

# HEPATOPANCREATICOBILIARY ABSTRACTS

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## THE INFLAMMATORY PATHWAY IS HIGHLY MUTATED AND OVEREXPRESSED IN GALLBLADDER CANCER

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**Introduction:** Gall bladder cancer (GBC) is the sixth most prevalent digestive malignancy and the most common biliary-tract carcinoma. GBC is characterised with delayed diagnosis, ineffective treatment and poor prognosis. Consequently, GBC has a 5-year survival rate varying from 0-12%. Studies have shown that the incidence of GBC varies by both location and ethnicity. Information about the genetic changes occurring during GBC is limited especially in Africa.

**Objectives:** This study aims to highlight genetic mutations and differentially expressed genes in South African GBC patients.

**Methods:** Ethics clearance was obtained from the Human Ethics Research Committee of the University of Witwatersrand. A pilot cohort of 10 Tru-cut biopsy tumours and 2 normal tissues were collected from consenting patients in Chris Hani Baragwanath Hospital, Johannesburg. Total RNA was extracted, and RNA sequencing performed. Differential gene and variant analysis was conducted using the CLC-Bio Genomics workbench. Functional analysis of dysregulated genes was conducted using reactome and DAVID. Identified variants were investigated using Polyphen-2, wANNOVAR and Fuma-gwas.

**Results:** Analysis showed that the inflammation pathway (mediated by cytokines and chemokines) contained the most mutated genes. Up to 94% of these mutations were novel with majority being missense mutations. Furthermore, genes commonly mutated across patients included pro-apoptotic genes and proto-oncogenes. Interestingly, we observed that the RGP6, a transcription factor, was the most commonly mutated.

**Conclusions:** Inflammation is known to be involved in inducing and promoting tumorigenesis, thus the identification of genes mutated in this pathway might provide future potential targets.

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## ENDOSCOPIC RESECTION OF DUODENAL TUMOUR OF THE MINOR PAPILLA

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**Introduction:** Endoscopic major papillectomy using a snare is recognized as a safe, effective and well-tolerated alternative to surgical therapy. A few papers have described endoscopic minor papillectomy since tumours of duodenal minor papilla are rare. We evaluated the technical feasibility, safety, and effectiveness of endoscopic snare minor papillectomy.

**Methods:** From March 2013 to March 2019, consecutive patients who underwent endoscopic resection of a duodenal tumour of minor papilla. All patients underwent an endoscopic ultrasonography (EUS) and biopsy. The minor papillary tumour resection was done using a snare electrocautery.

**Results:** The twenty-five patients underwent endoscopic snare minor papillectomy. Of the 25 patients, 7 patients also underwent endoscopic snare major papillectomy. Endoscopically, 19 cases of the minor papillary tumour were observed as subepithelial lesions (SELs), and 6 cases were observed as mucosal lesions. In all patients, en-bloc and complete resection of duodenal minor papilla were achieved without immediate complications. Of the 19 cases that were observed like SELs, 15 cases were ectopic pancreas (78.9%, 15/19), 2 cases were neuroendocrine tumor (10.5%, 2/19) and 2 cases were Brunner's gland hyperplasia. And of the 6 cases that were observed mucosal lesions, 4 cases were tubular adenoma and 2 case was chronic inflammation. Post minor papillectomy bleeding occurred in only 1 case (4%, 1/25). Also, no other complications, such as pancreatitis, perforation, were occurred.

**Conclusion:** Our data suggest that endoscopic resection of a duodenal tumour of the minor papilla is technically feasible, safe and associated with favourable clinical outcomes. Duodenal SELs of the minor papilla on endoscopy and EUS were an almost ectopic pancreas and neuroendocrine tumour.

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## EVALUATION OF LAPAROSCOPIC CHOLECYSTECTOMIES IN A TERTIARY TEACHING HOSPITAL IN SOUTH AFRICA

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**Introduction:** Symptomatic cholelithiasis is a common surgical condition encountered in the public health sector in South Africa. Laparoscopic cholecystectomy (LC) is the procedure of choice in management. Grey's Hospital is a tertiary referral centre for all complicated gallbladder pathology in the Western KwaZulu-Natal drainage area. Grey's Hospital is also a teaching hospital for General Surgery Registrars and HPB Fellows. The objective of this study was to evaluate the laparoscopic cholecystectomies performed here.

**Methods:** This was a retrospective study of all patients who underwent LC between December 2012 and December 2016. The Department of Surgery's electronic database and patient's case files were used. Patient demographics and case details were reviewed. Surgical details and complications were also assessed.

**Results:** A total of 511 patients underwent LC. The majority of patients were female (86.9%). Thirty-nine cases were converted to open procedure (7.6%). Conversion rate was 4.95% in females and 25.4% in males. The average

time taken to perform a LC was 1 hour 21 minutes. Forty-seven (9.9%) of the patients underwent laparoscopic partial cholecystectomies, with an average duration of 2 hours 1 minute. Major complications included two iatrogenic bile duct injuries (0.39%) and one bowel injury (0.2%).

**Conclusion:** The complexity of the gallbladder pathology encountered and the prolonged waiting periods due to lack of resources, make LC in Grey's hospital challenging with protracted operative times. However, LC has still been performed safely, even despite having an emphasis on Registrar and Fellow training.

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### **PREDICTING THE NEED FOR INTERVENTION IN PATIENTS PRESENTING WITH ASYMPTOMATIC GALLSTONES: CONSTRUCTION AND VALIDATION OF A RISK STRATIFICATION TOOL**

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**Introduction:** Optimal management of asymptomatic gallstones (AG) remains controversial and factors associated with intervention have not been documented. Our aim was to perform big data analysis to identify associated factors and develop a risk stratification tool (RST) to aid in patient consultations.

**Methods:** A validated natural language algorithm was used to screen radiological reports to identify patients with AG. Each individual electronic medical record (EMR) was then screened using a second algorithm to identify patients who subsequently underwent intervention including cholecystectomy (C), endoscopic retrograde cholangiopancreatography (ERCP), or percutaneous cholecystostomy (PC). The indication for each intervention (chronic or acute cholecystitis, acute pancreatitis, cholangitis, or gallbladder cancer) was recorded. Kaplan Meier curves were constructed to analyse time to intervention, and both cumulative incidence ratios and hazard estimates were calculated. Forward stepwise cox-regression identified factors associated with future intervention and these were used to develop the RST. Area under the receiver operating characteristics (AUROC) curves were calculated and internally validated using 1000 boot-strapped resamples.

**Results:** 22,257 patients were identified between 1996-2016. Median follow-up was 4.5 years (inter-quartile range [IQR]: 1.8-7.9 years). 1762 patients (7.9%) underwent intervention [C (n = 1273); PC (n = 66); ERCP (n = 592)] within a median of 3.9 years (IQR 1.4-6.9 years) of initial presentation. The cumulative incidence of intervention increased linearly up to 25% at 15 years. Factors associated with intervention included age, gender, ethnicity, tobacco use, obesity, haemolytic anaemia, hyperlipidaemia, statin use, and ultrasonic characteristics of the gallstones. The AUROC of the RST was 0.66 (95%CI, 0.64-0.67) for the initial sample and a 1000 boot-strapped resample yielded an AUROC of 0.66 (95%CI, 0.64-0.67) indicating good internal validity.

**Conclusions:** Intervention following diagnosis of AG is common, increasing linearly from initial presentation to 25% at 15 years. An RST, if externally validated, may identify associated risk factors and provide prognostic information for patient counselling.

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### **AN ANALYSIS OF EARLY POSTOPERATIVE COMPLICATIONS FOLLOWING BILIARY RECONSTRUCTION OF MAJOR BILE DUCT INJURIES USING THE MODIFIED ACCORDION AND ATOM CLASSIFICATIONS**

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**Introduction:** Few studies have reported patient outcome after surgical repair of bile duct injury (BDI) using a standardised, validated classification system. This is the first analysis to investigate the correlation between the Anatomic, Timing Of and Mechanism (ATOM) Classification of BDI and severity of postoperative complications classified using the Modified Accordion Grading System.

**Methods:** Patients undergoing index hepaticojejunostomy repair of BDI in laparoscopic cholecystectomy at a tertiary referral centre from 1993-2018 were included. Patient demographics, geographic distance from referral centre, time to referral, ATOM classification and highest Accordion Grade complication were retrieved from a prospective database. The primary outcome was determined using correlation statistics to assess the relationship between level of injury and severity of postoperative complication.

**Results:** One hundred and twenty-eight patients were included. There was no correlation between level of injury and severity of postoperative complication (rs (128) = -0.113, p = 0.203). Seventy (54.7%) patients had an injury less than 2 cm from the hepatic duct bifurcation and 52% of patients developed a postoperative complication, most mild to moderate in severity. Geographic distance resulted in substantial delays in referral (p < 0.001) but did not affect complication rate (p = 0.523).

**Conclusion:** In this prospective analysis the short-term complication rate was higher than previous retrospective reports, but the distribution of the severity of complications and spectrum of injury type were similar. There was no correlation between severity of injury and postoperative complications. Geographic distance from referral centre resulted in substantial differences in referral delay but had no statistically significant effect on outcome.

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## MIND THE GAP! EXTRALUMINAL PERCUTANEOUS-ENDOSCOPIC RENDEZVOUS WITH A SELF-EXPANDING METAL STENT FOR RESTORING CONTINUITY IN MAJOR BILE DUCT INJURY

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**Introduction:** Treatment of major iatrogenic and non-iatrogenic bile duct injury (BDI) often requires delayed surgery with interim external biliary drainage. Percutaneous transhepatic cholangiography (PTC) with biliary catheter placement and endoscopic retrograde cholangiography (ERC) with stent placement have been suggested to bridge the defect. In some patients, transpapillary cannulation of the bile duct cannot be achieved through ERC or PTC alone.

**Methods:** Two patients with major BDIs, one iatrogenic and one non-iatrogenic underwent an extraluminal PTC/ERC rendezvous with placement of a fully covered self-expandable metal stent (SEMS) for the acute management of BDI with substantial loss of bile duct length.

**Results:** In both patients the intraperitoneal PTC/ERC rendezvous with SEMS placement was successful with no complications after 12- and 18-months follow-up, respectively.

**Conclusion:** This study is the first to report a standardized approach to the acute management of iatrogenic and non-iatrogenic major BDIs using intraperitoneal PTC/ERC rendezvous with placement of a fully covered SEMS. The described technique may serve as a “bridge to surgery” strategy and is particularly useful for patients who have previously failed ERC and/or PTC alone, and in whom immediate surgical repair is not an option. However, long-term data of the success of this technique, specifically the use of a SEMS to bridge the defect, are lacking and further investigation is required to determine its role as a definitive treatment of BDIs with substance loss.

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## COMPARISON OF CROSS-SECTIONAL IMAGING IN PATIENTS PRESENTING WITH HEPATIC HYDATID DISEASE WITH AND WITHOUT HIV CO-INFECTION

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**Background:** Observations from case studies have raised the hypothesis that co-infection of HIV and Echinococcus granulosus (EG) may lead to a more severe clinical presentation of hepatic hydatid disease (HHD). This study assessed this hypothesis by comparing pre-operative cross-sectional imaging in patients with HHD with and without HIV co-infection.

**Methods:** Patients presenting at the Surgical Gastroenterology unit, Groote Schuur Hospital, South Africa with HHD

between 2012 and 2018, for whom the HIV status was known and with cross-sectional imaging (CT and/or MRI) available for review, were included. Images for each patient were reviewed by two experienced HPB surgeons in a blinded fashion. Where assessment did not concur, consensus was reached through combined re-assessment. Cyst number, size, location and findings were classified according to the WHO and Gharbi classifications.

**Results:** The study included 16 HIV+ and 16 HIV- patients. Right liver predominance was found in all HIV+ patients, compared to 50% in the HIV- group ( $p = 0.007$ ). Extrahepatic cysts were equally prevalent. There were no significant differences between cyst number, size or multilocularity between the two groups. Radiological suspicion of cyst rupture was found in 3/16 HIV+ and 4/16 HIV- patients ( $p = 0.685$ ). No differences were found in the Gharbi classification or WHO classification types between the two groups.

**Conclusion:** This is the first comparative study on imaging between HIV+ and HIV- HHD patients. A more severe clinical presentation for HIV+ patients, as previously postulated, was not reflected in the comparison as equitable cyst characteristics and type were observed. An unexplained right liver predominance was demonstrated in HIV+ patients.

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## OUTCOMES OF INTENDED CHEMOTHERAPY TREATMENT OF PATIENTS WITH PANCREATIC ADENOCARCINOMA TREATED AT A TERTIARY HOSPITAL

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**Introduction:** In patients with pancreatic adenocarcinoma (PAC) chemotherapy is used for conversion of borderline resectable patients, for post-operative adjuvant treatment and palliative treatment. There is sparse data on the proportion of patients that would qualify for chemotherapy, but actually commence and complete chemotherapy, particularly so in developing countries. To assess this and factors influencing oncologic treatment, a cohort of patients that presented with PAC to Groote Schuur Hospital, University of Cape Town, South Africa were assessed.

**Methods:** All patients presenting to the Surgical gastroenterology service from 1 January to 31 December 2017 were analysed. Oncologic management was documented in terms of whether patients were referred to oncology, which treatment was planned, whether patients commenced the intended treatment and whether treatment was completed.

**Results:** A total of 98 patients presented with PAC of whom only 40 (40.8%) were assessed by oncology. Of 7 patients in whom neo-adjuvant chemotherapy was recommended, only 3 received treatment, with no one completing the course. In 11 patients where adjuvant chemotherapy was intended, 7 commenced treatment, of whom 6 completed the intended

number of cycles. In 20 patients that were planned for palliative chemotherapy 9 commenced treatment, none of whom could complete the intended number of cycles. Poor performance status and defaulting were the most common reasons for not receiving intended chemotherapy.

**Conclusion:** In the studied cohort of patients presenting with PAC 6% completed chemotherapy. Chronic and infective diseases has a high prevalence in the served patient population, contributing to poor performance, a major factor affecting oncologic treatment.

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### RECALCITRANT EMBEDDED BILIARY SELF-EXPANDING METAL STENTS: A NOVEL TECHNIQUE FOR ENDOSCOPID EXTRACTION

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**Introduction:** Endoscopic placement of uncovered self-expanding metal stents (uSEMS) is the palliative treatment of choice for jaundice due to a hilar malignant biliary obstruction. However, it is particularly challenging to remove inadvertently placed uSEMS for assumed malignant lesions following subsequent diagnosis of benign conditions. We present a case describing a new technique for removal of bilateral, embedded biliary uSEMS 6 weeks after placement for a presumed gallbladder carcinoma that was subsequently diagnosed as benign.

**Methods:** At endoscopic retrograde cholangiography a guidewire was passed through two fenestrations in the distal uSEMS. The end was caught with a polypectomy snare and pulled through the channel. The sheath of a lithotripter was advanced over both ends of the guidewire. The sheath was then connected to the handle and the stent was gently pulled into the sheath by rotating the handle. This technique results in a perpendicular force over a limited surface of the biliary wall, minimising trauma.

**Results:** There were no complications. The patient was discharged post-procedure day one. Subsequent biopsies of the bile ducts showed benign histology. Histology from an elective cholecystectomy showed chronic cholecystitis.

**Conclusions:** Endoscopic stent removal for inadvertently placed uSEMS is possible, safe and cost effective using this new technique.

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### ENDOSCOPIC VARICEAL LIGATION PERFORMS BETTER THAN INJECTION SCLEROTHERAPY IN DECOMPENSATED CIRRHOTIC PATIENTS WITH ACUTE VARICEAL BLEEDING: A REAL WORLD COMPARATIVE COHORT ANALYSIS

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**Introduction:** Endoscopic variceal ligation (EVL) and injection sclerotherapy (EIS) are both used to control acute

bleeding. However, no detailed data exist on the relative efficacy of each method in patients who present with actively bleeding (spurting) oesophageal varices (BOV). This study compared the efficacy, safety and outcome of EVL with EIS in controlling actively bleeding oesophageal varices.

**Methods:** A prospectively maintained single-centre database was used to identify cirrhotic patients with acute BOV observed at the index endoscopy and who were treated between 2000 and 2018. Forty patients who received EVL were compared with 40 who had EIS to control bleeding. Control of acute variceal bleeding, recurrence of varices, rebleeding, endoscopic complications, eradication and survival were recorded using Baveno VI assessment criteria.

**Results:** Demographic data, cause of cirrhosis and Child-Pugh grade of both groups were similar. Failure to control acute bleeding occurred in 2.5% (n = 1) in the EVL group and 10% (n = 4) in the EIS group. Rebleeding during the index admission in the 2 groups was similar (EVL n = 6 vs EIS n = 7). Endoscopic-related complications and bleeding from treatment-induced oesophageal ulceration and mucosal slough was less common in EVL than in EIS (2 vs 8). There was no significant difference in mortality rates (EVL n = 13, EIS n = 10) during the index admission, in subsequent deaths (EVL n = 6, range: 1 month-6 years; EIS n = 7, range: 1 month-9 years) and survival (alive EVL n = 21, range: 1-8 years; EIS n = 23, range: 3 months-12 years).

**Conclusion:** EVL was better than EIS in terms of acute variceal bleeding control, lower rates of rebleeding, less procedure-related complications and a higher rate of variceal eradication but had no influence on ultimate survival. EVL is safe and effective and the preferred method of treating acutely bleeding oesophageal varices.

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### LIMITATIONS OF ENDOSCOPIC VARICEAL LIGATION IN ACHIEVING COMPLETE ERADICATION AND PREVENTING VARICEAL RECURRENCE

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**Introduction:** Endoscopic variceal ligation (EVL) is widely used to control acute variceal bleeding and prevent recurrent bleeding. This study assessed whether repeated EVL achieves complete eradication of oesophageal varices (OV) in patients with bleeding oesophageal varices (BOV).

**Methods:** A prospectively maintained single-centre database was used to identify patients with BOV who were treated between 2000 and 2018. 140 patients (100 men, 40 women; mean age 50 years; range, 21-84 years; Child-Pugh grade A = 32; B = 58; C = 60) underwent 160 emergency and 298 elective EVL interventions during a total of 928 endoscopy sessions. Control of acute bleeding, variceal recurrence, rebleeding, eradication and survival were analysed using Baveno VI assessment criteria.

**Results:** EVL controlled acute bleeding during the index admission in 134 of 140 patients (95.7%). Six patients required balloon tamponade for control and 4 had a salvage TIPPS. Overall 5-day failure to control bleeding was 7.1% (n = 10). Index admission mortality was 14.2% (n=20). Twenty-six (21.7%) of the surviving 120 patients had 31 subsequent rebleeding episodes after discharge from hospital. OV were eradicated in 50 of 111 patients (45%) who survived >3 months (median: 2 EVL procedures, range: 1-13 over a median of 6 months, range 0.5-55) of whom 31 recurred and 3 rebled. Sixty-nine (49.3%) of the 140 patients died during follow-up (liver failure n = 46, multi-organ failure n = 14, hepatorenal failure n = 4, pneumonia n = 1, HCC n = 2, MI n = 2). Cumulative survival for the 140 patients was 71.4% at 1 year, 65% at 3 years, 60% at 5 years and 52.1% at 10 years.

**Conclusion:** Complete eradication was achieved in <50% of patients. Although varices recurred in >50% of those eradicated, few of these rebled.

#### **A RETROSPECTIVE REVIEW OF PERCUTANEOUS TRANSHEPATIC GALLBLADDER DRAINAGE FOR NON-RESPONSIVE OR OTHERWISE NON-OPERABLE ACUTE CHOLECYSTITIS IN A TERTIARY HOSPITAL**

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**Background:** Percutaneous transhepatic gallbladder drainage (PTGBD) is described in the 2018 Tokyo Guidelines as an alternative to laparoscopic cholecystectomy (LC) for sepsis control, in specific clinical settings of acute cholecystitis (AC).

In South Africa, patients often present late or with recurrent AC. LC may be possible but is limited by emergency access to operating theatres. The safety and efficacy of PTGBD has not been described in South Africa. There is no universal consensus on the optimal timing of interval cholecystectomy following PTGBD. The aim is to demonstrate the outcomes of PTGBD in patients with AC, not suitable for LC or not responding to antimicrobials.

**Materials and Methods:** A retrospective review of radiology records was performed of patients who underwent PTGBD for AC in Groote Schuur Hospital, Cape Town, over a three-year period between May 2013 and July 2016. Patients with PTGBD for malignancy or acalculous cholecystitis were excluded. Technical success (correct placement of tube in the gallbladder), clinical response, procedure-related morbidity and mortality were recorded. Interval LC parameters were investigated.

**Results:** 37 patients had PTGBD, with technical success and clinical improvement in 29 (78.38%). Malposition (3/37) was the most common complication (8.11%). Two patients required emergency surgery (5.4%), while one tube was dislodged. Mean tube placement duration was 36.83 days (Range 1- 211). 16 patients (43.24%) went on to have LC. Eight required conversion to open surgery (50%). Four had subtotal cholecystectomy (25%). Average surgical time was 135 minutes (Range 60-300). There were no procedure-related mortalities. Eight patients (21.62%) died in the 90- day period following tube insertion.

**Conclusions:** PTGBD is safe for high- risk patients with AC, with high technical success and low complication rate. Subsequent LC should be performed but is usually challenging. The requirement for PTGBD may predict disease process associated with poor outcome.