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ABSTRACTS

FREE PAPER PRESENTATIONS

FP01 Clinical Impact of Postoperative Pancreatic Fistula after Minimally Invasive and Open Pancreatoduodenectomy

Caro Bruna[1,2,3], Anouk Emmen[1,2,3], Renyi Qin[4], Robert Sutcliffe[5], Baiyong Shen[6], Guiseppe Fusai[7], Yi-Ming Shyr[8], Igor Khatkov[9], Stuart Robinson[10], Leia Jones[1,2,3], Alberto Manzoni[1], Jin-Young Jang[11], Ugo Boggi[12], Mustafa Kerem[13], Bas Groot Koerkamp[14], Clarissa Ferrari[1], Olivier Saint-Marc[15], Quintus Molenaar[16], Claudio Bnà[17], Safi Dokmak[18], Rong Liu[19], Marc Besselink[2,3], Mohammed Abu Hilal[1]

[1]Department of General Surgery, Istituto Ospedaliero Fondazione Poliambulanza, Brescia, Italy., Italy. [2]Amsterdam UMC, location University of Amsterdam, Department of Surgery, Amsterdam, the Netherlands., Netherlands. [3]Cancer Center Amsterdam, the Netherlands., Netherlands. [4]Department of Biliary-Pancreatic Surgery, Affiliated Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China, China. [5]Department of Hepatopancreatobiliary and Liver Transplant Surgery, University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom, United Kingdom. [6]Department of General Surgery, Pancreatic Disease Center, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China, China. [7]7Department of HPB Surgery and Liver Transplantation, Clinical Service of HPB Surgery and Liver Transplantation, Royal Free London NHS Foundation Trust, London, United Kingdom, United Kingdom. [8]General Surgery, Department of Surgery, Taipei Veterans General Hospital and National Yang Ming Chiao Tung University, Taipei, Taiwan, Republic of China, Taiwan. [9]Department of Surgery, Moscow Clinical Scientific Center, Moscow, Russia, Russian Federation. [10]Department of Hepatobiliary, Pancreatic and Transplant Surgery, Department of Surgery, Freeman Hospital, Newcastle upon Tyne, UK, United Kingdom. [11]Departments of Surgery and Cancer Research Institute, Seoul National University College of Medicine, Seoul, Korea, Korea, Republic of. [12]Department of Surgery, University Hospital of Pisa, Pisa, Italy., Italy. [13]Department of General Surgery, Gazi University, School of Medicine, Ankara, Turkey., Turkey. [14]Department of Surgery, Erasmus University Medical Center Cancer Institute, Rotterdam, the Netherlands., Netherlands. [15]Department of Surgery, Centre Hospitalier Regional Orleans, Orleans, France., France. [16]Department of Surgery, University Medical Center Utrecht, Utrecht, the Netherlands., Netherlands. [17]Department of Radiology, Istituto Ospedaliero Fondazione Poliambulanza, Brescia, Italy., Italy. [18]Department of HPB Surgery and Liver Transplantation, Beaujon Hospital, University Paris Cite, Clichy, France., France. [19]Faculty of Hepatopancreatobilairy Surgery, Chinese PLA General Hospital, China

Background: Postoperative pancreatic fistula (POPF) after pancreatoduodenectomy (PD) are the biggest contributor to surgical morbidity and mortality. The impact of POPF could be influenced by the surgical approach. This study aimed to assess the clinical impact of POPF in patients undergoing minimally invasive PD (MIPD) and open PD (OPD).

Methods: This retrospective study included patients after MIPD and OPD from 39 centers in 14 countries (2005-2020). In patients with POPF (defined as ISGPS B/C), propensity-score matching was performed in a 1:1 ratio. Primary outcome was the presence of a second clinically relevant (ISGPS grade B/C) complication (post-pancreatic hemorrhage (PPH), delayed gastric emptying (DGE), bile

leak or chyle leak) besides POPF. Subgroup analysis was performed for robot-assisted versus laparoscopic MIPD.

Results: Overall, 1130 patients with POPF were included (558 MIPD and 572 OPD). Hereof, 336 patients after MIPD were matched to 336 OPD. After MIPD-POPF, 55.3% of patients experienced a second complication, compared to 35.4% after OPD-POPF (p<0.001). PPH rate was higher after MIPD-POPF (20.9% vs 7.5%;p<0.001), while bile leak rate was lower (12.5% vs 19.2%;p=0.032). MIPD-POPF was associated with a longer hospital stay (median 27d vs 22d;p<0.001) and more reoperations (21.1% vs 7.3%;p<0.001). In-hospital/30-day mortality did not differ significantly between groups (6.8% vs 4.7%;p=0.483). Subgroup analyses revealed comparable second complication rates between robot-assisted and laparoscopic MIPD-POPF (54.9% vs 56.5%;p=0.952).

Conclusions: After MIPD, the presence of POPF is more frequently associated with other clinically relevant complications than after OPD, which suggests the need to reconsider its patient selection.

FP02 The impact of a terminated randomized controlled trial on nationwide utilization and outcomes of minimally invasive pancreatoduodenectomy

Nine de Graaf[1], Sheraz Markar[2], Koop Bosscha[3], Michael Gerhards[4], Bas Groot Koerkamp[5], Ignace de Hingh[6], Tom Karsten[4], Daan Lips[7], Quintus Molenaar[8], Olivier Busch[1], Sebastiaan festen[4], Marc Besselink[1], Misha Luyer[6], Jony van Hilst[1]

[1]Amsterdam UMC, Netherlands. [2]Oxford University, United Kingdom. [3]Jeroen Bosch Ziekenhuis, Netherlands. [4]OLVG Hospital, Netherlands. [5]Erasmus MC, Netherlands. [6]Catharina Hospital, Netherlands. [7]MST, Netherlands. [8]UMC Utrecht, Netherlands

Background
The implementation of minimally invasive pancreatoduodenectomy (MIPD) in the Netherlands was hampered by the premature halt of the LEOPARD-2 RCT (laparoscopic (LPD) versus open pancreatoduodenectomy (OPD)), due to safety concerns. This study investigated the impact of LEOPARD-2 on the utilization and outcomes of MIPD in the Netherlands.

Methods
Nationwide retrospective analysis including all consecutive pancreatoduodenectomies (MIPD and OPD) from the mandatory nationwide Dutch Pancreatic Cancer Audit (DPCA;2014–2022). Patients were categorized based on surgery before, during or after LEOPARD-2 (07-03-2016 to 14-11-2017). Use of approach, hospital-volume and safety-outcomes (in-hospital/30-day mortality and major morbidity [Clavien-Dindo≥3]) were assessed before and after the termination of LEOPARD-2.

Results
Overall, 6,443 pancreatoduodenectomies were performed in 18 centers, of which 1,279 (19,9%) were performed minimally invasive (354 LPD & 925 RPD) in 10 centers. Before LEOPARD-2, five centers performed LPD. After LEOPARD-2, 3/5 switched to robot-assisted pancreatoduodenectomy (RPD) and 2/5 stopped performing MIPD. Median annual LPD center volume before LEOPARD-2 was 19(range 15-23) and the median annual RPD center volume after LEOPARD-2 was 20(range 8-34). After LEOPARD-2, the use of LPD decreased from 8% to 2%(P<0.001) while RPD use increased from 0% to 22%(P<0.001). Before and after LEOPARD-2, no significant differences were observed in major morbidity (37.8%vs 41.5%,P=0.45 and mortality (3.4%vs4.2%, P=0.66) after MIPD.

Conclusions
The outcomes of the LEOPARD-2 trial resulted in a significant reduction in the use of LPD in the Netherlands, and a concomitant substantial increase in RPD use. Importantly, safety outcomes remained similar before and after LEOPARD-2.

FP03 Identifying risk factors and novel screening techniques to improve the early detection of pancreatic ductal adenocarcinoma

Mr Declan McDonnell[1,2], Dr Paul Afolabi[2], Dr Sam Wilding[2], Professor Jonathan Swann[2], Professor Christopher Byrne[2,1], Mr Zaed Hamady[1,2]

[1]University Hospital Southampton, United Kingdom. [2]University of Southampton, United Kingdom

Background
Surgical resection of pancreatic ductal adenocarcinoma (PDAC) is only available to a minority of patients with the condition. Identification of suitable candidates is reliant recognising individuals at highest risk of developing PDAC, and novel investigations that could be utilised to facilitate prompt diagnosis.

Methods
The UK Biobank was studied using Cox Proportional Hazard Models to identify variables associated with incident PDAC cases.

Additionally, participants with resectable PDAC and healthy controls were recruited to a study using a 13C mixed triglyceride breath test (13C-MTGBT) to determine if it can discriminate between PDAC and healthy volunteers. Plasma samples were also taken to develop a metabolomic profile associated with PDAC.

Results
A total of 499,804 participants from UK Biobank were studied, and 1,157 incident PDACs were identified over an 11 year period. A HbA1c ≥48mmol/mol in those without a known history of diabetes had the greatest association with incident PDAC within the first 12 months of testing glycaemic levels (aHR 8.55 (95% CI: 4.58 – 15.99, $p < 0.001$) compared to those with normoglycaemia.

There were 23 resectable PDAC cases and 24 healthy controls recruited over a 12 month period. The 13C-MTGBT was able to discriminate between PDAC and healthy volunteers (Area under receiver operator characteristic curve 0.83 (95% CI: 0.70 – 0.96). Plasma metabolite profiles associated with PDAC include increased amounts of 3-hydroxybutyrate and decreased amounts of glutamine.

Conclusions
Novel breath and blood tests may facilitate early detection of PDAC if utilised in high risk groups such as new onset diabetes.

FP04 Extracellular Vesicle MicroRNAs derived from plasma show differential expression in patients with pancreatic ductal adenocarcinoma

Daniel S.K. Liu[1], Jisce R. Puik[2,3], Bhavik Y. Patel[4,5], Professor Luca Morelli[6], Annalisa Comandatore[6], Tessa Y.S. Le Large[2,3], Laura L. Meijer[7], Rutger-Jan Swijnenburg[2,3,8], Professor Marc Besselink[3,8], Professor Long R. Jiao[1], Professor Geert Kazemier[2,3], Jonathan Krell[1], Professor Elisa Giovannetti[3,9], Adam E. Frampton[1,4,5]

[1]Department of Surgery & Cancer, Imperial College London, Hammersmith Hospital, Du Cane Road, London, United Kingdom. [2]Amsterdam UMC Location Vrije Universiteit Amsterdam, Department of Surgery, De Boelelaan 1117, Amsterdam, Netherlands. [3]Cancer Center Amsterdam, Imaging and Biomarkers, Amsterdam, Netherlands. [4]Section of Oncology, Dept. of Clinical and Experimental Medicine, Faculty of Health and Medical Sciences, The Leggett Building, University of Surrey, Guildford, Surrey, United Kingdom. [5]HPB Surgical Unit, Royal Surrey NHS Foundation Trust, Guildford, Surrey, United Kingdom. [6]Division of General Surgery, University of Pisa, Italy. [7]Department of Surgery, Erasmus University Medical Center, Rotterdam, Netherlands. [8]Amsterdam UMC, Location University of Amsterdam, Department of Surgery, Amsterdam, Netherlands. [9]Cancer Pharmacology Lab, Fondazione Pisana per la Scienza, Pisa, Italy

Background: MicroRNAs (miRNAs) are small non-coding RNAs that regulate cancer gene expression at the post-transcriptional level. They are transported in extracellular-vesicles (EV) in blood and biofluids. We aimed to identify plasma EV-miRNAs that can differentiate malignant from benign pancreaticobiliary disease.

Methods: Patients were recruited at first presentation to HPB units in London and Amsterdam. Plasma cell-free RNA was extracted using TRIzol in a cohort of 41 patients (London: 26 PDAC, 5 CCA, 10 benign). Plasma EVs were obtained using size exclusion chromatography (SEC) from 20 patients (London: 10 PDAC, 10 benign) and EV-RNA isolated. Both sources of EV-RNA were analysed by small-RNA sequencing (Illumina NextSeq 500 single-end 75bp). Candidate EV-miRNAs biomarkers were validated by RT-qPCR in London: 31 benign and 30 PDAC, and in Amsterdam: 30 benign, 32 CCA and 33 PDAC.

Results: Clinical data showed higher bilirubin levels in patients with malignancy($p<0.0001$). No difference was detected in CRP levels. Plasma EV-miR-200 family were found to be significantly up-regulated in malignant patients. In London: this generated a diagnostic AUC was 0.82 (sensitivity 70%; specificity 87.1%) for detecting PDAC. Combining this model with serum CA 19-9 levels improved the AUC to 0.96 (sensitivity 89.3%; specificity 100%). Based on this data, including expression levels of 5-miRNAs, a diagnostic model with cut-off value was generated and applied to the Amsterdam samples: AUC was 0.97 (sensitivity 87.8%; specificity 100%).

Conclusion: Plasma EV-miRNAs can differentiate malignant from benign pancreaticobiliary disease at presentation. We are evaluating these biomarkers as prognostic indicators. Further multicentre validation is warranted.

FP05 Bile Microbiome Signatures associated with Pancreatic Ductal Adenocarcinoma compared to Benign Disease: a UK pilot study.

Mr Nabeel Merali[1,2,3], Mr. Julien Terroire[4], Dr Ayse Demirkan[4], Dr Nicola Annels[1], Professor Adam Frampton[1,2,3]

[1]University of Surrey, Section of Oncology, Department of Clinical and Experimental Medicine, Faculty of Health and Medical Science, Guildford, United Kingdom. [2]Minimal Access Therapy Training Unit (MATTU), Royal Surrey County Hospital NHS Foundation Trust, Guildford, United Kingdom. [3]HPB Department, Royal Surrey County Hospital NHS Foundation Trust, Guildford, United Kingdom. [4]University of Surrey, Section of Statistical Multi-Omics, Department of Clinical and Experimental Medicine, Faculty of Health and Medical Science,, Guildford, United Kingdom

Background: The intra-tumoural microbiome can influence pancreatic tumourigenesis and chemo resistance, and therefore patient survival. The role played by bile microbiota in PDAC is unknown. We aimed to define bile microbiome signatures that can effectively distinguish malignant from benign tumours in patients presenting with obstructive jaundice.

Methods: Prospective bile samples were obtained from 31 patients who underwent either ERCP or PTC. Variable regions (V3–V4) of the 16S rRNA genes of microorganisms present in the samples were amplified by PCR and sequenced. The cohort consisted of 12 PDAC, 10 choledocholithiasis, 7 gallstone pancreatitis and 2 primary sclerosing cholangitis patients. Unfortunately, 2 benign samples were excluded.

Results: Using the 16S rRNA method, we identified a total of 135 genera from 29 individuals (12 PDAC and 17 benign). Bile microbial beta diversity significantly differed between patients with PDAC vs. benign disease (Permanova p= 0.0012). We found three genera to be of significantly lower abundance among PDAC samples vs. benign adjusting for false discovery rate (FDR). These were Escherichia (FDR= 0.002), and two unclassified genera one from Proteobacteria (FDR= 0.002) and one from Enterobacteriaceae (FDR=0.011). In the same samples, the genus Streptococcus (FDR= 0.033) was found to be of increased abundance in the PDAC group.

Conclusion: We show that patients with obstructive jaundice caused by PDAC have an altered microbiome composition in the bile, compared to those with benign disease. These bile-based microbes could be developed into potential diagnostic biomarkers for PDAC and warrant further investigation.

FP06 Impact of donor liver blood tests on liver transplant outcomes and utilisation: National cohort study

Mr Samuel Tingle[1], Mr Joseph Dobbins[1], Miss Rebecca Bramley[1], Mr Michael Goodfellow[1], Miss Emily Thompson[1], Mr Georgios Kourounis[1], Mr Stuart McPherson[2], Prof Steve White[1], Prof Colin Wilson[1]

[1]Newcastle University, United Kingdom. [2]Freeman Hospital, United Kingdom

Background: Safely increasing organ utilization is a global priority. Donor serum transaminase levels are often used to decline livers, despite minimal evidence to support such decisions. This study aimed to investigate the impact of donor "liver blood tests" on transplant outcomes.

Methods: This retrospective cohort study used the National Health Service registry on adult liver transplantation (2016-2019); adjusted regression models were used to assess the effect of donor "liver blood tests" on outcomes and utilisation.

Results: A total of 3299 adult liver transplant recipients were included (2530 following brain stem death, 769 following circulatory death). Peak alanine transaminase (ALT) ranged from 6 to 5927 U/L (median=45). On multivariable analysis, adjusting for a wide range of factors, transaminase level (ALT or aspartate aminotransferase) did not predict graft survival, primary nonfunction, 90-day graft loss, or mortality. This held true in all examined subgroups. Even livers from donors with extremely deranged ALT (>1000 U/L) displayed excellent posttransplant outcomes. During the same time-period, peak ALT was an independent predictor of organ decline (aOR=1.279, 1.218-1.342, P<0.001). Avoiding decline based on donor ALT would lead to a predicted 48% decrease in organ decline in DBD donors with ALT >40; this corresponds to 37 additional livers per year in the UK.

Conclusions: Donor transaminases do not predict posttransplant outcomes, and therefore should not be used in utilisation decision-making. Avoiding unnecessary decline of organs based on donor transaminases will increase organ utilisation. This provides a safe, simple, and immediate option to expand the donor pool.

FP07 The role of the complement system in mediating ischaemic cholangiopathy in DCD liver transplantation

Mr Balaji Mahendran[1], Miss Chloe Connelly[1], Dr Beth Gibson[1], Mr Samuel Tingle[1,2], Mr Abdullah Malik[2], Miss Lucy Bates[1], Professor Kevin Marchbank[3,1], Professor Neil Sheerin[1], Professor Colin Wilson[1,2]

[1]Blood and Transplant Research Unit, Newcastle University, United Kingdom. [2]Department of HPB & Transplant Surgery, Freeman Hospital, Newcastle, United Kingdom. [3]Translational and Clinical Research Institute, I & I theme, Newcastle University, United Kingdom

Background
The discrepancy between available organs and the number of patients on the waiting list have led to an increasing number of donor after circulatory death (DCD) liver grafts being used. DCD liver grafts suffer from a higher risk of ischaemic cholangiopathy, the pathophysiology of which is poorly understood. We hypothesized that the complement system mediates damage to the arterial endothelium, thereby affecting the ability of cholangiocytes to regenerate.

Methods
Livers declined for clinical transplantation were perfused for up to 10 hours with anti-coagulated packed red cells at 37° with or without complement inhibition. Levels of circulating complement components, tissue binding of complement proteins, and organ damage markers were measured.

Results
5 DBD and 5 DCD livers were perfused, and 5 further DCD livers being perfused with eculizumab. C3 production was significantly higher in the untreated DCD cohort compared to DBD livers at 10 hours (52.68 µg/ml vs 8.62 µg/ml, $p<0.005$). C5b-9 deposition on the arterial endothelium of the portal tracts was significantly higher in the untreated DCD cohort compared to the treated DCD livers (mean 0.9 R.U vs 0.4 R.U, $p<0.05$). There was a non-significant difference in bile production and composition between the treated DCD and untreated DCD cohort.

Conclusions
There is evidence that the complement system mediates the damage to the arterial endothelium within the portal tracts of the liver. This damage could be ameliorated by complement inhibition. Further work to correlate this findings with clinical outcomes will be required.

FP08 Targeting the host in Pancreatic Cancer: A Novel Combination Therapeutic from Bench to Bedside

Mr Keaton Jones

University of Oxford, United Kingdom

We have designed a novel therapeutic approach to improve immunity whilst reversing immune suppression in pancreatic cancer. Radiotherapy can cause the release of tumour antigens from lethally irradiated cells, as well as the generation of neopeptides resulting from novel mutations. In addition, Eganelisib, a small molecule inhibitor that blocks the pathway responsible for the phenotypic switch towards a suppressive phenotype in myeloid cells (PI3K-gamma) promotes antitumour immunity. We hypothesise that combined treatment will improve anti-tumour immunity in pancreatic cancer.

To generate primary pancreatic tumours, (KPC) cells were injected directly into the pancreas. Radiotherapy was delivered in 3 fractions of 6Gy via CT guidance. For immune phenotyping, tumours were analysed by flow cytometry, multiplex immunohistochemistry and RNA sequencing. Combination treatment has been applied to primary human tissue slices (Avatars) in dynamic perfusion culture.

In a preclinical model of pancreatic cancer, combined treatment with radiotherapy and Eganelisib resulted in significantly increased survival. Analysis of the tumour microenvironment in this group revealed decreased numbers of suppressive myeloid cells and increased numbers of cytotoxic CD8 T cells. RNA sequencing demonstrated that pathways associated with innate inflammation and adaptive antitumor immunity were significantly elevated.

We have used our preclinical data to drive the translation of this novel therapeutic combination. Preclinical data has provided robust evidence that this combination approach results in effective antitumour immunity that may render tumours sensitive to immune checkpoint therapy. We are currently designing a Phase I clinical trial combining MR-LINAC guided radiotherapy with Eganelisib for patients with locally advanced pancreatic cancer

FP09 International multidisciplinary consensus guidelines on the optimal pathology assessment and multidisciplinary pathways of non-pancreatic neoplasms in and around the ampulla of Vater (PERIPAN)

Mohammad Abu Hilal[1], Bas Uijterwijk[1,2,3], Marc Besselink[2,3], Aldo Scarpa[4], Bas Groot Koerkamp[5], Sergio Alfieri[6], Fabio Ausania[7], Adnan Alseidi[8], Ugo Boggi[9], Christos Dervenis[10], Massimo Falconi[11], Giovanni Marchegiani[12], Michele Milella[13], Roberto Salvia[14], Ajith Siriwardena[15], Guiseppe Malleo[14], Horacio Asbun[16], Volkan Adsay[17], Caroline Verbeke[18]

[1]Department of Surgery, Fondazione Poliambulanza, Brescia, Italy, Italy. [2]Amsterdam UMC, location University of Amsterdam, Department of Surgery, Amsterdam, the Netherlands, Netherlands. [3]Cancer Center Amsterdam, The Netherlands, Netherlands. [4]Department of Pathology and Diagnostics, University of Verona, Verona, Italy, Italy. [5]Department of Surgery, Erasmus Medical Centre, Erasmus University Rotterdam, Rotterdam, The Netherlands, Netherlands. [6]Digestive Surgery Unit, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy, Italy. [7]Hospital Clinic, IDIBAPS, University of Barcelona, Spain, Spain. [8]Department of Surgery, University of California, San Francisco, CA, USA, USA. [9]Department of Surgery, University of Pisa, Pisa, Italy, Italy. [10]Department of Surgery, Medical School, University of Cyprus, Nicosia, Cyprus, Greece, Greece. [11]Department of Surgery, IRCCS San Raffaele Scientific Institute, Milan, Italy, Italy. [12]Hepato Pancreato Biliary and Liver Transplant Surgery, Department of Surgery, Oncology and Gastroenterology (DiSCOG), Padua University, Italy, Italy. [13]Department of Medical Oncology, University and Hospital Trust of Verona, Verona, Italy, Italy. [14]Department of General and Pancreatic Surgery, Pancreas Institute, University of Verona Hospital Trust, Verona, Italy, Italy. [15]Department of Surgery, Manchester Royal Infirmary, Manchester, UK, United Kingdom. [16]Division of Hepatobiliary and Pancreas Surgery, Miami Cancer Institute, Miami, Florida, USA, USA. [17]Department of Pathology, Koç University Hospital and Koç University Research Center for Translational Medicine (KUTTAM), Istanbul, Turkey, Turkey. [18]Department of Pathology, University of Oslo, Oslo University Hospital, Oslo, Norway, Norway

Background: The absence of multidisciplinary workflow guidelines and clear definitions and classifications for non-pancreatic neoplasms in and around the ampulla of Vater, including distal cholangiocarcinoma, duodenal carcinoma, and the (intestinal/pancreatobiliary/mixed/hybrid) subtypes of ampullary cancer, results in inconsistencies in research and impacts patient care. These international multidisciplinary consensus guidelines aimed to standardize the multidisciplinary diagnostic workflow and to achieve consensus on uniform definitions and classifications.

Methods: The consensus questions consisted of two parts, the multidisciplinary team (MDT) guidelines and the pathology guidelines. The Scottish Intercollegiate Guidelines Network methodology, including the Delphi methodology and the AGREEII tool for were used to create evidence-based consensus guidelines. 45 experts (pathologists, oncologists, surgeons, gastroenterologists, radiologists) from 12 countries were involved.

Results: Overall, 37.061 articles were screened of which 229 were included for final literature assessment. Based on the latter and the expert teams' expertise, 39 consensus questions with 57 recommendations were created for eight multidisciplinary pathway and eight pathology topics,

through three Delphi rounds. The PERIPAN consensus guidelines were presented and externally validated in an open access conference.

Discussion: The PERIPAN MDT guidelines provide clear agreements for optimal multidisciplinary patient workflow whereas the PERIPAN pathology guidelines provide clear definitions and classification criteria for patients with non-pancreatic neoplasm in and around the ampulla of Vater. Utilizing these guidelines, standardized information transmission and specimen handling across specialists and uniform definitions and classification will improve patient outcomes and future research, ultimately leading to tailored treatment for each specific type of cancer in the periampullary region

MINI ORAL PRESENTATIONS

AB01 Detection and treatment of recurrent pancreatic ductal adenocarcinoma – a European prospective, snapshot study

Drs. Paul Andel[1], Drs. Iris van Goor[1,2], Drs. Simone Augustinus[3], Prof. dr. Frederik Berrevoet[4], Prof. dr. Marc Besselink[3], Dr. Rajesh Bhojwani[5], Prof. dr. Ugo Boggi[6], Dr. Stefan Bouwense[7], Dr. Lodewijk Brosens[8], Dr. Geert Cirkel[9], Drs. Coen van Dam[10], Dr. Angela Djanani[11], Dr. Dimitri Dorcaratto[12], Dr. Stephan Dreyer[13], Dr. Marcel den Dulk[7], Prof. dr. Casper van Eijck[10], Dr. Isabella Frigerio[14], Dr. Poya Ghorbani[15], Dr. Mara Goetz[16], Dr. Bas Groot Koerkamp[10], Dr. Camila Hidalgo Salinas[17], Prof. dr. Ignace de Hingh[18], Prof. dr. Martijn Intven[19], Dr. Rosa Jorba Martin[20], Dr. Emanuele Kauffmann[6], Dr. Reinhold Klug[21], Dr. Mike Liem[22], Dr. Maartje Los[23], Prof. dr. Misha Luyer[24], Prof. dr. Manuel Maglione[11], Dr. Elena Martin-Perez[25], Dr. Mark Meerdink[26], Prof. dr. Vincent de Meijer[26], Dr. Vincent Nieuwenhuijs[27], Dr. Andrej Nikov[28], Dr. Vitor Nunes[29], Dr. Elizabeth Pando Rau[30], Prof. dr. Konstantinos Tepetes[31], Dr. Natalie Poortmans[32], Dr. Dejan Radenkovic[33], Dr. Mihaela Raicu[34], Prof. dr. Geert Roeyen[35], Dr. Francisco Sanchez-Bueno[36], Dr. Alejandro Serrablko[37], Dr. Joost Sprakel[22], Dr. Ernesto Sparrelid[15], Dr. Rohan Thakkar[38], Dr. George Tzimas[39], Dr. Faik Uzunoglu[16], Prof. dr. Helena Verkooijen[40], Prof. dr. Ulrich Wellner[41], Prof. dr. Alessandro Zerbi[42], Dr. Vincent Groot[1], Prof. dr. Quintus Molenaar[1], Prof. dr. Lois Daamen[1,40], Prof. dr. Hjalmar van Santvoort[1]

[1]Regional Academic Cancer Center Utrecht, UMC Utrecht Cancer Center & St. Antonius Hospital Nieuwegein, Department of Surgery, Utrecht, Netherlands. [2]UMC Utrecht Cancer Center, Department of Radiation Oncology, Utrecht, Netherlands. [3]Amsterdam UMC, location University of Amsterdam, Department of Surgery, Amsterdam, Netherlands. [4]University Gent, Department of General and HPB Surgery, Gent, Belgium. [5]Santokba Institute of Digestive Surgical Sciences , Santokba Durlabhji Memorial Hospital, Department of Surgery, Jaipur, India. [6]University of Pisa, Department of Translational Research on New Technologies in Medicine and Surgery, Pisa, Italy. [7]Maastricht University Medical Center , Department of Surgery, Maastricht, Netherlands. [8]Regional Academic Cancer Center Utrecht, UMC Utrecht Cancer Center & St. Antonius Hospital Nieuwegein, the Netherlands, Department of Pathology, Utrecht, Netherlands. [9]Regional Academic Cancer Center Utrecht, UMC Utrecht Cancer Center & Meander Medical Center, Amersfoort, the Netherlands, Department of Medical Oncology, Utrecht, Netherlands. [10]Erasmus Medical Center, Department of Surgery, Rotterdam, Netherlands. [11]Medical University Innsbruck, Department of Visceral, Transplant, and Thoracic Surgery, Innsbruck, Austria. [12]Hospital Clínico, University of Valencia, Biomedical Research Institute (INCLIVA), Department of Surgery, Valencia, Spain. [13]Glasgow Royal Infirmary, Department of Surgery, Glasgow, United Kingdom. [14]Pederzoli Hospital, Pancreatic Surgical Unit, Peschiera del Garda (Verona), Italy. [15]Karolinska Institutet at Karolinska University hospital, Division of Surgery, Department of Clinical Science, Intervention and Technology, Stockholm, Sweden. [16]University Hospital Hamburg-Eppendorf, Department of General, Visceral and Thoracic Surgery, Hamburg, Germany. [17]Royal Free Hospital, Department of Surgery, London, United Kingdom. [18]Catharina Hospital, Department of Surgery, Eindhoven, Netherlands. [19]UMC Utrecht Cancer Center, Utrecht, the Netherlands, Department of Radiation Oncology, Utrecht, Netherlands. [20]Hospital Universitari de Tarragona Joan XXIII, Department of Surgery, Tarragona,

Spain. [21]Comunity Hospital Horn, Department of General-, Visceral- and Vascular Surgery, Horn, Austria. [22]Medical Spectrum Twente, Department of Surgery, Enschede, Netherlands. [23]Regional Academic Cancer Center Utrecht, UMC Utrecht Cancer Center, Department of Medical Oncology, Utrecht, Netherlands. [24]Catharina Hospital Eindhoven , Department of Surgery, Eindhoven, Netherlands. [25]University Hospital La Princesa, Department of General and Digestive Surgery, Madrid, Spain. [26]University of Groningen and University Medical Center Groningen, Department of Surgery, Groningen, Netherlands. [27]Isala, Department of Surgery, Zwolle, Netherlands. [28]Military University Hospital Prague, Department of Surgery, Prague, Czech Republic. [29]Hospital Prof Doutor Fernando Fonseca EPE, Department of Surgery, Amadora, Portugal. [30]Hospital Vall d'Hebron, Department of Hepato-pancreatobiliary and Trasplant Surgery, Barcelona, Spain. [31]University Hospital of Larissa, Department of Surgery, Larissa, Greece. [32]Universitair Ziekenhuis Gent, Department of General and HPB Surgery, Gent, Belgium. [33]University Clinical Centra of Serbia, Clinic for Digestive Surgery, Belgrade, Serbia. [34]St. Antonius Hospital Nieuwegein, Department of Pathology, Nieuwegein, Netherlands. [35]Antwerp University Hospital, Department of HPB, Endocrine and Transplantation Surgery, Edegem, Belgium. [36]Hospital Clinico Universitario "Virgen de la Arrixaca", Department of General and Digestive Surgery, Murcia, Spain. [37]Miguel servet university hospital, Department of General and Digestive Surgery, Zaragoza, Netherlands. [38]Newcastle Freeman Hospital, Department of Surgery, Newcastle upon Tyne, United Kingdom. [39]Hygeia Hospital, Department of Hepatobiliary Surgery, Marousi, Greece. [40]University Medical Center Utrecht, Utrecht, the Netherlands, Division of Imaging and Oncology, Utrecht, Netherlands. [41]UKSH Campus Lübeck, Clinic of Surgery, Lubeck, Germany. [42]IRCCS Humanitas Hospital and Humanitas University, Department of Pancreatic Surgery, Rozzano, Italy

Background: The impact of routine postoperative imaging on treatment and survival of pancreatic ductal adenocarcinoma (PDAC) recurrence remains unclear. This collaborative European-African-Hepato-Pancreato-Biliary-Association (E-AHPBA) study assessed surveillance strategies, treatment, and survival in patients with PDAC recurrence.

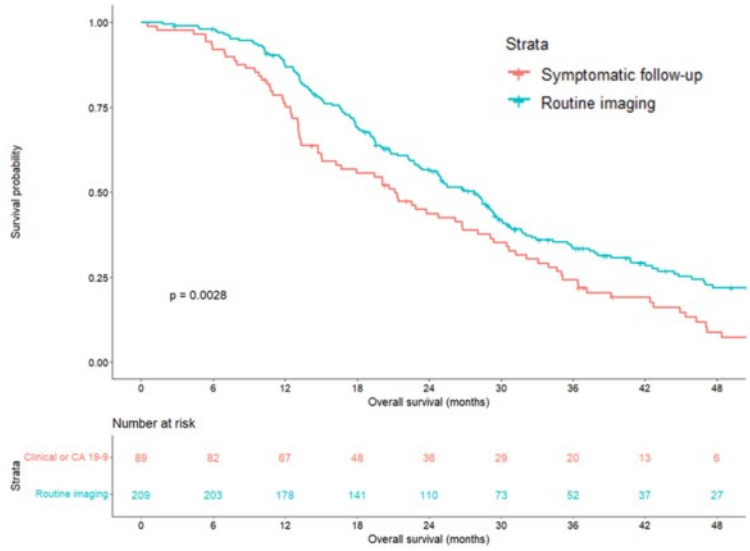
Methods: Patients who underwent primary PDAC resection and who were diagnosed with disease recurrence in 33 E-AHPBA centres from 13 countries (2020-2021) were included in this prospective, multicentre 'snapshot' study. Patients were stratified according to surveillance strategy: symptomatic follow-up (i.e. without routine imaging) or routine imaging. Overall survival (OS) (i.e. time between start treatment until death/last follow-up) was estimated with Kaplan-Meier curves and compared using the log-rank test. Predictors for OS were analyzed using multivariable Cox regression analysis and predictors for receiving recurrence treatment were evaluated using multivariable logistic regression analysis.

Results: 327 patients with PDAC recurrence were identified. Of these, 92 patients (27%) received symptomatic follow-up and 235 patients (68%) routine imaging. After a median follow-up of 36 months (IQR 25-54), OS was 21 months (95%-CI: 15-28) versus 28 months (95%-CI: 24-30) respectively (P=0.003). Routine imaging was independently associated with prolonged OS (HR: 0.71, 95%-CI: 0.52-0.95, P=0.022) and with receiving recurrence-focused treatment (OR: 2.74, 95%-CI: 1.26-5.97; P=0.011).

Conclusion: This international E-AHPBA snapshot study demonstrates that most patients receive routine imaging after PDAC resection, even though this is not recommended in European guidelines.

Patients with routine imaging more frequently undergo recurrence treatment and have a prolonged OS following initial resection.

Figure 1 - Kaplan-Meier curves comparing OS in patients who received routine imaging versus symptomatic follow-up



AB02 Variability in ASA physical status classification in patients undergoing hepato-pancreato-biliary surgery (MILESTONE-2): an international survey among surgeons and anesthesiologists

Simone Augustinus[1], Jasper P. Sijberden[1], Matthanja Bieze[1], Vandana Agarwal[2], Luca A. Aldrighetti[3], Adnan Alseidi[4], Francisco C. Bonofiglio[5], Douglas Campbell[6], Kevin C.P. Conlon[7], Katia Donadello[8], Joris Erdmann[1], Christina Ferrone[9], Michael Guertin[10], Ronald Harter[10], Maria E. Franceschetti[11], Guiseppe K. Fusai[12], Bas Groot Koerkamp[13], Thilo Hackert[14], Jin-Young Jan[15], Thomas Kander[16], Tobias Keck[17], Dominik Krzanicki[12], Ho-Jin Lee[15], Keith Lewis[18], Giuseppe Natalini[11], Carla Nau[19], Timothy M. Pawlik[10], Henry A. Pitt[20], Rafaella Reineke[21], Roberto Salvia[22], Eduardo de Santibanes[5], Shailesh V. Schrikhande[2], Martin Smith[23], Attila Szjiarto[24], Bobby Tingstedt[16], Alice C. Wei[25], John Windsor[26], Mohammed Abu Hilal[11], Manuel Pardo[4], Markus W. Hollmann[1], Marc G. Besselink[1]

[1]Amsterdam UMC, location University of Amsterdam, Netherlands. [2]Tata Memorial Hospital, India. [3]Ospedale San Raffaele, Italy. [4]University of California, USA. [5]Hospital Italiano de Buenos Aires, Argentina. [6]Auckland City Hospital, New Zealand. [7]Trinity College Dublin, Ireland. [8]University Hospital Integrated Trust of Verona, Italy. [9]Massachusetts general Hospital, USA. [10]The Ohio State University Wexner Medical Center & College of Medicine, USA. [11]Istituto Fondazione Poliambulanza, Italy. [12]Royal Free Hospital, United Kingdom. [13]University Medical Center Rotterdam, Netherlands. [14]University Hospital Hamburg-Eppendorf, Germany. [15]Seoul National University College of Medicine, Korea, Democratic People's Republic of. [16]Skåne University Hospital, Sweden. [17]UKSH Campus Lübeck, Germany. [18]Rutgers Robert Wood Johnson Medical School, USA. [19]University Medical Centre Schleswig-Holstein, Germany. [20]Rutgers Cancer Institute of New Jersey, USA. [21]IRCCS San Raffaele Scientific Institute, Italy. [22]University and Hospital Trust of Verona, Italy. [23]University of the Witwatersrand, South Africa. [24]I. sz. Sebészeti Klinika, Hungary. [25]Memorial Sloan Kettering Cancer Center, USA. [26]University of Auckland, New Zealand

Background: Patients undergoing Hepato-pancreato-biliary (HPB) surgery are preoperatively evaluated using the American Society of Anesthesiologists (ASA) classification, also used for case mix adjustment to compare outcomes among centers. This study aimed to define interrater variability of the ASA classification, and characterize the most relevant explanations for the variability, within HPB surgery.

Methods: International survey study including case-vignettes (2022-2023). Anesthesiologists and surgeons from (inter)national societies were invited to participate. The survey consisted of 23 questions and 8 case-vignettes.

Results: Overall, 1283 participants from 55 countries responded, 85% anesthesiologists and 16% surgeons. The ASA classification was commonly used, clinically (95%) and for research (96%); 79% of respondents declared that the score impacted perioperative strategy. There was considerable interrater variability (Kappa 0.26-0.42) in all case-vignettes. Interrater variability differed within and among geographic regions for each case. Over 80% of respondents stated that they would take the underlying disease (e.g., cancer) into account, but this barely changed the ASA score within the case-vignettes (1% difference). Only 11% of respondents would take the type of operation into account (e.g., complex surgery), nevertheless this did change the preferred score in the case-vignettes (13%

difference). Most common suggestions to improve the ASA score were to clarify whether type of operation should be considered, create a more extensive definition, and provide more examples.

Conclusions: Considerable variability in the ASA scoring for surgical HPB patients was observed, which reportedly will impact perioperative strategy. Additional guidance to classify patients according to ASA is urgently needed.

AB03 Feasibility of biodegradable stents to reduce pancreatic fistula rates in high-risk anastomoses

Dr. med. Laura-Ann Sahan, Dr. med. Omid Ghamar-Nejad, Dr. med. Rizky Widyaningsih, Dr. med. Dr. habil. Gregor Alexander Stavrou

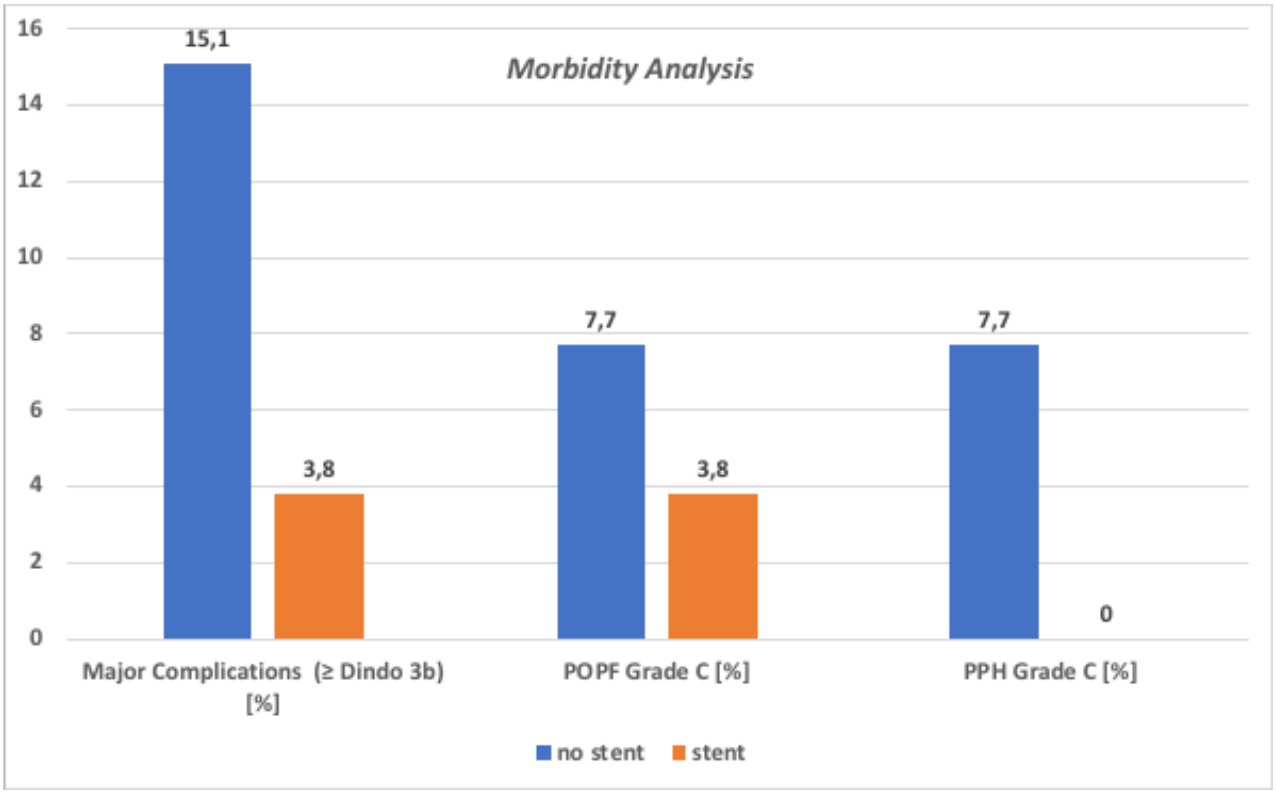
Department of General-, Visceral- and Thoracic Surgery, Klinikum Saarbrücken, Germany

Background
Postoperative pancreatic fistula (POPF) after pancreaticoduodenectomy (PD) is a serious complication. Splinting the anastomosis has been advocated for prevention. Recently, internal biodegradable stents are available as an alternative to plastic catheters.

Methods
All PDs performed at our institution were divided into two groups (stent vs. no stent). A transanastomotic Mono-J catheter was used as stent, from 2022 we used a biodegradable stent in selected high risk cases. A standardized, two-layer pancreaticojejunostomy was performed. All patients were evaluated for Charlson Comorbidity Index (CCI), technical feasibility, complications (Clavien-Dindo), pancreatic fistula (POPF), postpancreatectomy haemorrhage (PPH), stent dislocation and hospital stay.

Results
Between 01.2018 and 03.2023 65 PDs were performed. A stent was used in 26 cases with small pancreatic ducts <3mm and soft pancreas (n=10 biodegradable stent) while 39 patients were operated without. Both groups had similar baseline demographics and CCI. The 6-month follow-up showed no stent related complications. POPF (grade C) occurred in 3,8% of stented and 7,7% of non-stented patients (p=0,644). No grade C-PPH cases occured in the stented group, but 7.7% in the non-stent group (p=0,269). Major complications occurred in 3.8% of stented whilst in 15,4% of non-stented patients (p= 0,228).

Conclusion
A stent was used only in patients with high-risk pancreatic anastomosis expected to have more complications. There were no statistically significant differences in both groups, but a lower rate of POPF, PPH and major complications was found when a stent was used. Transanastomotic Stenting could be considered in all cases but especially in high-risk anastomosis.


Morbidity Analysis
16
14
12
10
8
6
4
2
0
15,1
3,8
7,7
3,8
7,7
0
Major Complications (≥ Dindo 3b) [%]
POPF Grade C [%]
PPH Grade C [%]
no stent
stent

AB04 Composite Outcome Score for Pancreatic Surgery (COMPOS-panc): A Study towards Worldwide Consensus on a Novel Holistic Outcome Score for Pancreatic Surgery

Drs Nine de Graaf[1,2,3], Prof Giovanni Marchegiani[4], Dr Clarissa Ferrari[5], Prof Andrew Cook[6], Prof Marc Besselink[2,3], Prof Mohammad Abu Hilal[1]

[1]Fondazione Poliabulanza Istituto Ospedaliero, Department of Surgery, Brescia, Italy. [2]Amsterdam UMC, location University of Amsterdam, Department of Surgery Amsterdam, Netherlands. [3]Cancer Center Amsterdam, Amsterdam, Netherlands. [4]University of Padua, Department of Surgical, Oncological and Gastroenterological Sciences (DiSCOG), Padua, Italy. [5]Fondazione Poliabulanza Istituto Ospedaliero, Department of Surgery, Research and Clinical Trials Office, Brescia, Italy. [6]University of Southampton, Public Health Medicine and Health Technology Assessment, Southampton, United Kingdom

Background: Proper outcome measurement is crucial to evaluate quality of care and surgical performance. In this study we identified the core short-term quality outcomes related to pancreatic surgery and developed a comprehensive multidimensional composite outcome score for pancreatic surgery (COMPOS-panc) for holistic outcome assessment.

Methods: This international, consensus-based study used a four-round modified-Delphi process to achieve consensus among experts, including surgeons, medical oncologists and gastroenterologists, involving two international patient organizations. In the first three rounds the individual core outcomes for pancreatic surgery were established, followed by a final round to weigh each outcome according to its respective severity. Validation was performed based on an international cohort of patients who underwent pancreatoduodenectomy.

Results: In total, 83 experts and 2 patient representatives completed the first explorative survey; 81 experts from 24 countries completed all survey rounds. After three rounds, consensus was reached on ten core outcomes for pancreatic surgery. Additional outcomes were integrated for minimally invasive surgery (1) and for malignant indications (2). The identified outcome measures were incorporated into a calculator as adverse events, with their respective severity weight, as based on survey 4. The calculator produces a continuous scale to rank the severity of different combinations of adverse events, from the worst result (death) “0”, to the highest achievable score (no adverse events) “100”.

Conclusions: COMPOS-panc reflects the overall success of a pancreatoduodenectomy procedure in a single continuous value for short-term outcome assessment. Future studies will focus on the validation for use as surgical quality indicator in registries and research.

Table 2. COMPOS-panc calculation tool including the core adverse events for outcome measurement after pancreatoduodenectomy

PANCREATODUODENECTOMY CALCULATOR				
Index	Events	Event options		
Intraoperative outcomes				
1	**Blood transfusion**	☐ Unplanned blood transfusion		
2*	**Reactive conversion**	☐ Emergency conversion to open surgery		
Postoperative outcomes (in-hospital or within 90-day postoperatively)				
3	**POPF**	☐ POPF grade B requiring only prolonged drainage >3 weeks	☐ POPF grade B requiring radiological or endoscopic intervention	☐ POPF requiring surgical intervention
4	**PPH**	☐ Bleeding requiring radiological (angiographic) or endoscopic intervention	☐ Bleeding requiring surgical intervention	
5	**DGE**	☐ DGE grade B	☐ DGE grade C	
6	**Bile leak**	☐ Bile leak grade B requiring a radiological or endoscopic intervention	☐ Bile leak grade C requiring surgical intervention	
7	**Other complications requiring intervention**	☐ Other complication requiring radiological or endoscopic intervention	☐ Other complication requiring surgical intervention	
8	**Multi-organ failure**	☐ Multi-organ failure		
9	**Mortality**	☐ Mortality		
10	**Length of hospital stay**	☐ 15-20 days	☐ ≥21 days	
11	**Readmission**	☐ Readmission requiring intervention		
Oncological outcomes				
12#	**Resection margin**	☐ R1	☐ R2	
13#	**Number of lymph nodes resected**	☐ 10-14 lymph nodes	☐ <10 lymph nodes	

POPF, postoperative pancreatic fistula; PPH, post-pancreatectomy hemorrhage; DGE, delayed gastric emptying; R1, tumor invasion <1 mm of resection margin; R2, macroscopic margin involvement
* Only scored for minimally invasive procedures
# Only scored for procedures for malignant indication

AB05 Microbiology of bile and duodenum in patients undergoing pancreatoduodenectomy: a side study of the multicenter randomized controlled SPARROW trial (perioperative versus prolonged antibiotic prophylaxis after pancreatoduodenectomy)

Drs. Daphne Droogh[1], Dr. Jannie Henderickx[2], Prof. Dr. Mark de Boer[1], Dr. Joffrey van Prehn[1], Dr. Bert Bonsing[1], Dr. Alexander Vahrmeijer[1], Dr. Sven Mieog[1]

[1]Leiden University Medical Center, Netherlands. [2]Center for Microbiome Analytics and Therapeutics, Netherlands

Background
Limited knowledge is available on the biliary and duodenal microbiome of patients with pancreatic cancer. Besides, the impact of extended use of antibiotics after pancreatoduodenectomy on the intestinal microbiome is unclear. This study will provide an in-depth exploration of the biliary and intestinal microbiome of patients undergoing pancreatoduodenectomy with contaminated bile to explore microbiome compositions of bile and duodenal fluid, and to assess the effect of extended antibiotic prophylaxis after pancreatoduodenectomy on fecal microbiome recovery.

Methods
This pilot study on ten patients participating in the SPARROW trial: a multicenter randomized controlled trial on 304 patients comparing perioperative versus prolonged antibiotic prophylaxis in patients undergoing pancreatoduodenectomy with biliarydrainage or ampullary malignancy. Microbiome analyses were performed on a perioperative biliary and duodenal sample, and three fecal samples on different time points (baseline, five-to-seven days after surgery and after three-to-four postoperative weeks). DNA was extracted from the samples for shotgun metagenomic sequencing.

Results
Microbiome analysis on the biliary, duodenal and fecal samples will be performed in January 2023. Therefore, we could present the preliminary results of this study during the ALPS meeting. Besides, the protocol of the currently recruiting SPARROW trial and its implications for guidelines on antibiotic prophylaxis will be discussed.

Conclusions
This study will explore the biliary and duodenal microbiome and fecal microbiome recovery after extended antibiotic prophylaxis following pancreatoduodenectomy. This knowledge will provide a basis to reduce postoperative morbidity and improve survival through personalized risk profiling and antibiotic treatment regimens in pancreatic cancer patients.

AB07 A volume-dependent outcome analysis of German hospitals compared to international benchmark data for primary liver tumours

Dr Jan Heil[1], Dr. Svenja Sliwinski[2], Dr. Laura-Ann Sahan[3], Dr. Dr. Gregor Stavrou[4], Prof. Wolf Otto Bechstein[5], Prof. Andreas Anton Schnitzbauer[6]

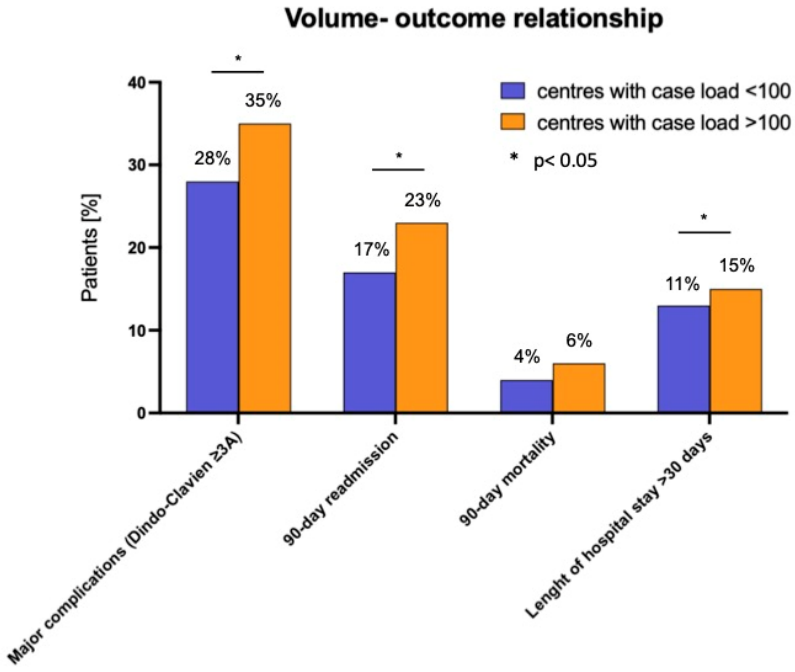
[1]JH, Germany. [2]SS, Germany. [3]LAS, Germany. [4]GS, Germany. [5]WOB, Germany. [6]AAS, Germany

Introduction: An unexpected high mortality after liver surgery was demonstrated in a recent analysis of hospital discharge data in Germany that was also shown to be caseload-depended as high-volume centres yielded a better outcome. This current study provides a volume-outcome analysis of liver resections for primary liver tumours and compares results with international benchmark data.

Method: A volume-outcome analysis was performed of all patients with hepato- or cholangiocelluar carcinoma entered into the retrospective StuDoQ liver registry of the German society for General and Visceral Surgery between 2019 and 2021. Depending on annual liver resections performed, participating centres were divided into two groups. Outcome quality was assessed by major complication (Dindo-Clavien ³3A), 90-day readmission and mortality rate, and length of hospital stay. Factors that might influence outcome quality were addressed in a multivariate analysis (MVA) using stepwise regression.

Results: A total of 4203 liver resections were entered into the registry, while 1371 (33%) of those had surgery for primary liver tumours. In centres with >100 annual liver resections (n=5), major complication and 90-day readmission rate, and length of hospital stay were significantly higher than in centres with <100 liver resections per year (n=25). There was no difference in mortality. In the MVA, outcome quality seemed not be affected by caseload of centres.

Conclusion: This study demonstrates differences in outcome quality between centres, whereas the caseload of centres per se seems not to allow to draw conclusion on outcome quality. Moreover, German (high-volume) centres provide comparable outcome quality to international benchmark data.


Volume- outcome relationship
centres with case load <100
centres with case load >100
* p< 0.05
Patients [%]
40
30
20
10
0
28%
35%
17%
23%
4%
6%
11%
15%
*
*
*
Major complications (Dindo-Clavien ≥3A)
90-day readmission
90-day mortality
Lenght of hospital stay >30 days

AB09 An international multicenter randomized controlled trial to compare combined portal and hepatic vein embolization with portal vein embolization alone in patients with primary liver cancers – The DRAGON PLC trial

Dr. Sinéad James[1,2], Jens Smits[1,2], Dr. Lisa van der Velden[1,3], Dr. Remon Korenblik[1,2], Dr. Maxime Dewulf[2], Dr. Christiaan van der Leij[1,2], Dr. Ronald M van Dam[1,2], * DRAGON Trials Collaborative[1]

[1]Maastricht University, GROW - School for Oncology and Developmental Biology, Netherlands. [2]Maastricht University Medical Center+, Department of Surgery, Netherlands. [3]Maastricht University Medical Center+, Department of Radiology and Nuclear Medicine, Netherlands

Background
Patients with primary liver cancers (PLC) are often ineligible for liver resection because an insufficient future liver remnant (FLR) poses too high a risk of post-hepatectomy liver failure. FLR hypertrophy can be induced by portal vein embolization (PVE), the current standard. Initial experiences of PVE combined with hepatic vein embolization (PVE/HVE) are promising, with an increased kinetic growth rate of the FLR and high resections rates. The aim of DRAGON PLC is to compare PVE/HVE with PVE regarding overall survival and resectability in patients with primarily unresectable PLC.

Methods
Over a two year period, 364 patients with perihilar cholangiocarcinoma (pCCC), intrahepatic cholangiocarcinoma (iCCC) or hepatocellular carcinoma (HCC) requiring preoperative FLR regeneration will be randomized to PVE/HVE or PVE (1:1, stratified by center and tumor type). Split primary endpoints are defined as FLR considered sufficient for resection 3 weeks after embolization and 5-year overall survival. Clinical and imaging data are collected 1, 3 and 6 weeks after PVE(/HVE) and during 5 years of follow-up. Data on FLR volume and function increase, quality of life and costs will be collected as secondary endpoints.

Results
The DRAGON PLC RCT has been granted funding by the Dutch Cancer Society and is due to start accrual in June 2024.

Conclusions
Within the DRAGON PLC trial, the effect of PVE/HVE on resectability and survival in PLC will be assessed. DRAGON PLC will provide evidence on this new treatment pathway, and its potential to ensure rapid, safe and cost-effective FLR hypertrophy.

AB10 Human liver response to pneumococcal infection during segmental ex-vivo perfusion: A 3Rs compliant directly translatable model for pharmacological, bacteriological and genetic research

Miss Trisha Kanani[1], Mr John Isherwood[1], Dr Wen Yuan Chung[1], Ms Shiying Tang[2], Ms Neama Alnabati[2], Professor Marco Rinaldo Oggioni[2], Professor Giuseppe Garcea[1], Professor Ashley Dennison[1]

[1]University Hospitals of Leicester NHS Trust, United Kingdom. [2]University of Leicester, United Kingdom

Background
We have previously presented the development of a human ex-vivo liver segmental perfusion model utilising surgically resected human liver segments (ALPS, 2023). The aim of this study was to compare in a human liver model the conclusions of work published in the Journal of Experimental Medicine which suggested that in a murine model high-virulence serotypes of Streptococcus pneumoniae exhibited an extraordinary ability to evade capture by Kupffer cells (An et al., 2022).

Methods
Following hemi-hepatectomy, a healthy liver segment was resected from the specimen and flushed. A segmental branch of the hepatic artery (HA) and portal vein (PV) were cannulated. Ten segments were subjected to normothermic machine perfusion for six hours with OxyglobinTM. Six segments were infected with different strains and serotypes of Streptococcus pneumoniae. Perfusate and biopsy specimen were analysed to evaluate bacterial clearance and co-localisation with Kupffer cells.

Results
Perfusate culture assays demonstrated no bacterial elimination by the liver. Furthermore, immunofluorescent staining of Kupffer cells and bacteria found no co-localisation of high and low virulence serotypes to hepatic macrophages after 30 minutes ($p=0.52$) and five hours ($p=0.14$) of infection.

Conclusion
Human liver segments did not eliminate pneumococcal strains in a serotype-specific manner or demonstrate preferential co-localisation of bacteria with macrophages based on serotype. These findings highlight issues when extrapolating findings from small animal models. Using perfused ex-vivo human liver from surgically resected specimens provides a metabolically and physiologically stable environment and is unique in providing results which can be directly translated to the clinical setting.

AB11 Liver Organ Quality Assessment (OrQA-L): A Machine Learning Model for Real-Time Visual Assessment of Steatosis During Transplant Retrieval

Mr Georgios Kourounis[1,2], Dr Ali Ahmed Elmahmudi[3], Dr Brian Thomson[3], Dr Robin Nandi[4], Mr Samuel Tingle[1,2], Prof James Hunter[5], Prof Hassan Ugail[3], Prof Colin Wilson[1,2]

[1]NIHR Blood and Transplant Research Unit, Newcastle University and Cambridge Universities, United Kingdom. [2]Institute of Transplantation, The Freeman Hospital, Newcastle upon Tyne, United Kingdom. [3]Faculty of Engineering and Informatics, Bradford University, Bradford, United Kingdom. [4]Digital Institute at Newcastle University, United Kingdom. [5]Nuffield Department of Surgical Sciences, University of Oxford, United Kingdom

Background: Macroscopic assessment of liver steatosis during transplant retrieval is currently subjective and reliant on surgeons' experience. Inter-rater variability may lead to unwarranted discard. Given the rising incidence of steatotic liver disease, developing an objective assessment tool is crucial. Our aim was to develop a machine-learning-based (ML) decision aid for objective steatosis assessment.

Methods: Two or more liver transplant surgeons scored 226 images on a 0-3 steatosis scale (None, Mild, Moderate, Severe). Post-augmentation, 404 images were split into 342 for training and 62 for testing. An additional 25 images from another collection were used for validation. The model aimed to predict these steatosis scores and was benchmarked against surgeon scores. All assessments were done via a web portal.

Results: Among the 62 testing images, Pearson's correlation coefficient between the model's predictions and surgeon scores was 0.705 ($p < 0.001$), with a mean-absolute-error (MAE) of 0.551(SD 0.350), and AUROC of 0.66. For the 25 validation images, the Pearson's correlation coefficient was 0.606($p = 0.0013$), with a MAE of 0.575(SD 0.398), and AUROC of 0.74. All images underwent processing and scoring in under 10 seconds.

Conclusions: The model demonstrates a consistent level of agreement with experienced liver transplant surgeons in the assessment of liver steatosis, highlighted by the small MAE between the model's predictions and the actual surgeon scores. Larger validation sets are needed for formal performance assessment. The quick processing time indicates its potential as a point-of-care tool. NB: If accepted, we would like to live demo OrQA-L.

AB12 Endoscopic ultrasound guided hepaticogastrostomy procedure: Lessons learnt in a tertiary academic centre.

Dr Neha Kumar, Dr Imraan Sardiwalla

Sefako Makgatho Health Sciences University, South Africa

Background
Endoscopic ultrasound-guided hepaticogastrostomy (EUS-HG) is a technically challenging procedure that is increasing in its application as a bail out procedure to obtain biliary drainage in palliative patients with advanced malignancies of the biliary tract. In our setting, we see that a vast majority of our patients with these malignancies present with advanced disease. Our unit has used EUS-HG extensively in our palliative management of these patients. Our aim was to evaluate the indications, techniques and outcomes of EUS-HG intervention in our tertiary academic centre.

Methods
A retrospective review was performed of our collected data on all EUS-HG procedures performed from January 2022 till currently. The data collected includes patient demographics, intraprocedural and postprocedural data, adverse events and re-interventions. All morbidities were defined according to American Society for Gastrointestinal Endoscopy lexicon's severity grading system. The primary outcomes of interest were technical success and post-procedural adverse events.

Results
A total of 205 interventional EUS procedures were performed in our unit since January 2022. Of these, 103 cases were EUS-HG procedures. The technical success rate was 98.2% and the clinical success rate was 93.8%. The mean procedure time range was 8.3-33 minutes. The mean duration of hospital stay was 4 days. There were no cases of post-intervention pancreatitis in our patient group.

Conclusions
EUS-HG is a useful method as an alternative biliary drainage method. This procedure has an acceptable morbidity with a high success rate. Further large studies are required to delineate its role better.

AB014 The value of adjuvant chemotherapy in patients after resection of pancreatic adenocarcinoma following preoperative FOLFIRINOX: An international multicenter study

Dr. Thomas F. Stoop[1,2,3], Toshitaka Sugawara[4,1], Atsushi Oba[5,4,6], Isabel M. Feld[2,3], Stijn Van Roessel[2,3], Eran Van Veldhuisen[2,3], Y. Andrew Wu[1,7,8], Jo Nishino[9], Mahsoem Ali[2,3], Adnan Alseidi[10], Alain Sauvanet[11], Antonio Sa Cunha[12], Arto Kokkola[13], Bas Groot Koerkamp[14], Daniel Pietrasz[12], Dyre Kleive[15], Giovanni Butturini[16], Giuseppe Malleo[17], Hanneke W.M. van Laarhoven[18,3], Isabella Frigerio[16], Jeanne Dembinski[11], Jin He[7,8], Johan Gagniere[19], Jörg Kleeff[20], José M. Ramia[21], Keith J. Roberts[22], Knut J. Labori[15], Marco V. Marino[23], Massimo Falconi[24], Michael B. Mortensen[25], Mickaël Lesurtel[12], Morgan Bonds[10], Nikolaos Chatzizacharias[22], Oliver Strobel[26,27], Olivier Turini[28], Oonagh Griffin[29], Oskar Franklin[1,30], Per Pfeiffer[31], Richard D. Schulick[1], Roberto Salvia[17], Roeland F. de Wilde[14], Safi Dokmak[11], Salvador Rodriguez Franco[1], Simone Augustinus[3,2], Stefano Crippa[24], Thilo Hackert[26,32], Timo Tarvainen[13], William R. Burns[7,8], Wells Messersmith[33], Johanna W. Wilmink[34,3], Richard A. Burkhart[7,8], Marco Del Chiaro[1], Marc G. Besselink[2,3]

[1]Division of Surgical Oncology, Department of Surgery, University of Colorado Anschutz Medical Campus, Aurora, Colorado, USA. [2]Amsterdam UMC, location University of Amsterdam, Department of Surgery, Amsterdam, Netherlands. [3]Cancer Center Amsterdam, Amsterdam, Netherlands. [4]Department of Hepatobiliary and Pancreatic Surgery, Graduate School of Medicine, Tokyo Medical and Dental University, Tokyo, Japan. [5]Department of Hepatobiliary and Pancreatic Surgery, Cancer Institute Hospital Japanese Foundation for Cancer Research, Ariake, Tokyo,, Japan. [6]Division of Surgical Oncology, Department of Surgery, University of Colorado Anschutz Medical Campus, Aurora, Colorado, Japan. [7]Division of Hepatobiliary and Pancreatic Surgery, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA. [8]The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins University, Baltimore, Maryland, USA. [9]Division of Bioinformatics, Research Institute National Cancer Center Japan, Tokyo, Japan. [10]Department of Surgery, Virginia Mason Medical Center, Seattle, Washington, USA. [11]Department of Surgery, Hôpital Beaujon Clichy, France. [12]Department of Hepato-Biliary-Pancreatic Surgery Liver Transplant Center, Université Paris-Sud Université Paris-Saclay, Villejuif, France. [13]Department of Gastroenterological Surgery, Helsinki University Hospital, Helsinki,, Finland. [14]Department of Surgery, Erasmus MC Cancer Institute, Rotterdam, Netherlands. [15]Department of Hepato-Pancreato-Biliary Surgery, Oslo University Hospital and Institute of Clinical Medicine, University of Oslo, Oslo, Norway. [16]Department of Surgery, Pederzoli Hospital, Peschiera, Italy. [17]Department of General and Pancreatic Surgery, The Pancreas Institute University of Verona, Hospital Trust, Italy. [18]Amsterdam UMC, location University of Amsterdam, Department of Medical Oncology, Amsterdam,, Netherlands. [19]Department of Digestive and Hepatobiliary Surgery-Liver Transplantation, University Hospital of Clermont-Ferrand, Clermont-Ferrand, France. [20]Department of Visceral Vascular and Endocrine Surgery, Martin Luther University, Halle-Wittenberg, Halle, Germany. [21]Department of Surgery, Hospital General Universitario de Alicante, Spain. [22]Hepato-Pancreato-Biliary Unit, Department of Surgery, University Hospitals of Birmingham, Birmingham, United Kingdom.

[23]General Surgery Department, Azienda Ospedaliera, Ospedali Riuniti Villa Sofia-Cervello, Palermo, Italy. [24]Department of Surgery, San Raffaele Hospital, IRCCS Vita-Salute University, Milano, Italy. [25]Department of Surgery, Odense Pancreas Center, Odense University Hospital, Odense, Denmark. [26]Department of General Visceral and Transplantation Surgery, Heidelberg University Hospital, Heidelberg, Germany. [27]Department of General Surgery, Division of Visceral Surgery, Medical University of Vienna, Vienna, Austria. [28]Department of Surgical Oncology, Aix-Marseille University, Institut Paoli-Calmettes, CRCM, Marseill, France. [29]National Surgical Centre for Pancreatic Cancer, St. Vincent's University Hospital, Dublin, Ireland. [30]Department of Surgical and Perioperative Sciences, Surgery, Umeå University, Umeå, Sweden. [31]Department of Medical Oncology, Odense University Hospital, Odense, Denmark. [32]Department of General, Visceral and Thoracic Surgery, University Hospital Hamburg-Eppendorf, Hamburg, Germany. [33]Division of Medical Oncology, Department of Medicine, University of Colorado School of Medicine, Aurora, Colorado, USA. [34]Amsterdam UMC, location University of Amsterdam, Department of Medical Oncology, Amsterdam, Netherlands

Introduction: Current evidence on the value of adjuvant chemotherapy in patients after resection of pancreatic adenocarcinoma following preoperative (m)FOLFIRINOX is conflicting, and studies do not take into account the duration of preoperative chemotherapy and type of adjuvant chemotherapy.

Methods: This international retrospective study included all consecutive patients after resection of pancreatic adenocarcinoma following 2-11 cycles preoperative (m)FOLFIRINOX chemotherapy followed by resection in 48 centers from 20 countries (2010-2018). Patients deceased within three months after resection were excluded. Primary outcome was OS from the three-months landmark. Cox regression analysis assessed the association between adjuvant chemotherapy and OS.

Results: Overall, 768 patients were included. Adjuvant chemotherapy was independently associated with prolonged OS (HR=0.66 [95%CI 0.49-0.87]). The interaction analysis was not significant, meaning that a different treatment effect in subgroups could not be confirmed. However, the association of adjuvant chemotherapy with OS was less in the subgroups of patients with ≥8 cycles preoperative (m)FOLFIRINOX, pancreatic head tumors, favourable radiological response, and ypN0. Both adjuvant (m)FOLFIRINOX (HR=0.57 [95%CI 0.41-0.80]) and other multi-agent regimens (HR=0.61 [95%CI 0.41-0.93]) were associated with prolonged OS as compared to no adjuvant chemotherapy whereas single-agent adjuvant chemotherapy was not associated with improved OS (HR=0.77 [95%CI 0.56-1.06]).

Conclusions: Use of adjuvant (m)FOLFIRINOX and other multi-agent chemotherapy regimens was associated with improved OS following resection of localized pancreatic adenocarcinoma after preoperative (m)FOLFIRINOX, whereas single-agent adjuvant chemotherapy was not. Future studies should assess the actual impact of adjuvant therapy in the identified subgroups.

AB15 Tissue shrinkage assessment during microwave ablation using fiducial markers: an ex-vivo liver predictor model

A.L. van der Velden[1,2], H. Rahmani[1,2], c.a.m. Verhagen[3], Dr. R. van Dam[4,2,5], Dr. M. C. Burgmans[3], Dr. R. Brecheisen[6], Dr. C. van der Leij[1]

[1]Department of Radiology, Maastricht University Medical Center+, Maastricht, Netherlands. [2]GROW-Department of Surgery, School for Oncology and Reproduction, Maastricht University, Maastricht, Netherlands. [3]Department of Radiology, Leiden University Medical Center, Leiden, Netherlands. [4]Department of Surgery, Maastricht University Medical Center, Maastricht, Netherlands. [5]Department of General, Visceral and Transplant Surgery, University Hospital RWTH Aachen, Aachen, Germany. [6]Department of Surgery, NUTRIM School of Nutrition and Translational Research in Metabolism, Maastricht University Medical Centre+, Maastricht, Netherlands

Introduction: Microwave ablation of liver tissue is associated with shrinkage of the ablated tissue. In general, the shrinkage is estimated to be around 20%, but the exact shrinkage factor is still not well studied. Besides, the shrinkage is not expected to be homogeneous across the ablation, which may result in misinterpretation of ablation margins on post-interventional imaging. The aim of this study is to investigate the direction and predictability of tissue contraction during microwave ablation with the use of fiducial markers in ex-vivo bovine liver.

Methods: Three grids consisting of 60 fiducial markers (Nanovi A/S, Lyngby, Denmark) are inserted into fresh bovine liver. The total size of each grid is 50x60 mm. Ablation needles are placed in the center of the grid. Pre-and post-ablation Computed Tomography (CT) scans are made to register and calculate displacements between pairs of corresponding markers. The following ablation duration and wattage will be used per grid: 1. HS Amica: 5 minutes and 60 Wattage, 2. Medtronic Emprint: 5 minutes at 60 Wattage, 3. Medtronic Emprint: 5 minutes and 100 Wattage.

Preliminary results will be presented, containing at least an analysis of the 2-dimensional grids (based on the original, pre-ablation marker positions) of displacement vectors (dx,dy,dz) combined with heatmap visualisations.