

6A HPB AND OESOPHAGOGASTRIC SURGERY

O138 CLINICAL FEATURES AND OUTCOMES OF PATIENTS WITH BREAST CANCER LIVER METASTASES TREATED BY SURGICAL RESECTION

ANS Silva, R Punde, JPA Lodge

St. James University Hospital, Department of Liver Transplantation and Hepatobiliary Surgery

Introduction: Breast cancer liver metastases (BCLM) are uncommon and therefore the characteristics of this subgroup of patients and their survival outcomes are poorly understood. Our aim was to study the cohort of patients who undergone liver resection for BCLM at SJUH, Leeds.

Method: Retrospective data collection using the Leeds Liver Surgery Database and Patient Pathway Manager of a total of 21 patients who had hepatectomies for BCLM from 2001-2016.

Result: Within 30 days of major hepatectomy (≥ 3 segments, 8 patients) or minor hepatectomy (< 3 segments, 12 patients), there was no mortality. The average hospital stay was 6 days and there were no major complications. Microscopically and macroscopically positive margins were present in 33% (R1) and 10% (R2). Following hepatectomy 3 patients (14%) developed isolated liver recurrences which required re-do liver resection. Median overall survival was 54 months with 10 (47%) patients alive and 9 (43%) patients alive at 5-years. There was no survival difference between patients with synchronous versus metachronous cancers, patients with extra-hepatic versus without extra-hepatic disease, patients with large tumours (≥ 3 cm) versus small tumours (< 3 cm) and patient's ≥ 50 years versus patients < 50 years (all p-values > 0.05). Patient with R0 margins had a marginally better survival than patient with R1/R2 (p=0.077). Patients without disease recurrence had better survival than patients with recurrence (p=0.045).

Conclusion: Recurrence of disease following post hepatectomy is associated with poorer survival in BCLM. BCLM are an uncommon phenomena therefore larger multicentre studies are needed to further evaluate this subgroup of patients

Take-home message:

Larger multicentre studies are needed to generate larger number in order to further evaluate this subgroup as Breast Cancer liver metastases (BCLM) are an uncommon disease process.

O139 PANCREAS PRESERVING DISTAL DUODENECTOMY: A VERSATILE OPERATION FOR A RANGE OF INFRA-PAPILLARY PATHOLOGIES

WK Mitchell, PF Thomas, AM Zaitoun, AJ Brooks, DN Lobo

Queens Medical Centre, Nottingham University Hospitals

Introduction: Neoplastic lesions of the duodenum are treated conventionally by pancreaticoduodenectomy. Lesions distal to the major papilla may be suitable for a pancreas preserving distal duodenectomy (PPDD), potentially reducing morbidity and mortality. We present our experience with this procedure.

Method: Patients were identified from a prospectively maintained database and outcomes determined from digital health records.

Result: Twenty-one patients were operated with intent of PPDD from 2003-2016. Eighteen successfully underwent PPDD. All had perioperative duodenoscopy to assess the relationship of the papilla to the lesion. After duodenal mobilisation and confirmation of the site of the lesion, the duodenum was transected distal to the papilla and a side-to-side duodeno-jejunal anastomosis was formed. One patient planned for PPDD proceeded to formal pancreaticoduodenectomy while two patients had unresectable disease. Median follow-up was 32 months. Pathologies resected included duodenal adenocarcinoma (n=6), gastrointestinal stromal tumours (n=4), adenomas (n=4), and lipoma, bleeding duodenal diverticulum, locally advanced colonic adenocarcinoma and extrinsic compression (n=1 each). Median postoperative length of stay was 8 days and morbidity was low [pain and nausea/ vomiting (n=2), anastomotic leak (n=1), pneumonia (n=1), overwhelming post-splenectomy sepsis (n=1, asplenic patient)]. The 90-day mortality was zero and fifteen patients are alive to date. One patient died of recurrent duodenal adenocarcinoma 18 months postoperatively; two died of unrelated disease (at 8 months and at 8 years).

Conclusion : PPDD is a versatile operation that can provide definitive treatment for a range of pathologies including adenocarcinoma and is associated with low morbidity and mortality. PPDD, pancreas preserving distal duodenectomy.

Take-home message:

Pancreas preserving distal duodenectomy is a versatile operation that can provide definitive treatment for a range of pathologies including duodenal neoplasia and is associated with low morbidity and mortality. Long-term results were also good.

O140 FREQUENT CO-AMPLIFICATION OF RECEPTOR TYROSINE KINASE AND DOWNSTREAM SIGNALLING GENES IN JAPANESE PRIMARY GASTRIC CANCER AND CONVERSION IN MATCHED LYMPH NODE METASTASIS

ANS Silva, J Coffa, V Menon, LC Hewitt, K Das, Y Miyagi, D Bottomley, H Slaney, T Aoyama, W Mueller, T Arai, IB Tan, N Deng, XB Chan , P Tan, A Tsuburaya, K Sakamaki, JD Hayden, T Yoshikawa, I Zondervan, S Savola , HI Grabsch

Wellcome Trust Brenner Building, Leeds Institute of Cancer and Pathology, University of Leeds

Introduction: Evidence suggests that co-amplification between receptor tyrosine kinase (RTK) and downstream signalling genes (DSS) and conversion between primary gastric cancer (primGC) and matched lymph node metastases (LNmet) are associated with resistance to targeted therapy. Therefore we aimed to establish the gene copy number status of RTK and DSS genes in primGC and matched LNmet.

Method: DNA from 237 Japanese primGC and 103 matched LNmet was analysed using a newly developed multiplex ligation-dependent probe amplification (MLPA) probemix to investigate RTK (EGFR, HER2, FGFR2, MET) and DSS (PIK3CA, KRAS, MYC, CCNE1) gene copy number status. Results were compared between primGC and LNmet and related to clinicopathological data including survival.

Result: 150 (63%) primGC had either RTK or DSS amplification. DSS co-amplification was more frequent than RTK co-amplification in primGC and LNmet. 70 (30%) GC showed a discordant RTK and/or DSS gene copy number status between primGC and LNmet, most common was negative conversion for DSS genes (n=40 GC). The presence of RTK amplification in primGC was related to poorer survival in univariate analysis (p=0.04).

Conclusion: This is the first and most comprehensive study in gastric cancer investigating the concordance between gene copy number status of targetable RTKs and downstream signalling oncogenes in primGC and LNmet. Future studies need to establish whether the relative high frequency of RTK and DSS co-amplification and/or the relative high rate of negative conversion in LNmet can potentially explain recent failures of RTK targeted therapy in GC patients.

Take-home message:

With exception of Trastuzumab, all other targeted therapies have failed in treatment of gastric cancer, the relative high rate of negative conversion in LNmet can potentially explain recent failures of RTK targeted therapy in GC patients.

O141 COMBINED RESECTIONS FOR LOCALLY ADVANCED RECTAL CANCER WITH SYNCHRONOUS LIVER METASTASES

B Creavin, A Heeney, E Ryan, D Winter
St Vincent's University Hospital

Introduction: Liver metastases is one of the commonest sites of metastatic disease in colorectal cancer with up to a quarter of patients having synchronous disease at diagnosis. Morbidity of rectal cancer surgery has led to apprehension in undertaking combined resections of primary rectal cancer and liver metastases. This study aims to review a single-institution experience of simultaneous resection in locally advanced rectal versus colon cancer with synchronous liver metastases.

Method: Patients with locally advanced metastatic rectal cancers were identified from prospectively maintained databases. Rectal cancer patients with liver metastasis were referred for neoadjuvant chemoradiotherapy and reassessed 6-8 weeks post treatment. Patients were referred for synchronous liver and rectal resections and followed up post operatively for short term and long term outcomes.

Result: Between Jan 2005 and July 2015, 35 consecutive patients with locally advanced rectal cancer and synchronous colorectal liver metastases (SCLM) were included and compared with 35 consecutive colorectal cancer and SCLM resections. One in hospital death occurred in both cohorts. There were no significant differences in overall morbidity (rectal 51.4% vs colonic 63%), minor or major complications between the two cohorts. There was no significant difference in overall survival or disease free survival.

Conclusion Synchronous resection of rectal and liver metastasis facilitates both treatment of primary and metastatic disease in selected patients.

Take-home message:

Synchronous resection of liver/rectal cancer is achievable in selected patients.

O142 FEASIBILITY OF ROBOTIC SURGERY FOR ADVANCED MINIMALLY INVASIVE HPB PROCEDURES

JA Logue, SM Robinson, RM Charnley, DM Manas, JJ French, SA White
Freeman Hospital, Newcastle

Introduction: Robotic surgery is gaining increasing acceptance in all fields of surgery. Experience in the UK is limited. We describe our experience and learning curve of robotic HPB procedures.

Method: Since 2013 we have performed 40 HPB procedures. Initial experience included cadaver lab training. Experience has been predominantly limited to two specialist laparoscopic surgeons. Procedures include cholecystectomy, distal pancreatectomy, fenestration of liver cysts and liver resections.

Result: Cholecystectomy (n=12) was used as our learning curve and to establish operative efficiency. There were no complications. Median operative time was 88.8 minutes, 5 were day cases. The next procedure to be introduced was distal pancreatectomy with or without spleen preservation (and adrenalectomy n=1) median operative time was 328 mins and median length of stay 9 days. 3 patients developed a Grade B pancreatic fistula (ISGPF classification). There were 2 conversions. 13 robotic liver procedures were performed eight of which were resections (left lateral/segmentectomy/metastectomy), 5 cases were fenestration of massive liver cysts. 2 patients developed bile leaks. There have been no deaths.

Conclusion: There is definitely an evolving role for complex robotic HPB surgery which is potentially far superior to conventional laparoscopic techniques. Our results demonstrate this is both safe and feasible

when introduced through an appropriate learning curve which involves cadaver lab training, mentoring and a gradual introduction to more complex procedures.

Take-home message:

Evolving role for robotic HPB surgery.

O143 DETOXIFICATION LOSS DRIVES ALDEHYDE METABOLIC REPROGRAMMING AND CONTRIBUTES TO GENOTOXICITY IN OESOPHAGEAL ADENOCARCINOMA

S Antonowicz (1), Z Bodai (1), T Wiggins (1), S Markar (1), P Boshier (1), H Kudo (1), F Rosini (1), R Goldin (1), H Gabra (1), RC Fitzgerald (2), Z Takats (1), GB Hanna (1)
(1) Imperial College London (2) MRC Cancer Unit, University of Cambridge

Introduction: Mutagenic aldehydes are enriched in oesophageal adenocarcinoma (OAC) patients' breath and biofluids, yet their origins and implications are unknown. This study aimed to (i) describe aldehyde metabolism in the malignant oesophagus from gene to metabolite, (ii) provide a mechanistic basis for aldehyde metabolic reprogramming, (iii) assess oncogenic sequelae of aldehyde enrichment.

Method: Mass spectrometry; candidate-based genetic driver discovery and validation; pharmacological and genetic perturbation studies in vitro.

Result: Multiple species of free aldehyde and aldehyde-DNA adducts were significantly enriched in oesophageal tissues from OAC patients, suggesting active carbonyl stress and genotoxicity, field effects, and a requirement for competent defences. Highly reactive enals and alkanals >C6 were particularly enriched. In all assessed legacy datasets, 5 to 8 isozymes of aldehyde dehydrogenase were consistently and significantly depleted in OAC tissues compared to normal mucosa ($P < 10e-8$ to -20); these findings were validated at the RNA ($n = 67$) and protein ($n = 436$) levels. In particular, low expression of ALDH3A2 was associated with progression and nodal metastasis, and independently predicted poorer survival (OR = 1.64, $P = 0.01$). ALDH3A2 mutations cause the metabolic error Sjogren-Larsson syndrome, characterised by hyperkeratosis and enriched fatty aldehydes. Mechanistically, stably expressing candidate ALDH genes in OAC cells improved aldehyde resilience and acted as a proliferative brake. Conversely, disrupting ALDH3A2 pharmacologically or with CRISPR-Cas9 editing was sufficient to enhance fatty aldehydes and proliferative phenotypes, verifying non-redundant tumour suppressor functions for this gene.

Conclusion: These data integrate aldehyde metabolic reprogramming and oesophageal genotoxicity, and support targeted aldehyde analysis for non-invasive theranostics.

Take-home message:

The oesophagus undergoes aldehyde stress; loss of coping mechanisms may be a hallmark of malignant change and maybe therapeutically exploitable.

O144 TOTAL PANCREATECTOMY AND AUTOLOGOUS ISLET CELL TRANSPLANTATION FOR CHRONIC PANCREATITIS - LONG TERM FOLLOW

JA Logue, WE Scott III, M Honkanen-Scott, J De Haviland, A Abou-Saleh, DM Manas, JAM Shaw, A Dickinson, Ashley R Dennison, RM Charnley, SA White.
Institute of Transplantation, Freeman Hospital, Newcastle

Introduction: Pancreatectomy and IAT is a controversial procedure with limited experience in the UK which is currently not funded by the NHS. We describe our experience and long-term follow-up in a new facility.

Method: We have performed 4 pancreatic resections combined with IAT for patients with chronic pancreatitis (3 hereditary, 1 idiopathic) Two had previous Frey procedures. Complications were graded according to the Clavien-Dindo classification.

Result: The islet yield was low as expected due to severe pancreatic fibrosis and previous pancreatic drainage procedures. The only complication was delayed gastric emptying in one patient. The first and last patient in our series are now completely opiate independent and the remaining 2 patients continue on reducing doses taking only 40mg morphine in 24hr. Pre-operatively this was 200mg and 320mg morphine respectively. All have a marked improvement in their quality of life. All require low dose insulin analogue therapy but continue to exhibit in vivo C-peptide secretion.

Conclusion: Pancreatectomy and IAT can be used as a salvage procedure for those patients who have failed all other therapy but in our opinion results are superior if performed much earlier in the course of their disease. Longer term follow-up demonstrates marked improvement in opiate requirements with complete cessation in two of the four patients when all other treatments have failed. Furthermore, in vivo C-peptide secretion affords protection from both the micro and macrovascular complications of diabetes mellitus.

Take-home message:

TP and IAT for chronic pancreatitis.