that the majority of training programs offers few complex HPB procedures as training opportunities. We accessed, through the Residency Review Committee of the Accreditation Council for Graduate Medical Education, the National Resident Report of operative logs submitted by general surgery residents at the completion of their training. The number of operations on the gallbladder, bile ducts, pancreas and liver were examined over the past 16 years (there were missing data for 3 years). Results were expressed as mean  $\pm$ SD and mode. From 252-279 programs participated. The results for cholecystectomy (laparoscopic and open), pancreatectomy (whipple and distal), major liver resection, and common bile duct exploration (CBDE) (open) are depicted. While the exposure to laparoscopic cholecystectomy seems robust, experience with other hepatic, biliary, and pancreatic surgery, even open cholecystectomy, is meager. For liver resection, the range was  $(SD) \pm 2-4$ . For pancreas resection the range was  $(SD) \pm 1-4$ . The mean mode (most frequently performed number) for liver resection was 0.5 (either 0 or 1), for pancreatic resections, less than 1.0 (either 0 or 1). Most residents perform only 2-4 of these cases during their general surgery residency. CBDE, as a means of providing familiarity with the extra-hepatic biliary tree, has steadily decreased in favor of other methods to treat choledocholithiasis. It is doubtful this experience in HPB surgery engenders confidence in finishing residents. Although there is pressure to develop centers of excellence in HPB surgery, attention should be focused on augmenting training in HPB surgery for general surgery residents perhaps through a combination of programmatic initiatives, *ex vivo* experiences, and mini-fellowships.

**159 UMBILICAL HERNIA REPAIR IN THE PRESENCE OF CIRRHOSIS AND ASCITES: RESULTS OF A SURVEY AND A REVIEW OF THE LITERATURE**

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**Introduction.** Umbilical hernias are common in cirrhotics, yet their management poses several challenges. The purpose of this study was to extensively review the available literature, plus conduct a survey to gather additional consensus evidence from experts in the field.

**Methods.** An extensive review of the literature since 1980 was performed. In addition, a survey was electronically distributed to 40 Canadian surgeons with a special interest in HPB.

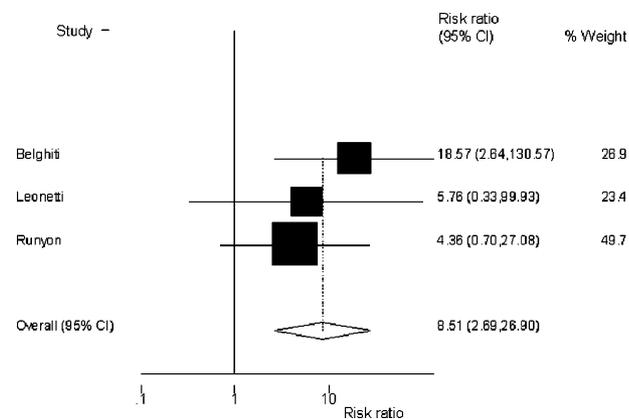
**Results.** 19 surgeons (45%) responded. Table 1 shows the scenarios where the respondents felt surgery was indicated. For asymptomatic hernias, all would operate in Child's A cirrhosis, but not in more advanced disease. These results seem to reflect the respondents' higher estimates of morbidity and mortality with more advanced liver disease. Their averaged estimates of mortality were 3.8%, 13.2% and 28.9% for class A, B, and C cirrhosis, respectively. However, recent literature demonstrates much lower morbidity and mortality than in the past. Of 135 patients reported in the literature since 1980, there were only 4 operative mortalities (2.7%) and the morbidity averaged 21%. Many now recommend early elective repair. Half of respondents would use prosthetic mesh, even in emergent situations with Child's B or C cirrhosis. The results of the 3 studies identified that examined the influence of uncontrolled ascites on hernia recurrence rates show that failure to control ascites appears to be strongly predictive of hernia recurrence (RR 8.5; 95% CI 2.7 to 26.9) (see Figure 1). This is consistent with the survey results where 69% of respondents would add a concomitant surgical procedure to control ascites, with most opting for a peritoneal drain until adequate healing is judged to have occurred.

**Conclusions.** Mortality and morbidity are much less than historically reported, and consideration should be given to early repair. The presence of ascites influences recurrence rates. Concomitant surgical procedures to control ascites should be considered when medical treatment is not enough.

Proportion of respondents offering repair of umbilical hernia according to different scenarios

	Child's A*	Child's B*	Child's C*	Respondent Total
Asymptomatic Hernia	100% (8)	0% (0)	0% (0)	8
Incarcerated Hernia	79% (11)	86% (12)	86% (12)	14
Ruptured Hernia (leaking ascites)	88% (14)	88% (14)	94% (15)	16
Impending Rupture (e.g. skin breakdown)	88% (14)	88% (14)	69% (11)	16
Total Respondents				16

\* Values represent percentage of respondents, with number of respondents in brackets.

**Figure 1.** Meta-analysis for influence of uncontrolled ascites on hernia recurrence rates.

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**SURGICAL TREATMENT OF PRIMARY HEPATIC MALIGNANCY IN THE UNITED STATES**

Joshua S Hill, MD, James T. McPhee, MD, Giles F. Whalen, MD, Mary E Sullivan, MS, Frederick A Anderson, PhD, Jennifer F Tseng, MD  
University of Massachusetts, Worcester, MA

**Introduction.** Over the past decades, the morbidity and mortality of hepatic resection has decreased. The purpose of the current study was to determine whether hepatic operations for primary liver cancer are increasing, and determine the underlying causal factors for any observed change.

**Methods.** All patient-discharges with a diagnosis of primary hepatic malignancy (ICD-9 code 155.0) were identified from the Nationwide Inpatient Sample (NIS 1998–2004). Surgical procedures were categorized as either enucleation/ablation of lesions, partial hepatectomy, or total hepatectomy/transplantation. Categorical data were analyzed by Chi Square tests. Mortality was examined using logistic regression with adjustments for patient demographics and comorbidities.

**Results.** 77,033 patients were identified with a discharge diagnosis of primary hepatic cancer. Between 1998 and 2004, there was a yearly increase in the number of patients with hepatic malignancy (6,861 to 15,556,  $P < 0.0001$ ). 11,337 patients underwent operative therapy with an increase in yearly volume (796 to 2,668). 34.4% of operative patients were female; 56.7% were white. Mean age was 61.9 years. Enucleation and/or ablation were performed in 36.6%, wedge resection in 30.9%, lobectomy in 31.0% and total hepatectomy/transplant in 1.5%; respective mortality rates were 4.0%, 6.2%, 10.6% and 14.5%. Over 7-years, the percentage of patients undergoing enucleation/ablation increased 10-fold, wedge resection and lobectomy both increased moderately and transplantation rates remained stable ( $P < 0.0001$  for trend). In-hospital mortality was 6.9% for operative cases. Hospital operative volume, liver and renal failure were inversely correlated with mortality (all univariate analyses  $P < 0.05$ ). An increasing percentage of patients were treated at high-volume centers in 2003–2004 versus 1998, which was associated with a concurrent trend toward reduction in national mortality.

**Conclusions.** Using the NIS 1998–2004, we have demonstrated that admissions for primary hepatic cancers are increasing, and that operations for these malignancies are increasing at an even faster rate. The cause of this increase in operative treatment is likely multi-factorial. An important factor may be the emergence of less-invasive techniques such as enucleation and ablation, which is supported by our data showing that these increased 10-fold. The overall mortality in patients undergoing surgery was 6.9%, which compares favorably to historic reports. As perioperative mortality continues to improve, an increasing number of patients with primary hepatic cancer may be referred for and benefit from operative treatment.

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**A SYSTEMATIC REVIEW ON THE EFFICACY OF REPEAT HEPATECTOMY FOR RECURRENT LIVER METASTASES FROM COLORECTAL CARCINOMA**

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**Background.** Despite the lack of level 1 evidence, hepatectomy has been considered the standard of care for liver metastases from colorectal carcinoma. Liver recurrence after hepatectomy is common and associated with a reduced survival if not treated aggressively. Many treatment centers advocate the use of repeat hepatectomy and have claimed that not only is it safe, but also it has similar survival results to initial hepatectomy. The purposes of this study were to critically appraise the quantity and quality of current clinical evidence and demonstrate the efficacy of repeat hepatectomy for colorectal liver metastases (CRLM).

**Methods.** Electronic literature searches in six databases were performed to identify all published peer-review medical articles on repeat hepatectomy for CRLM. The reference lists of all retrieved articles were manually reviewed for further identification of potentially relevant studies. Original studies using repeat hepatectomy for recurrent CRLM with a curative intent were searched for inclusion. All studies selected were human trials, published in English language. The two investigators then independently appraised each included article, using the recommended guidelines from the National Health Service Center for Reviews and Dissemination case series quality assessment criteria. Clinical effectiveness was synthesized through a narrative review with full tabulation of results of all included studies.

**Results.** Thirty-six original studies were identified allowing 1261 patients to be included. All studies were classified as observational studies without control groups (level 4 evidence). Seventeen studies had more than 20 patients, including 4 relatively large series ( $n > 100$ ). Their median follow-up since repeat hepatectomy ranged from 19 to 59 months. Their median survival after repeat hepatectomy ranged from 23 to 56 months, with 1-, 2-, 3- and 5-year survival rates vary from 77–100%, 37–89%, 27–68% and 13–49%, respectively. The disease-free interval after repeat hepatectomy was 19 to 35 months. The perioperative morbidity ranges from 11–30% and mortality varies from 0–5%. Intra-abdominal abscess and bile leak rates were 0–23% and 1–10%, respectively. The mean blood loss ranged from 450 to 928 cc. The median hospital stay varied from 8 to 26 days.

**Conclusions.** Repeat hepatectomy achieves similar survival results to that after initial hepatectomy. It is associated with moderate morbidity and mortality in the reported series. Although the level of evidence is low, the current literature suggests that repeat hepatectomy is efficacious in treating selected patients with liver recurrence from colorectal carcinoma.

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**FACTORS INFLUENCING PERIOPERATIVE BLOOD TRANSFUSIONS IN PATIENTS UNDERGOING MAJOR HPB PROCEDURES**

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**Background.** Patients undergoing major HPB resections are at risk for blood loss and transfusion (TF) requirements. Boosting preoperative hemoglobin levels with synthetic erythropoietin (EPO) offers the rationale to reduce TF needs and TF related morbidity. To assess such feasibility, we critically reviewed TF utilization in a HPB practice experience.

**Methods.** Information of perioperative PRBC TFs was collected prospectively over a 5-year period in a single surgeon academic practice. Outcome measures of interest were TF needs, amount of PRBC units required, postoperative morbidity, and length of stay (LOS). Perioperative clinical and laboratory parameters were tested for TF impact.

**Results.** Out of 344 patients who underwent a major operation, 231 were HPB procedures (67%). The median age was 63 (range: 26–88), and 55% were female. HPB cases included pancreatic ( $n = 130$ , 56%), hepatobiliary ( $n = 89$ , 39%), and other combined operations with a HPB component ( $n = 12$ , 5%). Median estimated blood loss (EBL, in cc) was 400 (pancreatic: 400, hepatobiliary: 400, other: 375,  $p = \text{NS}$ ). PRBC TFs were given in 50 cases (22%), at a median of 2 units (1–16). TF frequency was 23% for pancreatic, 16% for hepatobiliary, and 50% for other resections ( $p = 0.02$ ). Preoperative TFs were given to 5 patients (10% of all TFs), and 11 individuals received blood postoperatively (22% of TFs). Significant univariate TF associations were found for ASA class, gender, emergency cases, palliative intent, procedure type, R category, blood loss, OR length, and the following preoperative serum laboratory parameters: Hgb, WBC, albumin, calcium, Na, CO<sub>2</sub>, Cr, and INR. Significant TF associations on multivariate analysis were only demonstrated for Hgb ( $p < 0.0001$ , OR 0.37, 95% CI 0.26–0.52) and intraoperative EBL ( $p < 0.0001$ , OR 1.004, CI 1.003–1.006). TFs (versus no TFs) were significantly linked to major complications (28 vs. 13%,  $p = 0.01$ ) and increased LOS (median 9 vs. 7 days,  $p = 0.0003$ ), but not lethal events (6% vs. 2.2%,  $p = \text{NS}$ ). A potential benefit for preoperative EPO to realistically avoid TFs (nonemergent case, Hgb  $< 12$ , no preoperative TF need,  $< 4$  PRBCs given) could be derived for only 30 patients (13% of the 231 major operations, or 12% of all patients for whom a major procedure had been planned preoperatively).

**Conclusions.** The results show the relatively low TF rate of 22% for patients who undergo major HPB resections. Aside from preoperative blood counts, few parameters are able to identify subgroups at high risk for TFs. The data from this experience would not support routine preoperative EPO administration to reduce perioperative TF need, as the cohort with predictable EPO benefit would only comprise 12% of patients potentially at risk.

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**MORBIDITY, MORTALITY AND RISK FACTORS IN DISTAL AND SUBTOTAL PANCREATIC RESECTIONS FOR PANCREATIC NEOPLASIA: AN ANALYSIS OF THE NATIONAL SURGICAL QUALITY IMPROVEMENT PROGRAM**

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**Background.** Distal and subtotal pancreatic resections are technically challenging surgical procedures. Outcomes for this procedure have been limited to small, single institution series. This study aims to describe the

30-day morbidity and mortality and to define risk factors utilizing multi-institutional data.

**Methods.** The National Surgical Quality Improvement Program prospectively collected data for distal and subtotal pancreatectomy (CPT 48140) during fiscal years 2002–2004 using trained nurse reviewers and standardized event definitions. Patients were included for review if ICD9 codes indicated pancreatic neoplasia. Demographics, pre-operative medical conditions and laboratory data, intra-operative variables and outcomes were reviewed. Stepwise logistic regression was used to construct models predictive of 30-day post-operative morbidity and mortality.

**Results.** Patients were gathered from 43 Veterans Affairs Medical Centers and 14 private sector hospitals. 227 patients were identified with a mean age of 60 years and male preponderance (56%). Major contributing comorbidities were: smoking (23%), alcohol use (4%), diabetes (18%), pulmonary disease (10% dyspnea and 7% COPD), weight loss (11%) and disseminated cancer (7%). Neoadjuvant therapy was given to 2.6% of patients. Common laboratory abnormalities included decreased hematocrit and albumin and elevated alkaline phosphatase, SGOT, and creatinine. Wounds were classified as clean in 39% and clean contaminated in 61%. Mean operative time was 4 hours and on average less than 1 unit of blood (0.6±1.6) was transfused. 3.5% of patients returned to the operating room for complications. The mean post-operative length of stay was 11.2±7.3 days. 30-day morbidity was 21% overall. Most complications were respiratory events (8%) with pneumonia (4%) and failure to wean from the ventilator (2%) being most prevalent. Urinary tract (7%) and wound (6%) infections were also common. No independent variables were identified as statistically significant predictors of 30-day morbidity in the logistic regression analysis because the c index was 0.56. 30-day mortality rate was 1.3% (3 of 227).

**Conclusion.** Distal and subtotal pancreatic resections are associated with a high rate of morbidity and low mortality. While medical co-morbidities are common, no specific factor can be identified that is predictive of patient morbidity and mortality. Improved strategies to prevent wound, urinary, and pulmonary infection would be useful in this population.

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POPULATION BASED STUDY OF MANAGEMENT OF PANCREATIC ADENOCARCINOMA**

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The majority of pancreatic adenocarcinoma (PA) is metastatic at presentation with survival of less than six months. Due to this short mean survival after diagnosis, enrolling PA patients in prospective population-based epidemiological studies is a challenge. To help overcome this obstacle, the Pathology

academic center, 24% (23) had positive margins (non-academic vs academic p=NS). Medical records review revealed that 41% of resected patients received adjuvant chemotherapy. Only 8% of all responders participated in clinical trials. In conclusion, our study utilizes novel methodology to provide a prospective snapshot of PA across the province. Despite the use of PIMS and e-Path, response rates remained low (<40%). Not surprisingly, nonresponders were older, had more advanced disease, and more commonly received care in non-academic centers. Responders, however, provide an excellent resource to answer specific clinical research questions. In addition, e-Path provides higher quality data for studies related to surgical management since pathology reports are complete and available for all eligible subjects. The use of adjuvant therapy and the rate of participation in clinical trials seems disappointingly low.

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FREQUENCY WITH WHICH SURGEONS UNDERTAKE PANCREATICODUODENECTOMY CONTINUES TO DETERMINE LENGTH OF STAY, HOSPITAL CHARGES, AND IN-HOSPITAL MORTALITY**

Alexander Rosemurgy, MD, Sarah M Cowgill, MD, Brian Coe, Sam Alsaadi, MD, Ashley Thomas, Jennifer Cooper, Sharona Ross, MD, Steven Goldin, MD, PhD, Emmanuel Zervos, MD  
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**Introduction.** Numerous studies purport that complex operations are best undertaken by “high volume” surgeons. It is unknown how these studies have impacted delivery of care. This study was undertaken to determine changes in the number of, frequency with which surgeons undertake, and outcomes after pancreaticoduodenectomy (PD) in Florida 8 years after a study denoted that in Florida the frequency with which surgeons undertake PD impacted outcome.

**Methods.** Using the State of Florida Agency for Health Care Administration database, we correlated the frequency with which surgeons undertake PD with average length of hospital stay (ALOS), in-hospital mortality, and hospital charges for identical 33 month periods in 1995–1997 and 2003–2005.

**Results.** Compared to 1995–1997, 88% more PD were undertaken in 2003–2005 by 6% fewer surgeons (Table). In 1995–1997 and 2003–2005, the majority of PD were undertaken by surgeons doing less than one PD every 2 months (76% of PD in 1995–1997 and 52% of PD in 2003–2005). From 1995–1997 to 2003–2005 ALOS decreased. Conversely, from 1995–1997 to 2003–2005 in-hospital mortality rate did not decrease (Table); in-hospital mortality rate significantly increased for surgeons undertaking less than one PD every 2 months (p=0.03). For 2003–2005, frequency with which PD was undertaken inversely correlated with ALOS (p=0.01) (Table), hospital charges (p=0.003), and in-hospital mortality (p<0.0001) (Table).

Pancreaticoduodenectomies (PD) in Florida over 33 mo. in 1995–1997 and 2003–2005 stratified by no. of PD per surgeon

# PD per surgeon over 33 months	Period	# Surgeons	#PD over 33 months	ALOS (days)	In-hospital mortality (%)
1–3	1995–1997	251	365	23	5.5
(≤1 PD every 12 months)	2003–2005	192	284	18	12.3*
4–9	1995–1997	21	111	20	9.9
(≤1 PD every 4 months)	2003–2005	50	287	16	7.3
10–16	1995–1997	4	52	18	0
(≤1 PD every 2 months)	2003–2005	9	113	15	7.1
≥17	1995–1997	6	170	17	2.6
(≥1 PD every 2 months)	2003–2005	15	630	15	2.2
TOTAL	1995–1997	282	698	21	5.1
	2003–2005	266	1,314	16	5.9

\*Significantly greater than in 1995–1997, p<0.01, chi-square test.

Information Management System (PIMS), relying upon electronic pathology reporting (E-path), was installed in all labs in the province of Ontario, Canada, to provide rapid case ascertainment based on pathologic diagnosis. The purpose of this study is to use our prospective, population-based registry of PA to describe the management of PA in the province of Ontario. Of 852 eligible patients contacted based on pathological diagnosis of PA from 2003 to 2006, 35% (301) enrolled in the study, 24% (203) were deceased at first contact, 27% (232) refused participation and 14% (116) are being worked up or were lost to follow-up. Medical records were obtained for all responders. Non-responders were older (67 vs. 64 yrs, p<0.001), more likely to have received treatment in non-academic centers (53% vs. 35%, p<0.0001) and were less likely to have undergone any operative management of their disease in compared to responders (21% vs. 43%, p<0.0001). Of the responders, the frequency of potentially curative resection was greater in patients less than 70 years of age (46% vs. 35%, p<0.0001). Of those undergoing any potentially curative operation, (n=148), 87% (129) had successful resectional surgery while 13% (19) were found to have unresectable and/or metastatic disease and resection was aborted. Within the curative resection group, 26% (34) were conducted in non-academic centers of whom 32% (11) had positive margins. Of the 74% (95) resections performed in an

**Conclusions.** More pancreaticoduodenectomies (PD) are now undertaken in Florida by fewer surgeons with a shorter ALOS. In-hospital mortality remains high due to surgeons infrequently undertaking PD. Lowest costs and mortality with PD are seen with surgeons frequently undertaking PD. While numerous studies purport that complex operations are best undertaken by “high volume” surgeons, most PD in Florida are still undertaken by surgeons who undertake PD infrequently with ensuing greater lengths of stay, hospital costs, and in-hospital mortality rates. Because of increased in-hospital mortality from 1995–1997 to 2003–2005, patients needing PD, to an even greater extent than previously demonstrated, are best served by surgeons frequently undertaking the procedure.

Pancreaticoduodenectomies (PD) in Florida over 33 mo in 1995–1997 and 2003–2005 stratified by number of PD per surgeon.

**166  
IMPORTANCE OF LYMPH NODE SAMPLING IN STAGING OF PERIAMPULLARY MALIGNANCIES**

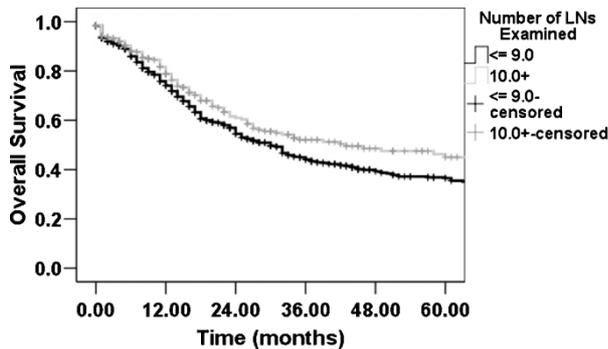
Juan C Gutierrez, MD, Alan S Livingstone, MD, Leonidas G Koniaris, MD  
University of Miami Miller School of Medicine, Miami, FL

**Objective.** To determine the impact of lymphadenectomy in prognosis and staging in pancreaticoduodenectomy for pancreatic, distal bile duct, duodenal or ampullary malignancies.

**Methods.** All pancreaticoduodenectomies for periampullary carcinomas from the SEER cancer registry were examined from 1993 through 2003.

**Results.** Overall, 6330 pancreaticoduodenectomies for non-metastatic periampullary carcinomas were identified. The cohort was comprised of 60.6% pancreatic, 18.7% ampullary, 13.2% distal bile duct and 7.5% duodenal cancers. A linear association between the number of lymph nodes (LNs) examined and overall survival was observed overall and for pancreas and distal bile duct cancers for node negative (N0) disease only. A trend towards improved survival was observed for ampullary and duodenal lesions. Median survival for all patients with localized, N0 disease improved from 30 months to 43 months with sampling of a minimum of 10 LNs, while two and five-year survival improved from 54.5% and 36.5% with <10 nodes examined to 61.0% and 45.0% with 10+ nodes examined ( $P=0.026$ ; see figure). Two and five-year survival in N0 pancreatic malignancies improved from 43.1% and 20.4% with <10 nodes examined to 49.5% and 33.5% with 10+ nodes examined ( $P=0.037$ ). A similar benefit was seen in N0 distal bile duct lesions where two and five-year survival rose from 53.8% and 32.6% with <10 nodes examined to 90.9% and 43.6% with 10+ nodes examined ( $P=0.042$ ). No significant improvement was observed in the setting of N1 disease.

**Conclusions.** Significantly better median survival and cure rates are observed following pancreaticoduodenectomy for localized periampullary adenocarcinoma when a minimum of 10 lymph nodes are examined. This benefit likely represents more accurate staging. No benefit is observed with increasing lymphadenectomy in the setting of node positive disease. In order to optimize the prognostic accuracy for individual patients and prevent staging errors in multicenter trials a minimum of 10 lymph nodes should be obtained and examined in the setting of node negative periampullary cancers.



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#### THE IMPACT OF EXTENDED LYMPH NODE DISSECTION ON THE SURGICAL RESECTION OF PANCREATIC HEAD ADENOCARCINOMA

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**Introduction.** The extent of lymph node dissection (LND) associated with resection of pancreas cancer is still largely debated. Adequately powered randomized trials to address the potential benefit of extended LND in these patients are unfeasible. Therefore, the primary aim of this study is to determine if the number of lymph nodes (LN) excised during surgical resection improves overall survival in patients with pancreatic head cancer by analyzing a large population database.

**Methods.** Using the Surveillance, Epidemiology, and End Results (SEER) registry, all patient records from 1988–2003 with surgically resected pancreatic head adenocarcinoma were queried. Patients with Stage 3 or 4 disease, multiple primary malignancies, or incomplete tumor grading, staging, radiation, demographic data, or number of LN examined were excluded. Kaplan-Meier methods and the log-rank test were used for survival. A Cox regression model was tested to determine the survival impact of LND. The number of LN excised were categorized into groups 1–5, 6–10, and >10. Gender, race, tumor grade, age >60 years, T-stage, and radiation were controlled co-variables in this model.

**Results.** Analyses were performed separately for patients with node negative [N–] (Stage IA/IB/IIA disease; 792 patients) and node positive [N+] (Stage IIB; 1243 patients) disease. Extent of LND was a statistically significant variable in terms of overall survival in both cohorts. For the N– cohort, patients who had 6–10 LN resected (HR=0.80; 95% CI 0.65–0.98;  $p=0.03$ ) and >10 LN resected (HR=0.79; 95% CI 0.64–0.97;  $p=0.02$ ) had a significantly improved survival over patients who had 1–5 LN resected. Similarly, in the N+ cohort, patients who had 6–10 LN resected (HR=0.83; 95% CI 0.70–0.99;  $p=0.03$ ) and >10 LN resected (HR=0.73; 95% CI 0.62–0.86;  $p<0.01$ ) had a significantly improved survival over patients who had 1–5 LN resected. Mean  $f/u$  time for all patients was 18.2 months

(mos). Median overall survival was significantly increased in both cohorts with extended LND. N– survival was 16 mos for 1–5 LN, 20 mos for 6–10 LN, and 21 mos for >10 LN ( $p=0.02$ ). N+ survival was 10 mos for 1–5 LN, 13 mos for both 6–10 & >10 LN ( $p<0.01$ ). In these models, extent of LND was an independent predictor of survival even after adjusting for the effects of gender, race, age, tumor grade, T-stage, and adjuvant radiation therapy.

**Conclusion.** These data suggest an overall survival benefit for extended LND with surgical resection for pancreatic head adenocarcinoma regardless of nodal status. Given the similar hazard ratios and survival outcomes for the 6–10 & >10 LND groups, these data appear to support the removal of at least 6 lymph nodes to gain a survival benefit.

#### Oral Posters II – Transplantation II

OP-08

4/21/07 4:15 to 6:15 pm

Abstract Numbers 168–177

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#### BUDD-CHIARI SYNDROME REPORT OF 3 UNIQUE CASES AND REVIEW OF THE LITERATURE

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**Background.** Budd-Chiari syndrome (BCS) is a clinical condition characterized by hepatic venous outflow obstruction due to a variety of underlying etiologies. Therapeutic modalities range from transjugular intrahepatic porto-systemic shunt (TIPS), to surgical shunt procedures and ultimately liver transplantation.

**Material and methods.** Retrospective chart review of 3 patients diagnosed with BCS at our institution from 2005 to 2006.

**Results.** All our cases involved female patients, age range from 10 to 50 years. Etiology of BCS included myelodysplastic syndrome, systemic lupus erythematosus (SLE) and Trisomy 8. Clinical presentation included symptomatic ascites (3/3), severe lower extremity edema (2/3) and liver dysfunction in (3/3) patients. Anatomically, the first patient had occlusion confined to the hepatic veins and the remaining two had additional occlusion involving the inferior vena cava. Therapeutic modalities included porta-caval shunt after failed TIPS for the first patient. The remaining 2 patients underwent simultaneous porta-caval and cavo-atrial shunts. One developed shunt dysfunction and despite repeated radiologic and surgical attempts of revascularization, ultimately required a liver transplantation. The other patient with dual shunting eventually underwent a kidney transplant for treatment of ESRD due to SLE. To our knowledge this is the first patient with BCS receiving initial surgical shunting and subsequent successful living related kidney transplantation. All patients remain on anticoagulation after surgical procedures. After a short term follow-up (7 to 9 months) no patients have had a recurrence of BCS. Initial clinical ascites and lower extremity edema have resolved and synthetic liver function remains normal. In the two patients not receiving liver transplantation, surgical shunts are patent to date corroborated by follow-up MRI.

**Conclusion.** Shunting and transplantation are satisfactory methods for treatment of BCS. Anatomic, physiological and clinical conditions dictate which one of the two procedures should be performed.

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#### LAPAROSCOPIC INCISIONAL HERNIA REPAIR AFTER LIVER TRANSPLANTATION

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**Purpose.** Incisional hernias occur in 4.6 to 17.2% of patients after liver transplantation. Laparoscopic ventral hernia repair is associated with fewer wound complications and a decreased incidence of recurrence when compared to open hernia repair. This study is to evaluate the results of laparoscopic incisional hernia repair after liver transplantation.

**Methods.** This is a retrospective review of 334 patients who underwent liver transplantation at the Mayo Clinic Arizona between 6/99 and 10/06. 14 of these patients subsequently had laparoscopic incisional hernia repair.

**Results.** Of the 14 patients, 86% (12) were male and 14% (2) were female. Age ranged from 51 to 69 with a mean of 61. 57% (8) of the patients had end stage liver disease secondary to hepatitis C. 14% (2) had primary sclerosing cholangitis, and the remaining patients were diagnosed with alcoholism and hemochromatosis. The time between transplant and hernia repair ranged from 4.5 to 38 months, with a mean of 19.5 months. 86% (12) patients had deceased donor transplantation, while 14%(2) had living donor liver transplantation. 21% (3) patients had five prior open abdominal surgeries, including umbilical hernia repair, cholecystectomy, appendectomy, and nephrectomy. None had prior incisional hernia repair or required re-operation following transplantation. Body mass index ranged from 21 to 37 with a mean of 27.8. Primary maintenance immunosuppression at the time of hernia repair was tacrolimus in 64% (9), sirolimus in 21% (3), and cyclosporine in 14% (2). 71% (10) patients were also on mycophenolate mofetil. All patients had been weaned off steroids by 4 months after

transplant by protocol. The hernias ranged from 208 to 1485 cm<sup>2</sup>, with a mean of 396 cm<sup>2</sup>. They were fixed with composite mesh ranging from 680 to 2365 cm<sup>2</sup>, with a mean of 873 cm<sup>2</sup>. All operations were completed with a laparoscopic approach, there were no conversions to open. Length of stay was 2 to 11 days, with an average of 5.5 days. Complications occurred in 14% (2) of patients. One patient developed infected seroma and mesh, requiring open operation and mesh removal. One patient developed a recurrence (7%) that required open operation and revision. This patient was on sirolimus. There were no graft losses or patient deaths.

**Conclusion.** Laparoscopic incisional hernia repair is safe in patients after liver transplantation, with a low risk of infection or recurrence.

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#### CHANGING CONTRAINDICATIONS TO LIVER TRANSPLANTATION WITH IMPROVED SURVIVAL: OBESITY, AGE >65 AND MALIGNANCY

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Historically absolute contraindications to transplantation included patients who were older (>65 years old), patients with severe obesity and patients with primary malignancy of the liver. With improvements in perioperative care and immunosuppressive strategies many centers began to liberalize the criteria for selection of patients. The proportions of the waiting list and survival across two eras was analyzed to determine the change and characteristics of those patients awaiting transplantation in the United States, as well as, any changes in survival across two distinct eras.

**Methods.** We compared patients in the UNOS database from two five year periods, 1/1/1994–12/31/1998 and 1/1/1999 to 12/31/2003 using both waiting list data and transplant data. The following variables were examined: age >65, diagnosis of cholangiocarcinoma, obesity characterized by BMI 30–40, BMI >30 (all obesity) and BMI >40 (morbid obesity) and diagnosis of hepatocellular carcinoma (HCC). We tested for change in proportion across eras. A survival analysis was done using the log rank test for equality over strata.

**Results.** Change in proportions across eras were significant at  $p < 0.0001$  for both waiting list data and transplant data; Age >65, BMI 30–40, BMI >30 and diagnosis of HCC. Graft survival rates across era were significant for patients with BMI 30–40, BMI >30 and diagnosis of HCC ( $p = 0.001$ ). Patient survival rates were significantly improved only for the group with a diagnosis of HCC across the two eras ( $p = 0.006$ ).

**Conclusion.** The acceptance of candidates for liver transplantation who are older, obese or with HCC has increased over the last decade. Improved graft survival has been seen in obese patients and in those patients with HCC. Additionally, patients with a diagnosis of HCC have also shown improved patient survival.

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#### WILL LIVER TRANSPLANT FOR HEPATOCELLULAR CANCER USING THE UCSF CRITERIA HELP?

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**Background.** Liver transplant (LT) is currently done for hepatocellular cancer (HCC) for patients that meet Milan criteria (single mass <5 cm or 3 tumors each less than 3 cm). There is controversy as to whether this should be extended to the UCSF criteria (single mass <6.5 cm or 3 tumors, largest of which is 4.5 cm and total diameter of <8.5 cm), but how this will impact on overall HCC survival is unknown.

**Methods.** We retrospectively reviewed a prospectively-collected database on HCC referred to our center from 1991–2006 for those who underwent LT or met Milan vs UCSF criteria.

**Results.** In 409 HCC patients, 33 underwent LT and 7 patients are currently on the LT waiting list. Of 114 patients who met Milan criteria, 21 underwent liver resection (LR), 52 had non-surgical therapies due to age/comorbidities, 41 did not undergo/complete LT evaluation for various reasons. Of 27 additional patients who met UCSF criteria, 6 underwent LR, 8 had non-surgical therapy due to age/comorbidities, and 5 did not undergo/complete LT evaluation. Eight patients were reasonable candidates for LT had UCSF criteria been used. Seven of these pts have died a mean 807 days and one is alive at 714 days after ablative therapies (chemoembolization/radiofrequency ablation). 1 and 3-yr survival were 67% and 43% in this group.

**Conclusions.** Using the UCSF criteria for LT for HCC may only affect small numbers of HCC patients (<2% in this series). Survival may be better than locally-ablative treatments but more data will be needed.

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#### MIDDLE HEPATIC VEIN OF THE RECIPIENT AS DRAINAGE FOR ANTERIOR SECTOR VEINS (SEGMENTS V–VIII) IN ADULT-TO-ADULT LIVING DONOR LIVER TRANSPLANTATION. (LDLT)

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**Introduction.** Controversy exists among the centers performing right lobe adult to adult living donor liver transplantation in terms of the preservation of the middle hepatic vein (MHV) in the donor. Some advocate that taking the MHV with the graft prevents congestion of the anterior sector, therefore decreasing the chances of a small-for-size syndrome. Others have described interposition grafts to the main tributaries of the MHV to prevent this congestion and improve graft function.

**Aim.** Describe a novel surgical technique in which the recipients MHV is dissected and anastomosed to the donor MHV tributaries of the anterior sector that are larger than 5 mm. Providing adequate functional mass without compromising donor safety.

**Methods.** This surgical technique was utilized in two adult-to-adult LDLT in both cases the MHV of the recipient was exposed approximately 5 cm from junction to the cava, this was done by blunt dissection of the liver parenchyma leaving a long trunk for the end-to-end anastomosis with the MHV tributary. The donor right lobe was brought to the operative field after back table flush, the recipient caval opening was anastomosed to the donor right hepatic vein orifice using 4-0 polypropylene running fashion. Donor segment 5 hepatic vein was anastomosed to the recipient middle hepatic vein with 6-0 polypropylene running fashion. Small branches of the recipients MHV were over sewn with 7-0 polypropylene; the left HV was closed with 4-0 polypropylene running fashion. The portal vein anastomosis was completed in standard fashion. Upon completion of the vascular anastomosis, portal vein flow was released, all clamps were removed and the liver was reperfused, no congestion of the right lobe graft was noted.

**Results.** Two female recipients (59 yo and 56 yo) with diagnosis of end stage liver disease secondary PSC in one case and HCV in the second were transplanted successfully with right lobe grafts from two male donors (26yo and 34yo) Routine Doppler ultrasound (DUS) was done on postoperative day #1, showing adequate outflow of the MHV to Segment V HV branch in both cases, patients were discharged from the hospital on postoperative day #9 and #12 respectively. There were no postoperative complications.

**Conclusions.** Donor safety and functional graft volume are the essence of LDLT, by utilizing the recipient's MHV for drainage of anterior sector veins with the described technique, congestion of the graft is prevented and early graft function optimized.

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#### INTRAOPERATIVE PLACEMENT OF AN EXPANDABLE METALLIC STENT FOR A PORTAL VEIN TROMBOSIS AFTER LIVING DONOR LIVER TRANSPLANTATION

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**Background.** Portal vein thrombosis, complicating living donor living transplantation by occurring in the intraoperative period is often managed with thrombectomy or splenorenal-shunt when is necessary.

**Objective.** To show a case of intraoperative portal vein thrombosis managed with an endovascular approach placing an expandable metallic stent.

**Population and Methods.** We report on an 8 month old female patient with biliary atresia who received a LDLT, and the portal vein thrombosed at the time of reperfusion, unsuccessfully managed with thromboendovenectomy.

**Results.** An angiography was performed through IMV to diagnose the anatomy and also showed the steal phenomena. Another catheter was placed in an iliac vein branch to access the SMV. With angiographic control it was placed a stent 6 mm diameter and 40 mm long to resolve the problem (Cordis PRECISE RX Nitinol Stent System®). The portal vein was patent on the Doppler US and angiographic control, also the steal phenomena disappeared. The postoperative follow up was done by Doppler US without stenosis or thrombosis. The patient was discharged at day 34 postoperative.

**Conclusions.** Endovascular techniques during liver transplantation can resolve some liver graft perfusion problems due to PVT and steal phenomena, especially with an unsatisfactory thromboendovenectomy. Although primary permeability of stents has been good, these results need to be confirmed in the long term follow up.

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#### REASSESSING THE IMPACT OF PERIOPERATIVE BLOOD TRANSFUSIONS ON OUTCOMES OF LIVER TRANSPLANTATION

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In the early experience with liver transplantation, the number of perioperative blood transfusions (PRBC) given was a strong predictor of poor patient outcomes after transplantation. With improved anaesthesia and intensive care, it is not clear whether the same negative implication of PRBC transfusions persists today.

**Methods.** We performed a retrospective review of outcomes in 555 adult patients who underwent orthotopic liver transplantation at our center between January 1998 and October 2005. PRBC transfusions were recorded as a continuous variable. Univariate and multivariate regression analyses were

performed to investigate whether postoperative outcomes (length of hospital stay, postoperative rise in transaminases, ALP, bilirubin, creatinine, graft failure, patient death) were influenced by perioperative variables including PRBC, year of transplantation, donor age, recipient gender, recipient age, MELD score, UNOS status, cold and warm ischemia times, acute *vs* chronic liver failure, and living *vs* cadaveric transplantation.

**Results.** Increased PRBC transfusions were associated with lower UNOS status, prolonged cold ischemic times, increased recipient age, and cadaveric liver transplantation, but not with higher MELD scores. In univariate regression analysis RPBC transfusions were significantly correlated with length of hospital stay, maximum postoperative creatinine, graft loss, and patient death. MELD score was significant for maximum postoperative creatinine, patient death and graft loss, while the UNOS status was associated with the length of hospital stay and maximum creatinine. However, in multivariate regression analysis the PRBC transfusion rate was an independent predictive factor only of the length of hospital stay and the maximum postoperative creatinine. MELD score was the only independent predictive factor for patient death, while cold ischemia time was the only independent predictive factor for postoperative max AST in our model.

**Conclusions.** In the modern era of transplantation, PRBC transfusion rates are associated with prolonged hospital stay and postoperative kidney dysfunction but not with graft failure or patient survival. These data highlight the impact of improved peri-operative anaesthesia and intensive care.

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#### CHOLEDOCHODUODENOSTOMY OFFERS AN ALTERNATIVE BILIARY RECONSTRUCTION TO CHOLEDOCHOJEJUNOSTOMY IN LIVER TRANSPLANTATION

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A standard Roux-en-Y choledochojejunostomy (CDJ) can be a difficult biliary reconstruction to perform in patients who have had previous abdominal surgery. A choledochooduodenostomy (CDD) can be an alternative procedure in these cases. However, the potential role of CDD in liver transplantation as an alternative to CDJ remains controversial with only limited reports in the literature. Here we report our experience using CDD during liver transplantation.

**Methods.** Since 2000 eleven patients undergoing cadaveric orthotopic liver transplantation (OLTx) at our center had a CDD performed instead of a CDJ. The first patient had the CDD performed as a biliary reconstruction of a duct-to-duct anastomotic stricture occurring 13 months after the OLTx. The remaining ten cases all had the CDD performed at the time of OLTx. Six patients were transplanted for primary sclerosing cholangitis, one for autoimmune hepatitis, one for laennec's cirrhosis, one for Wilson's disease, one for primary biliary cirrhosis and one for biliary atresia (previous Kasai procedure). The patients MELD scores at the time of OLTx ranged from 18 to 31. In all patients, a tension-free CDD anastomosis was performed over an internal stent using interrupted, 5-0 resorbable monofilament sutures. All patients received conventional immunosuppression.

**Results.** The median follow up time to date is 13.9 months with a mean of  $17.9 \pm 7.11$  months and a range of 2.0-84.3 months. No patient developed a bile leak or bleeding from the CDD anastomosis in the post operative period. One patient has had an episode of suspected cholangitis that resolved on a short course of oral antibiotic treatment. No patient is on prophylactic antibiotic treatment and no patient has developed signs of a biliary stricture. All patients have normal liver function tests.

**Conclusion.** CDD can be performed as an alternative to CDJ during liver transplantation with potential benefits over the CDJ including easier post-OLTx endoscopic evaluation and absence of an entero-entero anastomosis. Furthermore, CDD seems to be associated with a low risk for early and late complications. Our experience warrants further investigation of the potential benefits of CDD over CDJ in liver transplantation.

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#### OUTCOME OF BILIARY STRICTURE AFTER RIGHT LIVING DONOR LIVER TRANSPLANT

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**Introduction.** The incidence of biliary complications (BC) ranges 20-40% in living donor liver transplant (LDLT). Scant information is available on the long-term outcome of BS after interventional or surgical treatment (TR) of biliary stricture (BS) in LDLT.

**Materials and methods.** In a 4 year period, 46 patients (pts) underwent right LDLT. Primary biliary anastomosis was either duct-to-duct (D-D) or Roux-en-Y (R-Y). The long-term outcome of percutaneous transhepatic bile duct dilatation/ stent placement (PTC) or R-Y anastomosis in pts with BS was studied. BS resolution was defined as absence of both clinical/imaging evidence and stents >1 year from TR.

**Results.** BS was diagnosed in 6 pts (13%), 5 after R-Y and 1 after D-D (see Table). Two pts with D-D had conversion to R-Y 5 days post LDLT. Three

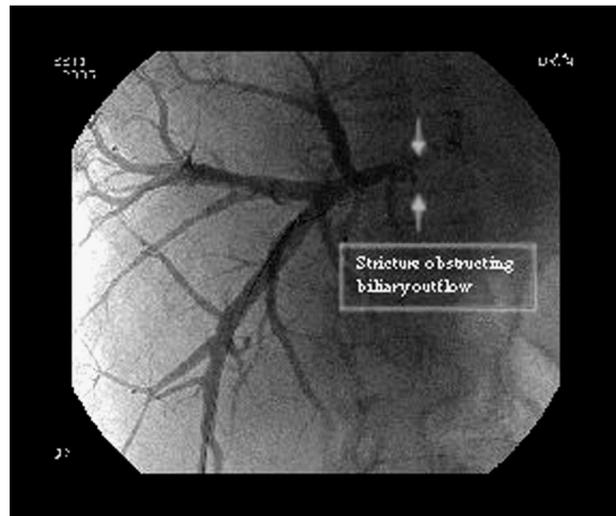
out of 6 pts were treated for biliary leak prior to BS. One pt with conversion of D-D to R-Y had BS resolution, F/U 1095 days. Three pts underwent R-Y redo and required additional PTC after surgery average 10.3 TR/pt (2-20). Average time of TR was 27 months (18-39). Of these pts, 2 are symptoms free/no stent at F/U at 1 and 3 months from last TR and 1 had to be re-transplanted after 2 R-Y redo. PTC was the only TR in 2/6 pts (see Figures 1-2), 1 pt is stent free 3 months after the last of 6 TR, 1 still has a stent after 12 TR. Pts and graft survival is 100% and 88.8% respectively. Pts without BS resolution have normal bilirubin and mean alkaline phosphatase 462 IU/L (206-626).

**Discussion.** Complete resolution of BS in right LDLT is difficult to achieve particularly after R-Y. Long term graft survival is achievable at the expenses of frequent intervention. Re-transplantation must be considered as definitive TR in many pts. D-D anastomosis, when technically feasible, seems to offer more TR opportunities.

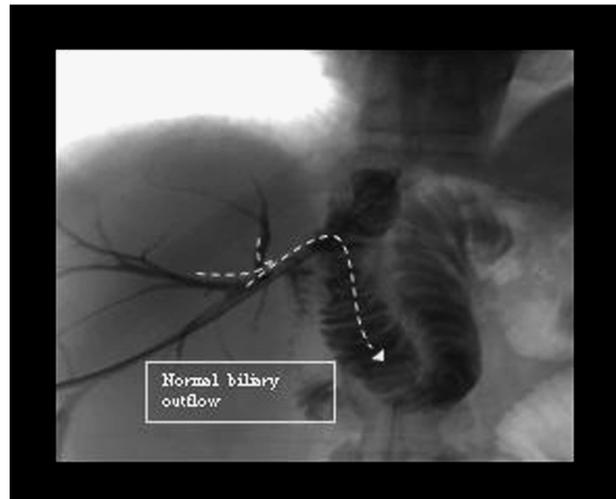
Pts	Primary Anastomosis	First Complication	# of treatments	F/U free disease days	Outcome
1	R-Y	POD 8: Leak	0 S 6 IR	75	ALK 622
2	D-D	POD 7: Leak T-tube obstruction, R-Y conversion	2 S 2 IR	0	ALK 729 ReTx
3	D-D	POD 5: HA thrombosis, R-Y conversion	1 S 20 IR	30	ALK 206
4	R-Y	POD 25: leak	0 S 12 IR	0	ALK 626
5	D-D	POD 150: stenosis	1 S 3 IR	1095	ALK 134
6	R-Y	POD 180: stenosis	1 S 9 IR	120	ALK 396

S=surgical treatment; IR=interventional radiology treatment; ALK=alkaline phosphatase; ReTx=re-transplanted. Pts 2 and 3 had early conversion to R-Y.

#### Pre-treatment



#### Post-treatment



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**PREDICTORS OF BILIARY COMPLICATIONS FOLLOWING LIVING DONOR LIVER TRANSPLANTATION**

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**Introduction.** Adult living donor liver transplantation (ALDLT) is most frequently complicated by biliary related issues. The reported incidence of bile leak is up to 30% in some series.

**Methods.** A retrospective review of a single center experience with ALDLT was performed to evaluate possible mechanisms for bile leaks. Parenchymal transection technique, biliary anatomy, type of reconstruction and timing of leak were reviewed.

**Results.** We performed 44 ALDLT grafting segments V–VIII without the middle hepatic vein from May 1999 to August 2006. Biliary anatomy was investigated using magnetic resonance cholangiography pre-operatively with intra-operative cholangiography for confirmation. In 19 cases a single right biliary duct (43.2%) was noted. In 25 cases multiple biliary ducts (56.8) were present. A single biliary anastomosis was performed in 28 cases (63.6%) and a double anastomosis was created in the remaining 16 (36.4%) cases. With a mean follow up of 698 days (range 44–2700 days), patient and graft survivals were 87.5% and 87.5% respectively. The incidence of biliary leak was 7/44 (15.9%). Biliary complications observed include: three instances of leak from the cut surface, three cases of anastomotic leak, and one leak noted from a transhepatic tube site. Two patients required operative interventions. All other patients were managed by interventional and/or endoscopic means.

**Conclusions.** Biliary complications were infrequent in this series of ALDLT. One leak contributed to a patient death early in the series secondary to sepsis and multiorgan failure. No other grafts were lost directly to biliary complications. Multiple biliary reconstructions were strongly related with bile leak. Method of transection did not have a significant effect on outcome.

**Oral Posters II – Biliary II: Benign and Pancreatitis OP-09**

4/21/07 4:15 to 6:15 pm

Abstract Numbers 178–188

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**LONGITUDINAL DUODENOTOMY FOR EXCISION OF BENIGN DUODENAL NEOPLASMS**B Dillard, J Hering, S Garrean, J Espat  
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**Introduction.** Given their rare occurrence and variable presentation, benign duodenal neoplasms (BDNs) pose an interesting surgical challenge, as optimal evidence-based treatment has yet to be defined. Though literature on this subject is scant, some reports suggest that, for BDNs not amenable to endoscopic polypectomy, choice of operation should be influenced by location of the lesion. As such, the operation of choice would be transduodenal excision for lesions in portion 1, pancreaticoduodenectomy for lesions in portion 2, especially near the ampulla, and segmental resection for lesions in portions 3 and 4.

**Purpose.** To present a recent experience with local transduodenal excision of symptomatic BDNs in the 2nd–4th portions of the duodenum.

**Methods.** Since 2001, 4 patients meeting these anatomic criteria with symptomatic BDNs have undergone excision at our institution.

**Results.** The mean age of the 2 males and 2 females in this series was 64 years. Presenting symptoms were dyspepsia (1 patient), epigastric pain (1 patient), and upper GI hemorrhage (2 patients). All patients underwent EGD with consequent localization of their duodenal tumors and further characterization via EUS. The characteristics of the BDNs are as follows: one 2 cm hamartomatous polyp on the antimesenteric wall of D2; one well differentiated 3 cm neuroendocrine tumor at D3; one 4 cm pedunculated GIST on

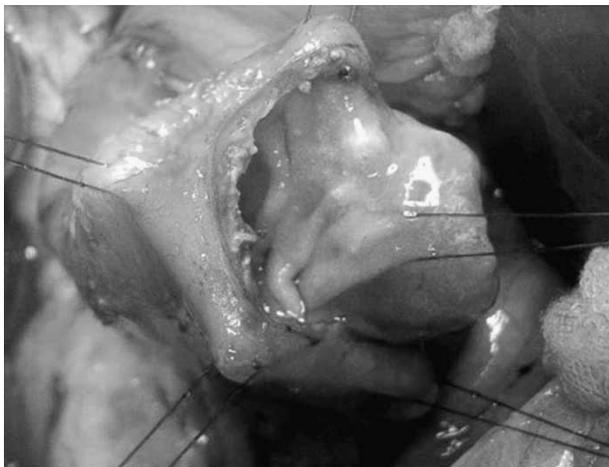


Figure 1. Excision of BDN via longitudinal duodenotomy.

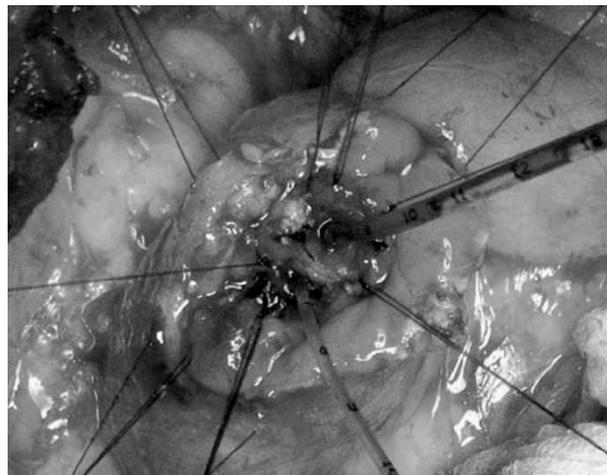


Figure 2. Reconstruction of common bile duct and pancreatic duct after ampullectomy.

the antimesenteric wall of D4, and one 3 cm ampullary tubulovillous adenoma. All operations were performed via a right subcostal incision. All non-ampullary BDNs were excised via longitudinal duodenotomy with transverse 2 layer closure. The single ampullary tubulovillous adenoma was excised via ampullectomy with subsequent septoplasty between the common bile duct and pancreatic duct, circumferential sphincteroplasty, and transverse 2 layer closure. In all cases, periduodenal JP drains were placed intraoperatively. Postoperatively, patients underwent a gastrografin upper GI study with no evidence of leaks or luminal narrowing. There were no postoperative complications and there was no mortality.

**Discussion.** This modest series supports that anatomic location is not a limitation for proceeding with local excision of BDNs via longitudinal duodenotomy with transverse closure. When necessary, ampullectomy with reconstruction is technically feasible. This procedure can be performed with minimal morbidity and, when possible, is preferable to the alternatives of pancreaticoduodenectomy or segmental resection.

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**DIC-CT AND INTRA-OPERATIVE CHOLANGIOGRAPHY FOR LAPAROSCOPIC CHOLECYSTECTOMY**

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In case of laparoscopic cholecystectomy (LC), we routinely examine preoperative DIC-CT to evaluate an anatomy of biliary tract, and also perform intra-operative cholangiography (IOC) to avoid intra-operative bile duct injury (IBDI). We investigated feasibility of DIC-CT and IOC for IBDI. During recent five years, we have experienced LC for 509 patients in our hospital.

**Results.** DIC-CT revealed anatomical anomaly on 30 patients out of 509 patients. IOC was performed completely on 96% of the patients. Four patients out of 509 patients who underwent LC encountered IBDI due to marked inflammation around the cystic duct, and two patients were treated surgically with T-tube drainage or direct repair of injured cystic duct under laparoscopic guidance, and these postoperative courses were uneventful. Four patients were successfully treated with ENBD or just intra-abdominal drainage which was placed intra-operatively. Summary: IOC is still controversially, however it is reported to be useful for intra-operative examination of CBD stones, and also to be useful to avoid injury of bile duct. Routine IOC during LC including dissection of cystic duct and catheterization into the cystic duct could improve skill of surgical procedures such as laparoscopic CBD exploration or laparoscopic gastrointestinal surgery.

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**LAPAROSCOPIC CHOLECYSTECTOMY IN PROGRESSIVE SYSTEMIC SCLEROSIS**Nihar R Dash, Devendra Gupta, MD, Rajan Saxena, MS  
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**Aim.** To discuss the challenges of laparoscopic cholecystectomy that can be posed in a patient with systemic sclerosing disease.

**Background.** Progressive systemic sclerosis or Scleroderma is a not so uncommon disease which is characterised by inflammation, vascular sclerosis and fibrosis of skin, viscera and other organs of the body. Laparoscopic cholecystectomy in these cases can be troublesome and challenging for the surgeon as well as the anaesthetist. Here in we, for the first time, report a case which addresses the issue. The Case: A 42 year old lady presented to us with symptomatic uncomplicated cholelithiasis. She was a diagnosed case of

scleroderma since last 22 years and was on steroid and penicillamine. In her case the manifestations were raynaud's phenomena, hardening of skin of upper half of the body associated with skeletal, pulmonary, endocrine, vascular, ocular and other connective tissue manifestations. High risk consent for general anaesthesia and high chance for conversion to open were taken. In the operation theatre exposure to cold was avoided. Intra venous cannulation, intubation, blood pressure recording and anaesthesia required skill and special measures. Pneumoperitoneum was created with veress needle. Because of circumferential hardening of the abdominal wall the inflation was restricted and coupled with the fatty mesentery, thickened bowel and unyielding liver, the working space was very limited. Two fan retractors were used for retraction of the bowel. The calot dissection and gall bladder removal were not problematic especially in the hand of an experienced surgeon of the department. Extra attention was given to hemostasis. Wounds closed with subcutaneous sutures only. The patient had a smooth post operative course.

**Conclusion.** Laparoscopic cholecystectomy in patients with scleroderma is of immense benefit to the patient if precautions are taken; as described in our case; according to the pathological changes, with the availability of advanced anaesthetic facilities and experienced surgeon.

#### 181 NEW APPROACHES FOR BLOODLESS LAPAROSCOPIC CHOLECYSTECTOMY IN THE CIRRHOTIC PATIENT

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**Introduction.** The prevalence of cholelithiasis in cirrhotic patients is reported to be twice that of the general population. Cirrhosis has represented a relative contraindication to laparoscopic cholecystectomy, however, technological advances in minimally invasive surgery and haemostatic devices have allowed advances in the field of high risk biliary surgery. A review of peri-operative outcomes in a series of high risk cirrhotic patients undergoing laparoscopic cholecystectomy was undertaken.

**Methods.** Records of cirrhotic patients undergoing laparoscopic cholecystectomy at a single institution performed by two surgeons were reviewed (1999–06). Demographic data, conversion to open surgery, haemostatic techniques, operative times, blood loss, length of stay, and 30-day mortality were assessed.

**Results.** 47 patients (25 males, 22 females) underwent an attempted laparoscopic cholecystectomy of which 4 cases were converted to laparotomy. Symptomatic cholelithiasis was the indication for operation in the majority of cases with acute cholecystitis representing only 2 of cases. All patients were Child's class A or B cirrhotics (42 A and 5 B). Median age was 55 and median length of stay was 1 day (1–13). Mean estimated blood loss was 115 (50–600 cc). Blood products were required in a only 4 patients: one patient required transfusion of packed red blood cells, two required platelet transfusions, and one fresh frozen plasma. Tissuelink electrocautery and argon beam coagulation were utilized in all cases. There were no reoperative cases for bleeding in the series. Intraoperative drains were left primarily for ascites in 14 cases and most were removed by the first post-operative day. Mean operative time was 126 minutes. There was no acute on chronic hepatic decompensation in the immediate post-operative period. Additionally, there was no 30-day mortality in these patients.

**Conclusion.** This series represents the second largest review of laparoscopic cholecystectomies in cirrhotic patients in the United States. Although operative interventions in the setting of cirrhosis may represent more challenging cases with respect to blood loss and other morbidity, laparoscopic cholecystectomy is feasible and safe with acceptable conversion rates and length of stay. Furthermore, utilizing advanced laparoscopic hemostatic devices can minimize both blood loss and transfusion rates. A representative video demonstration of the laparoscopic hemostatic techniques described above will also be included.

#### 182 HEMOCONCENTRATION AS AN EARLY MARKER OF SEVERITY IN THE ACUTE BILIARY PANCREATITIS

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**Purpose of the Study.** Studies that associate the hemoconcentration with the development of necrotizing acute pancreatitis, are present in literature. The aim of this study was to evaluate if the hemoconcentration can be an early marker of necrotizing pancreatitis.

**Methods.** In the period January 1998–June 2005, 60 patients admitted with diagnosis of acute biliary pancreatitis; 24 had a CT-scan within 36–72 hours; Ranson's criteria were applied in all patients. Seven of the 24 patients had a necrotizing pancreatitis (Balthazar's score). The hematocrit (Hct) was retrospectively evaluated and associated with the CT-scan morphological data.

**Results.** The regression analysis showed an association between pancreatic necrosis, by means of CT evaluation, and the hemoconcentration. Hematocrit more than 43% in the males and more than 39% in the females within the first 24 hours from the admission, was a marker of severity and pancreatic

necrosis. In 6 of the 7 patients with necrotizing pancreatitis there was critical value of Hct and only in 4 of the 17 patients with edematous pancreatitis there was a high value of Hct, showing the statistical significance of the proposed criteria ( $p < 0.01$ ). The negative predictive value of the hemoconcentration was 94.7% for the evolution in pancreatic necrosis.

**Conclusions.** The prognostic value of the hemoconcentration is comparable with the score of Ranson. So, it is an early and simple marker of the necrotizing evolution of the acute pancreatitis, because of its high negative predictive value: the patients with acute pancreatitis without hemoconcentration will rarely develop a necrotizing pancreatitis.

#### 183 REFRACTOMETRY ROLE FOR DIAGNOSIS OF PATHOLOGIC PROCESS IN ACUTE PANCREATITIS

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Acute pancreatitis (AP) is a disease characterized by unpredictable outcomes. In most AP cases the process is controlled at the phase of the gland edema. In a number of cases the disease develops into the phase of pancreonecrosis (PN). The 3rd phase is that of suppurative complications (SC). These phases make up a single whole the manifestations of which as well as transitions of one phase into another are, at first, caused by enzymatic autoaggression degree and, then, by an infection. It's known that the 1st phase is from 1 to 3 days long, and the 2nd one is up to 7 days long. Later, there can appear resorption of necrotic infiltration – from 2 to 8 weeks long, aseptic sequestration or necrosis foci infection, i.e. transition into the 3<sup>rd</sup> phase. The SC phase is usually evident on the 15th day or later. The time of transition of one phase into another is relative. Its diagnosis is especially difficult. The main difficulties appear during diagnosis of infiltrate infection and SC course. This is followed by delayed intervention. To make the transition of 1 phase into another more exact, to determine suppurative process and its course in pancreas, to perform a surgical intervention in time we propose to evaluate the index of blood serum refraction (IBSR) by refractometry method. We examined 30 patients having various AP forms using this method and made up the following groups of patients: 1st gr. - patients with pancreas edema. 2nd gr. - patients with "aseptic" pancreonecrosis. 3<sup>rd</sup> gr. - patients at the phase of SC. The following results were obtained: On admission mean IBSR of the patients in the 1st gr was 1.3472. While the patients were improving IBSR was decreasing and to the time of their discharge from the hospital it was 1.3454. In the 2nd gr mean IBSR on admission was higher than in the 1st gr and made up 1.3500; on discharge it became 1.3475 that also demonstrated their clinical improvement. All the patients from this group recovered. In the 3<sup>rd</sup> gr mean IBSR on admission was 1.3490, in the course of treatment it was lowering. And on discharge mean IBSR of the three recovered patients was 1.3448 that showed a clinical course of improvement as well. Three patients died during SC phase. Mean IBSR of these patients on admission was 1.3497. One should pay attention to IBSR decrease, the patients' state becoming worse and the treatment being unsuccessful. Thus, preliminary study of IBSR importance for the changes taking place in pancreas, for the course of pathologic process demonstrates IBSR diagnostic value. While AP is progressing the IBSR figures have a tendency to go up and the process of recovery is accompanied by a decrease in these figures.

#### 184 MINIMALLY INVASIVE PROCEDURES FOR THE TREATMENT OF ACUTE PANCREATIC PSEUDOCYSTS

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**Background.** The treatment of acute pancreatic pseudocyst has been open surgery for a long time. However, in the last years, minimally invasive techniques have been performed more frequently, with less morbidity and mortality rates.

**Objective.** To show the experience at a single Center with laparoscopic, endoscopic and percutaneous approach for the treatment of acute pancreatic pseudocysts, and to define the use of the "open" surgery nowadays.

**Population and Methods.** We performed a retrospective analysis of the last 10 years. We analyzed patients with acute pancreatic pseudocyst. We reviewed procedures, morbidity, mortality and effectiveness rates.

**Results.** Between 1996–2006, we treated 39 patients with 43 acute pancreatic pseudocysts. We performed 7 open surgeries (2 because surgeon preference and 5 because diagnostic doubts). In 19 patients we performed laparoscopic surgery; 12 cystojejunostomies, 1 double cystojejunostomy, 2 cystogastrostomies, 1 external drainage and 1 splenopancreatectomy. We converted 2 laparoscopic surgery to open fashion because of a technique problem. Only one patient had recurrent pseudocyst. In 5 patients we performed endoscopic approach, 2 transgastric drainage, 2 transpapillar drainage and one transduodenal drainage with excellent results. In 9 patients who were approached percutaneously, 3 failed and required surgery.

**Conclusions.** The "open" surgery should be indicated only when the percutaneous approach fails and/or exists diagnostic doubts. The minimally invasive surgery should be taken as the first option because of its excellent successful rate.

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**ADULT CONGENITAL CHOLEDOCHAL CYST**

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**Background.** There are five types of choledochal cyst, which are anomalies that involve intrahepatic or extrahepatic bile ducts, or both. These lesions are found most frequently in patients who are Asian, female, infants but are recognized with increasing frequency in adults. It has been estimated that the actual clinical incidence of choledochal cyst ranges from 1 in 13,000 to 1 in 2 million patients. Biliary cyst account for approximately 1% of all benign biliary disease. The frequency of bile duct cyst in decreasing order is type I choledochal cyst (80%); followed by type IV, 13%; type III, 4%; and type II, 2.6%. Multiple intrahepatic bile duct cyst without an extrahepatic component occurs in less than 1% of the patients.

**Patients and Methods.** A retrospective review of clinical files of all patients with choledochal cysts diagnosed between 2003 and 2006 was performed.

**Results.** We have managed 7 patients with this anomaly. All were female. The mean age was 44 years (range 32–60 years) and there were 7 type I cysts. Procedure used to diagnose cyst included Computed Tomography (CT) in combination with retrograde cholangiopancreatography (ERCP) in three patients, CT/magnetic resonance cholangiopancreatography (MRCP) three patients, ultrasonography/ERCP one patient. Presenting complaints included abdominal pain in three patients, pancreatitis in two patients, and jaundice in two patients. Our operative treatment included choledochal cystectomy, cholecystectomy, and Roux-Y hepaticoyeyunostomy. There was no mortality. Surgical morbidity was limited to two patients with pneumonia and empyema (20%), respectively. Hospital stay range was nine to 42 days with an average of 20 days. Operative time range 210–360 minutes with a mean time of 275 minutes. Surgical bleeding range was 250–1110ml, mean bleeding was 535 ml. Median follow-up was 21 months. All patients are symptom free.

**Conclusions.** MRCP provides essential information of the duct anatomy without the risk of pancreatitis. Management of choledochal cysts is successful after their complete removal. Biliary continuity after cyst resection is best established by Roux-Y hepaticoyeyunostomy.

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**TREATMENT OF BENIGN BILIARY STENOSIS WITH TEMPORARY SELF-EXPANDABLE METALLIC STENT**

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**Introduction.** Metallic self-expandable stent (MSES) are commonly use for treatment of neoplastic biliary stenosis. Recently MSES for treatment of benign biliary stenosis (bile duct injury, chronic pancreatitis, post-tranplantation stenosis) have been reported with good results. Thus, the aim of our study is to evaluate the safety and feasibility of temporary MSES in different type of benign stenosis.

**Patients and Methods.** Between November 2004 and Mars 2006, 8 patients (1 woman and 7 men with a mean age of 55 y.o.) underwent MSES insertion to treat a benign stenosis. The origin of benign stenosis was: post-liver transplant (n=4), chronic pancreatitis (n=3), choledochocoele (n=1). All, but one, patients were treated with multiple dilatations and plastic prosthesis insertion before the use of MSES. The indication of MSES was a persistent stricture despite optimal endoscopic treatment, poor surgical candidate, poor tolerance of the procedure, adverse local conditions. For one patient with a very poor general condition, MSES was use immediately to avoid multiple endoscopic procedures.

**Results.** The mean interval between first dilatation and the MSES insertion was 126 days (range: 0 to 338). The average number of endoscopic procedures before insertion of MSES was 1.6 (range: 0 to 4). There were 2 complications after MSES insertion: 1 pancreatitis and 1 cholangitis. MSES retrieval was performed without difficulties and complications (mean: 288 days after insertion; range: 100 to 453) in 7 patients. The follow-up is 141 days.

**Conclusions.** The treatment of benign biliary stenosis with MSES is safe and feasible. Moreover, MSES can be removed without complications after a few months, used as a temporary method for dilatation. It is also an alternative for selected patients in poor medical condition or in whom the local duodenal conditions make repeated ERCP hazardous. A longer follow-up will be necessary to evaluate the long term efficacy of this method of dilatation for resolution of benign strictures.

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**LIVER RESECTION COMBINED TO BILE DUCT REPAIR AFTER A BILE DUCT INJURY DURING LAPAROSCOPIC CHOLECYSTECTOMY**

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**Introduction.** Laparoscopic cholecystectomy increases the risk of major bile duct injuries. The aim of this study was to define the place of liver resection combined to bile duct repair in the treatment of major bile duct injuries.

**Methods.** A retrospective study of 23 patients (16 women and 7 men with a mean age of 51.4 y.o.). We analyze the following criteria: gallbladder disease, injuries diagnosis time, Strasberg classification of injuries, type of bile duct repair and long-term results.

**Results.** Between 1991 and 2005, 123 patients were referred for a biliary tract injury; 23 patients (28.3%) required a liver resection combined to bile duct repair. The bile duct injury was recognized during the surgery for 7 patients or following the surgery in 16 patients. The Strasberg classification was: 3 type E3, 16 type E4 and 4 type E5. Before the 23 patients were referred, 12 have had hepaticoyeyunostomies, 5 primary closures, 3 drainage of bilioma (2 percutaneous and 1 open approaches) and 3 conservative treatments. After referral, we have had to perform an intrahepatic hepaticoyeyunostomy combined to 9 central hepatectomies and 14 right hepatectomies. There is one postop mortality (4,3%), and 17 patients (74%) had  $\geq 1$  postop complications. The mean follow-up was 88 months. During the long-term follow-up, 2 patients developed a secondary biliary cirrhosis and 1 an anicteric cholestasis.

**Conclusions.** Liver resection combined to bile duct repair may be necessary in the treatment of bile duct injury in order to obtain the best results, especially in patients with Strasberg E4 bile duct trauma.

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**PARENCHYMAL SPARING CENTRAL HEPATECTOMY FOR HILAR STRICTURE**

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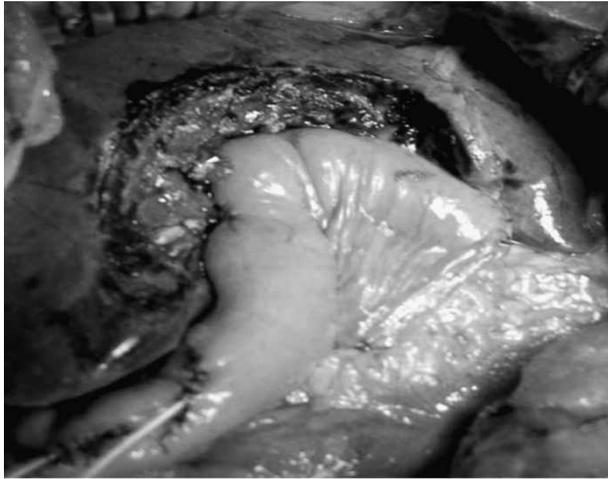
**Introduction.** The role of parenchymal sparing central hepatectomy (PSCH) for hilar biliary stricture is not well established. In this study, we report 4 cases of hilar strictures which were treated with PSCH.

**Methods.** Liver resections performed at our center from 1/98 to 8/06 were retrospectively reviewed.

**Results.** A typical preoperative hilar stricture is shown in Fig 1. Among 221 cases, 4 required the partial resection of segments V and IV with multi-segmental biliary reconstruction via RNY hepaticoyeyunostomy, Fig 2. A typical postoperative cholangiogram is seen in Fig 3. Case 1 involved a gallbladder cancer which invaded the hilum. PSCH was performed with en-bloc extended cholecystectomy and biliary reconstruction as shown. The hospital course was uncomplicated. Patient received adjuvant chemoradiation and survived 7 months. Case 2 involved a benign hilar stricture consistent with sclerosing cholangitis which presented as painless jaundice. He is doing well at 13 months after PSCH. Case 3 involved a cholangiocarcinoma found in 83 y.o. woman treated with PSCH. Her recovery was complicated by pulmonary embolus but she is doing well at 1 year without undergoing adjuvant therapy and has no evidence of recurrence. The 4th PSCH case involved 2.5 cm cholangiocarcinoma in the setting of micro-nodular cirrhosis which was found intraoperatively. His postoperative course was complicated by a late onset of ascites and sepsis resulted in multiorgan failure and death in 5 months. Postoperative cholangiograms obtained in all patients demonstrated no biliary leaks.

**Conclusion.** In selected cases of hilar strictures, parenchymal-sparing central hepatectomy can be useful. It is particularly attractive for benign lesions and for lesions in the presence of limited hepatic reserve. Although complex, multisegmental biliary reconstruction can be safely performed.





**Oral Posters II – Basic Science II  
OP-10**

4/21/07 4:15 to 6:15 pm  
Abstract Numbers 189–199

**189  
AGE INCREASES MURINE RESTING GALLBLADDER VOLUME**

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**Introduction.** Age, obesity and diabetes are known risk factors for cholesterol gallstone formation. We have previously demonstrated that young, obese, diabetic mice have increased resting gallbladder volume and decreased *in vivo* gallbladder emptying compared to young lean mice. However, the influence of ageing on gallbladder volume and response are unknown. Therefore, we tested the hypothesis that old mice would have increased resting gallbladder volume and impaired gallbladder emptying compared to young mice.

**Methods.** Thirteen lean, nondiabetic (C57BL/6J) and 12 obese, diabetic, leptin-deficient (Lep<sup>ob</sup>) female mice were fed a nonlithogenic diet for three weeks. Fourteen mice (7 lean, 7 obese) were young (3 months) while 11 mice (6 lean, 5 obese) were old (12 months). After an overnight fast, *in vivo* gallbladder volume was measured by ultrasound before and after an injection of cholecystokinin 1 nmol/kg. Gallbladder ejection fraction was calculated. Serum was drawn for glucose and insulin levels, and HOMA (an index of insulin resistance) was calculated. Data were analyzed by ANOVA and Student's t test.

**Results.** Gallbladder resting volume, residual volume, ejection fraction (EF) and serum data are presented in the table.

Group	Resting Vol (ml)	Residual Vol (ml)	EF (%)	Glucose (mg/dl)	Insulin (μIU/L)	HOMA Index
Lean-Young	15 ± 2	3 ± 1	80 ± 9	134 ± 19	1 ± 1	0.2 ± 0.1
Lean-Old	23 ± 2	5 ± 2	81 ± 7	215 ± 11*	7 ± 3	3.3 ± 1.3
Obese-Young	28 ± 5*	4 ± 2	87 ± 4	290 ± 21*	29 ± 11*	20.3 ± 8.1*

Table (Continued)

Group	Resting Vol (ml)	Residual Vol (ml)	EF (%)	Glucose (mg/dl)	Insulin (μIU/L)	HOMA Index
Obese-Old	62 ± 5 <sup>†</sup>	17 ± 7 <sup>†</sup>	73 ± 11	180 ± 41 <sup>§</sup>	53 ± 11 <sup>Δ</sup>	24.8 ± 10 <sup>Δ</sup>

\*p < 0.05 vs Lean-Young, †p < 0.01 vs Others, §p < 0.05 vs Obese-Young, Δp < 0.06 vs Lean-Old.

**Conclusions.** These data suggest that age, obesity and diabetes all 1) increase resting gallbladder volume but 2) do not alter *in vivo* gallbladder response to cholecystokinin and that 3) age increases residual gallbladder volume in obese mice. Therefore, we conclude that age contributes to gallstone pathogenesis by enhancing gallbladder stasis.

**190  
DEVELOPMENT OF A REVERSIBLE SURGICAL MODEL OF GALLBLADDER INFLAMMATION AND CHOLESTASIS**

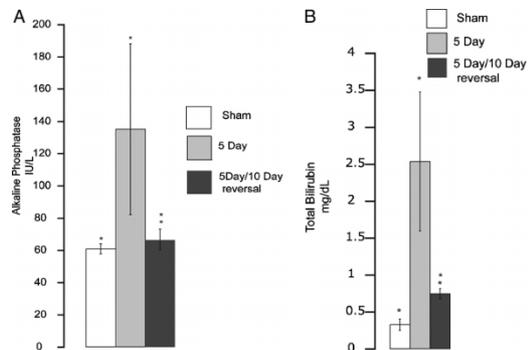
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**Introduction.** Previous mouse models of gallbladder inflammation used ligation of the cystic duct alone that resulted in inflammation that is histologically different from that seen in human cholecystitis. Ligation of the common bile duct (CBD) is popular method used to induce biliary inflammation because it induces histological changes identical to acute cholecystitis. In mice, however, CBD ligation results in a high early post-operative mortality rate, which may be due to post-operative traumatic pancreatitis. To overcome this problem, we developed a simplified model of gallbladder inflammation in mice, which minimizes post-operative death, maintains an effective inflammatory response, and is easily reversible.

**Methods.** Mice were anesthetized. At laparotomy, without tissue dissection, a 1 mm titanium clip is applied across the distal CBD. To reverse the obstruction, a fine silk suture was incorporated into the clip during initial placement and secured to the abdominal wall. The suture was removed on postoperative day 5, thereby reversing CBD obstruction without repeat surgery. Mice were allowed to recover for 10 days after relief of obstruction.

**Results.** Obstruction for 5 days caused distension of the gallbladder and CBD. The gallbladder showed marked hypertrophy (8-fold increase in wall thickness) and inflammation (17-fold increase in tissue myeloperoxidase activity) compared to sham controls. Serum levels of alkaline phosphatase and bilirubin were markedly elevated, indicating injury to the biliary epithelium. Early (day 0–2) survival was 100% and later (day 3–5) survival was 85% (n = 54 mice). We successfully reversed biliary obstruction (n = 10 mice), with one death from infection 2 days after clip removal. Of the surviving animals, gross examination showed complete biliary decompression, reduced inflammation and resolution of jaundice. Histological findings confirmed reduced epithelial damage, edema and neutrophil infiltration. Serum alkaline phosphatase and bilirubin levels also returned to within normal levels.

**Conclusion.** We have developed a new and reversible technique to induce bile duct obstruction in mice. Obstruction of the CBD causes injury and inflammation in the gallbladder, which resolves after reversal. This reversible model of cholestasis can be applied to genetically altered mice to further define molecular mechanisms of biliary inflammation.



**Serum Alkaline phosphatase (A) and total bilirubin levels (B) in sham operated animals (n=6), 5 day CBD ligated (n=6), and 5 day CBD ligated/10 day reversal (n=9)**

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CHALLENGES IN PRIMARY STEATOTIC HEPATOCYTE ISOLATION PROCEDURES**

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The use of primary human hepatocytes is essential for basic research and pharmaceutical arenas. To meet this demand, viable hepatocytes are being procured from residual tissues of hepatic resections. The tissue is preserved with a standard cold-storage solution. Hepatocytes are then isolated using a collagenase solution to dissolve the extracellular matrix and purified via a density gradient separation. The increasing prevalence of human liver steatosis offers a technical hurdle for the isolation of viable hepatocytes due to differences in cell density compared to normal hepatocytes. In order to determine the significance of liver steatosis in hepatocellular yield, we conducted a retrospective analysis of 75 samples. Steatosis was broken into the following groups: none/minimal, mild/moderate, and severe using conventional analysis of H&E stained slides. Initial cell yields (after collagenase digestion) showed no difference in average cells/gram tissue between the none/minimal and mild/moderate steatosis groups ( $21.6\text{A} \pm 15.5$  cells/gm tissue vs  $20.9\text{A} \pm 13.6$ , respectively), but severe steatosis significantly decreased initial yield versus both groups ( $8.60\text{A} \pm 2.4$ ,  $p < 0.001$ ). This trend was similar to the results for a final cell yield (after density gradient purification), however the differences were not statistically significant (none/minimal:  $9.1\text{A} \pm 9.9$ , mild/moderate:  $9.9\text{A} \pm 7.5$ , severe:  $3.8\text{A} \pm 5.1$ ). Interestingly, there were no significant differences in the percentage yield (final yield/initial yield) within the groups, indicating high variability in yield after purification. Steatosis of increasing severity decreases the cell yield after whole tissue perfusion for isolation of human hepatocytes. The problems appear to lie with the collagenase perfusion and not with the density gradient purification. Our data shows a significant difference in initial yield immediately after the tissue digestion and not in the final yield. Most surprising was that when the final yield was divided by the initial yield, no differences in ratios were observed between groups. This indicates that our methods for compensating for hepatocellular steatosis are adequate during the density separation. However, because so much variability in yield exists in all groups, other factors should be evaluated, including ischemia times, degree of necrosis/fibrosis, etc, which may affect the hepatocyte purification. Because steatosis clearly affects the initial yield, these results implicate either the quality of perfusion or enzymatic digestion. Further analysis will be necessary to determine which step is responsible.

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#### HEPATIC FIBROSIS INDUCED BY XENOSERA IS FEATURED BY INCONSPICUOUS INFLAMMATION BUT ROBUST ECM REMODELING

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**Objective.** Hepatic cirrhosis in rats induced by injection of pig sera (IPS) represents a model of fibrogenesis caused by immunological injury. However, the underlying pathogenesis is not well characterized. This study was carried out to determine the interrelation between hepatic inflammation and fibrous proliferation.

**Methods.** A chronic model of liver cirrhosis introduced by IPS in rats was studied. An acute model of cholestatic cirrhosis induced by common bile duct ligation (BDL) served as comparison. Liver tissue was collected for histology, histochemistry and quantitative real time PCR (qPCR) analysis to quantify the mRNA expression of genes relating to inflammation (IL-1, IL-6, MCP-1, MIP-1, TNF- $\alpha$ , RANTES, TGF- $\beta$ , PDGF and CD44) and fibrogenesis (collagen 1,  $\alpha$ SMA, MMP-9 and TIMP-1).

**Results.** IPS resulted in an insidious development of liver fibrosis characterized by intensive septum formation, collagen I deposition and  $\alpha$ SMA+ myofibroblast proliferation, without prominent hepatic parenchymal changes and limited inflammation. Immunohistochemistry showed limited number of T cells (CD3+), macrophages (CD68+) and total leukocytes (CD45+) in the cirrhotic livers. qPCR demonstrated that mRNA coding for genes relating to ECM remodeling such as collagen 1,  $\alpha$ SMA, MMP-9 and TIMP-1 were significantly up-regulated in the IPS livers when compared with normal control. However, mRNA transcripts coding for inflammation-related cytokines TGF- $\beta$ , PDGF, IL-1, IL-6, TNF- $\alpha$ , CD44, MIP-1 and MCP-1 were at levels comparable with normal control. Only RANTES was mildly up-regulated. In contrast, the BDL livers exhibited histological changes with hepatocyte degeneration/necrosis, bile duct proliferation and portal inflammation. BDL liver gene expression was remarkable for up-regulation of all the pro-inflammation genes examined in association with increased expression of collagen-1,  $\alpha$ MSA, MMP9 and TIMP-1, indicating that in BDL livers robust inflammation coincides with fibrous proliferation.

**Conclusion.** Unlike BDL livers which exhibited remarkable up-regulation of various pro-inflammation cytokine genes, cirrhotic livers induced by IPS exhibit robust extracellular matrix remodeling in the absence of notable hepatic inflammation. The insidious nature of cirrhosis development seen in this IPS model mimics certain types of liver cirrhosis in the humans.

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#### LIVER SINUSOIDAL ENDOTHELIAL CELLS: PHENOTYPIC CHARACTERIZATION BY ELECTRON MICROSCOPY

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**Introduction.** The liver possesses several unique immunological functions, including the induction and maintenance of peripheral tolerance. Thus, the immune functions of cells within the sinusoids are of particular interest. Liver sinusoidal endothelial cells (LSECs) comprise the major cell type within the hepatic sinusoids and interact directly with the portal and systemic circulations. Therefore, LSECs are strategically placed to play a critical role in the immune functions of the liver. LSECs have been shown to have high antigen uptake and processing capacity, similar to other antigen presenting cells. Some studies have shown that LSECs express surface molecules such as CD-80, CD-86, and MHC class II allowing LSECs to stimulate T-cells; in contrast, other studies show data indicating that LSECs do not express these surface molecules and are thus unable to stimulate T-cells. These previous studies used flow cytometric analysis after LSEC isolation to study the phenotypic characteristics of LSECs. In our study, we use electron microscopy as a novel technique to analyze LSECs directly and further elucidate their phenotypic characteristic.

**Methods.** Adult C57BL/6 mice were anesthetized per standard protocol. The left ventricle was cannulated and the animal perfused with PBS followed with 5 ml of 4% paraformaldehyde and 0.1% glutaraldehyde. The liver was extirpated, cryoprotected and frozen. Liver sections were placed on glass super frost slides and kept at  $-80\text{C}$ . Liver sections were stained with anti-CD45 and anti-MHC II primary antibodies. Goat anti-mouse Alexa Fluoro nanogold antibody was used as the secondary antibody. Slides were then prepared for analysis with electron microscopy using standard protocols.

**Results.** High resolution electron microscopy images at magnifications ranging between 6,000 and 12,000 $\times$  allowed LSECs to be identified by morphology. These cells expressed neither MHC class II nor CD45. In contrast, macrophages and dendritic cells, which were identified by morphology, clearly demonstrated the positive staining for MHC class II and CD45 that is characteristic of professional antigen presenting cells.

**Conclusions.** Electron microscopy is an effective method to further elucidate the phenotypic characteristics of liver sinusoidal endothelial cells. Using this technique, we have phenotypically characterized LSECs and demonstrated that they lack the phenotypic characteristics usually associated with antigen presenting cells. This may represent a powerful tool to further characterize LSECs in terms of molecules such as CD-80, CD-86, and MHC I, and hopefully further our understanding of the immunological role of these cells.

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#### CELLULAR HETEROGENEITY OF HEPATIC MACROPHAGES: ISOLATION AND CHARACTERIZATION OF TWO SUBSETS OF ED2 (CD163) POSITIVE CELLS IN THE RAT LIVER

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**Objective.** ED2 is a mouse monoclonal antibody which is widely used for recognizing rat CD163, a cell surface marker for tissue macrophages. Using flow cytometry we have recently identified two distinct subsets of ED2+ cells from the rat liver. The current study was conducted to isolate and characterize these ED2+ liver cells subsets.

**Methods.** Adult F344, ACI or LEW rats were used in this study. Total liver cells were obtained by *in vivo* perfusion /digestion of the livers with collagenase solution, followed by gradient centrifugation. ED2+ liver cells were isolated by FACS. Phenotypes of the sorted cells were determined by quantitative PCR for gene expression of selected lineage differentiation markers. Primary cultures were established for studies of cell growth and phagocytosis. Transmission electron microscopy was used to define the ultrastructures of the cells.

**Results.** Flow cytometry detected 2 subsets of hepatic macrophages positive for ED2. The first subset exhibited an ED2<sup>high</sup>/AF<sup>high</sup> (autofluorescence) phenotype while the second subset was ED2<sup>dim</sup>/AF<sup>dim</sup>. The ED2<sup>high</sup>/AF<sup>high</sup> cells in culture exhibited morphology, growth pattern and phagocytic activity consistent with the general description of Kupffer cells. On the other hand, the ED2<sup>dim</sup>/AF<sup>dim</sup> cells were smaller in size, monocyte-like in cellular appearance and weak in phagocytosis. In addition to expression of low levels of macrophage-related surface markers such as ED1 (CD68), ED8 (CD18), and CD172a, the ED2<sup>dim</sup>/AF<sup>dim</sup> cells expressed moderate levels of mRNA encoding for myeloid lineage differentiation markers c-fms, ERMP12 (PECAM) and ERMP20 (Ly-6C). Transmission electron microscopy demonstrated that these two subsets of ED2+ cells were characteristic of myeloid cells. Gadolinium treatment effectively eliminated the ED2<sup>high</sup>/AF<sup>high</sup> population but had no effect on the ED2<sup>dim</sup>/AF<sup>dim</sup> cells.

**Conclusion** The data suggest that the ED2<sup>high</sup>/AF<sup>high</sup> population of non-parenchymal liver cells represent the conventional Kupffer cells. The ED2<sup>dim</sup>/AF<sup>dim</sup> cells, however, belong to a subset of non-Kupffer cell hepatic macrophages with functions and origin yet to be defined.

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Withdrawn

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**LEUKOCYTE-ENDOTHELIUM INTERACTIONS IN ACUTE PANCREATITIS AFTER TNF-ALPHA MODULATION: AN INTRAVITAL MICROSCOPIC STUDY**

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**Background.** Leukocyte-endothelium interaction is known to be a remarkable event at the beginning of systemic inflammatory response syndrome. Leukocyte activation and infiltration are believed to be critical steps in the progression from mild to severe pancreatitis and responsible for many of its systemic complications. The aim of this study was to evaluate leukocyte-endothelium interactions in mesenteric postcapillary venules and cytokines serum levels in experimental acute pancreatitis followed by inhibition of TNF-alpha production.

**Methods.** Severe pancreatitis was induced in Wistar rats with a injection of 0.5ml of 2.5% sodium taurocholate into the pancreatic duct. Eighteen rats were divided in 3 groups: Sham (surgical procedure without AP induction), Pancreatitis (AP Induction), and Pentoxifylline (AP induction plus administration of 25 mg/kg pentoxifylline). Intravital microscopy was used to observe inflammatory leukocyte rolling, adhesion, and transendothelial migration in small venules *in vivo* (venule diameter, 15–25 µm). TNF-alpha, IL-6, and IL-10 levels were measured by ELISA.

**Results.** Modulation of TNF-alpha by pentoxifylline shows beneficial effects in this experimental model. The Pentoxifylline group had a statistically significant reduction of leukocyte rolling, adhesion, and transendothelial migration *in vivo* and a statistically significant reduction of inflammatory cytokines levels (IL-6, IL-10, and TNF-alpha).

**Conclusion.** Modulation of TNF-alpha reduced systemic inflammatory response in this experimental model. Moreover, our data suggest that TNF-α induce accumulation (adhesion, and transendothelial migration) of leukocytes in acute pancreatitis.

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**THE EFFECT OF ISCHAEMIC PRECONDITIONING IN HUMAN LIVER SINUSOIDAL ENDOTHELIAL CELLS FOLLOWING HYPOXIA-REOXYGENATION**

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**Background.** Ischaemic preconditioning (IPC) is known to have protective effects against ischaemic-reperfusion injury following major liver resection and transplantation. However, its effect on liver regeneration is still undetermined. We aimed to assess the cytokine and growth factor production by human liver sinusoidal endothelial cells (HLSEC) and evaluate the effect of IPC on these mediators in an *in vitro* hypoxia-reoxygenation (H-R) model mimicking ischaemic-reperfusion injury.

**Methods.** Confluent culture flasks of HLSEC were subjected to H-R (1 hour hypoxia+1 hour reoxygenation), IPC with H-R (10 minutes hypoxia+10 minutes reoxygenation+1 hour hypoxia+1 hour reoxygenation) and compared to untreated Controls. Production of interleukin (IL)-1β, IL-1 receptor antagonist (IL-1ra), IL-6, IL-8, transforming growth factors (TGF)-α, granulocyte-colony stimulating factor (G-CSF) and tumour necrosis factor (TNF)-α were determined over a 48 hour period.

**Results.** IL-6, IL-8 and G-CSF were produced by HLSEC, while IL-1β, IL-1ra, TGF-α and TNF-α were not. IPC prior to H-R increased IL-6 (36% and 38%) and G-CSF (31% and 85%) production compared to H-R alone after 36 and 48 hours respectively. IPC prior to H-R decreased IL-8 output by 9% and 7% compared to H-R alone after 36 and 48 hours respectively. Although there was a trend in increased IL-6 and G-CSF production, there was no significant difference in IL-6, IL-8 and G-CSF production between the IPC-treated group and non-IPC-treated groups.

**Conclusion.** HL-SEC produces pro-regenerative mediators such as IL-6, IL-8 and G-CSF. Although IPC affects IL-6, IL-8 and G-CSF release in HLSEC between 24 to 48 hours following H-R, this was statistically not significant. The final effect on liver regeneration would depend on the interaction of various liver cells and studies on co-culture models are required.

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**ISCHEMIC PRECONDITIONING AND INTERMITTENT CLAMPING INCREASE THE TOLERANCE OF FATTY LIVER TO HEPATIC ISCHEMIA-REPERFUSION INJURY IN THE RAT**

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**Introduction.** Liver ischemia-reperfusion (I/R) injury is a well-known cause of morbidity and mortality following liver surgery and transplantation. Hepatic steatosis increases the extent of cellular injury incurred during I/R injury. Further investigation is warranted to identify measures that reduce the untoward sequelae of liver I/R injury.

**Methods.** Male Zucker rats were subjected to 75-minutes of 70% hepatic ischemia and three hours of reperfusion. The ischemic periods were based on following protocols: Continuous clamping (CC) for 75-minutes; Intermittent clamping (IC) with 5 cycles of 15-minutes clamp on and 5-minutes clamp off; or Ischemic preconditioning (IP) with 10-minutes clamp on, 15-minutes off, and 60-minutes on. Each group was further subdivided (7 rats in each subgroup) into control and treatment (methylprednisolone- MP) arms. The rats were pretreated with intravenous methylprednisolone (2 mg/kg) or normal saline (NS) prior to the induction of ischemia. Warm I/R injury was evaluated using serum levels of aspartate aminotransferase (AST), serum IL-6, hematoxylin and eosin staining, and a specific marker of apoptosis (TUNEL staining).

**Results.** Hepatocellular injury was significantly reduced with IP and IC compared with CC (AST- 3285 ±122.3 and 2875 ±285.4 compared with 5436.3 ±984.7 units/L, respectively (P <0.01). Serum IL-6 level was also significantly reduced with IP and IC compared CC (70 ±8.8 and 76 ±6.2 compared with 147 ±8.5 ng/l respectively (P <0.01). Histologic analysis also revealed that IC and IP provided significant protection as compared with CC group. TUNEL-positive cells were clearly reduced in hepatic tissue of IC and IP groups compared to CC. Interestingly, pretreatment with MP was associated with an increase in serum AST, IL-6, and worsening histologic features in all groups compared to the NS arm.

**Conclusions.** IC and IP increase the tolerance of fatty liver to hepatic ischemia-reperfusion injury in the steatotic liver. MP is associated with increased hepatic I/R injury in the fatty liver.

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**ISCHEMIC PRECONDITIONING VERSUS INTERMITTENT CLAMPING ON HUMAN LIVER SINUSOIDAL ENDOTHELIAL CELLS: EFFECTS ON CYTOKINES AND GROWTH FACTORS**

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**Background.** Ischaemic preconditioning (IP) with continuous clamping and intermittent clamping (IC) of the portal triad are distinct protective strategies against ischaemic-reperfusion injury (IRI) following liver surgery but their effect on liver regeneration is still undetermined. Therefore, we aimed to evaluate the effect of IP and IC on cytokine and growth factor production by human liver sinusoidal endothelial cells (HLSEC) in an *in vitro* hypoxia-reoxygenation (H-R) model to mimic IRI.

**Methods.** Confluent culture flasks of HLSEC were subjected to H-R (1 hour hypoxia+1 hour reoxygenation), IP with H-R (10 minutes hypoxia+10 minutes reoxygenation+1 hour hypoxia+1 hour reoxygenation), IC (15 minutes hypoxia+5 minutes reoxygenation x3+1 hour reoxygenation) and compared to untreated Controls. Differences in production of interleukin (IL)-1β, IL-1 receptor antagonist (IL-1ra), IL-6, IL-8, transforming growth factors (TGF)-α, granulocyte-colony stimulating factor (G-CSF) and tumour necrosis factor (TNF)-α were determined over a 48 hour period.

**Results.** The production of IL-1β, IL-1ra, TGF-α and TNF-α was undetectable in all groups. IP prior to H-R featured increased levels of IL-6 (36% and 38%) and G-CSF (31% and 85%) compared to H-R alone after 36 and 48 hours, respectively. IP prior to H-R exhibited a decrease in IL-8 profile by 9% and 7% compared to H-R alone after 36 and 48 hours, respectively. By contrast, IC increased IL-6 production (22% and 42%) and G-CSF (57% and 107%) compared to H-R alone after 36 and 48 hours, respectively. IC decreased IL-8 production by 8% and 1% compared to H-R alone after 36 and 48 hours, respectively. There was no significant difference in IL-6, IL-8 and G-CSF production between IP-treated and IC-treated groups.

**Conclusion.** Both IP and IC appear to equally influence the expression of pro-regenerative mediators such as IL-6, IL-8 and G-CSF in HLSEC. Both IP and IC seem to influence the release of IL-6, IL-8 and G-CSF between 24 to 48 hours following H-R. These results suggest that both IP and IC could potentially affect the liver regeneration signaling cascade. Hence, both strategies require further evaluation using co-culture models to determine their final effect on these mediators of liver regeneration.

**Oral Posters II – Pancreas II: Techniques, Neoplasm Potpourri OP-11**

4/21/07 4:15 to 6:15 pm  
Abstract Numbers 200–211

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### A SINGLE-INSTITUTION RETROSPECTIVE REVIEW OF LAPAROSCOPIC AND OPEN DISTAL PANCREATECTOMIES

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Laparoscopic surgical techniques are being used more frequently in the treatment of pancreatic disease with minimal morbidity and mortality. In this retrospective review, we compare multiple variables and outcomes in the laparoscopic and open distal pancreatectomies performed at our institution over a four-year period. We reviewed the medical records of 116 patients undergoing distal pancreatic resection from 2002 to 2006. Data gathered included demographics, pancreatic pathology, operative time, estimated blood loss, control of pancreas stump, pancreatic leak and other post-operative complications, and length of stay. Student t-test, median test, and chi-square analyses were used to determine significant differences between laparoscopic and open groups. A p-value of less than 0.05 was considered significant. Of 116 distal pancreatectomies, 26 were performed laparoscopically and 90 open (including 9 laparoscopic cases converted to open). Difficult dissection due to adherent tumor (5), bleeding (2), and technical limitations (2) were reasons for conversion. There were no significant differences in demographics, median operative time, pancreatic leak rate (7.7% versus 8.2%) or overall complication rate (22.7% versus 25.6%). Twenty-five laparoscopic cases were performed for benign disease and one for malignant disease versus 36 for benign and 49 for malignant disease in the open group ( $p < 0.0001$ ). Median EBL was 250 mL in the laparoscopic group versus 750 mL in the open group ( $p < 0.0001$ ). A stapling device was used in 92.3% of the laparoscopic cases to control the pancreatic stump whereas sutures were used in 61.9% of the open cases ( $p < 0.001$ ). Laparoscopic patients had a median length of stay of 5 days versus 7 days in the open group ( $p < 0.006$ ) with 34.8% of the laparoscopic group staying more than 5 days versus 67.1% of the open group staying more than 5 days ( $p < 0.005$ ). Laparoscopic distal pancreatectomy yields comparable surgical results with significantly shorter hospital stays than open pancreatectomy. Pancreatic leak and overall complication rates appear similar. Laparoscopic distal pancreatectomy is a safe, effective treatment option for select cases of pancreatic disease.

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### OPEN AND LAPAROSCOPIC SPLEEN-PRESERVING, SPLENIC VESSEL-PRESERVING DISTAL PANCREATECTOMY: INDICATIONS AND OUTCOMES

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**Background.** Historically, distal pancreatectomy included removing the spleen because of the relations of the splenic artery and vein with the tail of the pancreas. Spleen preserving distal pancreatectomy has been described lately in order to reduce the risk associated with splenectomy. The aim of this study is to report a series of open and laparoscopic distal pancreatectomies with spleen and splenic vessel preservation.

**Methods.** From June 2001 to June 2006, a total of 29 distal pancreatectomies were performed. Spleen and splenic vessel preservation was possible in 10 patients (35%). Both open and laparoscopic approaches were performed. The main variables recorded were demographic data, intra and postoperative complications, length of stay, final pathology results, and incidence of pancreatic leak. A closed suction drain close to the pancreatic stump was placed in every patient. Amylase levels on the drain output were checked on postoperative day two and five.

**Results.** All ten spleen-preserving pancreatectomies were performed successfully. Laparoscopic resection was possible in six patients. Only one patient suffered an intraoperative splenic artery injury, which was repaired without consequence. Postoperative morbidity consisted of one pancreatic fluid collection, which was drained successfully by interventional radiology. Ninety percent of the patients presented high amylase levels on postoperative day two. However, all drains were removed on the first outpatient clinic visit, once the patients were tolerating a regular oral diet. The median length of stay for the open and laparoscopic approach was 4.5 and 7.5 days, respectively. Overall, median length of stay was 5.5 days. Final pathology results revealed serous cystadenoma in 40% of the cases, neuroendocrine tumor of the pancreas in two cases, two mucinous cystadenomas, one carcinoid tumor and one intrapancreatic spleen. With an average follow-up of 18.6 months, no splenic vein thrombosis was detected.

**Conclusions.** Open or laparoscopic spleen-preserving distal pancreatectomy (with splenic vessel preservation) appears to be a feasible and safe procedure. The laparoscopic approach resulted in shorter length of hospital stay and was associated with minimal morbidity. In selected cases of cystic lesions and low grade neoplasms, distal pancreatectomy with splenic preservation is possible.

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### CYSTIC PANCREATIC NEUROENDOCRINE TUMORS: A RARE ENTITY?

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**Introduction.** Pancreatic incidentalomas including non-functioning cystic neuroendocrine tumors (CNETs) are being detected with increasing frequency. CNETs are rare premalignant conditions with fewer than 60 cases reported and the largest published series comprised of only 4 patients. Computed tomography (CT) has been the diagnostic study of choice but only occasionally demonstrates the hypervascular border characteristic of NETs. Endoscopic ultrasound (EUS) with fine needle aspiration (FNA) and immuno-histochemistry may be a more consistent means to establish the diagnosis, but no data on the role of EUS is available. The current review aims to report the largest series of CNETs treated to date, to describe the management of CNETs in that series and document the role of EUS in the diagnosis of CNETs.

**Methods.** Our experience with CNETs treated at an academic medical center between 1995 and 2006 was reviewed with regard to patient demographics, preoperative radiologic/endoscopic evaluation, operative approach, pathology, and perioperative/long-term outcomes.

**Results.** Ten CNETs were treated. The mean age at diagnosis was  $55.9 \pm 10.8$  years. Nine patients were male, one female. One patient had symptoms consistent with a functional tumor (hypoglycemia). The others were non-functional and either asymptomatic (2) or presented with epigastric pain (4) or pancreatitis (3). Nine tumors were detected by CT, but only two demonstrated peripheral hypervascularity. Nine lesions were studied with preoperative EUS and FNA, and all nine demonstrated strong staining for synaptophysin and chromogranin. Tumors were evenly distributed throughout the pancreas with four in the pancreatic head and 6 in the body or tail. All were resected: 1 by enucleation, 3 by pancreaticoduodenectomy, and 6 by distal pancreatectomy. Average tumor size was  $2.3 \pm 0.9$  cm. Perioperative morbidity occurred in 30% (2 intra-abdominal abscesses, one pancreatic fistula). All patients survived surgery. The average length of follow-up was  $2.7 \pm 1.7$  years. One patient had evidence of lymph node involvement at the time of resection and had late hepatic recurrence treated with hepatic artery embolization. The remaining nine have had no evidence of recurrence. All ten are alive presently.

**Conclusions.** Cystic neuroendocrine tumors are rare pancreatic neoplasms which are being detected with increasing frequency as diagnostic CT becomes ever more prevalent. Endoscopic ultrasound with aspiration is an accurate method to establish the diagnosis preoperatively. Surgical resection is safe. Long term outcomes following resection are excellent.

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### CYSTIC PANCREATIC NEOPLASMS: AN EMERGING PROBLEM

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**Background.** Widespread usage of advanced abdominal imaging has resulted in an increased finding of cystic lesions in the pancreas. Greater than 90% of cystic pancreatic lesions are of inflammatory origin. The critical issue confronting the specialists managing these patients is differentiating these inflammatory lesions from neoplastic ones.

**Materials and methods.** Encompassing the duration from June 2001 to June 2006, we performed 121 pancreatic resections. Herein, we report their preoperative workup, operative management, pathologic findings, complications and follow-up.

**Results.** 121 pancreatic resections were performed with 16 (13.2%) patients having cystic pancreatic neoplasms. Our series comprised mostly females (13/16, 81%), with a mean age of 56 (range 22-90). The most commonly utilized preoperative imaging modalities were contrast enhanced computed tomography and gadolinium enhanced magnetic resonance imaging. The lesions were fairly evenly distributed through the pancreas with 5 (5/16, 31%) in the head, 6 (6/16, 38%) in the body and 5 (5/16, 31%) in the tail. Based on pathologic findings 6 (6/16, 38%) tumors were mucinous cystic neoplasms, 1 of which was borderline malignant, 6 (6/16, 38%) were serous cystadenomas, 2 were intraductal papillary mucinous neoplasm, also known as IPMNs (2/16, 12%) and 1 each (1/16, 6%) of neuroendocrine (non-functioning islet cell) and pseudo-papillary types. Operative procedures tailored to location consisted of distal pancreatectomy and splenectomy, pancreaticoduodenectomy (Whipple's procedure) and isolated head resection. Ileus, (>5 days) or poor tolerance of oral diet (>7 days), including delayed gastric emptying, was the most common complication and noted in 6 (6/16, 38%) of patients. This was followed closely by pancreatic leak in 4 patients (25%). Pancreatic leaks were divided equally between proximal and distal pancreatic resections. Three patients were managed with closed suction drains; either by maintaining operatively placed drains or additional drains placed by interventional radiology. Other complications were deep venous thrombosis (1), fascial dehiscence (1), pneumothorax (1), psoas abscess (1) and new onset

pancreatic insufficiency. We had no in-hospital or 30 day mortality. Our follow-up radiographic data (range 4–48 months, mean follow-up duration 21 months) does not show any recurrences at this time.

**Conclusions.** Our results are comparable to other high volume centers. Complications, if and when they arise need prompt diagnosis and quick resolution the availability of specialists, intensive care facilities, interventional radiology services and expert anesthesiologists cannot be overemphasized.

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#### CURRENT DIAGNOSIS AND MANAGEMENT OF SOLID PSEUDOPAPILLARY TUMORS OF THE PANCREAS

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We reviewed our recent institutional experience with solid pseudopapillary (papillary cystic-solid) tumors in order to characterize the presentation and current methods of diagnosis and surgical management of these uncommon tumors of the pancreas. Through an electronic search of patients treated from 2003 until the present, patients with the pathologic diagnosis of a solid pseudopapillary tumor of the pancreas were identified, and their medical records were reviewed. A total of 10 patients (nine females, one male) ranging in age from 14 to 53 (median 33) were identified. In eight patients the tumor was asymptomatic and was found incidentally on abdominal imaging studies; in two patients the tumor was found during evaluation of related symptoms. Radiologic diagnoses included neuroendocrine tumor, mucinous cystic neoplasm, and an unspecified solid mass of the pancreas. The preoperative diagnosis of a solid pseudopapillary tumor was established in 7 patients by means of an EUS-guided biopsy and in one patient by means of a CT-guided biopsy. EUS-guided biopsy was non-diagnostic in one patient, and preoperative biopsy was not performed in 1 patient. In two patients the tumor was located in the head of the pancreas and was treated by means of a Whipple procedure. In eight patients, the tumor was located in the body or tail of the pancreas. Six of these patients underwent a laparoscopic distal pancreatectomy. An open distal pancreatectomy was instead performed in two patients because of the size of the tumor (11 cm) or the patient's body habitus. In all patients negative margins of resection were achieved. In one patient malignant features (capsular invasion, perineural and vascular invasion) were found, but to date (followup 2–36 months, median 21 months) there have been no recurrences. Solid pseudopapillary tumors are considered rare tumors of the pancreas. Our recent institutional experience suggests, however, that they have been underdiagnosed because they frequently remain asymptomatic despite reaching large size. EUS-guided biopsy should be performed as it provides an accurate means of establishing the diagnosis of a solid pseudopapillary tumor. While confirmation of this diagnosis is not necessary to determine the need for surgical resection, establishing the diagnosis of a solid pseudopapillary tumor avoids inappropriate enucleation of such tumors and permits consideration of laparoscopic resection for tumors located in the body or tail of the pancreas.

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#### INCIDENCE, PREVALENCE AND MANAGEMENT OF INTRA-DUCTAL PAPILLARY MUCINOUS NEOPLASM IN OLMDST COUNTY, MINNESOTA, 1976–2005: A POPULATION STUDY

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**Background.** IPMN is being recognized with increasing frequency around the world but the true incidence of Intraductal Papillary Mucinous Neoplasm remains unknown.

**Methods.** We used the records-linkage system of the Rochester Epidemiology Project to ascertain incident cases of Intraductal Papillary Mucinous Neoplasm in Olmsted County, Minnesota from January 1, 1976–December 31, 2005. We also evaluated the number of prevalent cases as of December 31, 2005. Age and sex-adjusted incidence rates for IPMN in residents aged 20 or older were estimated for the period, 1976–2005.

**Results.** We identified 28 incident cases of IPMN. The age- and sex-adjusted cumulative incidence for IPMN Olmsted County MN is 1.63 cases per 100,000 persons (95% CI 1.02, 2.23) from 1976–2005. Point prevalence on December 31, 2005 was 25.96 cases per 100,000 persons (95% CI 14.53) or one per 3,852. Restricting to County residents aged 60 and older the point prevalence is 101.86 cases per 100,000 persons (95 CI 57.22, 146.50) or one per 981 persons. Thirty-two percent of patients were treated surgically while the remainder was followed annually with imaging studies, primarily abdominal CT and EUS. The five year survival rate after diagnosis was 59.6%. The cause of death was pancreatic cancer in four of the eight patients that died.

**Conclusion.** The incidence of IPMN in Olmsted County is low but appears to be increasing. Most patients with this disease were followed annually with imaging studies while about a third of the patients required surgical resection. While our data does not depict an epidemic more epidemiologic studies from other populations are required.

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#### IS SURGERY NECESSARY FOR THE TREATMENT OF PRE-OPERATIVE DIAGNOSED AMPULLA OF VATER ADENOMA?

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**Background.** Ampullary adenoma is very rare and is truly premalignant neoplasm. Current methods of endoscopic biopsy and even intraoperative frozen sections are limited in their ability to rule out co-existing foci of carcinoma. Recently therapeutic endoscopic physician preferred endoscopic snare excision (ESE) even in case of relatively large adenoma. In this study we evaluate diagnostic accuracy of ampullary adenoma and when we should do perform transduodenal local resection (TDLR) or pancreaticoduodenectomy (PD).

**Methods.** The records of 37 patients who admitted at Yonsei Medical Center from January 1986 to December 2005 and with a endoscopic biopsy result was ampullary adenoma were retrospectively reviewed. Final pathologic result, recurrence and re-treatment result in case of margin positive after endoscopic snare excision or TDLR or PD were analyzed and long-term follow-up was ascertained.

**Results.** Among 37 patients, 32 were treated by ESE, TDLR or PD, but 5 were observed without further treatment or follow-up loss. Among these 32 patients, 13(40.6%) were pathologically confirmed adenoma with adenocarcinoma. In these 32 patients, ESE, ESE+PD(PPPD), TDLR and PD(PPPD) were performed for 2, 3, 2 and 6 patients respectively. All patients were alive from 2 to 115 months after treatment except one operation mortality, one recurrence 2months after ESE and one follow-up loss. For 24 patients with adenoma, ESE, TDLR and PD(PPPD) were performed in 14, 1 and 4 patients respectively. Among 14 ESE patients, seven(50.0%) were lateral or base margin positive. In these seven patients, six patients were treated by re-ESE and two patients had recurrence 18 and 19 months after re-ESE.

**Conclusions.** For the management of ampullary tumor, complete removal of tumor should be obtained. For adenoma with adenocarcinoma, we recommended TDLR of PD(PPPD) and for adenoma ESE is one of acceptable treatment modality and margin negative resection is important for long-term good result.

**Key Words.** ampullary adenoma, endoscopic snare excision, surgery.

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#### SOMATOSTATINOMA: A 20-YEAR SURGICAL EXPERIENCE

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**Objective.** The objective of this study was to identify and describe the characteristics of patients diagnosed and treated for somatostatinomas at a single institution.

**Methods.** The pathology and operative databases were queried to identify patients with the histologically confirmed diagnosis of somatostatinoma from the time period of 1986 until 2006. Following patient identification, inpatient charts were reviewed and clinicopathologic data were analyzed. All tumors were re-examined and were confirmed to be somatostatinomas.

**Results.** The results of the search identified six patients with histologically confirmed somatostatinomas. Of the six patients, four presented with significant weight loss (>15 lbs) and abdominal pain, while two patients presented as an incidental finding. All of the patients identified underwent pancreaticoduodenectomy, where four patients had tumor located in the pancreas, while two patients had tumor located in the duodenum. One patient underwent liver resection for metastatic disease. The average size of the primary tumor was 1.0 ± 0.5 centimeters (0.3–1.5 cm). While all tumors were described as strongly positive for somatostatin, immunohistologic staining also demonstrated three of six tumors to be positive for chromogranin. At a median follow up of 4 years (range 4 months to 17 years), five patients were alive without evidence of recurrent disease and one patient, who presented with weight loss and liver metastasis, was alive with recurrent disease.

**Conclusions.** Although rare, six cases of somatostatinoma were identified and treated at a single institution in a 20-year period. Weight loss was the presenting symptom in four patients and two patients were asymptomatic. Long term survival can be expected following surgical resection regardless of symptoms.

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#### IS THERE AN INDICATION FOR INITIAL CONSERVATIVE MANAGEMENT OF CYSTIC LESIONS OF THE PANCREAS?

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**Background.** The evaluation and surgical recommendation for small pancreatic and peri-pancreatic cystic lesions presents a clinical challenge. Our traditional bias has been an aggressive surgical approach based on the "malignant potential" of even small cystic lesions.

**Methods.** We reviewed our experience with patients (n = 78) who presented with a presumed cystic pancreatic lesion and who underwent operative management between 1995 and 2005.

**Results.** There were 55 (71%) females; median age 63 years. Patients presented with an incidental finding (48%), pain (40%), acute pancreatitis (4%), other (8%). The median lesion size was 4 cm (range 1–30 cm). Operations were distal pancreatectomy (n = 48), pancreaticoduodenectomy (n = 14), other (n = 26). Most patients had a non-malignant lesion (n = 65, 83%) (mucinous cystadenoma (n = 29), serous cystadenoma (n = 15), IPMN without invasion (n = 8), pseudocyst, other benign). Malignant lesions (adenocarcinoma, neuroendocrine tumor, and other) were found in 13 patients (17%). The risk of malignancy increased with size: <3 cm (n = 25), 4%; 3–5 cm (n = 23), 13%; and >5 cm (n = 30), 30%. The median size (range) of tumors was: adenocarcinoma (n = 7) 8 cm (3–15 cm); neuroendocrine (n = 2) 2.7 cm (2.4–3 cm); and other (n = 4) 8 cm (5–30 cm). Pre-operative cyst fluid cytology was performed in 41 patients. The negative predictive value (NPV) of cytology for malignancy was 88% and the positive predictive value (PPV) was 100%. Pre-operative serum CA 19-9 was measured in 40 patients (normal <37). The NPV of CA 19-9 for malignancy was 90%; the PPV was 50%.

**Conclusion.** These data support a role for initial conservative management of small cystic pancreatic lesions as the risk of associated malignancy is very low. Cyst fluid cytology and a serum CA19-9 may help select patients with cystic lesions for conservative management. The role of CT and PET for monitoring small cystic lesions is currently being evaluated.

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#### FRANTZ-GRUBER TUMOR – A SPECTRUM OF DISEASES AND SURGICAL TREATMENT OPTIONS: PANCREATICODUODENECTOMY TO LAPAROSCOPIC DISTAL PANCREATECTOMY

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Frantz-Gruber tumor, also known as solid and cystic pseudopapillary tumor of the pancreas, is an uncommon disease that occurs predominantly in young females. Surgical resection remains the treatment of choice as it offers excellent prognosis. Herein, we present three cases of Frantz-Gruber tumor, highlighting the varied presentation and spectrum of surgical options for this disease.

**Methods.** A review of the HPB database was conducted to identify patients who underwent resection for Frantz-Gruber tumor.

**Results.** Three patients were identified; all young females presenting with a variety of clinical features, including upper abdominal pain, mass, and obstructive jaundice. Based on tumor location, the surgical approach consisted of either pancreaticoduodenectomy or laparoscopic distal pancreatectomy. Two patients underwent a Whipple procedure for tumors in the head of the pancreas, while one patient had a laparoscopic distal pancreatectomy and splenectomy for a pancreatic tail tumor. In all cases, disease was confined to the pancreas with no vascular involvement or distant metastases. All three patients underwent a successful, margin-negative resection of their tumor and are alive and disease-free today. Patient #1: A 22 y/o female was referred for evaluation of a periampullary mass detected on physical exam and CT scan. Staging laparoscopy revealed an 8.5 cm resectable mass in the head of the pancreas. Pancreaticoduodenectomy was performed. Final pathology showed a pT2N0M0 pseudopapillary tumor. The patient remains alive and disease-free four years later. Patient #2: A 26 y/o female presented with epigastric pain of several months duration. CT of the abdomen revealed a 5 cm mass in the pancreatic tail; endoscopic ultrasound-guided biopsy showed pseudopapillary cells. She underwent resection of her tumor via a laparoscopic approach. Patient #3: A 22 y/o female with history of obstructive jaundice presented to the surgical clinic for evaluation of a pancreatic head mass. She had undergone a biliary/duodenal bypass and failed resection attempt at an outside institution. CT of the abdomen showed a resectable 8 cm pancreatic head mass, diagnosed as pseudopapillary tumor by biopsy. The patient underwent a Whipple procedure and remains disease-free nearly 3 years later.

**Conclusion.** Frantz-Gruber tumors may vary considerably in their presentation and location in the pancreas. While surgical resection offers a uniformly excellent prognosis and is the treatment of choice, the approaches to resection are diverse and must be tailored to the tumor's location within the pancreas.

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#### OUTCOMES FOLLOWING AGGRESSIVE SURGERY FOR MALIGNANT NEUROENDOCRINE TUMOURS OF THE PANCREAS

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**Background.** Pancreatic neuroendocrine tumours (PNET) often present a diagnostic and therapeutic challenge. Besides the morbidity and mortality associated with surgery, recurrence of disease has hampered its wider application. This study evaluates the outcome of patients following aggressive surgery.

**Methods.** From 1999–2005, records of patients undergoing surgical resection were reviewed. Patients with benign PNETs were excluded. Outcomes studied were patient demographics, radiological investigations, surgical procedures, pathologic characteristics, complications, mortality and disease free survival.

**Results.** Twelve patients were identified with a median age at diagnosis of 54 years (Range: 22–79 years) and a male to female ratio of 7:5. The most common presenting symptoms were abdominal pain (n = 7). Two patients presented with synchronous liver metastasis. Surgical procedures included total pancreatectomy (n = 3), pancreaticoduodenectomy (n = 4) and distal pancreatectomy and splenectomy (n = 5, 2 were laparoscopic). Additional procedures included hepatic resection (n = 2), adrenalectomy (n = 1) and portal vein reconstruction (n = 2). Histological diagnosis was non-functioning PNET (n = 9), Multiple Endocrine Neoplasia (MEN)-1 (n = 2) and malignant insulinoma (n = 1). The median tumour size was 3 cm (Range: 1–14 cm). Eight (66%) had lymph node metastasis and 7 had evidence of angioinvasion (58%). Overall morbidity was 33% with one post-operative death. The median follow-up was 27 months (Range: 2–72). Completeness of resection (p = 0.015), nodal involvement (p = 0.008), and vascular invasion (p = 0.002) were independent predictors of disease recurrence on multivariate analysis. The overall actuarial survival rate at 2-years was 91% and the disease free survival was 69%.

**Conclusion.** In selected patients, aggressive surgery for malignant PNET may improve survival rates with low morbidity. Tumour vascular invasion and nodal involvement are associated with early disease recurrence and poor survival.

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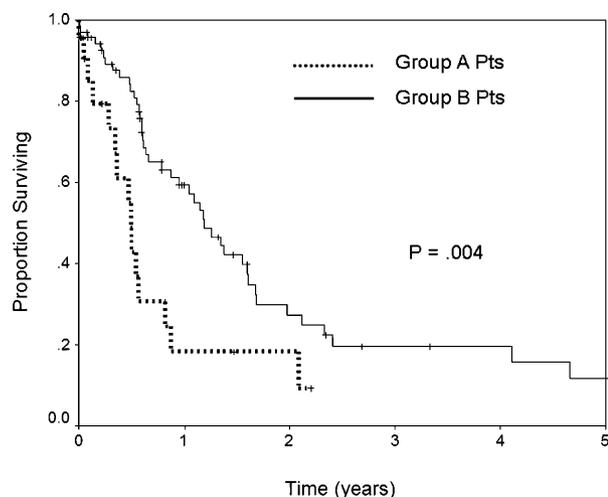
#### IS RESECTION OF PERIAMPULLARY OR PANCREATIC ADENOCARCINOMA WITH SYNCHRONOUS HEPATIC METASTASES JUSTIFIED?

Timothy M Pawlik, MD, MPH, Ana Gleisner, MD, Jordan Winter, MD, Michael Choti, MD, MBA, Richard Schulick, MD, John Cameron, MD, Johns Hopkins  
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**Introduction.** There is no consensus regarding what tumors are appropriately managed with hepatic metastectomy. Specifically, the role of hepatic resection for metastatic periampullary or pancreatic adenocarcinoma remains controversial. We report the morbidity and survival of patients (pts) with periampullary or pancreatic adenocarcinoma who underwent simultaneous hepatic resection for synchronous liver metastasis.

**Methods.** Between 1995 and 2005, 1563 pts underwent surgery for periampullary (n = 608) or pancreatic adenocarcinoma (n = 955). A matched 1:3 paired analysis was used to compare pts with synchronous metastatic disease who underwent primary tumor resection + simultaneous hepatic metastectomy (Group A) to pts without evident metastatic disease who underwent primary tumor resection alone (Group B).

**Results.** Of 1563 pts undergoing resection of periampullary or pancreatic adenocarcinoma, 22 (1.4%) underwent hepatic resection for synchronous liver metastasis. The primary tumor site was ampullary (n = 1), duodenal (n = 2), distal bile duct (n = 2), or pancreas (head, n = 10; tail, n = 7). The majority of pts (86.4%) had a solitary hepatic metastasis; median size of the lesion was 0.6 cm. Hepatic metastectomy included wedge resection (n = 20), segmentectomy (n = 1), and hemi-hepatectomy (n = 1). Group A



pts were matched to Group B pts based on primary tumor histology, location, and size, as well as nodal and surgical margin status. On matched analysis, perioperative complications were similar (Group A, 45.5% vs. Group B, 48.4%;  $p = .99$ ), but post-operative mortality (Group A, 18.2% vs. Group B, 4.5%;  $p = .06$ ) was increased in pts undergoing hepatic resection. Median survival of Group A pts was 5.9 mon compared to 14.2 mon for Group B ( $p = .004$ ) (Fig). In pts undergoing resection of synchronous liver metastasis, pancreatic (median, 6.2 mon) vs. non-pancreatic (median, 7.1 mon) primary tumor histology was not associated with survival ( $p = .09$ ).

**Conclusion.** Resection of periampullary or pancreatic adenocarcinoma with resection of synchronous metastatic liver disease was associated with higher perioperative mortality. Long-term survival for even well-selected pts with low volume metastatic liver disease was uncommon. Simultaneous resection of periampullary or pancreatic carcinoma with synchronous liver metastasis may not be justified.

#### Oral Posters II – Pancreas III: Staging, Prognosis, Technical Issues OP-12

4/21/07 4:15 to 6:15 pm

Abstract Numbers 212–222

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#### THE ROLE OF PANCREATOCODUODENECTOMY IN THE TREATMENT OF COMPLEX PANCREATIC TRAUMA

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**Objectives/background.** This study evaluated the role of pancreaticoduodenectomy in the management of complex proximal pancreatic injuries.

**Patients and Methods.** Demographic data, mechanism and extent of injury, Abdominal Trauma Index, operative procedure, postoperative course, complications and outcome were analyzed in 64 patients who had pancreatic injuries between January 2001 and December 2005.

**Results.** 8 patients (median age 27 years; 4 gunshot, 3 blunt trauma, 1 stab) had cephalic pancreaticoduodenectomy for complex duodeno-pancreatic injury. 2 had IVC and 1 portal vein injuries. Three patients had a pylorus-preserving PD and five patients had a standard Kausch-Whipple resection. The mean ATI was 47 (range 34–76). The median intraoperative blood replacement was 1200 ml (range 600–6300 ml). The median duration of surgery was 5 h 25 min (range 4 h 10 min to 6 h 50 min). One patient died postoperatively of multi-organ failure. Complications included anastomotic leaks due to pancreatic (1) and biliary (1) fistulae, delayed gastric emptying (2). Factors complicating surgery were shock on admission, the number of associated injuries, coagulopathy, hypothermia and gross bowel oedema.

**Conclusions.** Pancreaticoduodenectomy is a life-saving procedure applicable to a small cohort of patients with complex unreconstructable or devitalized injuries to the pancreatic head. ATI score accurately predicted severity and mortality.

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#### ANTHROPOMETRIC ASSESSMENT OF THE “STAGING WINDOW” PRIOR TO PANCREATOCODUODENECTOMY

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**Introduction.** Although several studies have examined peri-operative nutritional supplementation in patients undergoing pancreaticoduodenectomy (PD) all provided support at various timepoints. In theory, the pre-operative period offers a therapeutic “window” for nutritional support. This study undertakes a detailed nutritional assessment in the pre-operative work-up period to identify whether there is a window for nutritional supplementation.

**Methods.** Data were collected prospectively on 25 patients undergoing PD under the care of an individual hepatobiliary surgeon in a regional HPB service from January 2005 through September 2006. Data were collected from index admission to discharge on: demography, clinical course, tumour-related data, anthropometric measurements, calorie intake, operative detail and outcome. All data refer to time from admission to HPB unit. The median age was 58 (range 32–75) yrs and 14 were female. 13 were in-patients at admitting hospitals prior to referral with a pre-HPB unit median hospital stay of 10 (1–31) days. Seven were jaundiced on arrival. Median delay from admission to surgery in the jaundiced group after stenting was 30 (3–46) days). Median delay from admission to surgery in the non-jaundiced group was 32 (1–65) days). Measured end-points were: body mass index (BMI), mid-arm circumference (MAC in cms), triceps skinfold thickness (TST in mms), Grip strength in kilopascals (kPa). Data were compared from admission to pre-op and from surgery to discharge with analyses being undertaken by non-parametric tests (Mann-Whitney U).

**Results.** Median in-patient stay was 33 (11–47) days. Twelve (48%) experienced some form of complication. There were no in-hospital deaths.

There was a significant fall in BMI from base to discharge ( $P = 0.02$ ) which was associated with a fall in MAC ( $P = 0.005$ ) indicative of loss of lean body muscle mass. However, there was no significant difference from admission to pre-op in any parameter, even in the jaundiced subgroup.

**Conclusions.** Although PD can be accomplished safely, it results in a drastic peri-operative fall in BMI. Even with a prolonged pre-operative staging period, there does not appear to be a likely benefit from pre-operative supplemental nutrition in excess of a normal diet.

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#### CHARACTERIZATION OF PERI-OPERATIVE BLEEDING AND TRANSFUSION UTILIZATION IN A MODERN SERIES OF PANCREATOCODUODENECTOMIES

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**Background.** Peri-operative bleeding requiring transfusion and/or re-operation has historically been a common complication following pancreaticoduodenectomy (PD). High cost and low supply of red blood cells, as well as short and long complications associated with transfusion warrant a critical analysis of bleeding and transfusion utilization.

**Methods.** We reviewed 50 PDs performed by 3 surgeons (2000–2005). Peri-operative bleeding and red blood cell transfusion utilization was analyzed in the context of patient’s presentation and operative findings.

**Results.** Median patient age in this series was 64 years (23–83 years); 50% male. Median pre-operative hematocrit was 37.3% (range 24.7–50.1%). Median intra-operative blood loss was 800 mL (range 200–3500 mL). Overall, 56% of patients received a red cell transfusion in this series; 46% of patients received an intra-operative transfusion. Among patients who received a transfusion, the median number of units transfused was 1.5 units (range 1–8 units). No patient in the series required re-operation for bleeding. Median post-operative day #1 hematocrit in patients not receiving an intra-operative transfusion was 33.5% (range 28.7–37) while median hematocrit in patients receiving a transfusion was 31.8% (range 24.2–42.1). Estimated blood loss was significantly higher in patients receiving perioperative transfusions (1311 mL) than those who received no transfusion (569.2 mL) ( $p < 0.001$ ). Age  $> 60$  ( $p < 0.05$ ) and pre-operative hematocrit  $< 35\%$  ( $p = 0.05$ ) were significantly associated with transfusion utilization. Peri-operative mortality was 2/50 (4%); causes of mortality were sepsis (POD 37) and aspiration (POD 10).

**Conclusions.** Transfusion utilization with PD remains high although bleeding requiring re-operation and bleeding associated mortality in this modern series is low. More selective intra-operative transfusion utilization may be indicated. Patients undergoing PD who are  $> 60$  years of age and those who have pre-operative hematocrit  $< 35\%$  would good candidates for aggressive transfusion prevention strategies.

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#### MODIFIED CATELL’S PANCREATICO-JEJUNOSTOMY, BUTTRESSING AND ISOLATED BILIO-PANCREATIC LOOP RESULTS IN BETTER OUTCOMES FOLLOWING PANCREATOCODUODENECTOMY

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**Aim.** Pancreaticoduodenectomy (PD) is considered as one of the most challenging and complex intra-abdominal procedures, with different technical variations having been described. We assessed outcomes following PD using the modified Catell’s method, with buttressing of soft pancreas and using an isolated bilio-pancreatic loop.

**Patients and Methods.** Over a 4 year period, between May 2002 and June 2006, 50 PDs were performed by a single surgeon using the modified Catell’s method. Post-operative morbidity, mortality, details of pancreatic texture, PD size were recorder prospectively.

**Results.** Median pancreatic duct size 4 mm (0.2–10 mm) respectively. The pancreas was found to be firm in 18 patients (36%), intermediate in 13 patients (26%) and soft in the remaining 19 patients (38%). Buttressing was performed in 21 (42%) of patients. Additional procedures included portal vein reconstruction ( $n = 5$ ) and metastectomies ( $n = 2$ ). Median intra-operative blood loss was 300 mls. There were no intra-operative and in-hospital mortalities in this cohort. Major complications occurred in 7 patients (5 requiring relaparotomy and 2 managed conservatively). The re-operated group included bleeding from the stapled jejunum-jejunal anastomosis ( $n = 4$ ), bowel obstruction from internal herniation ( $n = 1$ ). Two patients with a biliary and pancreatic leak respectively were successfully managed conservatively.

**Conclusion.** Our early results suggest, the Modified Catell’s Pancreatico-jejunosotomy with buttressing for soft pancreas using an isolated bilio-pancreatic loop are safety measures for better outcomes following Pancreaticoduodenectomy.

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### SURGICAL ASPECTS OF LIVER ARTERIALIZATION AFTER PANCREATECTOMY WITH CELIAC AXIS RESECTION FOR LOCALLY ADVANCED CANCER OF THE PANCREATIC BODY

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The main reason for unresectability in locally advanced cancer of the pancreatic body (ACPB) is the invasion of major vessels such as the common hepatic artery and celiac axis.

**Aim.** To present different surgical techniques and results of liver arterialization after radical pancreatectomy with en bloc resection of the celiac axis in patients with ACPB.

**Methods.** Between May 2004 and October 2006, 4 patients with carcinoma of the body (3) and head-body (1) of the pancreas underwent radical resection. Vascular invasion was observed on preoperative three-dimensional CT angiographic scan. Encasement of the celiac axis (CA) (4), common hepatic artery (CHA) (4) and splenic artery (SA) (4) were noted, as well as infiltration of superior mesenteric vein (SMV) (1). No regional or general dissemination was demonstrated. In all 4 patients, complete macroscopic tumor removal (R0) was achieved by body and tail pancreatectomy (3) and total pancreatoduodenectomy (1) with en bloc resection of the CA, CHA, SA and left gastric artery. Combined resection of SMV vein was required (1). The adequacy of liver blood supply was assessed by manual palpation and Doppler study. Appleby operation was performed with intraoperative radiation in 1 patient with hepatic arterial flow through the pancreatoduodenal arcade from the superior mesenteric artery. 3 patients underwent arterial reconstruction: Direct end to end anastomosis (CHA-stump CA) was feasible in 2 patients. An interposition of a PTFEt prosthesis of 6 mm in diameter was required in 1 patient.

**Results.** Operative time ranged from 350 to 820 minutes. Red blood transfusions of 3, 5, 6 and 8 Units were administered during the surgery, respectively. The serum concentrations of AST and ALT on postoperative day 1 were 210–620 and 130–590 in the three patients who underwent arterial reconstruction. The patient with Appleby operation had significantly higher values; 1200 and 1080, respectively. AST and ALT recovered to the preoperative level within 11 days. Postoperative mortality (30 days) was 1/4. The patient, with radiotherapy and chemotherapy previous treatment died as a result of sepsis fifteen days after the operation. No vascular or digestive complications could be demonstrated.

**Conclusions.** Pancreatectomy with CA resection to treat locally advanced ACPB is feasible. The surgical procedure offers a high resectability and radicality. Late outcome should be further studied.

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### NODAL SAMPLING IN PERIAMPULLARY CANCER: DOES IT CHANGE YOUR APPROACH?

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**Objective.** To evaluate the predictive value of regional pancreatic nodal sampling in periampullary tumors.

**Background.** Lymph node status in periampullary cancers has been discussed as a way to avoid proceeding with pancreaticoduodenectomy at an early stage in exploration. Common hepatic artery and common bile duct nodal groups (lymph node groups of 8 and 12 respectively according to Japan Pancreas Society Classification) are among the first nodal groups that are exposed during initial exploration for pancreaticoduodenectomy. Although lymph node sampling and the idea of sentinel lymph node biopsy have been proposed as a guide for treatment selection, the predictive value of lymph node sampling has not been addressed.

**Study design.** 45 patients underwent pancreaticoduodenectomy in a single institution and by a single surgeon between September 2005 and September 2006. 36 patients had a diagnosis of periampullary tumor and had regional node sampling at the beginning of the procedure. In a retrospective analysis, we evaluated the predictive value of regional nodal sampling on overall nodal status.

**Results.** Of the 36 patients with diagnosis of periampullary tumor, 23 had both negative nodal sampling and final regional nodal involvement for metastatic tumor; 9 patients had a negative nodal sampling but positive final nodal involvement; 4 patients had both positive nodal sampling and final nodal involvement for metastatic tumor (see table).

**Conclusion.** Sampling of common hepatic artery and common bile duct nodal groups has a negative predictive value of (0.718) and positive predictive value of (1) in evaluating regional pancreatic nodal status. Therefore, decision regarding performing a pancreaticoduodenectomy and prediction of final nodal status can not be based on initial nodal sampling.

Patients (n)	Sentinel Node †	Regional Nodal Status
23	Negative	Negative
9	Negative	Positive
4	Positive	Positive

† Hepatic artery and common bile duct nodal groups.

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### LYMPH NODE RATIO AS A PREDICTIVE FACTOR IN PANCREATIC ADENOCARCINOMA

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**Background.** Survival after curative resection for pancreatic adenocarcinoma remains poor. Lymph node status has been reported as an important prognostic factor. This study evaluates the impact of lymph node ratio (positive lymph nodes to total number of lymph nodes removed) on the survival of patients who underwent a curative resection for pancreatic adenocarcinoma.

**Methods.** A review of the institutional pancreatic cancer database identified 408 patients diagnosed with pancreatic ductal adenocarcinoma between 1971–2005. Demographic data and clinico-pathologic information for patients who underwent a curative resection was reviewed. Prognostic variables for the patients who underwent a curative resection were analyzed.

**Results.** Of the 395 patients, 67 (17%) were resectable and 328 (83%) were inoperable. Of these 328 patients, 239 (58.5%) had distant metastatic disease at presentation. The 67 resectable patients underwent a curative pancreatectomy with regional lymphadenectomy. Of these 67 patients, 10 patients died within 12 months and were excluded from the study. Median follow up for the remaining 57 patients was 26.8 months. Median number of lymph nodes removed was 14 (range: 1–47). Of the 57 patients, 33 patients had positive and 24 had negative lymph nodes. Median survival for all patients was 42 months. Number of harvested lymph nodes had no impact on overall survival in the node- negative or node-positive patient populations. When lymph node ratio was examined as a continuous variable a Relative Risk ratio of 3.115 (p value = 0.0947) was noted (Table).

**Conclusion.** The data suggests that lymph node ratio may be predictive of survival in patients with resected pancreatic adenocarcinoma. A larger sample size will be required to fully evaluate its role.

Variable	P-Value	Relative Risk	95% RR confidence limits	
Total nodes	0.7576	0.994	0.956	1.033
Positive nodes	0.4285	1.027	0.962	1.095
Node ratio	0.0974	3.115	0.822	11.812

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### ROLE OF PREOPERATIVE 18-FDG-PET IN PANCREATIC MASSES

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**Background.** Pancreatic cancer is a lethal disease. The role of 18-fluorodeoxyglucose positron emission tomography (18-FDG-PET) in the preoperative evaluation of pancreatic masses is incompletely understood.

**Aim.** To determine a role of preoperative 18-FDG-PET in the clinical evaluation and management of a pancreatic mass.

**Methods.** During January 2004–December 2005, 54 patients who were evaluated for pancreatic mass subsequently underwent surgical resections. Final pathology reports were available for all 54 patients. Twenty-nine patients had 18-FDG-PET in addition to the standard preoperative workup. These 29 cases formed the basis of this retrospective report.

**Results.** Among the 29 cases with preoperative 18-FDG-PET, the pathology of the malignant tumors included 20 ductal adenocarcinoma (DA), 1 metastatic renal cell (RCC) carcinoma, 1 gastrointestinal stromal neoplasm (GIST), and 2 intraductal papillary mucinous neoplasms with dysplasia (IPMN), and 2 neuroendocrine neoplasms (Neu.) The benign pathology included 1 chronic pancreatitis (CP), and 2 cystadenoma. The preoperative 18-FDG-PET was positive showing the hypermetabolic foci in the pancreas in 18 of DA, 1 Neu, and 1 GIST. The 18-FDG-PET was negative in 2 DA, 1 RCC, 1 Neu, 2 IPMN, 1 CP, and 2 cystadenomas.

**Conclusion.** Preoperative 18-FDG-PET correlates well with pancreatic adenocarcinoma. However, 18-FDG-PET did not change the clinical decision and management of the primary pancreatic cancer. The role of 18-FDG-PET in IPMN, nonpancreatic malignancies, and recurrent pancreatic cancer remains to be determined.

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**PANCREATIC RESECTION FOR METASTATIC RENAL CELL CARCINOMA TO THE PANCREAS**Kamran M. H. Karimi, MD, David W. Mcfadden, MD  
West Virginia University, Morgantown, WV

**Background.** Although extremely rare for most primary malignancies, the presence of metastases to the pancreas is usually a harbinger of diffuse systemic involvement. Clear cell renal cell carcinoma (RCC) of the kidney differs in that respect. Metastatic deposits tend to be isolated and diffuse systemic involvement may be absent.

**Materials and methods.** An IRB approved retrospective review of 3 cases of histologically confirmed RCC metastases to the pancreas was performed. We present their pre-operative workup, surgical treatment, histopathological findings and postoperative course.

percutaneous drainage is optimal for large abscesses. The appearance of blood in a surgical drain or the gastrointestinal (GI) tract following PD suggests arterial pseudoaneurysm. Angiography proves the diagnosis, and angiographic embolization generally provides definitive therapy. Control of concomitant pancreatic fistula is mandatory. Pancreaticojejunostomy stricture is a late complication after PD, presenting with post-prandial pain, and/or diarrhea. Magnetic resonance cholangiopancreatography (MRCP) with secretin stimulation proves the diagnosis; treatment is by surgical revision. Hepaticojejunostomy stricture is also a late complication after PD, usually presenting with post-prandial right upper quadrant pain. MRCP proves the diagnosis; percutaneous transhepatic cholangiography (PTC) allows treatment by stenting.

**Conclusions.** With increased performance of PD, "unusual" complications will be seen more frequently. Early recognition and treatment of these complications will contribute to optimal patient outcome.

Complication	Timing	Symptoms	Diagnosis	Treatment
SMV/PV Thrombosis	Early	Increased fluid sequestration	Ultrasound	Anticoagulation, surgical revision
Chylous fistula	Early	Chyle in drain	↑ triglyceride in drain fluid	TPN, sandostatin
Afferent limb obstruction	Early/Late	Postprandial pain, diaphoresis	Abdominal CT	Endoscopy, Surgical revision
Hepatic abscess	Early	Fever, mental status change	Abdominal CT	Antibiotic, drainage
Pseudoaneurysm	Late	Blood in drain, GI bleed	Angiography	Embolization, control fistula
Pancreaticojejunostomy stricture	Late	Postprandial pain	MRCP (secretin)	Surgical revision
Hepaticojejunostomy stricture	Late	Right upper quadrant pain	MRCP/PTC	Stent

See text for abbreviations

**Results.** Three out of 121 pancreatic resections performed in the last five years at the our institution have been for the indication of RCC metastasis to the pancreas. All 3 of our patients were female. Their ages ranged from 56 to 70 years (mean age = 63 years). The time interval between nephrectomy and detection of the pancreatic recurrence ranged from 5 to 15 years (mean = 11.6 years). Two of our patients had Stage I disease at the time of initial diagnosis of primary RCC and one had Stage III. Only one out of three patients was symptomatic with fatigue, for the other two the lesions were detected either during surveillance or during workup of an unrelated illness. Surgical procedures were performed at a mean interval of 3.6 months (range 3–4 months) from the time of diagnosis and referral. Multimodal preoperative imaging with magnetic resonance (MR) scan and combined computed tomography with positron emission tomography (CT-PET) was utilized in all cases. None of our patients underwent any preoperative tissue diagnosis. The surgical procedure in all cases was distal/subtotal pancreatectomy and splenectomy. Solitary metastases were found in two and multiple in one of our patients. We had one complication in the form of a pancreatic leak, which required a combined surgical and interventional approach to effect a resolution. We did not encounter any in-hospital or 30-day mortality.

**Conclusions.** Three patients, all women, underwent distal pancreatectomy and splenectomy. Mean time period between nephrectomy and findings of pancreatic metastasis was 11.6 years. One patient had a major complication with a pancreatic fistula. Two patients have developed extrapancreatic recurrences. Resection of RCC metastases to the pancreas may offer a survival advantage in select group of patients. Development of metastatic deposits after a prolonged disease-free period may actually be a negative prognostic indicator, implying a rapid and uncontrollable change in tumor biology.

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**UNUSUAL EARLY AND LATE COMPLICATIONS OF PANCREATICOJUNOSTOMY: RECOGNITION IS PARAMOUNT TO DIAGNOSIS**Nicholas J Zyromski, MD, Attila Nakeeb, C. Max Schmidt, MD, PhD, Henry A Pitt, MD, Keith D Lillemoe, MD, Thomas J Howard, MD  
Indiana University, Indianapolis, IN

**Background.** Pancreaticoduodenectomy (PD) is being performed more frequently; common complications are well described. A number of unusual complications are less well characterized.

**Methods.** Review of a prospectively collected database.

**Results.** Superior mesenteric vein/portal vein (SMV/PV) thrombosis may occur early or late after PD. Unusually large fluid requirements (early) or sudden appearance of ascites (late) should prompt SMV/PV ultrasound to confirm the diagnosis. Anticoagulation should be instituted immediately; immediate re-operation is appropriate in select patients. Chylous fistula presents with high-volume, milky drain effluent. This diagnosis is confirmed by elevated triglyceride level in drain fluid. Institution of total parenteral nutrition (TPN) and sandostatin is effective therapy in most patients. Colicky post-prandial epigastric pain and diaphoresis suggests afferent limb obstruction. Abdominal computed tomography (CT) may demonstrate a dilated afferent limb; treatment is by endoscopy (early) and operative revision (definitive). Hepatic abscess may present with low-grade fever, chills, diaphoresis, or subtle mental status alteration. Abdominal CT proves the diagnosis. Antibiotic therapy alone may successfully treat small abscesses;

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**LIFE-THREATENING BLEEDING FROM DUODENUM DUE TO PANCREATIC DISEASES**Yuki Sakurao, MD, Mitsugi Shimoda, MD, PhD, Masato Katoh, MD, PhD, Kyu Rokkaku, MD, PhD, Tokihiko Sawada, MD, PhD, Keiichi Kubota, MD, PhD  
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**Introduction.** Although some bleeding from the duodenum is frequently observed in patients with pancreatic head tumors, life-threatening bleeding from the duodenum due to pancreatic diseases is an extremely rare condition. Here we report two such rare cases treated by pancreatoduodenectomy (PD). [Case 1] A 60-year-old man was admitted to our department with upper abdominal pain and tarry stool. Abdominal CT and angiography showed arterio-venous malformation (AVM) of the pancreas head. Endoscopy revealed bleeding from the duodenal varices caused by portal hypertension induced by AVM. After placement of embolization coil in the gastroduodenal artery, PD was performed. Histological examination showed AVM of the pancreas head. Postoperatively, the bleeding was stopped. [Case 2] A 63-year-old man was admitted to our department with jaundice and tarry stool. CT demonstrated no definite tumor. Endoscopy revealed severe bleeding from a duodenal ulcer of the second portion. Under a tentative diagnosis of post-bulbar ulcer, PD was performed immediately. Histological examination revealed pancreatic cancer invading the duodenal wall, causing a huge ulcer.

**Conclusion.** Only PD can cure the rare conditions of life-threatening bleeding from the duodenum due to pancreatic diseases.

**Oral Posters II – Liver IV: Metastatic Disease**

OP-13

4/21/07 4:15 to 6:15 pm

Abstract Numbers 223–234

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**SURGICAL INTERVENTIONS FOR METASTATIC LESIONS TO THE LIVER: A NATIONAL PERSPECTIVE**James T Mcphee, MD, Joshua S Hill, MD, Zachary Hurwitz, MS, Giles F Whalen, MD, Mary E Sullivan, RN, Jennifer F Tseng, MD  
University of Massachusetts Medical School, Worcester, MA

**Background.** Metastatic lesions to the liver are associated with an exceedingly poor prognosis. Complete surgical resection, when feasible, remains the gold standard and has been shown to improve five-year survival for primary colon lesions. Optimizing outcomes for the peri-operative period are imperative to improve one's chance of long-term survival. The purpose of this study was to evaluate operative outcomes for hepatic resections for metastatic disease at the national level.

**Methods.** The Nationwide Inpatient Sample was queried to identify all patient discharges that occurred for hepatic resection of metastatic lesions from the years 1998–2004. Patients were identified by appropriate ICD9-CM diagnostic and procedural codes. Inpatient mortality was the primary measured outcome. Categorical variables were analyzed by chi square. A multivariate logistic regression was performed with mortality as the

dependent variable. The regression was adjusted for patient age, sex, race, and selected co-morbidities. In addition adjustments were made for certain hospital level characteristics including geographic location, teaching status, and annual surgical volume.

**Results.** Over the seven-year period of the study, an estimated 42,000 patient-discharges occurred for the surgical treatment of a metastatic liver lesion. 50% of patients were women; 82% were white. Overall, 23% of patients undergoing resection underwent a hepatic lobectomy, 44% underwent a wedge resection and 33% underwent enucleation/local destruction of their lesion, with respective mortality rates of 4.3%, 2.7%, and 1.5%. By univariate analysis, in aggregate form, procedures performed at teaching hospitals had a lower mortality (3.3 vs. 2.5%,  $p < 0.05$ ). Teaching hospitals also performed a higher percentage of hepatic lobectomies compared to non-teaching hospitals (26% vs. 11%,  $p < 0.05$ ). There was no correlation between annual hospital surgical volume and operative mortality on univariate or multivariate analysis ( $p > 0.05$ ).

**Conclusions.** Based on a large retrospective administrative survey, patients with metastatic lesions to the liver have acceptable operative mortality rates when they undergo resection. While teaching and non-teaching hospitals have similar mortality rates, teaching hospitals perform higher-mortality procedures such as hepatic lobectomy more frequently than non-teaching hospitals. These data suggest that heterogeneous procedures such as liver resection for metastatic disease may require more complex analyses to ascertain the true effects of factors such as hospital procedure volume and academic status on mortality.

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### MULTIMODAL TREATMENT OF LIVER METASTASIS FROM GASTROINTESTINAL STROMAL TUMOURS

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**Introduction.** Gastrointestinal Stromal Tumours (GIST) clinical behaviour is unpredictable and surgery alone does not cure recurrent GIST. Metastatic liver disease is a major determinant of patient's survival.

**Methods.** Database and records of patients with liver metastasis from GIST ( $n = 13$ ) treated at our unit between January 2002 and June 2006 were reviewed. Treatment modalities included surgical resection, radio frequency ablation, hepatic artery chemoembolisation, imatinib mesylate, and selective internal radiation therapy using Yttrium microspheres (SIRTEX). Patient demographics, clinicopathological characteristics of the primary tumour and the extent of intrahepatic and extrahepatic metastatic disease were recorded.

**Results.** There were 6 (46%) males and 7 (54%) females. The mean age at time of diagnosis of the primary tumour was  $65.5 \pm 9.7$  years (range 45–80). Five patients (38%) had synchronous metastasis at presentation. The primary tumour site was the stomach in six patients (46%), terminal ileum three patients (23%), duodenum two patients (15%) and the pelvis in two patients (15%). The mean size of the metastatic liver lesions was  $8.03 \text{ cm} \pm 4.33$  (SD). In 7 patients liver resections were performed (in 3 patients repeatedly). RFAs were performed in 4 patients, in two patients repeatedly. In two patients trans-arterial chemoembolisation (TACE) was performed and one patient was treated with SIRTEX treatment. 5 patients were treated with imatinib, two patient received repeated series. One patient received 8 therapeutic modalities, 2 patients 7 modalities and another patient received 4 treatment modalities. The more modalities were given the longer survival time was observed. Resection and imatinib treatment significantly improved the survival time in comparison with imatinib treatment alone ( $p = 0.031$ ). Of all patients who underwent hepatectomy, three patients survived more than 5 years (23%) after the initial hepatectomy. The average survival was 35.14 month.

**Conclusion.** Multimodal approach for patients having liver metastasis from GIST provides better survival rates. Well-conducted prospective studies are needed to further evaluate the different treatment options.

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### HEPATIC RESECTION FOR METASTATIC GASTRO-INTESTINAL AND PANCREATIC NEUROENDOCRINE TUMOURS: OUTCOME AND PROGNOSTIC PREDICTORS

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**Background.** Treatment modalities of hepatic metastases from neuroendocrine tumours (NET) include surgery, somatostatin analogues or chemoembolization. The aims of this study were to evaluate the outcome of patients following surgery and identify prognostic predictors of recurrent disease.

**Methods.** Retrospective clinico-pathological analysis of patients managed with hepatic NET metastases over a 13-year (January 1993–December 2005) period.

**Results.** 18 patients with hepatic metastases from NET were identified with a median age of 53 (31–75) years. The localization of the primary tumour was the terminal ileum ( $n = 8$ ), pancreas ( $n = 7$ ), appendix ( $n = 2$ ) and duodenum ( $n = 1$ ). 12 patients had synchronous hepatic metastases and 6

patients developed metachronous hepatic tumours over a median period of 20 (6–144) months. Presenting symptoms included abdominal pain ( $n = 13$ ), recurrent diarrhoea ( $n = 7$ ) and flushing ( $n = 7$ ). 15 patients underwent surgery with curative intent and 3 patients had palliative resection. The overall 2- and 5-year actuarial survival rates were 94% and 86%, respectively. The 2- and 5-year disease-free rates following hepatic resection with curative intent were both 66%. Partial or complete control of endocrine-related symptoms was achieved in all patients following surgery. Recurrent disease occurred in 4 patients. Resection margin involvement was associated with developing recurrent disease. The overall morbidity was 22% with one post-operative death. The overall follow-up period was 45 (9–93) months.

**Conclusion.** Surgical resection for hepatic NET metastases may improve survival in selected patients and a clear resection margin predicts disease-free interval.

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### PARTIAL HEPATECTOMY FOR HEPATIC NEUROENDOCRINE MALIGNANCY: WHO BENEFITS?

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**Introduction.** Controversy persists regarding the indications for and timing of surgical resection of hepatic neuroendocrine (NE) tumors. Aggressive strategies of resection or debulking have often been adopted. However, guidelines for patient selection are lacking, and long-term outcomes of resection in the setting of multimodal therapies remain unclear.

**Method.** We reviewed a prospectively maintained database of patients undergoing resection of hepatic NE tumors between 1992 and 2004. Clinicopathological variables were analyzed to identify factors associated with overall survival (OS), progression-free survival (PFS) and symptom control.

**Results.** Sixty patients were identified. Two-thirds underwent prior or concomitant resection of primary tumor. One-third presented with hormonal symptoms. Median extent of liver involvement by disease was 40%. Sixty percent underwent at least a hemihepatectomy; complete resection was performed in 63%. After a median follow-up of 52 months, median OS was 61 months. Recurrent or progressive disease was observed in 88%; the liver was the site of initial recurrence or progression in 83%, and median PFS was 12 months. All patients with hormonal symptoms experienced complete relief for a median of 27 months. Eighty percent received additional therapy after resection, including 53% who underwent hepatic arterial embolization. Absence of extrahepatic disease and prior or concomitant resection of primary tumor were associated with improved OS on multivariate analysis; ability to perform a complete resection was associated with improved PFS.

**Conclusion.** Partial hepatectomy can be performed safely with effective control of hormonal symptoms. Long-term survival outcomes appear reasonable, but recurrence or progression is usually observed. Extrahepatic disease and the absence of primary tumor resection are associated with significantly poorer survival; inability to perform a complete resection is associated with faster time to disease progression. These findings suggest that certain oncological characteristics can identify those patients who may not expect to benefit from surgical intervention.

	median survival (months)	multivariate p
extrahepatic disease	(OS) 91 vs 34	0.04
primary tumor resection	(OS) 91 vs 48	0.04
complete resection	(PFS) 18 vs 6	0.01

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### SIMULTANEOUS RESECTION OF COLORECTAL TUMORS AND LIVER METASTASES

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**Introduction.** Recent advances in hepatobiliary and colorectal surgery had permitted to do simultaneous resection of a primary colorectal tumor and liver metastases. The aim of this study is to compare our surgical results in colorectal synchronous liver metastases resection versus staged liver metastases resection from a previously treated colorectal cancer.

**Methods.** A retrospective database of patients who underwent liver metastases resection from a colorectal primary tumor from 1990 to August 2006 was reviewed. From 2003 up to now, data were obtained from a specific prospective designed protocol. Non anatomical resections were excluded. Two groups were defined: Group I: Patients with a simultaneous colorectal and liver metastases resection, Group II: Patients with staged colorectal and hepatic resection. Demographic characteristics, technical aspects, postoperative liver function, morbidity and mortality were reviewed. Statistical significance was obtained by t test.

**Results** In this period, 67 patients underwent a hepatic resection from colorectal liver metastases, of which 48 fulfilled the inclusion criteria. Group I; n=13, Group II n=35. Both groups were comparable in demographic variables. Mean number of resected Couinaud's Segments was 2.5 in Group I and 3.5 in Group II. The most frequent hepatic resection was a left lateral segmentectomy in the synchronous group and a right hepatectomy in the metachronous group. There were no statistical differences in mean intraoperative blood loss (838 ml in Group I, 1116 ml in Group II), mean red blood cell units transfused (0,6 versus 1) and mean operative time (268 and 244 minutes, respectively). Mean post-operative stay was 11,1 days for the first group and 11,3 days for the second.) In Group I, 5 of 13 patients developed a postoperative complication, and 17 of 35 in Group II. In each group, 2 patients had a postoperative liver failure, with good response to medical support. There was no perioperative mortality.

**Conclusion.** Simultaneous resection of large bowel and liver parenchyma is a feasible and safe alternative in patients with a primary colorectal tumor and liver metastases.

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### SURVIVAL AFTER RESECTION OF HEPATIC AND PULMONARY COLORECTAL METASTASES

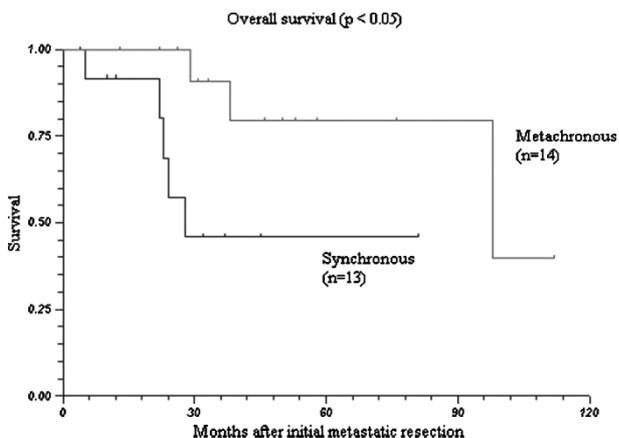
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**Introduction.** While benefits from resection of isolated pulmonary and hepatic colorectal metastases (CRM) are well recognized, outcomes after resection at both sites are not established. The objective of this retrospective study is to determine long-term survival in patients who undergo resection of hepatic and pulmonary CRM.

**Methods.** Clinicopathologic, operative, and long-term survival data were reviewed from patients identified from a hepatectomy database who underwent resection of pulmonary and hepatic CRM. Survival was calculated with Kaplan-Meier analysis and compared with the log-rank test.

**Results.** From 1997–2006, 27 patients underwent resection of hepatic and pulmonary CRM. 13/27 (48%) presented with synchronous disease at both sites; 5/13 (38%) underwent simultaneous pulmonary and hepatic resections. No patient presented with CRM outside the lung or liver at the time of resections. Median patient age was 52 years, 14/27 (52%) patients had multiple hepatic CRM, 11/27 (41%) patients had multiple pulmonary CRM, 4/27 (15%) patients had bilateral pulmonary CRM, 7/27 (26%) patients underwent anatomic pulmonary resection, and 22/27 (81%) patients underwent major hepatectomy ( $\geq 3$  segments). 26/27 (96%) patients were treated with chemotherapy before or after resection of initial metastases. There were no cases of post-operative mortality. After a median patient follow-up of 45 months, actuarial 3-year and 5-year survival after resection of initial metastases was 72% and 64%. 3-year and 5-year survival after resection of primary tumor was 96% and 64%. The only factor associated with survival was timing of hepatic and pulmonary CRM (Figure). Patients with synchronous metastases at both sites had shorter overall survival after resection of initial metastases than metachronously presenting patients (5-year 46% vs. 80%,  $p < 0.05$ ).

**Conclusion.** Excellent long-term survival and low post-operative mortality can be achieved after resection of hepatic and pulmonary colorectal metastases in selected patients presenting without extra-pulmonary or extra-hepatic disease and who are heavily treated with chemotherapy. The favorable survival demonstrated in this series in comparison to older reports may reflect better lesion identification with current imaging techniques in addition to more effective chemotherapeutic regimens.



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### OUTCOMES AFTER HEPATIC RESECTION IN THE PATIENTS WITH COLORECTAL CANCER LIVER METASTASES: A RETROSPECTIVE COMPARISON WITH NON-RESECTION CASES

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**Background.** The survival benefit in patients with colorectal cancer liver metastases (CLM) underwent the curative surgical resection has been demonstrated. However, the resectability may be determined differently at the discretion of each departments.

**Patients and Methods.** From Feb 2001 through Feb 2006, 140 patients were diagnosed with CLM. 27 patients with CLM were treated with hepatic resection (Group A, n=27). Palliative managed patients were 113. Among them, 21 patients who had resectability at initial diagnosis or after chemotherapy were selected. (Group B, n=21). For this assessment, two expert surgeons and two radiologists conducted the re-evaluation for resectability. The authors compared outcomes between Group A and Group B.

**Results.** In total 48 patients, the median age was 61 years (32–86) and mean size of the masses was 4.3 cm (0.8–14), which were not different significantly among two groups, including performance status, liver function, CEA level, stage, and hepatic lesion numbers. The median number of mass was 4 (1–14) in group A and 3 (1–9) in group B ( $P = 0.123$ ). After a median follow up duration of 31.3 months, estimated 3-year overall survival (OS) rates was  $71.1 \pm 16.9\%$  in group A and  $14.29 \pm 7.0\%$  in group B ( $P = .0001$ ). The median OS in group A was 23.6 months, while it was 14.8 months in group B.

**Conclusion.** Accurate lesion detection, aggressive surgical resection, and optimal adjuvant/neo-adjuvant chemotherapy should be performed for long term survival in the patients with CLM. Therefore, expert surgeons, gastroenterologists, oncologists, and radiologists might be cooperated to decide the adequate treatment plan the optimal time of surgery in the CLM patients.

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### PROGNOSTIC FACTORS IN HEPATIC RESECTIONS FOR THE COLORECTAL CANCER METASTASES

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**Background.** Liver resection currently serves as the only one curative therapy for liver metastases from colorectal carcinoma. Appropriate criteria for surgical resection are controversial.

**Aim.** The aim of this study was to determine the characteristics of the disease which affected prognosis.

**Methodology.** Between March 1999 and December 2005, 135 patients with hepatic metastases from colorectal carcinoma underwent anatomical liver resection at our institution. There were 77 men and 58 women, with a mean age of 56.9 years (range 22–74). The follow-up period ranged from 2 to 69 months. The survival rate was estimated by the Kaplan-Meier method and compared by log-rank test.

**Results.** 76 of the primary lesions were located in the colon and 59 in the rectum. There were 42 Dukes B, 54 Dukes C and 39 Dukes D. Liver metastases were detected synchronously in 45 and metachronously in 90 patients at the time of diagnosis. The operative mortality rate within 30 postoperative days was 3.1%. During the follow-up period we registered tumor recurrence rate of 14.1%. The overall 5-year survival rate was 31.8%. Multivariate analysis shows a significant correlation between 5-year survival and solitary ( $p < 0.05$ ) and unilobar ( $p < 0.01$ ) metastases. The survival rate did not significantly correlate with gender, age, location of primary tumor, Dukes classification, time of diagnosis or CEA level.

**Conclusions.** According to our results, number and localization of metastatic liver lesions represents the prognostic factors of significant importance. Without an effective therapeutic alternative, liver resection is still recommended and represent a "gold" standard in the treatment of colorectal liver metastases.

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### PREDICTORS OF EARLY DISEASE RECURRENCE FOLLOWING HEPATIC RESECTION FOR COLORECTAL CANCER METASTASIS

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**Background.** With the broadening indications of hepatic resection for colorectal liver metastases (CRLM), the exact group of patients who would benefit from surgery is still debatable. The aim of this study was to identify predictors for early recurrence, defined as recurrence within 6 months of CRLM resection, in order to identify those patients that may require further pre-operative radiological staging of the disease prior to surgical resection.

**Methods.** Prospectively collected dataset of 430 patients undergoing curative resection for CRLM. Exclusion criteria were patients who had a previous liver resection and those who received neo-adjuvant chemotherapy.

**Results.** Eighty-six (20%) patients developed early recurrence. Early recurrence was associated with poorer outcome when compared to late recurrences,  $p < 0.001$ . The predictor of early recurrence on multivariable analysis was the presence of numerous (8 or more) metastases,  $p = 0.036$ . Numerous metastases also predicted for extra-hepatic recurrent disease.

**Conclusion.** We have identified a group of patients with numerous metastases who recur early following resection of CRLM. We suggest that these patients should be considered for additional pre-operative radiological workup in the form of PET scanning to identify those patients that would be deemed suitable for resection.

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### THE PATHOLOGY OF LIVER NODULES AFTER NEOADJUVANT CHEMOTHERAPY IS ASSOCIATED WITH OUTCOME FOR COLORECTAL CANCER METASTASES

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**Background.** Colorectal cancer (CRC) is the second leading cause of cancer-related deaths in Western countries. Due to the improved response rates achieved by irinotecan and oxaliplatin-based chemotherapeutic regimens, and the introduction of biological therapies, an increasing number of patients can be treated with intent to cure. Neo-adjuvant chemotherapy offers several advantages: 1) downsizing of tumors, making unresectable lesions resectable; 2) gauge the effectiveness of the regimen to tailor post-operative therapy; 3) allow treatment of occult systemic disease and control of synchronous lung metastases for subsequent resection.

**Aim.** To determine if the use of a neoadjuvant treatment strategy is associated with increased rate of R0 resection, systemic disease control and to correlate this with pathologic findings.

**Methods.** We conducted a retrospective chart review of patients who underwent resection for CRC metastases between March 2003 and June 2004.

**Results.** 26 patients with liver metastases from CRC were treated with either irinotecan-based or oxaliplatin-based therapy prior to hepatectomy. Seventeen patients presented with synchronous liver metastases, while two also had concurrent lung involvement. The median clinical risk score (1) was 3. Nineteen patients (73%) achieved complete resection of all nodules. Six patients had a complete pathological response to neoadjuvant treatment. Mild to moderate steatosis of the background liver was found in 52%. There was no grade 3 or 4 complications or mortality related to liver insufficiency. A survival at two years and a status of disease-free at last follow-up were associated with a significantly increased amount of fibrosis and a decreased percentage of viable tumour cells in their liver nodules on pathologic analysis ( $p < 0.05$ ). The amount of necrosis and mucin were not significantly associated. The median follow-up was 30 months. Twenty (77%) patients were alive at two years and thirteen (50%) are currently without disease.

**Conclusion.** The use of neoadjuvant chemotherapy may provide early systemic disease control allowing for complete resection of involved liver and long-term disease-free survival. The percentage of fibrosis and tumour viability after neoadjuvant chemotherapy correlates with the success of metastectomy.

**Reference.**1. Fong Y, Fortner J, Sun RL, Brennan MF, Blumgart LH. Clinical score for predicting recurrence after hepatic resection for metastatic colorectal cancer: analysis of 1001 consecutive cases. *Ann Surg.* 1999 Sep; 230(3):309–18; discussion 18–21.

233 (will not be presented)

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### RESECTION FOR COLORECTAL AND NON-COLORECTAL LIVER METASTASES: A COMPARATIVE STUDY

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**Background.** Surgical treatments results in patients with colorectal (CR) liver metastases have been analyzed in different series in the world. However for non-colorectal liver metastases this matter has not been perfectly studied. Therefore, it has been observed that surgical treatment increase free time of disease and survival in both cases.

**Aim.** To compare long term results in patients with metastases treated with liver resection.

**Patients and Methods.** A retrospective study in 81 patients with liver metastases from CR and NCR cancer, treated with liver resection in the

Instituto Nacional de Cancerologia de México and Centro Médico ISSE-MyM from August 1995 to September 2006 was performed. Data were analyzed from the clinical records and included epidemiological data and survival.

**Results.** Of a whole of 81 patients with liver metastases surgically treated with a mean age of 41 years old (range 15 to 71), 45 (55%) were female and 36 (45%) were male. Thirty three patients (40.74%) had metastasis from CR and 48 (59.3%) from NCR. The primary tumor in nine (18.75%) of them was from breast cancer, nine (18.75%) from carcinoid tumors, six (12.5%) from testicle cancer, five (10.41%) from ovarian cancer and 17 (35.42%) from other places. The mean time of follow up was 14 months, the status from the patients treated with metastases from CR is as follows: 60.6% alive without tumoral activity, 18.18% died without tumoral activity and 21.22% died with tumoral activity. The mean survival was 23.53 months for this group, and only eight (24.24%) patients had tumor recurrence. Comparing to the patients treated with metastases from NCR, 50% are alive without tumoral activity, 10.4% are alive with tumoral activity, 8.3% died without tumoral activity and 31.3% died with tumoral activity. This group presented a mean survival of 28.46 months, and sixteen (33.33%) patients had tumor recurrence.

**Conclusions.** Surgical resection of liver metastases from NCR is an effective treatment in a well selected group of patients. Our results in these group of patients are similar to those resected with CR. However, it is necessary to increase the number of patients to confirm these results.

### Oral Posters II – Liver V: Ablation OP-14

4/21/07 4:15 to 6:15 pm  
Abstract Numbers 235–246

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### AN EXPERIMENTAL STUDY OF THE TREATMENT OF LIVER INJURY WITH INLINE RFA

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**Background.** The liver is the most frequently injured abdominal organ after trauma. Hemorrhage is often the major cause of death after liver injury. Hemostasis however sometimes may be very difficult to achieve, liver resection is occasionally required in the trauma setting.

**Aim.** In this study we examined the use of InLine RFA device (ILRFA, Resect Medical Inc, Fremont CA) designed for liver resection, in the entirely different setting of simulated liver trauma where the injury is actively bleeding prior to an attempt at surgical control.

**Materials and methods.** Six pigs were tested in this study. We created two types of grade III to IV liver injury: peripheral (cut off the edge of one lobe) and central (cut an incision on the central part). Then treatment with InLine RFA was compared to conventional diathermy and suture, totally 32 surgeries were performed: peripheral injury (12 InLine versus 6 diathermy+suture); central injury (8 InLine versus 6 diathermy+suture). Blood loss was measured by determining the difference in the weights of dry sponges and blood stained sponges after resection. The weight difference was expressed as the blood loss in grams.

**Results.** Six pigs were used to simulate a total of 32 liver trauma injuries. This resulted in 20 simulated liver injuries which were then treated with the InLine and 12 controls which were treated with conventional diathermy and suture. No massive bleeding occurred, and no animal died during the experiment. After surgery, pigs were euthanized. The reduction of blood loss was 63.88% in peripheral injury and 53.57% in central injury respectively. There were highly significant differences in both two types of injuries: blood loss ( $p < 0.001$ ), blood loss per  $\text{cm}^2$  ( $p < 0.001$ ).

**Conclusions.** In this study we examined the use of ILRFA for the coagulation and hemostasis of simulated liver trauma. After the InLine RFA device is deployed into the liver parenchyma, it seals small arterial and venous vessels; therefore hemostasis was achieved with a significant reduction of blood loss (63.88% in peripheral injury and 53.57% in central injury) compares to conventional diathermy plus suture. We believe that ILRFA will be an interesting device to evaluate in certain liver injuries in man.

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### BENIGN LIVER TUMORS: ROLE FOR LAPAROSCOPIC ULTRASOUND-GUIDED RADIOFREQUENCY ABLATION

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**Introduction.** The treatment decision for benign liver lesions must be individualized and based upon risk of treatment versus the risks of observation. The role of laparoscopic RFA is studied.

**Methods.** The records of all patients who presented with initial diagnosis of benign liver mass between 06/03–10/06 were reviewed, and those who underwent laparoscopic ultrasound guided RFA were identified. Indications included hepatocellular adenoma, indeterminate lesion by 3 imaging studies (ultrasound, three-phase computed tomography (CT scan) and gadolinium magnetic resonance imaging (MRI)), growth of the lesion, and clear tumor related symptoms during follow-up. Demographics, underlying liver disease (if present), history of estrogen use, tumor size, location, and number were noted. Results of intra-operative core needle biopsy were noted. Initial results

of ablation were assessed with postoperative CT scan one month after the procedure. Follow-up data including survival, complications, and quality of life were gathered.

**Results.** Sixty-nine patients with initial diagnosis of benign liver mass were evaluated; 25 (36.2%) were symptoms free, had clear radiological findings of hemangioma or focal nodular hyperplasia (FNH), and were not considered surgical candidates. Seventeen (24.6%) were observed with follow-up imaging every 3–6 months; 27 (39.1%) patients had surgical intervention. 14 of them had history of long term use of estrogens. Nine (13.0%) had symptomatic lesions >5 cm, and underwent open surgical enucleation or resection. Eighteen (26.1%) met the criteria for laparoscopic surgical intervention. The mean age was  $47.2 \pm 13.6$ ; all patients were females. Two patients had 4 lesions, one had 3 lesions, 4 had 2 lesions, and 11 patients had one lesion. Two patients had underlying liver disease (1 hepatitis C, 1 alcoholic liver disease). Procedures included laparoscopic intra-operative ultrasound of the liver, RFA, and 4 patients had additional cholecystectomy. Mean length of stay was  $1.8 \pm 1.2$  days. Mean tumor diameter was  $2.6 \pm 1.1$  cm (range 2–5 cm). Pathology demonstrated 10 cases of FNH, 6 hepatocellular adenomas, 1 macroneoplastic nodule, and 1 fatty infiltration. Mean follow-up was  $17.6 \pm 13$  months (range 1–39). There were no deaths. Three patients developed postoperative right side pleural effusion. Two resolved with diuretic therapy, and one required one time thoracentesis. All patients were symptoms free 3 months after the procedure.

**Conclusions.** Laparoscopic ultrasound guided RFA is a safe modality that achieves excellent local control of liver tumors. When combined with intra-operative core needle biopsy it offers excellent diagnostic and therapeutic solution for patients with benign liver tumors.

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#### THE HEAT SINK EFFECT MAY LEAD TO LOCAL RECURRENCE: A COMPARATIVE STUDY OF RADIOFREQUENCY, CRYOTHERAPY AND MICROWAVE IN THE LIVER

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**Background.** The majority of primary and secondary liver tumours are unresectable. Ablative modalities such as microwave (MTA), radiofrequency (RF) and cryotherapy are alternative treatment modalities in current use. Blood flow adjacent to ablation zones may cause inconsistencies in ablation morphology and impair the cytotoxic abilities of these modalities. This is known as the heat sink effect.

**Aims/Objectives.** To assess the ability of the heat sink phenomenon to alter the ablation morphologies of MTA, RF and cryotherapy.

**Methods.** Twenty-one rats received microwave, 21 RF and 21 cryotherapy ablations to their liver at laparotomy. Twenty-one rats were used as a control arm. Livers were analysed 48 hours after ablation by H&E staining.

**Results.** All livers showed sharp macroscopic demarcation between treated and unablated tissue. Histological analysis showed MTA to have the clearest ablated/unablated boundary with little inflammatory reaction and no perivascular hepatocyte survival. Coagulative necrosis of all portal structures in the ablation zone was noted. Cryotherapy showed evidence of an increased inflammatory reaction with perivascular cell survival within the ablation zone. An irregular burn edge was seen with RF with evidence of perivascular and intra-lesional hepatocyte survival.

**Conclusion.** A relatively higher proportion of tumour recurrences, with cryotherapy and radiofrequency, occur at sites ablated in proximity to vascular structures; this may be due to the heat sink effect. Cryotherapy and radiofrequency rely on conduction to induce their cytotoxic effects and hence due to the increased treatment time required, are more prone to loss of thermal energy to blood flow. MTA on the other hand creates a field effect and causes uniform tissue destruction within a radiated field, thereby markedly reducing treatment times and subsequent corruption of the ablation morphology.

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#### LIVER RESECTION USING A FOUR-PRONG RADIOFREQUENCY COAGULATION DEVICE (HABIB 4X, RITA MEDICAL)

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**Objective.** To assess the efficacy of liver resection using a four-prong radiofrequency coagulation device.

**Background.** Advances in surgical technique and perioperative care have reduced mortality from liver resection over recent years. A significant focus has been on the reduction of blood loss during parenchymal division. Intraoperative hemorrhage during parenchymal transection and need for transfusion remain a predictor of perioperative morbidity.

**Methods.** From August 2005 to October 2006, 29 patients with hepatic lesions underwent resection using a four-prong radiofrequency (RF) device. The use of bipolar RF energy and multiple prongs rapidly creates a zone of necrosis within the liver substance approximately 1 cm wide and

nearly as deep as the needles are placed. Intraoperative ultrasound was performed to delineate the tumor location and assess for other lesions. The selected line of transection is thermoablated using the device. The parenchyma is then cut using a scalpel or parenchymal fracture (clamp or finger fracture). Surgical clips are selectively used to ensure vessel and bile duct ligation. The patients charts were reviewed for estimated operative blood loss, procedure time, need for transfusion, length of stay, and perioperative mortality and morbidity.

**Results.** No drains were used. There were 5 right hepatic lobectomies, 4 left hepatic lobectomies, and 20 segmental resections. A synchronous colonic resection was performed on three patients having segmentectomies. Mean operative blood loss was 354 ml (range = 100–1500). Mean procedural time was 244 minutes (range = 97–557). There were no intraoperative deaths. Average LOS was 8 days (range = 4–18). There were 6 perioperative complications: 4 hepatic abscesses, one pulmonary embolus, and one upper GI bleed from a peptic ulcer. Two of the patients who had hepatic abscesses had a synchronous colon resection. There was one perioperative mortality, which was secondary to a cardiac arrhythmia. Two patients required transfusions. One of these patients was transfused for a bleeding peptic ulcer.

**Conclusions.** Use of the four-prong radiofrequency dissecting device for liver resection is safe. This novel device offers a new tool for near bloodless hepatic parenchymal transection.

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#### A MULTICENTRE CONTROL STUDY OF INLINE RADIOFREQUENCY ABLATION DEVICE FOR LIVER TRANSECTION

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**Background.** Surgical resection is the best established treatment known to provide long-term survival for liver malignancy. Intraoperative blood loss has been the major concern during major liver resections, and mortality and morbidity of surgery is clearly associated with the amount of blood loss. We have previously demonstrated that the use of InLine Radiofrequency Ablation Device (Resect Medical Inc<sup>®</sup>, Fremont CA) to pre-coagulate the liver transection plane prior to resection is safe and effective in significantly reducing intraoperative blood loss and transection time in both animal experiments and human trials.

**Aims.** To study blood loss, transection time and postoperative complications in patients in a multicentre using ILRFA pre-coagulation and conventional CUSA in liver resection.

**Materials and methods.** 102 liver resections were performed in 4 institutions from Nov 2003 to Oct 2006: 51 (29 men and 22 women) were ILRFA pre-coagulation followed by CUSA transection and 51 (28 men and 22 women) were performed only by CUSA transection as control, these were prospective sequential series. The average age were 62.9 (30–85) in the ILRFA and 61.9 (28–79) in the control group. group had cirrhotic liver. Pringle manoeuvre was applied only when required. Blood loss was measured from sponge weights and suction bottle contents.

**Results.** The type of liver resection was very similar in both groups, included 14 non-anatomic and 37 anatomic resections (formal lobectomies or extended resections) in the ILRFA, 19 non-anatomic and 32 anatomic resections in controls. Median number of RFA deployments was 3 (range 1–12) with a median coagulation time of 9 (range 3–36) minutes. Median operation blood loss was  $165.33 \pm 20.38$  ml (range 5–675 ml) in the ILRFA and  $598.53 \pm 79.36$  ml (range 80–3600 ml) in the control, a 72.4% reduction and  $P < 0.05$ . The median transection surface area was not different in the ILRFA and control groups. The median transection blood loss per unit resection area was  $3.35 \pm 0.42$  ( $0.14 \sim 12.33$ ) ml/cm<sup>2</sup> in the ILRFA patients compared with  $6.09 \pm 0.72$  ( $0.92 \sim 36$ ) ml/cm<sup>2</sup> in controls, the reduction was 45.0% and  $P < 0.05$ . The median transection time was 27 (2–219) minutes in the ILRFA and 35 (5–62) minutes in controls.

**Conclusions.** ILRFA pre-coagulation is a safe, effective technique for liver resections which significantly reduces blood loss.

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#### RADIOFREQUENCY ABLATION OF SMALL HEPATIC MALIGNANCIES PROVIDES EQUAL LOCAL CONTROL TO RESECTION

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**Background.** The efficacy of ablative techniques in the treatment of hepatic malignancies is limited by the size of the tumor. We hypothesize that ablation of appropriately sized lesions can produce local control similar to resection.

**Methods.** A retrospective analysis of a single-surgeon consecutive series was performed on patients with metastatic colorectal carcinoma (mCRC) or hepatocellular carcinoma (HCC) who underwent operative ablation (radiofrequency (RFA), cryosurgery or fulguration) and/or resection at a single institution from 1998–2005. Local recurrence (LR), defined as lesion enlargement or satellite lesion on imaging, and adverse prognostic factors were analyzed by operative technique.

**Results.** One hundred nineteen patients (97 mCRC, 22 HCC) received surgical treatment for 241 hepatic lesions (90 ablations and 151 resections). Lesion size (median, range) was significantly larger in resected lesions (3.0 cm, 0.4–26.0) than lesions treated by RFA (2.5 cm, 0.3–8.0), cryosurgery (2.5 cm, 0.9–10.8) or fulguration (1.0 cm, 0.5–2.7) ( $p=0.02$ ). With a median 16-month follow-up, LR did not differ significantly across procedure type with rates of 13.5%, 16.7%, 20% and 8.7% for RFA, cryosurgery, fulguration and resection, respectively. LR of lesions greater than 3 cm treated with RFA was significantly greater than for similarly treated lesions 3 cm or less (36.4% vs. 7.3%,  $p=0.007$ ). LR of lesions 3 cm or less treated by RFA was comparable to similarly sized lesions treated by resection (7.3% vs. 8.1%,  $p$  value = 0.88). Using a Cox proportional hazard model, factors that significantly decreased survival included cryosurgery, lesion size of > 3 cm, extra-hepatic recurrence, and absence of LSLR, while adjuvant chemotherapy significantly increased survival. Factors that did not affect survival included RFA, primary histology, and presence of more than 4 hepatic lesions.

**Conclusion.** RFA of small (3 cm or less) hepatic lesions is as effective as resection in preventing LR from mCRC and HCC and is not associated with an adverse outcome. This confirms that multiple operative techniques may be considered for this patient population.

#### 241 IS RADIOFREQUENCY-ASSISTED LIVER RESECTION SAFE AND ONCOLOGICALLY-SOUND?

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Data was prospectively collected on consecutive liver resections with the TissueLink™ device. Morbidity, blood loss, transfusion, inflow occlusion, failures, haemoglobin, mortality and resection margin was collated. 153 patients were opened for hepatic resection over 3 years by one surgeon (RH). 10 (6.5%) had no treatment. 11 (7.2%) had open radiofrequency ablation. 132 (86.3%) patients had hepatic resection. 18 of those resected (13.6%) did not undergo radiofrequency-assisted technique – 8 Kelly clays, 3 laparoscopic, 2 total vascular exclusion and 5 CUSA. Of these resections, only 4 were converted from tissueLink™ to another method. The failure rate was 3.4%. 114 patients underwent radiofrequency-assisted resection. 61 males. Mean age 58.5 (32–84). Pre-operative chemotherapy was given to 51.5% of patients. Pre-operative portal vein embolisation was used in 16 (14%). Significant co-morbidity was present in 18.4%. There were 10 bowel resections, 2 pancreatic, 1 portal vein resection, 1 reversal Hartmans and 1 gastrectomy. 11 patients had 2 stage hepatectomy and 6 patients had re-hepatectomy. There were 68 colorectal metastasis resections, 5 breast, 12 other primary sites, 2 unknown primaries, 7 neuroendocrine, 6 hepatomas, 4 biliary malignancies and 10 benign. Median operating time = 3.5 hours. 78.1% of patients had no inflow occlusion. Central venous pressure was not controlled. Median blood loss was 300 mls. Mean in-hospital transfusion requirement was 0.9 units with median transfusion 0 units. 4.3% of patients had fresh frozen plasma in hospital. 7.8% had vitamin K for elevated INR. There was no significant difference between admission/discharge haemoglobin. Median hospital stay was 10 days (5–60). 60 day mortality was 0.87%. Morbidity was 27% including that from associated procedures and hepatic failure. There was one biliary stricture due to thermal damage early in the series (0.87%). Hilar dissection has since not been carried out with the device. Bile leaks occurred in 5 cases (4.3%), 3 being stented. Median margin of clearance for colorectal liver metastases was 4 mm, for hepatoma 2 mm, biliary malignancy 15 mm and other malignancies 5.5 mm.

**Conclusion.** Radiofrequency-assisted resection using an anatomically-based method is a safe method of parenchymal transection. It appears to allow for appropriate resection margins.

Hepatic resections	
Resection type	Number
3 or more Couinaud segments	55
2 or more Couinaud segments	25
Other	34
Total	114
Formal right hepatectomy	20
Formal left hepatectomy	7
Trisectonectomy	17

#### 242 THE EVOLUTION AND PERIOPERATIVE COURSE OF PATIENTS UNDERGOING RADIOFREQUENCY ABLATION OF LIVER TUMORS BETWEEN 1996 AND 2006

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**Purpose.** Radiofrequency ablation (RFA) is widely touted as a safe and effective means of liver tumor destruction. More data is required before this technique can be accepted as an appropriate part of the standard management algorithm. The purpose of this study is to examine the perioperative course and complications following RFA of liver tumors at a single high volume institution over a 10-year period.

**Methods.** Between September 1996 and June 2006, data was collected prospectively on ablations in 192 patients. All procedures were performed under the direction of a single surgeon. Substantial changes occurred in ablation technology during this period, including increases in maximum power generation and alterations in tip design.

**Results.** Patients included 80 women and 112 men, with an average age of 63 years (SD ± 23). A total of 464 tumors were ablated for an average of 2.4 tumors per patient. Mean tumor size was 2.4 cm (SD ± 1.70, range 0.7 to 13 cm). Average operative time was 172 minutes and blood loss for all ablations averaged 116 ml with a mean EBL for the 15 open procedures of 832 ml. Laparoscopic ablations were used in 147 patients, 15 patients had open treatments, 26 were CT guided and 4 thoracoscopic (transdiaphragmatic). Major intraoperative complication occurred in 7 patients including 1 tumor rupture during ablation, 1 thermal bowel injury, 1 gallbladder thermal injury, 3 enterotomies, and 1 bowel trocar injury. Major post-operative complications occurred in 17 patients and included 1 cardiac death, 6 RFA site abscesses, 5 PE/pneumonia, and 5 patients had significant hepatic dysfunction. Overall, major complications occurred in 24/192 (12.5%) of patients.

**Conclusions.** Radiofrequency ablation has rapidly become a popular treatment modality for hepatic tumors, especially in patients who are poor operative candidates. Although overall morbidity is reduced compared to open surgical resection, major complications do occur. We have reviewed our short-term outcomes with the intention of better understanding how to incorporate RFA into our management algorithm.

#### 243 RESECTION OF HEPATIC RECURRENCE FOLLOWING RADIOFREQUENCY ABLATION FOR LIVER METASTASES

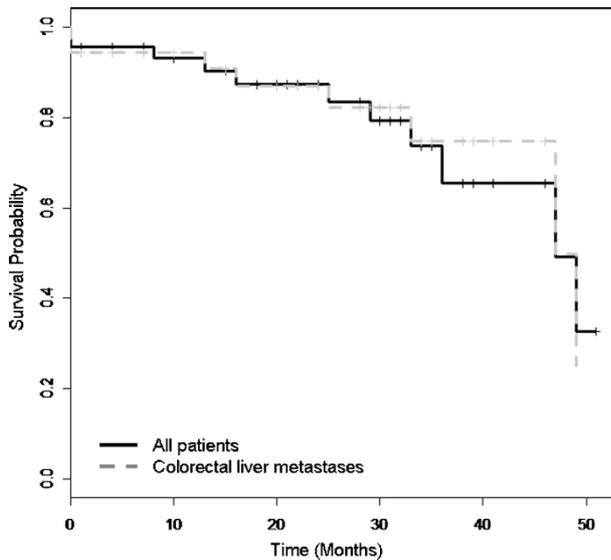
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**Background.** Advances in surgical technique have enabled selected patients with recurrent liver metastases (LM) to undergo repeat hepatic surgery with curative intent. The utility of hepatic resection after radiofrequency ablation (RFA) of LM has not been studied. The purpose of this study was to examine early outcomes following hepatic resection for recurrence at any site in the liver in patients who previously underwent RFA of LM.

**Materials and Methods.** Using a prospective hepatobiliary database, 45 patients were identified with LM treated by RFA who subsequently underwent hepatic resection of recurrence between 1998 and 2006. Safety and early outcomes of hepatic resection were analyzed.

**Results.** Indications for RFA were inadequate liver remnant ( $n=22$ , 49%), liver disease ( $n=5$ , 11%), prohibitive comorbidities ( $n=1$ , 2%), and referral following RFA ( $n=17$ , 38%). Thirty-five patients had colorectal LM; 10 patients had LM of other origins (4 sarcoma, 4 pancreatic, 1 breast, and 1 carcinoid). Recurrence occurred at a median of 12 months (range 1–64) after index RFA. Chemotherapy was administered before or after hepatic resection in 38 patients (84%). Preoperative portal vein embolization was performed in 4 patients. Resections included 13 hemihepatectomies, 8 extended hepatectomies, 9 mono- or bisegmentectomies, 4 wedge resections, and 11 resections combined with RFA. Seventeen patients (38%) required additional resection (10 diaphragm alone, 5 diaphragm combined with adjacent structures, and 2 other). Median operating time, median blood loss, and transfusion rate were 186 minutes (range 71–516), 425 ml (range 50–10,000), and 18%. Most patients had a single recurrent tumor ( $n=29$ , 64%); median tumor size was 4 cm. Ninety-day morbidity and mortality rates were 49% ( $n=22$ ) and 4% ( $n=2$ ), respectively. At median follow-up of 25 months, median overall survival was 47 months for all patients and also 47 months for the subgroup with colorectal metastases. Median disease-free survival was 10 months for both groups.

**Conclusion.** Although morbidity and extent of resection are significant, resection in patients with hepatic recurrence after RFA is safe. In this selected group of patients, median and overall survival rates at early follow-up are similar to previously published rates for up-front resection.



#### 244 SURVIVAL RESULTS OF NON-SURGICAL TREATMENT MODALITIES FOR MALIGNANT LIVER TUMOURS

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**Introduction.** Surgical resection provides the best survival for patients with primary and secondary liver cancer. It is only possible in 15%–20% of patients. Non-surgical treatment modalities remain the only option.

**Material and methods.** From November 2004, patients whose liver tumours were not amenable for surgery were considered for chemotherapy, radiofrequency ablation, trans-arterial chemoembolization and yttrium-90 microspheres treatment after discussion at our multidisciplinary meeting. None of the patients had extrahepatic disease.

**Results.** A total of 123 patients were considered for chemotherapy (n=27), radiofrequency ablation (RFA) (n=41) trans-arterial chemoembolization (TACE) (n=20) and yttrium-90 microspheres treatment (n=14). They were 71 men and 52 women with a mean age of 57. Among them 58 had colorectal liver metastases (CLM), 27 had Hepatocellular carcinoma (HCC) and the remaining 38 were grouped as others. The mean survival time for each treatment group was 18.8 months, 18.1 months, 18.7 months and 15.1 months for RFA, yttrium-90 microspheres treatment, chemotherapy and TACE respectively. As for type of diseases, patients with colorectal liver metastases had 75%, 56% and 24% survival rates at 1-, 2-, and 3 years respectively, compared with 60%, 43% and 13% for the noncolorectal group. The HCC group had 43%, 18% and 10% survival rates over the same period. **Conclusion.** Patients survival is more correlated to the tumour histopathologic type than the non-surgical treatment modality used. Younger patients survived longer and this we attribute to co-morbidities in the elderly.

#### 245 MICROWAVE ABLATION IS AN EFFECTIVE TOOL TO TREAT UNRESECTABLE PRIMARY AND SECONDARY LIVER TUMOURS

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**Background.** Microwave tumour ablation (MTA) is one of 3 thermal ablative modalities available to treat unresectable liver tumours. Radiofrequency and cryotherapy have poor local control rates and have been associated with high recurrence rates. We have successfully used microwave ablation to treat liver tumours since 2001.

**Aims.** To assess the safety and efficacy of MTA to treat patients with less than 5 unresectable liver tumours.

**Methods.** Thirty-six patients with unresectable liver metastases received MTA between 2001 and 2006. A total of 84 tumours (mean 23 mm; range 4–70 mm) were ablated. Tumour types included colorectal carcinoma secondaries (28), Parathyroid metastases (PTH) (1), HCC (6) and carcinoid (1). All patients underwent pre- and post-operative cross sectional imaging. Most tumours were treated between 2–3 minutes at 150 W. Seven patients had a left hemi-hepatectomy and MTA, 10 right hemi-hepatectomy and MTA and 19 had MTA alone.

**Results.** No bleeding, abscess formation, bile duct injury or microwave related complications were observed. Fifteen patients are alive post ablation of whom 8 are disease free (mean f/u 19 months; range 6–35), 7 are alive with tumour recurrence (mean f/u 24 months; range 12–42), of whom 2 patients have developed local recurrence, probably due to tumour proximity to major hilar vessels. Of those with recurrence, 72% of patients are alive more than 2 years post ablation. There were 3 deaths in the immediate 30 day post-operative period, all unrelated to MTA, and at post-mortem were confirmed to be secondary to significant co-morbidities of the patients. The other 18 patients survived an average of 18 months (range 2–42 months).

**Discussion.** MTA is a safe treatment option and is related to a low recurrence rate compared to radiofrequency and cryotherapy. As with all surgical techniques a learning curve is often evident and the 3 post-op deaths were between 2001 and 2002. Stringent patient selection has reduced our 30 day patient mortality and the local recurrence rates compare favourably to other ablative treatment options.

#### 246 NOVEL HIGH SPEED RADIO FREQUENCY (HSRF) TISSUE ABLATION SYSTEM-INITIAL CLINICAL EXPERIENCE

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We report an evaluation of a new and novel High Speed Radio Frequency (HSRF) tissue ablation system (RFA Medical, Inc., Fremont California). This system is unique in both its speed and ability to use a variety of existing RFA generators currently available in many hospitals around the world as the energy source. Our experience included various generators such as the Radio Therapeutics Corporation (Boston Scientific, Boston MA), Celon LabPower (Celon – Olympus, Teltow – Berlin Germany), and the Rita 1500 and 1500X (Rita Medical Systems, Fremont CA). We evaluated use of the device in-vitro (explanted bovine liver), in-vivo (ovine liver), and clinically in a ten patient prospective study. In this study patients which were scheduled for resection of their liver tumours underwent tumor ablation followed by the planned resection. Following the liver resection the ablated tissue was bread loafed and the ablation size was noted. The total ablation time was also recorded. Patient and procedure details for this study included gender, age, tumor type, the use of any inflow occlusion, and operative or postoperative complications. There was no significant difference within the demographics between patients. The amount of time required to achieve the target ablation size was significantly less than any RFA device currently available. Although operation of each generator varies slightly, there was no significant effect noted between uses of the different generators. In each case the desired ablation was achieved at a significantly reduced ablation time as compared to the experience of either our institution or in published literature with standard RFA devices. The target ablation size, achieved ablation size, and ablation time was noted and recorded.

Ablation Sizes with Ablation Times

Target Ablation Size (cm)	Ablation Size Mean / SD (cm)	Ablation Time (min)
5	5.0 / 0.3	5
7	6.9 / 0.4	12

Based on our results we have concluded that this HSRF (High Speed Radio Frequency) tissue ablation system is safe, effective, and requires only a small fraction of the time that current ablation devices require.

**Free Papers**  
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**FP-08**  
**4/22/07 7:30 to 9:30 am**  
**Abstract Numbers 247–254**

#### 247 A STANDARDIZED APPROACH TO TEACHING LAPAROSCOPIC CHOLECYSTECTOMY ELIMINATES COMMON BILE DUCT INJURY IN AN INNER CITY UNIVERSITY TEACHING HOSPITAL

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The purpose of this study was to evaluate if teaching laparoscopic cholecystectomy (LC) in a University Hospital using an approach focused on obtaining “the critical view of safety” while avoiding dissection in an inflamed triangle of Calot would prevent common bile duct injury.

**Methods.** We retrospectively reviewed 601 consecutive patients undergoing attempted laparoscopic cholecystectomy (LC) for cholecystitis and/or

cholelithiasis between 1999 and 2005. If the critical view of safety could not be achieved by a retrograde approach, alternative measures were employed including fundus-first LC (FFLC); partial cholecystectomy (PC); cholecystostomy tube; or conversion to open cholecystectomy (COC). Main outcomes were death, common or segmental bile duct injury, cystic duct leak, conversion to OC, and length of stay.

**Results.** 30-day mortality was zero and there were no common bile duct injuries. There were 5 bile leaks (0.8%), and 89 conversions to OC (15%). Average length of stay was 1 day for patients having successful LC, and 5 days for patients who were converted to open cholecystectomy. PC was performed in 19 patients (3%) and cholecystostomy tube was placed in 9 (1%). Intraoperative cholangiography was performed selectively in 344 patients (57%). There were 2 right posterior sector duct injuries caused by a single surgeon and both occurred in patients who had dissection performed within an inflamed triangle of Calot during RLC prior to obtaining the critical view. There were 3 post operative cystic duct leaks; 2 occurred from necrosis of the gallbladder neck and/or cystic duct and one occurred in a patient whose inflamed gallbladder neck was stapled close.

**Conclusions.** Obtaining the "critical view of safety" by dissection that begins lateral and high on the gallbladder wall is a good technique to avoid common bile duct injury during RLC. When the critical view cannot be achieved in this manner, especially in the presence of inflammation, alternative measures are indicated which include: FFLC, PC; or cholecystostomy tube while avoiding dissection below the gallbladder neck. If FFLC or PC cannot be safely accomplished, conversion to OC combined with IOC are indicated. This step-wise approach to teaching cholecystectomy to residents dealing with a high acuity patient population substantially reduces the risk of bile duct injury during laparoscopic cholecystectomy.

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#### MICROWAVE ABLATION IS EXTREMELY EFFECTIVE AT GAINING LOCAL CONTROL OF LARGE LIVER TUMOURS

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**Background.** Large primary or secondary unresectable liver tumours have always been a challenge to treat. Several ablative modalities such as radiofrequency and cryotherapy have been tried but often failed to gain local control over tumours greater than 35 mm. Microwave tumour ablation (MTA), has been successfully used in our centre since 2001.

**Aims.** To assess the efficacy of MTA to gain local control over tumours greater than 35 mm.

**Methods.** We have treated over 60 patients and performed 208 microwave ablations since 2001. Fourteen patients with either single or multiple tumours had 1 or more tumour measuring 35 mm or larger. All patients underwent pre-operative cross-sectional imaging. A total of 34 tumours were treated, 17 of which were 35 mm (mean 47 mm; range 35–70 mm) or greater. Ten patients had colorectal liver metastases, 3 patients had HCC and 1 a parathyroid carcinoma metastasis. All patients with colorectal secondaries were treated at laparotomy under ultra-sound guidance. The parathyroid metastases (4 cm) and 1 patient with HCC (7 cm), were treated laparoscopically at 100 watts for 4 mins and 6 mins respectively. Most tumours were treated with 150 Watts of power for 2–3 minutes only by a single insertion of the applicator. Ten patients underwent MTA alone, 1 a formal right hemihepatectomy and 3 a left hemihepatectomy along with MTA. All patients had 3 monthly cross-sectional imaging post-operatively.

**Results.** There were no ablation related complications, such as bile leaks, abscess formation or bleeding. Six patients are alive of whom 3 are disease free (mean 25 months; range 6–35). Three have recurrence of disease (mean 29 months; range 16–42) of whom one has local recurrence of a tumour impinging on the hilar vessels. Seven evaluable patients died (mean 19 months; range 2–42) of either hepatic or extra-hepatic disease progression, none had evidence of local recurrence on their latest scan. One patient died day 1 post-procedure of an MI, a post-mortem report did not site microwave ablation as a cause of death.

**Discussion.** Microwave is capable of effectively treating tumours greater than 35 mm. Of those patients initially declared in-operable, 50% were alive more than 2 years post-ablation and of those surviving more than 1 year post-ablation (10/14), 90% had no evidence of local recurrence on cross-sectional imaging. MTA is capable of producing complete tumour ablation of large (35–70 mm in diameter) liver tumours without the need for multiple insertions of the applicator. Other alternative ablation modalities such as radiofrequency have a poor local control rate and a high local recurrence rate, particularly with large tumours.

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#### PREOPERATIVE STAGING FOR EXTRAHEPATIC CHOLANGIOCARCINOMA USING MDCT PRIOR TO BILIARY DRAINAGE

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Preoperative staging and management of extrahepatic cholangiocarcinoma (CC) had been very complicated.

**Aim.** To clarify the efficacy of our new strategy using multidetector row CT (MDCT) prior to biliary drainage for preoperative staging and management of extrahepatic CC.

**Patients and Methods.** Sixty-six consecutive patients with extrahepatic CC, who underwent resection with curative intent between September 2002 and August 2006, were enrolled in this study. Among 66 patients, 36 had upper or hilar CC and 30 had middle or lower CC. In principle, MDCT study was performed before biliary drainage with a plain scan followed by a four-phasic contrast-enhanced CT at 20sec, 40sec, 70sec, and 120sec after an injection of 150ml of non-ionic contrast medium. Axial images, coronal images, and CT angiography of the hepatic artery and portal venous system were routinely obtained. Diagnostic criteria of longitudinal cancerous extension along the biliary system were 1) caliber change of the dilated proximal ducts and 2) thickened bile duct wall with contrast enhancement. After assessment of cancer extent by MDCT, the operative procedure was decided. Biliary drainage was performed only for the future remnant hepatic segments in cases with upper or hilar CC. Preoperative portal vein embolization was performed if necessary and angiography was not done as a general rule.

**Results.** MDCT study prior to biliary drainage was carried out in 25 patients (69%) with upper or hilar CC and 14 patients (47%) with middle or lower CC. Major hepatic resection with caudate lobectomy was performed for all patients with upper or hilar CC. Pancreaticoduodenectomy was carried out in 29 patients with middle or lower CC and extrahepatic bile duct resection was done in one patient. Curative resection with negative surgical margins was achieved in 31 patients (86%) with upper or hilar CC and 27 patients (90%) with middle or lower CC. A cumulative 3-year survival rate for upper or hilar CC was 72.4% and for middle or lower CC 70.4%.

**Conclusions.** MDCT prior to biliary drainage provides us with reliable information for tumor staging and decision making of the operative procedure of extrahepatic CC.

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#### CT VS. MRCP: OPTIMAL CLASSIFICATION OF IPMN

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Intraductal papillary mucinous neoplasms (IPMNs) of the pancreas are being diagnosed with increased frequency. Utilizing CT scanning as the sole source of imaging prior to definitive surgical management is not uncommon. We hypothesize MRI/MRCP may provide greater accuracy in identification of IPMN type and extent.

**Methods.** From 1991 to 2006, 214 patients with IPMN were treated at our tertiary care center; of these, 150 underwent 157 operations. Preoperatively, 30 patients had both CT and MRCP. Of these, 18 met criteria of high quality and close proximity to operation. Two independent readers performed retrospective blinded analysis using standardized criteria for IPMN type, focality, distribution (diffuse = >1 surgical site), number, size of the index lesion and main duct dilation.

**Results.** The mean time from MRCP and CT to operation was 76 and 78 days respectively ( $p=0.96$ ). A lesion characteristic of IPMN was identified on CT and MRCP in all patients. MRCP showed 13 (72%) branch, 4 (22%) mixed, and 1(6%) main duct type IPMN, whereas CT showed 9 (50%) branch, 6 (33%) mixed, and 3 (17%) main duct type IPMNs. IPMN type was different in 7 (39%); 4 (22%) of these were read on CT as having main duct involvement, but no main duct disease was seen on MRCP or identified on surgical pathology. MRCP showed multifocal disease in 13 (72%) versus only 9 (50%) on CT. A different distribution was seen in 9 (50%). MRCP showed non-diffuse disease in 6 (33%) where CT indicated diffuse disease; conversely, MRCP showed diffuse disease in 3 (17%) where CT indicated non-diffuse disease. Finally, there were 101 branch lesions identified on MRCP compared to 46 on CT.

**Conclusions.** While CT is cost-effective, it should not be the only test to classify IPMN. CT overestimates main duct involvement, a significant predictor of malignancy. This is due to the inability to consistently differentiate main duct dilation from multifocal branch duct dilations. Small branch duct cysts are more often identified on MRCP, decreasing the chance they will go undetected preoperatively. Based on this study, CT is not adequate as the sole method of evaluating IPMN type and extent. MRCP should be employed for optimal management of these patients.

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#### ANTRAL PRESERVING PANCREATODUODENECTOMY: IMPACT ON EARLY POST-OPERATIVE DELAYED GASTRIC EMPTYING

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In an effort to diminish the occurrence of early post-operative delayed gastric emptying following pancreaticoduodenectomy one of the authors (FRS)

changed the type of gastroduodenal resection utilized in his performance of pancreatoduodenectomy from pylorus preserving to an "antral preserving" resection. This variant of gastroduodenal resection is characterized by the margin of gastric resection being located immediately proximal to the pylorus. To determine if this change in practice has produced the desired effect we compared proxy indicators for the occurrence of delayed gastric emptying, duration of nasogastric intubation and length of hospital stay, between patients that underwent pylorus preserving pancreatoduodenectomy (PPPD) and antral preserving pancreatoduodenectomy (APPD). The study series was comprised of 99 consecutive patients that underwent pancreatoduodenectomy between January 1998 and August 2006. Data was accrued from a prospective data base and supplemented with retrospective review of medical records. In the series 29 patients had a PPPD and 70 had undergone APPD. There was no evidence that these two groups differed in age, pre-operative comorbidities or proportion of malignant diagnosis. There was no in-hospital mortality for the series. The incidence of morbidity was 48% and the incidence of "major" morbidity ( $\geq$ Clavien grade III) was 34%. Eight of the 99 patients (8.1%) had their post-operative course complicated by pancreatic fistula, there was one biliary leak and six patients in the series (6.1%) required a second operation to deal with post-operative complications. Included in this group was one patient whom had undergone APPD that required a remedial operation nine months later for stenosis at the gastrojejunostomy due to marginal ulceration. Of note, following APPD patients were not routinely maintained on acid suppressive therapy. Median duration of nasogastric intubation was significantly less for APPD than for PPPD, 3 vs. 7 days ( $p < 0.001$ ). Median length of hospital stay was shorter following APPD than for PPPD, 12 vs. 14 days, however this difference did not reach statistical significance ( $p = 0.063$ ). APPD is an attempt to draw upon the strengths of both "classical" pancreatoduodenectomy and PPPD by, respectively, minimizing early delayed gastric emptying and long-term post gastrectomy sequelae. Based on these results it appears that the adoption of APPD has had a favourable influence on early post-operative delayed gastric emptying. Future work will aim to study long-term sequelae and evaluate gastrointestinal quality of life in patients undergoing this variant of gastroduodenal resection in pancreatoduodenectomy.

#### 252 DOES PANCREATIC DUCT SIZE PREDICT THE RISK OF FISTULA AFTER PANCREATODUODENECTOMY?

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Postoperative pancreatic fistula (POPF) is the most common complication following pancreatoduodenectomy (Whipple Procedure). The reported incidence ranges from 1% to 30%. The large range of this complication is due to varying definitions of POPF along with the patient profile of those undergoing surgery. We and others have hypothesized that in pancreatic adenocarcinoma and chronic pancreatitis the pancreas has a more fibrotic consistency and is more likely to maintain anastomotic integrity of the pancreatojejunostomy than those with soft normal gland consistency. Thus we hypothesized that pancreatic duct size could be used as a surrogate for pancreas gland fibrosis and may predict the risk of POPF.

**Methods.** 126 patients underwent a Whipple procedure by the Transplant and Hepatobiliary Surgical Unit between January 2000 and July 2006. Information on Pancreatic duct size was available for 106 patients. Drain data was available for sixteen of the remaining 20 patients and only 1 had evidence of POPF. Pancreatic duct measurements were available through computed tomography, ERCP, endoscopic ultrasound, and/or direct operative calibration. Two groups were identified; those patients with ducts less than or equal to 3 mm (small duct) and those with duct size greater than 3 mm (large duct). POPF was defined as drain fluid amylase greater than 5 times normal on or after day 4 with a 24 hour volume greater than 30 ml. Patient demographic and clinical outcome data was analyzed to correlate with the duct size. Histologic examination for fibrosis was also reviewed. Data was evaluated by chi square, student's T test and Cox proportional hazards ratio.

**Results.** Overall postoperative fistula formation was 13 of 122 (10.6%). Nine of 44 (20.4%) patients in the small duct group developed POPF, while only 3 of 62 (4.8%) patients in the large duct group developed a fistula post-operatively ( $P < 0.0001$ ). Age, sex, post op length of stay, and estimated blood loss was no different between the two groups. Overall 30 day mortality was 2 of 126 (1.5%).

**Conclusions.** Large ( $>3$  mm) pancreatic duct size predicts a lower risk for pancreatic fistula formation after Whipple procedure. A large pancreatic duct is an indicator of obstruction and often results in increased fibrosis in the pancreatic parenchyma. Preoperative measurement of duct size may allow for a more accurate prediction of post-operative pancreatic fistula and may allow for improved individual patient risk assessment.

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#### SELF-EXPANDABLE ENTERAL METALLIC STENTS FOR TREATMENT OF GASTRIC OUTLET OBSTRUCTION: A SINGLE CENTRE EXPERIENCE IN 67 PATIENTS

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**Introduction.** Gastric outlet obstruction (GOO) is a late stage complication of a variety of malignancies of the biliopancreatic area. Palliative treatment through self-expandable metallic stent (SEMS) insertion is an option. It is a minimally invasive alternative with a lower morbidity and mortality than surgical bypass. The aims of this study were to assess the feasibility, efficacy and complications associated with enteral SEMS insertion.

**Patients and Methods.** Between February 2002 and September 2006, 67 patients (33 women, 34 men; mean age 66 years) were referred for endoscopic enteral stenting for GOO caused by various malignancies of the biliopancreatic area.

**Results.** The causes of obstruction were pancreatic neoplasm ( $n=42$ ), gallbladder and bile duct neoplasm ( $n=16$ ), gastric neoplasm ( $n=7$ ) and others ( $n=2$ ). Forty-eight patients had a biliary tract obstruction and underwent biliary stenting. Enteral stenting was successful in 63 patients (94%) and failed in 4 patients (1 severe gastroparesis without mechanical obstruction and 3 major duodenal strictures). Nine patients required a second stent for various reasons: inadequate length ( $n=3$ ), tumour progression ( $n=5$ ) and stent migration ( $n=1$ ). The morbidity rate was 24%. The complications were as followed: duodenal perforation ( $n=2$ ), acute cholecystitis or cholangitis ( $n=2$ ), food impaction ( $n=1$ ), inadequate stent length ( $n=3$ ), stent migration ( $n=1$ ) and stent obstruction secondary to tumour progression ( $n=6$ ). Two patients died from complications related to the stent insertion. The median hospital stay was 8 days. Four patients were lost at follow-up. Food tolerance was analyzed in 57 patients: excellent (normal diet) ( $n=42$ ), average (soft or liquid) ( $n=7$ ) and poor (frequent vomiting) ( $n=8$ ). Median survival post stent insertion was 75 days.

**Conclusion.** Endoscopically inserted enteral SEMS for malignant gastric outlet obstruction was successful in 63 of 67 patients. Palliation of symptoms was satisfactory in 86% of patients with an acceptable morbidity and mortality.

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#### LAPAROSCOPIC DISTAL PANCREATECTOMY: COMPARISON WITH OPEN SURGERY

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Laparoscopic surgery has become the standard technique for the management of gallstones, gastroesophageal reflux disease and achalasia. The laparoscopic approach also has become the preferred technique for the majority of patients requiring adrenalectomy and splenectomy. In recent years, laparoscopic surgery of the colon, liver and pancreas also have been introduced. However, the least experience has been gained with the pancreas, and no concurrent comparative data are available. Therefore, the aim of this analysis is to compare the results of laparoscopic and open distal pancreatectomy.

**Methods.** From April, 2004 through September, 2006, 47 laparoscopic distal pancreatectomies were undertaken at our institution. From a 10-year database of open distal pancreatectomies, 40 patients who were age-, gender- and disease-matched were chosen for comparison. Thirty of the 40 open control patients (75%) underwent surgery during the past three years. Records were reviewed for splenic preservation, operative time, blood loss, complications and length of hospital stay (LOS).

**Results.** The mean age of the laparoscopic and open patients was 57 and 55 years, respectively, and 60% versus 65% were female. Three of the laparoscopic patients (7%) were converted to an open procedure. The most common diagnoses for the laparoscopic and open patients was benign mucinous tumor (43 vs 56%), chronic pancreatitis (13 vs 16%), and islet cell tumor (13 vs 11%). Four patients with malignant lesions (2 adenoCA and 2 malignant neuroendocrine tumors) underwent laparoscopic resection. Operative and postoperative results are shown in the table.

**Conclusions.** These data suggest that laparoscopic distal pancreatectomy is associated with a) a higher rate of splenic preservation, b) increased operative time, c) decreased blood loss and d) decreased length of stay. We conclude that laparoscopic distal pancreatectomy can be performed safely and can be undertaken by surgeons experienced in both laparoscopic and pancreatic surgery.

Distal Pancreatectomy	N	Spleen Preservation	Op time (min)	Blood loss (ml)	Pancreatic fistula	LOS (days)
Laparoscopic	47	60%	270	587	8%	5.5
Open	40	6%*	230*	1200*	20%	7.7*

\*  $p < 0.05$  vs laparoscopic

## Free Papers

## Liver II

## FP-09

4/22/07 7:30 to 9:30 am

Abstract Numbers 255–262

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## CLINICOGENOMIC CHARACTERIZATION OF PRIMARY COLORECTAL CARCINOMA ASSOCIATED WITH LIVER METASTASES

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**Purpose.** Approximately 20% of patients with colorectal carcinoma (CRC) present with hepatic metastases. Genome-wide alterations that occur during the metastatic progression of CRC remain poorly understood. Using a clinicogenomic CRC database, we have sought to compare clinical variables as well as microarray gene expression profiles between metastatic and non-metastatic primary CRCs.

**Methods.** From 1993 to 2003, primary CRC specimens were collected from patients consenting to our tissue bank protocol. RNA was extracted from tissue collected at surgery. All specimens underwent gene profiling using the Affymetrix 133 Plus 2.0 Gene chip. We identified a total of 96 analyzable cases. Clinical data were collected by chart review, and statistical comparisons performed using the Fisher Exact Test. Gene expression data were normalized and compared using the Mann-Whitney non-parametric test. A Q-value analysis was used to estimate the false discovery rate (FDR). MetaCore software was used to identify potential pathways and interactions between differentially expressed genes.

**Results.** We identified 66 patients without evidence of nodal or distant metastases. An additional 30 patients were noted to have either synchronous or metachronous hepatic metastases. The study population was comprised of 58 males and 38 females with a median age of 72 years (range 39–90). Patients with metastatic disease were more likely to present with weight loss (44% vs. 16%  $p=0.006$ ) and higher T (3 or 4) stage (72% vs. 100%;  $p=0.004$ ). There were no significant differences between the 2 groups with respect to grade and perineural or lymphovascular invasion. At a FDR of 1%, metastatic tumors displayed a total 234 upregulated genes (0 downregulated) as compared to non-metastatic CRCs. Amongst the most upregulated genes were EGF Receptor (+1.7 fold change) and genes associated with the ubiquitin proteolytic pathway (UMF1+1.5, EDD1+1.4, UBE2W+1.3, UBE2E3+1.3). By MetaCore analysis, 15 pathways were significantly altered, of which 11 were associated with cell adhesion functions (Cytoskeleton remodeling;  $p=0.0005$ , TGF/Wnt  $p=0.0007$ ; Integrin mediated cell adhesion  $p=0.001$ ).

**Conclusions.** CRCs with metastatic potential display a dramatically altered panel of differentially expressed genes that are associated with upregulation of EGFR, ubiquitin proteolysis and various aspects of cell adhesion. Our data add to the understanding of the biologic processes involved in tumor metastasis and have the potential to contribute to the development of novel modalities for CRC diagnosis, prognosis and targeted therapies.

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## NEOADJUVANT CHEMOTHERAPY PRIOR TO MAJOR HEPATIC RESECTION OF COLORECTAL METASTASES IS ASSOCIATED WITH INCREASED MORTALITY AND HIGHER COMPLICATIONS RATE

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**Introduction.** Although Neoadjuvant approach to treat hepatic colo-rectal metastases is widely accepted, there is insufficient data regarding its impacts on postoperative morbidity and mortality.

**Methods.** Patients with resectable colo-rectal hepatic metastases were assigned to either an immediate surgery (group 1) or to neoadjuvant treatment with Irinotecan or Oxaliplatin together with Bevacizumab (Avastin) followed by surgery (group 2). Selection was based on the oncologist's and patient's preference and was guided by the estimated risk of recurrence. A multivariate analysis was conducted to identify risk factors for various postoperative complications.

**Results.** Of 106 included patients, 54 were operated immediately and 52 following neoadjuvant treatment. Overall mortality rates were 1.9% (1/54) in group 1 and 9.6% (5/52) in group 2 ( $p=0.07$ ). Mortality rates following extended lobar resections ( $\geq 5$  segments) were 8% (1/12) within group 1, and 41% (5/12) in group 2. The only other outcome measure that was different significantly is wound complications (infection, dehiscence and hernia; 7.4% vs. 23% respectively,  $p=0.03$ ). The rates of other infectious complications (pulmonary, line, UTI, intraabdominal collection) and the mean length of stay were also higher in the group 2, but these did not reach statistical significance. Interestingly, synchronous GI surgery was not an independent risk factor of post-operative complications.

**Conclusions.** Neoadjuvant chemotherapy is associated with increased mortality and morbidity following major hepatic resections. The oncological justification of neoadjuvant approach should be balanced accordingly.

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## TOTAL LOSS OF FDG AVIDITY IN COLORECTAL CANCER LIVER METASTASES AFTER CHEMOTHERAPY IS INFREQUENTLY ASSOCIATED WITH A COMPLETE PATHOLOGICAL RESPONSE

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**Introduction.** Newer chemotherapeutic regimens, especially those including biologic agents such as bevacizumab, have improved outcomes in patients with metastatic colorectal cancer. In some cases, dramatic responses have been associated with loss of FDG uptake on follow-up PET scans. It is unclear how often loss of FDG avidity in the face of continuing presence of a lesion on CT or MRI scan is associated with complete tumor destruction. This information is of importance in determining further management.

**Methods.** This is an analysis of a specific subset of patients undergoing neoadjuvant chemotherapy for hepatic metastases from colorectal adenocarcinoma. The inclusion criteria were: 1) whole body PET scan demonstrating FDG-avid hepatic lesions prior to initiation of neoadjuvant therapy; 2) whole body PET scan demonstrating loss of FDG-avidity of the same hepatic lesions after completion of neoadjuvant therapy; and 3) histopathological sampling of hepatic lesions by biopsy or resection to document extent of response to treatment.

**Results.** 16 patients treated from 6/2002 to 6/2006 fit inclusion criteria, including 12 since 1/2005. Median age was 58.5 years (range: 32–84 years), twelve were male, and fifteen had either stage 3 or 4 disease at the time of resection of the primary colorectal cancer. The chemotherapeutic regimen used in 13/16 patients was 5-fluorouracil-based (either FOLFOX or FOLFORI) combined with bevacizumab. No patient had focal FDG uptake in the liver after chemotherapy – 12/16 had uniform uptake of FDG in the liver, and 4/16 had heterogeneous uptake. On microscopic examination of resected tumors (15 patients) or biopsies (1 patient), viable tumor was present in 13 patients (81%). Complete response (only necrotic tumor identifiable) was declared when no viable tumor was present in a completely resected tumor. This was found in only 3 cases (19%).

**Conclusion.** Most patients with colorectal cancer whose hepatic metastases become FDG-PET negative after newer neoadjuvant chemotherapy regimens still have active residual tumor in the liver. Curative resection of liver metastases in these patients should not be deferred on the basis of FDG-PET negativity.

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## RIGHT HEPATIC LOBECTOMY USING THE STAPLE TECHNIQUE IN 101 PATIENTS

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**Background.** Application of linear stapling devices for extra-hepatic vascular control in liver surgery has been well-established. However, the technique for use of stapling devices in hepatic parenchymal transection is not well defined.

**Purpose.** To describe the safety and efficacy of our technique for use of endo-vascular stapling devices in hepatic parenchymal transection during open right hepatic lobectomy (Right Hemihepatectomy).

**Methodology.** We reviewed our experience with 101 consecutive open right hepatic lobectomies performed by a single surgeon between January 2003 and July 2006, in which endovascular staplers were utilized for the parenchymal transection phase.

**Results.** Of the 101 patients who underwent resection, 53 (52%) were female. The mean age was 58 years. Malignant disease was the indication for resection in the majority of patients (88%). Of those with cancer, 78% (69 of 89) had metastatic colorectal cancer, 6% (5 of 89) had metastatic neuroendocrine tumor, 4% (4 of 89) had hepatocellular carcinoma, 4% (4 of 89) had cholangiocarcinoma, and the remaining 8% were other metastatic cancers. 12 patients (12%) underwent resection for hepatic adenoma or symptomatic benign disease (FNH or hemangioma). 48 patients (48%) underwent a major ancillary procedure at the time of hepatic resection. 39 patients (39%) had a non-anatomic wedge resection of a left lobe lesion, 27 patients (27%) had one or more lesions treated with radiofrequency ablation (RFA), and 6 patients (6%) were treated with a synchronous bowel resection. The median total operative time was 336 minutes (range 155–620 minutes). A Pringle maneuver for temporary vascular inflow occlusion was utilized in all cases, with a median time of 9 minutes (range 4–17 minutes). 10 patients (10%) required blood transfusion during surgery or in the post-operative period. The maximum transfusion was 2 units of pRBC in 7 patients, and 1 unit of pRBC in 3 patients. The mean nadir post-operative hematocrit was

28.2%. All patients with malignant disease had tumor free margins at the completion of the procedure. The average hospital length of stay was 6.0 days. One patient (1%) developed a clinically significant bile leak requiring a post-operative ERCP. No patient required re-operation. Thirty and ninety day survival was 100%.

**Conclusion.** These findings indicate that application of endovascular stapling devices for parenchymal transection in major hepatic resection is a safe technique, with low transfusion requirements and minimal post-operative bile leak. The technique allows for rapid transection of the entire right hepatic lobe in under 10 minutes.

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#### HEPATECTOMY FOLLOWING COLORECTAL CANCER RESECTION IN THE ELDERLY IN THE UNITED STATES

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**Introduction.** After colectomy for colorectal cancer (CRC), patients have a 50% lifetime risk of developing metastases, with the liver as the most common site. It is estimated that approximately 20% of CRC liver metastases are resectable. Despite the proven benefit of liver resection for metastatic disease for long term survival, it is not known whether elderly metastatic CRC patients are appropriately offered liver resection for metastatic disease.

**Methods.** Patients with resected CRC aged between 65 and 75 years at the time of diagnosis were identified from the linked Surveillance, Epidemiology and End Results (SEER) – Medicare program from 1991 through 2003. Patients without continuous part A and B Medicare coverage, or had HMO coverage at any time from diagnosis of CRC to date of death were excluded. Patients with any cancers other than CRC were also excluded. Medicare claims data was used to determine whether resected CRC patients received a hepatectomy at any time following their colorectal resection. Overall survival (OS) was analyzed using the Kaplan Meier method and log-rank test.

**Results.** A total of 32652 patients were identified. The mean age at CRC diagnosis was 70.5, with 50% males. Of these patients, 596 (1.8%) received a subsequent liver resection. For patients who received a liver resection, mean age was 69.9 years at CRC diagnosis and 71.0 years at liver resection. The extent of hepatectomy was as follows: 131 (22%) formal right hepatectomy; 41 (7%) formal left; 35 (6%) trisegmentectomy; and 389 (65%) lobectomy not otherwise specified. There were 368 (62%) and 228 (38%) patients who received a hepatectomy for synchronous (within 6 months of the CRC resection) and metachronous metastases, respectively with no clinical difference in median survival for either group (24 and 25 months, respectively). One, three and five year OS for resected patients was 76%, 27% and 7.3%, respectively. Age and sex adjusted rates of liver resection by SEER region varied from 1.0% to 2.5%.

**Conclusions.** A lower than expected rate (2%) of hepatic metastatectomy was found among patients with previously resected colorectal cancer in the SEER-Medicare program. No difference in mortality was found between patients with synchronous or metachronous disease. Not unexpectedly, the long term overall survival rates among this older group were lower than that from literature series of younger patients. Further study is warranted to examine both access to and selection for hepatic resection for metastatic CRC in this population.

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#### RECURRENCE AND SURVIVAL OUTCOMES AFTER HEPATIC RESECTION WITH AND WITHOUT CRYOTHERAPY FOR COLORECTAL LIVER METASTASES

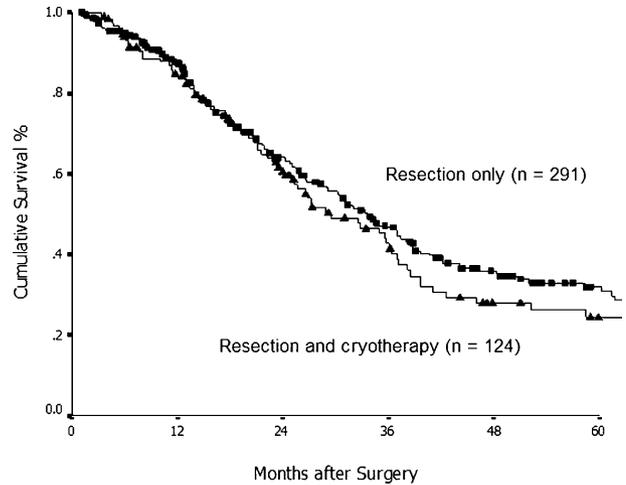
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**Introduction.** Only 10% of patients with colorectal liver metastases (CRLM) are amenable to resection. Ablative techniques have increased the proportion of patients that can undergo potentially curative treatment. Some reports support resection combined with cryotherapy for multiple bilateral liver diseases that would otherwise be ineligible for curative treatment. This series demonstrated long-term results of 415 patients with CRLM who underwent resection with or without cryotherapy.

**Method.** From January 1990 to December 2005, 291 patients were treated with resection only, 124 were treated with combined resection and cryotherapy. Resection was performed where technically possible, while cryotherapy was used to complement resection in bilobar disease. Hepatic arterial chemotherapy was used in patients who had more than 2 lesions. Recurrence and survival outcomes were analyzed. Kaplan-Meier and Cox-regression analyses were used to identify significant prognostic indicators.

**Result.** Median length of follow-up was 25 months (1 to 124). The 30-day perioperative mortality rate was 3.1%. Overall median survival was 32 months (1 to 124), with 1-, 3- and 5-year survival of 85%, 45% and 29% respectively. The overall recurrence rates were 66% and 78% for resection and resection/cryotherapy groups, respectively. Median lengths of disease-free intervals were 13 months and 8 months for resection and resection/cryotherapy groups, respectively. For the resection group, the median survival was 34 months, with 1-, 3- and 5- year survival of 88%,

47% and 32%, respectively. For the resection/cryotherapy group, the median survival was 29 months, with 1-, 3- and 5-year survival of 84%, 43% and 24%, respectively ( $p=0.206$ ) (Figure 1). Three factors were independently associated with an improved survival in multivariate analysis: absence of extrahepatic disease at diagnosis ( $p=0.026$ ; HR=1.490; 95% CI=1.049–2.116), largest lesion size  $\leq 4$  cm ( $p=0.012$ ; HR=0.271; 95% CI=0.098–0.752) and a low postoperative CEA ( $p < 0.001$ ; HR=1.887; 95% CI=1.369–2.6).



**Conclusions.** Long-term survival results of resection combined with cryotherapy for multiple bilobar CRLM are comparable to that of resection alone. An presence of extrahepatic disease at diagnosis,  $>6$  lesions with largest lesion size  $\geq 4$  cm and a postoperative CEA  $>5$  ng/ml are associated with a reduced survival outcome.

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#### COLORECTAL LIVER METASTASES: RECURRENCE AND SURVIVAL FOLLOWING HEPATIC RESECTION, RADIOFREQUENCY ABLATION, AND COMBINED RESECTION/ABLATION

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**Introduction.** Radiofrequency ablation (RFA) is increasingly accepted as an option for patients (pts) with colorectal liver metastases (CRLM). Long-term data following treatment of CRLM using RFA with or without hepatic resection are limited.

**Methods.** Between 1984 and 2006, 383 pts with CLRM were treated surgically at a single institution. Data were analyzed using univariate and multivariate analyses. To account for clinical differences between the RFA and resection group, a matched case control analysis was performed.

**Results.** Median number of treated hepatic lesions was 2 (range, 1–15); median size of the largest lesion was 3.5 cm (range, 0.2–15 cm). 310 (80.9%) pts underwent resection only, 61 (15.9%) resection+RFA, and 12 (3.2%) RFA only. The perioperative complication rate was 19.3% and 90-day mortality rate was 1.4%. At a median follow-up of 20.5 months, 184 (48.0%) pts had recurred. Factors associated with overall recurrence included primary tumor nodal status, tumor number, and history of RFA (all  $P < .05$ ). On multivariate analysis, pts who had undergone RFA remained over twice as likely to recur (HR=2.81,  $P < .001$ ). Pts who underwent either ablation alone (35.2%) or RFA+resection (40.0%) also had a higher rate of local recurrence within the liver compared with pts who underwent resection alone (9.8%) ( $P < .001$ ). The median actuarial survival for the entire cohort was 49.6 months and the 5-year survival rate was 42.6%. Patients who underwent resection only (61.4 months) had a longer median survival compared with pts who had either RFA alone (45.2 months) or RFA+resection (29.0 months) (both  $P < .001$ ). For pts treated with RFA, as tumor number increased so did the risk of disease-specific death (one lesion, HR=2.24; 2–3 lesions, HR=3.28;  $>3$ , HR=3.73) (all  $P < .001$ ). Pts who underwent RFA+resection were matched to pts who underwent resection only based on metastatic lesion size and number, as well as primary tumor T- and N-stage. On matched analysis, pts who underwent RFA+resection still had a higher risk of recurrence and disease-specific death vs. pts who underwent resection alone (Table).

**Conclusion.** Pts with CRLM who were treated with RFA alone or in combination with resection had a higher risk of hepatic recurrence and disease-specific death. When feasible, hepatic resection should remain the treatment of choice for pts with CRLM.

Risk of Recurrence and Disease-Specific Death Stratified by Surgical Procedure

	Hepatic Recurrence (Percent, %)	Any Recurrence (Percent, %)	5-year Disease-Specific Death (Percent, %)
<b>Unmatched Analysis</b>			
Resection Only	9.8	55.8	49.7
Resection + RFA	40.0	92.8	93.7
RFA Only	35.2	75.0	76.9
<b>Matched Analysis</b>			
Resection Only	16.6	58.7	52.6
RFA ± Resection	69.9	91.2	91.3

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**MICROWAVE HEPATIC TUMOR ABLATION RESULTS OF ONGOING PHASE 2 TRIAL**

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**Background.** Microwave hepatic tumor ablation represents a new and expanding technology in hepatic tumor ablation techniques. A majority of the initial experience had been in Asia and the United Kingdom. Microwave ablation has been demonstrated to be effective in the treatment of hepatic tumors in multiple treat and resect studies. This study represents our ongoing phase 2 evaluation of microwave ablation as the primary therapy in patients with hepatic malignancies.

**Method.** A prospective multi-institutional study of microwave ablation of hepatic tumors from 3/2004 until 5/2006 is presented. A standard bracketed technique of placing multiple (maximum 3) probes around the periphery of the tumor was utilized. In all cases multiple ablations of hepatic lesions was performed simultaneously.

**Results.** Two hundred and fifty-four hepatic tumors were ablated in 107 patients (45 colorectal, 28 hepatocellular, 13 breast, 21 other), in 108 ablation sessions. The median tumor number was 3 (range 1–13) with a median size of 3 cm (range 1.5 to 5.0 cm). Multiple types of microwave probes were utilized depending on location and size, with 56 open, 7 laparoscopic, and 45 percutaneous. 18 patients underwent additional procedures including partial hepatectomies, colectomy, and gastrectomy. Total median ablation time was 10 minutes (range 5 to 22.5), with median ablation volume 50.5cc (range 21 to 147). There were two peri-operative mortalities, with peri-operative morbidity occurring in 22 patients. After a median follow up of 22 months there have been 7 (2.8%) ablation recurrences and 46 (43%) regional recurrences.

**Conclusion.** Microwave hepatic tumor ablation is a safe and effective technique for tumor ablation. The ability to perform multiple ablations simultaneously allows for a more efficient surgical procedure, especially in patients with multiple lesions. The ability to perform bracketed ablations in tumors that are not perfectly spherical may result in more complete initial ablations and fewer ablation recurrences. Continued evaluation in ongoing trials in specific malignant histology's and specific hepatic parenchyma is needed to optimize this and other ablation technologies.

**Free Papers****Biliary II**

FP-10

4/22/07 10:15 to 11:45 am

Abstract Numbers 263–268

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**GALLBLADDER BILE CHANGES IN PATIENTS TREATED WITH PREOPERATIVE TOTAL PARENTERAL NUTRITION**

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Total parenteral nutrition increases the risk of gallbladder sludge and gallstones. Although the cause of this association has been studied in animal models, little data on bile composition with TPN exists in humans. In animal models, changes in bile salt secretion, bile salt profiles, gallbladder bile calcium, bilirubin, and biliary phospholipids have been reported with TPN. Whether any of these gallbladder bile changes occur in patients on TPN is unknown. We investigated gallbladder bile composition and bile salt profiles in 16 surgical patients on preoperative TPN (7days to 4 weeks) and compared this to gallbladder bile from 17 patients with normal oral intake undergoing operation for elective surgery (12 colectomy, 1 wedge liver resection, 2 gastric resection, 1 Nissen, 1 distal pancreatectomy). None of the patients had gallstones. Bile was analyzed for Ca<sup>++</sup>, total Ca, electrolytes, cholesterol and phospholipids (Wako and Boehringer-Mannheim

kits). Bilirubin profiles and bile salt profiles were analyzed with respective hplc assays.

**Results.** Gallbladder bile calcium (both ionized and total), bilirubin and bile salt concentrations, sodium, potassium, and bile acidification were similar in patients on preoperative TPN and patients with normal oral intake preoperatively. Similar to findings in animal models, TPN was associated with decreased phospholipids concentrations in gallbladder bile. Neither the concentration, nor the profile of bile acids changed, yet the percent of bile acids conjugated with taurine as compare to glycine was decreased in patients on TPN.

Gallbladder Bile values	Oral intake	TPN
Calcium (mM)	6.4 ± 0.7	6.5 ± 1.4
Bilirubin (mg%)	295 ± 52	204 ± 55
Bile salt (mM)	138 ± 13	148 ± 24
Cholesterol (mM)	7.7 ± 1.7	8.0 ± 1.9
Phospholipids (mM)	46.4 ± 5.9	31.4 ± 4.6*
%Taurine conjugated bile salts	36 ± 4	19 ± 4*

\* Significant difference, p < 0.05, t-test.

**Conclusion.** Gallbladder bile from patients on preoperative TPN did not show changes in calcium, bilirubin nor bile salt concentration as seen in animal models on TPN. Whereas the bile composition of cholic acid, chenodeoxycholate and deoxycholate conjugates did not change, the percent of bile salts conjugated with taurine decreased. Biliary phospholipid concentrations decreased similar to that seen in several animal models. A reduction in biliary phospholipids may alter the solubility of cholesterol in bile and predispose to gallstones in patients fed intravenously.

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**UNCONSCIOUS BIAS INFLUENCES THE DIAGNOSIS OF LAPAROSCOPIC BILE DUCT INJURIES**

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**Purpose.** Framing (assumptions about context, that leads to assigning meaning to certain observations and discounting others deemed irrelevant) channels all types of human decision-making, including the diagnosis of bile duct injuries. The clinician's ability to frame data using well-developed pattern-matching confers expertise. But, this can sometimes lead to diagnostic errors (eg. if the clinician frames symptoms of bile ascites as ileus rather than bile duct injury). Another common diagnostic error (premature closure) occurs when an initial diagnosis is given more credence than the evidence supports and subsequent disconfirmatory findings are discounted. In 74% of injuries resulting from a laparoscopic cholecystectomy, the complication is undetected until sometime later in the post-operative period. We analyzed the thinking patterns that eventually led to the diagnosis.

**Methods.** Of 303 bile duct injuries, the 224 (74%) that were detected postoperatively were grouped by presentation: bile ascites (Fist) or biliary obstruction (Obst), and whether jaundice (bili ≥ 3) was present. Time to diagnoses, number of encounters (clinic/ER visit, hospitalization, etc.) before diagnosis, and the effect of prior diagnostic hypotheses on final diagnosis was tabulated.

**Results.** 53% of these injuries were diagnosed at first presentation (Rec), 70% presented with Fist and 30% with Obst. Among those with Fist, only 45% were Rec (45% vs 71%, Fist vs Obst, P = 0.003). When accompanied by jaundice, Fist cases were Rec more often (60% vs 40%, with vs without jaundice, P < 0.05). 43% of cases with persistent bilious drainage were observed for > 2 weeks (range 1–140 days) before obtaining diagnostic studies. Injuries initially missed were more likely to be missed on subsequent encounters: 58% were missed on the 2nd encounter, 24% were missed again on the 3rd-5th encounters (P < 0.0001); and recognition time was longer (7 vs 27 days, Rec vs missed, P < 0.0001). This pattern was repeated at each point of missed injury (opened without recognition, missed during hospitalization, clinic, etc.).

**Conclusions.** Inadequate framing (failure to appreciate the significance of bile leaks) and premature closure (giving excessive credence to the initial hypothesis) accounted for most diagnostic delays. Increasing awareness that most laparoscopic bile duct injuries present with bile ascites rather than obstructive jaundice (better framing), and a more balanced weighting of the diagnostic findings would lead to earlier diagnosis, earlier treatment, and less morbidity. Understanding the innate idiosyncrasies of human decision-making is critical for improving outcomes.

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**EVOLUTION OF THE SURGICAL REPAIR OF BILE DUCT INJURIES: THE TRANSITION TO INTRAHEPATIC REPAIR**

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The most frequent technique used for reconstruction is a Roux en Y hepatojejunostomy. Long-term results of reconstruction are related to several technical and anatomic factors, but an ischemic duct play a mayor role. We report the results seen during the transition of low extrahepatic repair to high intrahepatic repair.

**Methods.** In 15 years a total of 355 patients have been referred to our hospital for bile duct repair. Thirty two cases have been repaired minutes to hours after the injury occurred. The remaining 323 patients arrived weeks after the injury with heterogeneous symptoms related to intrabdominal collections, external fistulae and occluded ducts. Surgical treatment was done when either the radiological or endoscopic approach were ruled out and when the general conditions of the patient allowed the surgical intervention for reconstruction. In all cases, a Roux en Y hepatojejunostomy was done. Partial resection of segment IV was performed in order to obtain non-inflamed, non-scarred, non-ischemic biliary ducts with the purpose of achieving a high quality bilioenteric anastomosis. This technique was done in 101 patients. In a total of 243 cases an anastomosis at the level of the confluence was attempted (in 163 we found the confluence preserved and in 80, the confluence was lost). In the remaining 80 patients, a low bilioenteric anastomosis was done at the level of the common hepatic duct. We compared the cases in which an intrahepatic repair was done (163) with those who had an extrahepatic one (80).

**Results.** All of the injuries were classified as Strasberg E. In all cases the confluence was preserved (N=243). In 163 a high intrahepatic repair was done, including the 101 patients in which resection of segment IV and V was part of the surgery. The anastomosis was made with 5-0 absorbable monofilament sutures, opening the anterior aspect of the left duct in order to obtain a wide, tension free anastomosis. In the remaining 80 cases (operated between 1990-1997) an anastomosis was done at the level of the common hepatic duct were the surgeon seemed to find a healthy duct. Twelve (15%) of the 80 cases with low extrahepatic anastomosis required a new intervention (surgical or radiological), compared to the 5 cases of the 163 (3%) that had a high intrahepatic anastomosis (P=0.00062). Good results were obtained in 85% and 97% of the cases with low extrahepatic anastomosis and high intrahepatic anastomosis respectively.

**Conclusions.** A high intrahepatic anastomosis warrants the finding of non-scarred, non-ischemic ducts, allowing a safe and high quality anastomosis with significant results compared to the low level anastomosis group.

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#### TREATMENT OF MAJOR BILE DUCT INJURIES AFTER LAPAROSCOPIC CHOLECYSTECTOMY – FIFTEEN YEAR EXPERIENCE IN A REFERENCE CENTER

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**Introduction.** Laparoscopic cholecystectomy increases the risk of major bile duct injuries. We report our fifteen year experience of treatment of these injuries in a referral center.

**Methods.** A retrospective study of 123 patients (93 women and 30 men; mean age: 49±17 years) referred between 1991 and 2005 in our tertiary center. We analyze: gallbladder disease, injuries diagnosis time, Strasberg classification of injuries, type of reparation procedures and long terms results of follow-up.

**Results.** Cholecystectomy was performed for 77 symptomatic chronic calculous cholecystitis and 46 acute calculous cholecystitis. The injury was diagnosed during the surgical procedure for 60 patients and in the post-operative time for 63 patients. The Strasberg classification of injuries was: 5 type A, 8 type E1, 28 type E2, 34 type E3, 36 type E4, 12 type E5. Before the transfer of patients, primary reparation procedure was: 39 primary closures, 23 hepatojejunostomies, 13 exploratory laparotomies, 17 percutaneous drainage of bilioma, 7 ERCP or transhepatic procedures and 24 medical treatments. In our center, 104 patients needed 1 to 4 surgical corrections with: 72 hepatojejunostomies, 12 surgical drainages, 23 hepatectomies and 1 liver transplantation. Forty-six ERCP or percutaneous therapeutic procedures and 16 percutaneous drainages were done. The median follow-up was 78 months. The mortality was 2.5%. Seven patients were lost during the follow-up. Long-term results were: 102 patients with normal hepatic blood tests and 88 with normal liver ultrasound examination.

**Conclusions.** Roux-en-y hepatojejunostomy is the best procedure for the repair of bile duct injuries and allows very good long-term results.

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#### MANAGEMENT OF BENIGN BILIARY STRICTURES: ANALYSIS OF MINIMALLY INVASIVE TECHNIQUES VERSUS SURGICAL TREATMENT

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**Introduction.** The effectiveness of various benign biliary stricture treatments has not been evaluated systematically. The authors reviewed the treatment and outcome of patients with benign biliary stricture who under-

went surgical treatment, minimally invasive treatment (ERCP, PTCD) or both.

**Methods.** Between 2002 and 2006 Patients(n=49) referred for treatment of benign bile duct strictures due to chronic pancreatitis (17), sclerosing cholangitis (12), bile ducts injuries (11), choledochal cysts (3), pancreatic pseudocyst (3), crohn's disease of the duodenum (2), Aberrant anatomy (1). Surgery and/or endoscopic treatment were performed according to the degree, the level (Bismuth-Collins classification) and the etiology of the stricture. Multivariate and univariate analysis of clinical and pathologic factors in relations to patient's outcome, hospitals stay and survival were performed.

**Results.** 28 patients had only endoscopic intervention (stenting, balloon dilatation). 16 patients were managed with both surgical and minimally invasive procedure. 5 patients underwent only surgical treatment. Repeated minimally invasive treatments gave less complications (4/28) than surgery alone (4/5) or surgery and endoscopy (15/16); as well as were correlated to a less initial hospital stay (P<0.01) and total hospital stay (P<0.01). There was no difference in the outcome according to the etiology and the level of the stricture. Recurrence rate was less in patients treated by surgery and endoscopy (P<0.01).

**Conclusion.** Successful management of benign biliary stricture requires a multidisciplinary approach. Initial endoscopic treatment should be attempted and repeated minimally invasive procedures are a real option. Combination of surgery and endoscopic intervention provides the best outcome.

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#### RECURRENT PYOGENIC CHOLANGITIS – THE ROLE OF SURGICAL INTERVENTION

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**Purpose.** To assess the outcomes of surgical management of Recurrent Pyogenic Cholangitis (RPC) at a North American tertiary care centre.

**Methods.** Retrospective analysis of 42 RPC patients, presenting between 1986-2005. Patients were identified through a search of hospital and hepatobiliary surgeons' clinical records.

**Results.** Mean age is 54 years (24-87), and 23 patients were female (55%). All subjects had recurrent episodes of bacterial cholangitis; sixteen patients (38%) had predominantly left-lobe disease, while 19/42 (45%) had bilateral disease. Twenty-seven patients (64%) underwent surgery, after failed attempt at stone removal by ERCP in 11 and by interventional radiology in 9. The principles of surgical management were: intraoperative stone extraction and provision of a Hutson choledochojunal access loop when necessary. Surgical procedures were: 10 CBD explorations with Hutson loop; 17 hepatectomies, 10 with, and 7 without Hutson loop. Liver resection was used in patients whose stone disease was dominant in one lobe. In the non-resection group, 7/10 had CBD dominant or bilobar stones; 2 had parenchymal atrophy but no significant intra-hepatic stones; and one had right-sided stones considered to be extractable. Operative mortality was zero; complication rate for hepatectomy (35%) was similar to that of CBD exploration (30%). Median follow-up was 24 months (3-228). Of 21 Hutson loops constructed, only 7 (33%) were subsequently used for percutaneous removal of stones, with three failures. Post-op need for interventional radiology (excluding Hutson access) occurred in 4 other patients. At completion of surgical therapy (i.e. operation±use of Hutson loop), 21/27 (78%) patients were free of stones. At last follow-up, no surgical patients had recurrent symptoms due to stones, while in the non-operated group 4/15 were symptomatic from stones (27%). Cholangiocarcinoma was identified in 6/42 (14%) patients; 5 were unresectable and one was an incidental in-situ carcinoma in the resected specimen.

**Conclusion.** Surgery appears to be a safe and effective treatment option for RPC, and hepatectomy is a valuable option for lobe-dominant disease with no apparent increased morbidity. Though Hutson loop has not been used frequently, it has low morbidity and provides for direct percutaneous removal of stones. The risk of cholangiocarcinoma is increased in RPC and often presents as advanced disease. Hepatectomy should be considered in patients with lobe-dominant RPC.

#### Free Papers

##### Liver III

FP-11

4/22/07 10:15 to 11:45 am

Abstract Numbers 269-274

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#### COMPARISON OF TWO METHODS OF FUTURE LIVER REMNANT VOLUME MEASUREMENT

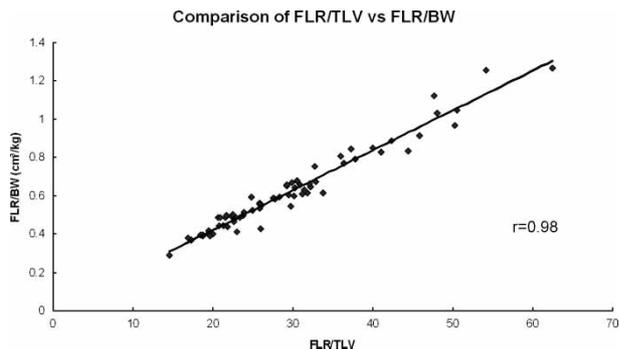
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**Background.** In liver transplantation, a minimal graft to patient body weight (BW) ratio is required for graft survival; in liver resection, total liver volume (TLV) calculated from body surface area (BSA) is used to determine the future liver remnant (FLR) volume needed for safe hepatic resection. These two methods of estimating liver volume have not previously been compared. The purpose of this study was to compare FLR volumes standardized to BW versus BSA and to assess their utility in predicting postoperative hepatic dysfunction following hepatic resection.

**Methods.** Records were reviewed of 68 consecutive noncirrhotic patients who underwent major hepatectomy after portal vein embolization between 1998 and 2006. FLR (cm<sup>3</sup>) was measured preoperatively with three-dimensional helical computed tomography; TLV (cm<sup>3</sup>) was calculated from patients' BSA. The relationship between FLR/TLV and FLR/BW (cm<sup>3</sup>/kg) was examined using linear regression analysis. Receiver operating characteristic (ROC) curve analysis was used to determine FLR/TLV and FLR/BW cutoff values for predicting postoperative hepatic dysfunction (defined as peak bilirubin level >3 mg/dl or prothrombin time >18 seconds).

**Results.** Regression analysis revealed that the FLR/TLV and FLR/BW ratios were highly correlated (Pearson correlation coefficient, 0.98; figure 1). The area under the ROC curve was 0.85 for FLR/TLV and 0.84 for FLR/BW (95% confidence interval, 0.71–0.97). Sixteen of the 68 patients developed postoperative hepatic dysfunction. ROC curve analysis yielded a cutoff FLR/BW value of ≤0.4, which had a positive predictive value (PPV) of 78% and a negative predictive value (NPV) of 85%. The corresponding FLR/TLV cutoff value of ≤20% had a PPV of 80% and a NPV of 86%.

**Conclusions.** Based on the strong correlation between the FLR measurements standardized to BW and BSA and their similar ability to predict postoperative hepatic dysfunction, both methods are appropriate for assessing liver volume. In noncirrhotic patients, a FLR/BW ratio of ≤0.4 and FLR/TLV ≤20% provide equivalent thresholds for performing safe hepatic resection.



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**STEATOSIS IS AN INDEPENDENT PREDICTOR OF POST-OPERATIVE MORBIDITY FOLLOWING HEPATIC RESECTION FOR COLORECTAL METASTASIS**

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**Background.** Hepatic resection is commonly performed for colorectal liver metastasis (CRLM). To date, few studies are available on the effect of steatosis on morbidity and mortality.

**Methods.** Patients undergoing hepatic resection for CRLM from January 2000 to September 2005 were identified from the Hepatobiliary database.

Data analyzed included demographics, laboratory analyses, extent of hepatic resection, blood transfusion requirements and steatosis.

**Results.** 386 patients were identified with a median age of 66 (32–87) years. 201 (52%) patients had at least one co-morbid condition and 192 (50%) patients had an ASA score of 1. 279 patients (72%) underwent anatomical resections and the remaining 107 (28%) had non-anatomical resections. 165 (43%) patients underwent additional procedures. 194 patients (50%) had steatosis and were classified on severity: mild (n = 122), moderate and severe (n = 72). Overall morbidity was 49% (n = 139) and mortality was 2% (n = 7). The presence of co-morbid conditions, higher ASA grade, major hepatic resection, additional procedures, steatosis and blood transfusion were associated with increased morbidity. ITU admission, morbidity, infective complications and changes in biochemical profile were associated with a greater severity of steatosis. Independent predictors of morbidity were steatosis, extent of hepatic resection and blood transfusion.

**Conclusion.** Steatosis is associated with an increase in morbidity following hepatic resection for CRLM. Other predictors of outcome were extent of hepatic resection and blood transfusion. Patients with steatosis, undergoing major hepatic resection and require blood transfusion should be considered high-risk and managed aggressively post-surgery.

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**INCREASED USE OF PARENCHYMAL-SPARING SURGERY FOR BILOBAR COLORECTAL LIVER METASTASES IS ASSOCIATED WITH REDUCED MORTALITY WITHOUT CHANGE IN ONCOLOGIC OUTCOME**

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**Introduction.** Resection of bilobar colorectal liver metastases has unique technical concerns and has been associated with worse oncologic outcome. We aimed to determine the association of operative variables with morbidity, mortality, and oncologic results for resection of bilobar liver metastases.

**Methods.** Patients were identified from a prospectively maintained database. The log-rank test was used to assess differences in survival, and the Pearson's chi-square test was used for morbidity. Cox regression was used for multivariate analysis. The Cochran-Armitage, Jonckhree-Terpstra, and log-rank trend tests were used to assess trends in categorical variables, continuous variables, and survival.

**Results.** From 7/1/1992–2/13/2003, 443 operations for bilobar colorectal metastases were performed in 440 patients. The complication rate was 51% with a liver-related complications rate of 24% and a major complications rate of 29%. The 30-day and 90-day mortality was 2.9% and 5.4%. Kaplan-Meier predicted 5-year survival was 30%, although 5-year recurrence was 82%. The 5-year hepatic disease-free survival was 39%. Positive resection margin independently correlated with worse disease-specific survival, and the use of wedge resection independently correlated with shorter liver recurrence-free survival. The number of liver segments resected was independently associated with liver-related complications. Vascular or biliary resection as well as intra-abdominal, extra-hepatic resections other than of the primary tumor was independently associated with major complications. There were too few deaths for multivariate analysis of operative mortality. Operative approach changed over time (Table) with greater use of multiple simultaneous liver resections, wedge resections, and ablations, as well as less use of major hepatectomies. This correlated with decreased mortality without change in disease-specific survival or liver recurrence.

**Conclusions.** Resection of bilobar colorectal liver metastases can be accomplished with acceptable morbidity, mortality, and oncologic results. Increased use of a parenchymal-sparing approach is associated with decreased mortality without compromise in cancer-related outcome.

Trends in Procedures and Outcome over Time

	1992–1994 (n = 96)	1995–1997 (n = 122)	1998–2000 (n = 144)	2001–2003 (n = 81)	p-value
Major procedure lobectomy or trisectionectomy	89 (93%)	106 (87%)	119 (83%)	60 (74%)	<0.001
Four or more segments resected	88 (92%)	98 (80%)	111 (77%)	57 (70%)	<0.001
Number of segments resected (median/mean)	5/4.7	5/4.4	4.5/4.2	4/3.9	<0.001
More than 2 simultaneous liver resections	2 (2.1%)	9 (7.4%)	17 (12%)	13 (16%)	<0.001
Wedge resection used	15 (16%)	28 (22%)	51 (36%)	31 (38%)	<0.001
Ablation used	1 (1.0%)	0 (0%)	4 (2.8%)	7 (8.6%)	0.001
Ninety day mortality	6 (6.3%)	13 (11%)	4 (2.8%)	1 (1.2%)	0.02
Median disease-specific survival (months)	45	34	34	NR	0.52
Median liver recurrence-free time (months)	22	20	20	15	0.43

NR = not reached.

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**RESECTABLE EXTRAHEPATIC DISEASE IS NO LONGER A CONTRAINDICATION TO HEPATECTOMY FOR COLORECTAL METASTASES**

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**Introduction.** The presence of extrahepatic disease, bilobar disease, and greater than three hepatic lesions have traditionally been considered contraindications to hepatectomy for colorectal metastases because of the perceived increased perioperative risk without improved long-term survival. Resectable extrahepatic disease (EHD) at the time of hepatic resection was considered to expand criteria for further treatment of colorectal metastases.

**Methods.** The charts of 328 patients who underwent hepatectomy for colorectal cancer metastasis from 1988 to 2005 were reviewed. Prior chemotherapy, if received, in these patients consisted of bolus 5-FU. Data were compared by Student's T-test and Fisher's Exact Test, where appropriate. Overall survival curves were constructed using the Kaplan-Meier method and compared by log-rank analysis. Multivariate analysis was undertaken to determine predictors of decreased survival and perioperative mortality.

**Results.** Fifty (15%) patients presented with EHD at the time of hepatectomy. There were no significant differences between patients with and without EHD with regard to age, gender, disease free interval, and the number and distribution of hepatic metastases. Patients with EHD were as likely to undergo complete (i.e. R0) resection as those with isolated liver metastases (58% vs. 72%,  $p > 0.05$ ). Perioperative mortality was 5.8% and was not affected by concomitant resection of EHD ( $p = 0.471$ ). Only increasing number of segments resected was predictive of perioperative mortality by multivariate analysis. Median overall survival was 19.7 months in patients with EHD compared to 34.0 months in patients without EHD ( $p < 0.001$ ). Only age and EHD remained significant predictors of decreased survival by multivariate analysis.

**Conclusion.** Despite similar populations, extrahepatic disease remains a poor prognostic indicator for survival after hepatectomy for colorectal metastasis. However, low perioperative mortality coupled with median survival of nearly 20 months emphasizes the potential of a curative approach to patients with traditionally incurable disease. The presence of resectable extrahepatic disease should no longer be a contraindication to hepatectomy for colorectal metastases, particularly when coupled with modern chemotherapy.

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**SURVIVAL FOLLOWING RADIOFREQUENCY ABLATION OF COLORECTAL LIVER METASTASES: A TEN YEAR EXPERIENCE**

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**Purpose.** The purpose of this study is to examine the outcomes and survival of patients who had radiofrequency thermal ablation (RFA) of colorectal liver metastases.

**Methods.** Between September of 1996 and Jun of 2006, perioperative and follow-up data were collected prospectively on 110 patients with isolated colorectal liver metastases who underwent 128 RFA procedures.

**Results.** The average patient age was 54 (SD ± 24). Cardiopulmonary comorbidities were present in 65 (59%) patients. Out of 128 procedures, there were 107 laparoscopic, 12 open, 7 CT guided, 1 thoracoscopic, and 1 US guided. 13 patients had two procedures and 6 patients had three procedures. The average number of tumors ablated per patient was 2.3, the average size of tumor was 2.63 cm (SD ± 1.5).

	RFA only	RFA/Resection	RFA/HAI	RFA/Resection/HAI
Laparoscopic	74	8	23	2
Open	3	4	1	4

There were 5 intraoperative complications (3 enterotomies, 1 minor skin burn, 1 GB burn) and 9 minor and two 2 major postoperative complications. One patient with a concomitant colostomy takedown had an anastomotic leak. One patient with a severe aortic valve gradient died three weeks postoperatively of pneumonia and an MI. Two patients with concomitant liver resections needed blood transfusions. The median follow-up is 20 months (range = 3 to 120). 78 (71%) patients have recurred, with a median of 9 months to first recurrence. Overall distant failure rate was 42 (38%). Overall RFA site failure was 22/110 (20%). Kaplan-Meier survival analysis was done and showed a mean and median survival was 38 and 32 respectively. Overall 5-year survival was 25%. A Cox regression analysis for overall survival showed the likelihood of death was 3.88 ( $p = 0.003$ ) for tumors > 5 cm in diameter and 2.41 ( $p = 0.043$ ) for patients with more than 1 tumor.

Site of 1st Recurrence	78/110
RFA site only	16 (14.5%)
New liver site only	14 (12.7%)
RFA and new liver only	6 (5.4%)
Extrahepatic only	22 (20%)
Extrahepatic and liver	20 (18.2%)

**Discussion.** We have shown that RFA is an effective means of tumor destruction with a low perioperative morbidity. RFA may have a role in the treatment of selected in patients with colorectal liver metastases.

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**HEPATECTOMY AND LUNG RADIOFREQUENCY ABLATION FOR HEPATIC AND SUBSEQUENT PULMONARY METASTASES FROM COLORECTAL CARCINOMA**

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**Background.** Liver and lung are the two most involved organs in colorectal carcinoma metastases. This reflects the porto-systemic spread of the disease. In selected groups of patients, hepatic resection has been regarded as the only curative treatment of colorectal liver metastases, achieving a median survival of 20 to 40 months and a 5-year survival of 30–50%. Despite hepatectomy with curative intent, many patients develop pulmonary metastases after initial hepatectomy. Resection of colorectal pulmonary metastases can achieve a 20–40% 5-year survival, but only in a small group of patients. Lung radiofrequency ablation (RFA) is a relatively safe procedure and may have a useful role in the management of non-surgical candidates with colorectal pulmonary metastases.

**Methods.** This study consists of 30 patients, who had previously undergone hepatectomy for colorectal liver metastases and subsequently developed pulmonary metastases, which were then treated with lung RFA. The primary aim of this presentation is to demonstrate survival in patients with two organ metastases, who are not candidates for surgical resection of colorectal pulmonary metastases. The secondary aim is to assess the prognostic indicators for survival after lung RFA. Lung RFA was performed percutaneously under local anaesthesia and conscious sedation, with fluoro-CT guided imaging, using the RITA 1500 generator. All patients were reviewed at one week, one month and every three months with repeat CEA and chest CT scans. The follow-up was complete.

**Results.** In the 30 patients involved in this study, there was no lung RFA related mortality. The periprocedural morbidity rate was 37%. The median survival after initial liver surgery was 64 months (range 15–118 months). The 1-, 3-, and 5-year survival rates were 100%, 77% and 53%, respectively. The median survival after lung RFA was 32 months (range 5 to 50 months). The 1-, 2-, and 3-year survival rates were 75%, 63% and 45%, respectively. The following 4 factors were found to significantly affect survival in the univariate analysis: the size of the largest pulmonary metastasis ( $p = 0.032$ ), the proximity of metastases to major pulmonary vessels ( $p = 0.003$ ), pre-lung RFA CEA levels ( $p = 0.013$ ) and post-lung RFA CEA levels ( $p = 0.022$ ).

**Conclusions.** Lung RFA is a relatively safe procedure in the management of non-surgical candidates with colorectal pulmonary metastases.