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Original Article

Pancreatic surgery outcomes: multicentre prospective snapshot study in 67 countries

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Abstract

Background: Pancreatic surgery remains associated with high morbidity rates. Although postoperative mortality appears to have improved with specialization, the outcomes reported in the literature reflect the activity of highly specialized centres. The aim of this study was to evaluate the outcomes following pancreatic surgery worldwide.

Methods: This was an international, prospective, multicentre, cross-sectional snapshot study of consecutive patients undergoing pancreatic operations worldwide in a 3-month interval in 2021. The primary outcome was postoperative mortality within 90 days of surgery. Multivariable logistic regression was used to explore relationships with Human Development Index (HDI) and other parameters.

Results: A total of 4223 patients from 67 countries were analysed. A complication of any severity was detected in 68.7 per cent of patients (2901 of 4223). Major complication rates (Clavien–Dindo grade at least IIIa) were 24, 18, and 27 per cent, and mortality rates were 10, 5, and 5 per cent in low-to-middle-, high-, and very high-HDI countries respectively. The 90-day postoperative mortality rate was 5.4 per cent (229 of 4223) overall, but was significantly higher in the low-to-middle-HDI group (adjusted OR 2.88, 95 per cent c.i. 1.80 to 4.48). The overall failure-to-rescue rate was 21 per cent; however, it was 41 per cent in low-to-middle- compared with 19 per cent in very high-HDI countries.

Conclusion: Excess mortality in low-to-middle-HDI countries could be attributable to failure to rescue of patients from severe complications. The authors call for a collaborative response from international and regional associations of pancreatic surgeons to address management related to death from postoperative complications to tackle the global disparities in the outcomes of pancreatic surgery (NCT04652271; ISRCTN95140761).

Introduction

Improvements in healthcare, including the delivery of surgical care, have been observed worldwide. These improvements, however, have not been uniform and disparity in the access to surgical treatment between high- and low-to-middle-income countries remains significant[1]. Global surgery, a commitment to advancing surgical care globally, has emerged as a response to address disparities in surgical care[2].

Pancreatic surgery-associated mortality has reportedly decreased to rates as low as 0–3 per cent[3–5]; however, these figures represent high-volume centres from countries with a high Human Development Index (HDI), a composite metric of life expectancy, education, and income per capita. Improvements in high-HDI countries have been attributed to better patient selection, surgical expertise, and standardization of postoperative care[6]. Several risk factors for postoperative complications have been identified, including age, ASA fitness grade, diabetes mellitus, poor nutritional status, blood loss, perioperative transfusion, and pancreatic texture at surgery[7]. Despite a reduction in perioperative mortality, the associated morbidity rate reported in current literature remains as high as 30–50 per cent[8–10], suggesting that the management of complications may be key to reducing mortality.

This international study of pancreatic surgery outcomes sought to record a snapshot of global pancreatic surgical practice, allowing analysis of current mortality, morbidity, and practice patterns.

Methods

Ethics

The chief investigator in the UK ensured that data recording was carried out in accordance with the Research Governance Framework for Health and Social Care, Second Edition, 2005, and its subsequent amendments. The principal investigator at each participating centre was responsible for their appropriate institutional research committee compliance, which was a prerequisite for data acceptance. In the UK, the National Research Ethics Service decision tool (https://www.hra-decisiontools.org.uk/research/) confirmed that this study would not be considered research by the National Health Service (NHS). This study was therefore registered at the Royal Free

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London NHS Foundation Trust audit tracker in accordance with Trust policy by the chief investigator (reference number RFH287_20/21). The study was registered prospectively with ClinicalTrials.gov (NCT04652271) and the ISRCTN registry (ISRCTN95140761).

Study design

The International Pancreatic Surgery Outcomes Study—PancreasGroup.org—was a prospective, multicentre, cross-sectional study undertaken to provide an overview of the current practice of pancreatic surgery worldwide. The study protocol was first introduced to the international community of pancreatic surgeons attending the International Hepato-Pancreato Biliary Association (IHPBA) meeting in 2020. The website was subsequently launched and advertised on social media platforms. Pancreatic surgeons practising across the world who were interested in the study could volunteer as country leaders to contribute to the recruitment of further centres in their respective country. The study design followed the Global Surgery Collaborative Snapshot Research approach[11] and results are reported according to the STROBE guidelines[12] (*Table S1*).

Study interval

The study design was initiated in January 2020 and the project was made available to the public with centre recruitment starting in September 2020. Patient recruitment took place in 2021, with 3-month prospective, consecutive patient enrolment. All patients were followed up prospectively until 90 days after surgery.

Centre recruitment

This study was announced worldwide through various sources including e-mail lists, universities, hospitals, associations, societies, social media, and personal contacts. Furthermore, country leaders worldwide were assigned the role to recruit centres in their region. The study protocol was translated into 10 different languages and made available on the study platform. Thus, all these efforts were made to avoid centre selection bias.

Participants and procedures

Recruited sites provided data on all adult consecutive patients undergoing pancreatic surgery. This comprised all indications (benign and malignant), open, laparoscopic or robotic, elective or emergency, partial or total pancreatectomies, as well as pancreatic tumour enucleations, procedures with concomitant vascular or other-organ resections, and surgical pancreatic duct drainage procedures for chronic pancreatitis. Exclusion criteria were: age less than 18 years, pancreas or islet cell transplantation, transcutaneous or transgastric imaging-guided ablation or electroporation, endoscopic procedures, as well as transgastric or surgical necrosectomies. This study aimed to recruit the maximum number of patients worldwide over the study interval. As a patient recruitment target, a 90-day mortality rate of 3 per cent was assumed. The aim was to recruit at least 3000 patients to allow meaningful analysis. To minimize patient selection bias, the participants were aware that data were to be reported anonymously, and not to be shared with any other institutions, societies, or government agencies.

Data

Patient and operation characteristics were collected. Morbidity until hospital discharge was recorded according to the Clavien–Dindo classification of surgical complications[13] and the Comprehensive Complication Index®[14] (LGID Foundation, 8008 Zurich, Switzerland) until 90 days after surgery. Major complications were defined as those with a Clavien–Dindo grade of at least IIIa, indicating any postoperative complication requiring an intervention, the patient developing organ failure, or the complication leading to death. The failure-to-rescue rate[15] was calculated by dividing the number of patients who died by the total number of patients with major postoperative complications. Data were collected via a case report form (CRF) available from the PancreasGroup.org platform[16]. This form was specially designed to include mandatory fields for case submission, including outcome data to ensure that there were no missing data important for the analysis. Cases with incomplete data were labelled as draft and were excluded from the analysis (*Table S3*) For cancer resections, data collection followed the AJCC, 8th edition, staging system[17]. Participating countries were classified into low-to-middle-, high-, and very high-HDI countries according to the United Nations Development Program 2021 report[18]. Briefly, HDI is a statistical composite index of life expectancy, education (mean years of schooling completed and expected years of schooling upon entering the education system), and per-capita income indicators, which is used to rank countries into four tiers of human development.

Complexity score

A new score of complexity of pancreatic surgery was developed based on seven clinically relevant parameters according to review of clinical data. Each parameter was associated with an increased risk of complications after pancreatic surgery in previous studies, clinical experiences, and in this data set. Receiver operating characteristic curve analysis was used to assess its predictive value, and the Youden's index was used to identify optimal cut-off points for morbidity and mortality. The score was further assessed in a separate multivariable analysis of mortality. For practical purposes, each of the following seven parameters was assigned a single point (that is equal weight) so that it can be used in daily clinical practice without the need for sophisticated calculators: BMI over 35 kg/m^2, soft pancreas, pancreatic duct smaller than 3 mm, pancreatoduodenectomy or total pancreatectomy, portomesenteric venous resection and reconstruction, arterial resection and reconstruction, and procedure extended to resection of additional organs (for example colon).

Statistical analysis

Continuous variables were compared using the Mann–Whitney *U* test or Kruskal–Wallis *H* test, as appropriate. Differences among proportions were analysed using Fisher's exact test or Pearson's χ^2 test, as appropriate. Patients with missing data on hospital stay as well as duplicate submissions were excluded from the analysis. No other patients were excluded as key CRF data were mandatory. Multivariable logistic regression was used to investigate 90-day mortality. All *P* values were two-sided and $P < 0.050$ was considered statistically significant. Statistical analysis was undertaken using R version 3.3.2 (R Core Team, R Foundation for Statistical Computing, Vienna, Austria), and R Studio version 1.0.44 (RStudio, Boston, MA, USA) with the

graphical user interface rBiostatistics.com© (rBiostatistics.com, London, UK).

Results

Participants

A total of 4223 patients were included in the analysis after excluding 123 submitted cases (2.8 per cent) with incomplete hospital stay data and 5 (0.1 per cent) sample case entries used to test the online CRF. This cohort was derived from all 7 continents, 67 countries, 255 cities, and 354 institutions; however, 641 institutions from 81 countries initially registered with PancreasGroup.org (*Figs S2–S4*). Overall demographics revealed that patients of both sexes were similarly represented; the median age was 64 (i.q.r. 55–72) years, and the median BMI was 24.7 (22.0–27.7) kg/m^2 (*Table S2*). A majority of patients (2129 of 4223, 50.4 per cent) had an ASA grade of II; the most common co-morbidities were diabetes mellitus (1146 of 4223, 27.1 per cent) and cardiac disease (789 of 4223, 18.7 per cent).

Operation characteristics

Overall, 679 patients (16.1 per cent) underwent minimally invasive surgery, including 189 (4.5 per cent) who had robotic pancreatic surgery (*Table 1*). Portomesenteric venous resection was required in 504 patients (11.9 per cent), whereas 119 (2.8 per cent) underwent arterial resection. End-to-end and tangential reconstruction modalities were most commonly used in portomesenteric resections (265 (51.6 per cent) and 217 (42.2 per cent) respectively), whereas graft reconstruction was required in 73 patients (14.2 per cent). The median intraoperative estimated blood loss was 300 (i.q.r. 150–500) ml and mean(s.d.) packed red blood cell transfusion amount was 0.5(1.5) units. The mean(s.d.) complexity of pancreatic surgery score was 1.8(1.0) (range 0–6).

The two most frequently performed operations were pancreatoduodenectomy (2501, 59.3 per cent) and distal

Table 1 Operation characteristics

	No. of patients* (*n* = 4223)
Surgical approach	
Open	3544 (83.9)
Laparoscopic	490 (11.6)
Converted to open	105 (2.5)
Robotic	189 (4.5)
Converted to open	24 (0.6)
Duration of operation (min), median (i.q.r.)	320 (240–420)
Operative procedure	
Distal pancreatectomy	1033 (24.5)
Spleen-preserving	194 (4.6)
Enucleation	62 (1.5)
Pancreatoduodenectomy	2501 (59.3)
Pylorus-preserving	808 (19.1)
Total pancreatectomy	291 (6.9)
Spleen-preserving	61 (1.5)
Other	219 (5.2)
Extended procedure to additional organs	599 (14.2)
Vessel resection and reconstruction	
Portomesenteric resection	504 (11.9)
Tangential reconstruction	217 (42.2)
End-to-end reconstruction	265 (51.6)
Autologous or cadaveric graft reconstruction	43 (8.4)
Prosthetic graft (biological or synthetic)	30 (5.8)
Arterial resection	119 (2.8)
Intraoperative findings	
Pancreatic texture	
Hard/fibrotic	1493 (41.4)
Soft/normal	2112 (58.5)
Pancreatic duct size (mm)†	
< 3	1178 (37.0)
3–8	1762 (55.3)
>8	245 (7.7)
Intraoperative blood loss	
Estimated blood loss (ml), median (i.q.r.)	300 (150–500)
Blood transfusion (units), mean(s.d.)	0.5(1.5)
Other information	
Use of surgical drain	4071 (96.5)
Intraoperative octreotide administration	1495 (35.7)

*Values are *n* (%) unless otherwise indicated. †Where applicable.

Table 2 Characteristics of patients diagnosed with pancreatic ductal adenocarcinoma

	No. of patients* (*n* = 1894)
Patient and disease characteristics	
Age (years), median (i.q.r.)	67 (59–73)
Sex ratio (F : M)	926 : 968
BMI (kg/m^2), median (i.q.r.)	24.6 (22.0–27.4)
Preoperative CA19-9 (units/l), median (i.q.r.)	78 (22–310)
Preoperative treatment	
Neoadjuvant therapy	445 (23.4)
Neoadjuvant chemotherapy	363 (19.2)
Neoadjuvant radiotherapy	79 (4.2)
Operative procedure	
Pancreatoduodenectomy	1335 (70.5)
Distal pancreatectomy	350 (18.5)
Total pancreatectomy	160 (8.5)
Other	48 (2.5)
Extended procedure (additional organs resected)	252 (13.3)
Vessel resection and reconstruction	
Portomesenteric resection	392 (20.7)
Arterial resection	75 (3.9)
Final pathological diagnosis†	
Tumour size (mm), median (i.q.r.)	30 (22–40)
Total no. of lymph nodes resected, median (i.q.r.)	20 (13–28)
Total number of positive lymph nodes resected, median (i.q.r.)	1 (0–4)
Lymphovascular invasion	1085 (63.5)
Perineural invasion	1324 (77.0)
Portal vein involvement	188 (14.1)
Disease stage (*n* = 1744)	
0	20 (1.2)
IA	186 (10.8)
IB	291 (16.8)
IIA	155 (9.0)
IIB	578 (33.5)
III	403 (23.4)
IV	109 (5.3)
Resection margins (*n* = 1771)	
R0	1300 (73.4)
R1	449 (25.4)
R2	22 (1.2)
Specific positive pancreatic resection margins (*n* = 1894)	
Anterior surface	62 (3.3)
Posterior margin	214 (11.3)
SMV margin	124 (6.6)
SMA margin	92 (4.9)
Pancreatic neck/transection margin	91 (4.8)
Proximal duodenal/gastric margin	15 (0.8)
Common bile duct margin	19 (1.0)
Distal duodenal margin	10 (0.5)
Portal vein resection margin	20 (1.0)
Other	23 (1.2)

*Values are *n* (%) unless otherwise indicated. †Data available for variable number of patients. CA19-9, carbohydrate antigen 19-9; SMV, superior mesenteric vein; SMA, superior mesenteric artery.

Table 3 Postoperative outcomes

	Overall (*n* = 4223)	Pancreatoduodenectomy (*n* = 2501)	Distal pancreatectomy (*n* = 1033)
Highest Clavien–Dindo complication grade at 90 days			
No complications	1322 (31.3)	671 (11.8)	409 (39.2)
Grade I—no treatment	744 (17.6)	450 (17.7)	202 (19.4)
Grade II—drug treatment	1067 (25.3)	706 (27.8)	229 (22.0)
Grade IIIa—intervention under LA	461 (10.9)	297 (11.7)	102 (9.8)
Grade IIIb—intervention under GA	277 (6.6)	182 (7.2)	61 (5.8)
Grade IVa—single organ failure	76 (1.8)	46 (1.8)	15 (1.4)
Grade IVb—multiorgan failure	52 (1.2)	35 (1.4)	5 (0.5)
Grade V—death	229 (5.4)	157 (6.2)	20 (1.9)
Clavien–Dindo grade at 90 days, grouped			
Complication of any severity	2901 (68.7)	1873 (73.6)	634 (60.8)
Grade ≥IIIa	1090 (25.8)	717 (28.2)	203 (19.5)
Grade ≥IIIb	629 (14.9)	420 (16.5)	101 (9.7)
Comprehensive Complication Index® score, median (i.q.r.)			
Until discharge	8.7 (0–29.6)	15.0 (0–20.9)	8.7 (0–20.9)
Until 90 days after surgery	20.9 (0–33.2)	20.9 (0–35.0)	8.7 (0–26.0)
Postoperative complications until hospital discharge			
Delayed gastric emptying	800 (18.9)	598 (23.5)	84 (8.1)
ISGPS grade (*n* = 3127)			
A	415 (10.8)	314 (13.4)	48 (5.0)
B	234 (6.1)	181 (7.7)	17 (8.6)
C	77 (2.0)	58 (2.5)	4 (6.5)
Pancreatic fistula	1053 (24.9)	658 (25.9)	326 (31.3)
ISGPS grade (*n* = 3892)			
A	539 (13.9)	313 (13.3)	167 (19.2)
B	407 (10.4)	253 (10.7)	132 (13.6)
C	105 (2.7)	90 (9.0)	10 (1.0)
Postoperative bleeding	435 (10.3)	310 (12.2)	56 (5.4)
ISGPS grade (*n* = 3434)			
A	142 (3.7)	100 (4.3)	20 (2.1)
B	126 (3.3)	95 (4.1)	19 (2.0)
C	132 (3.4)	100 (4.3)	8 (0.8)
Biliary fistula	187 (4.4)	144 (5.7)	n.a.
Gastrojejunostomy leak	68 (1.6)	43 (1.7)	n.a.
Chyle leak	212 (5.0)	147 (5.8)	33 (3.2)
Portal vein thrombosis	58 (1.4)	29 (1.1)	14 (1.3)
Pulmonary complications	473 (11.2)	307 (12.1)	91 (8.7)
Gastrointestinal complications	349 (8.2)	217 (8.5)	62 (5.9)
Cardiac complications	250 (5.9)	163 (6.4)	48 (4.6)
Urological complications	185 (4.3)	115 (4.5)	34 (3.3)
Infection	890 (21.0)	634 (24.9)	123 (11.8)
Neurological complications	123 (2.9)	70 (2.8)	21 (2.0)
COVID-19	69 (1.6)	45 (1.8)	12 (1.2)
Other	574 (13.6)	334 (13.1)	111 (10.6)
Treatment offered within 90 days of surgery			
Insulin administration	929 (25.1)	461 (20.7)	181 (19.8)
Pancreatic enzyme supplementation	2152 (57.3)	1456 (63.8)	358 (39.0)
Chemotherapy offered	1758 (50.1)	1301 (59.9)	292 (33.3)
Radiotherapy offered	106 (2.9)	70 (3.1)	18 (2.0)
Other postoperative outcomes			
Duration of IMC/HDU stay (days), median i.q.r.)	0 (0–1)	0 (0–1)	0 (0–1)
Duration of ICU stay (days), median (i.q.r.)	1 (0–2)	1 (0–2)	0 (0–1)
Duration of hospital stay (days), median (i.q.r.)	11 (7–17)	12 (8–19)	8 (6–13)
Hospital readmission rate until 90 days	723 (19.7)	440 (19.7)	184 (20.2)
Failure-to-rescue rate	229 of 1090 (21.0)	157 of 717 (21.9)	20 of 203 (10.0)
Cost (US $), mean(s.d.)	22 317 (15 146)	23 465 (16 661)	19 770 (11 419)

Values are *n* (%) unless otherwise indicated. LA, local anaesthesia; GA, general anaesthesia; ISGPS, International Study Group on Pancreatic Surgery; n.a., not applicable; IMC/HDU, intermediate medical care/high-dependency unit; ICU, intensive care unit.

pancreatectomy (1033, 24.5 per cent) (*Table S3*). Of all distal pancreatectomies, only 381 (36.5 per cent) were carried out minimally invasively, and 194 patients (18.8 per cent) underwent a spleen-preserving distal pancreatectomy. Interestingly, a total of 56 different combinations of pancreatic stump closure was identified in patients undergoing distal pancreatectomy. The most frequently used pancreatic stump closure techniques were handsewn (268, 25.8 per cent), stapler (542, 52.2 per cent), and reinforced staple line (175, 16.9 per cent).

Pancreatic ductal adenocarcinoma

Based on histopathology results, an operation was performed for cancer in 3299 patients (78.1 per cent), of whom 1894 (45.1 per cent) were found to have pancreatic ductal adenocarcinoma (*Table 2*). Neoadjuvant therapy was administered to 445 patients with pancreatic ductal adenocarcinoma (23.4 per cent). Portomesenteric venous resection was required in 392 patients (20.7 per cent) to facilitate resection. Although 449 patients (25.4 per cent) who underwent pancreatoduodenectomy had an

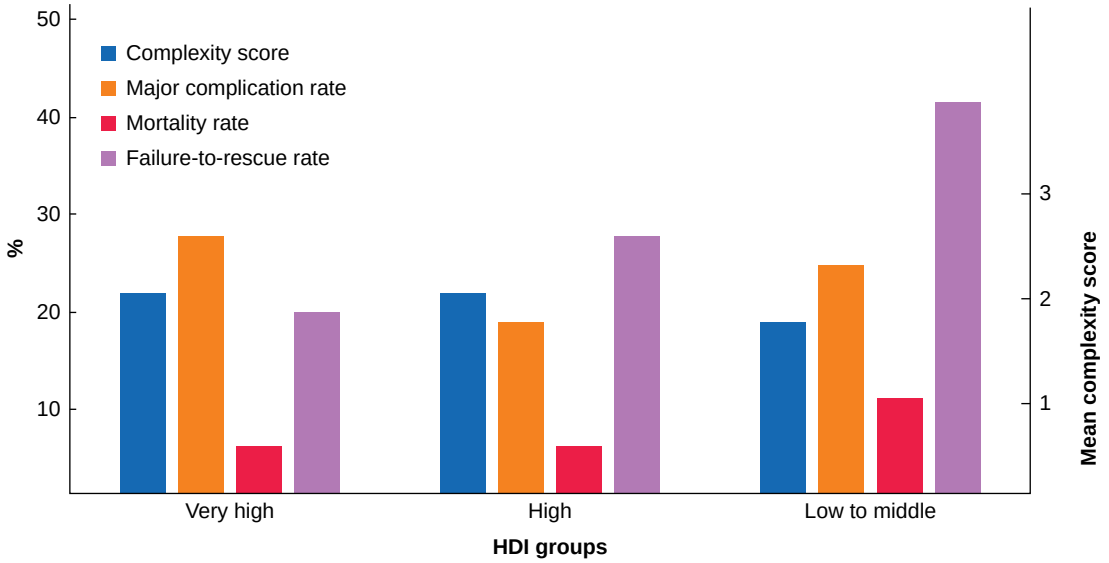


Fig. 1 Complexity of pancreatic surgery score, and major complication, mortality, and failure-to-rescue rates among the low-to-middle-, high-, and very high-Human Development Index groups

The complexity score bar scale is 10-fold for better interpretation. HDI, Human Development Index.

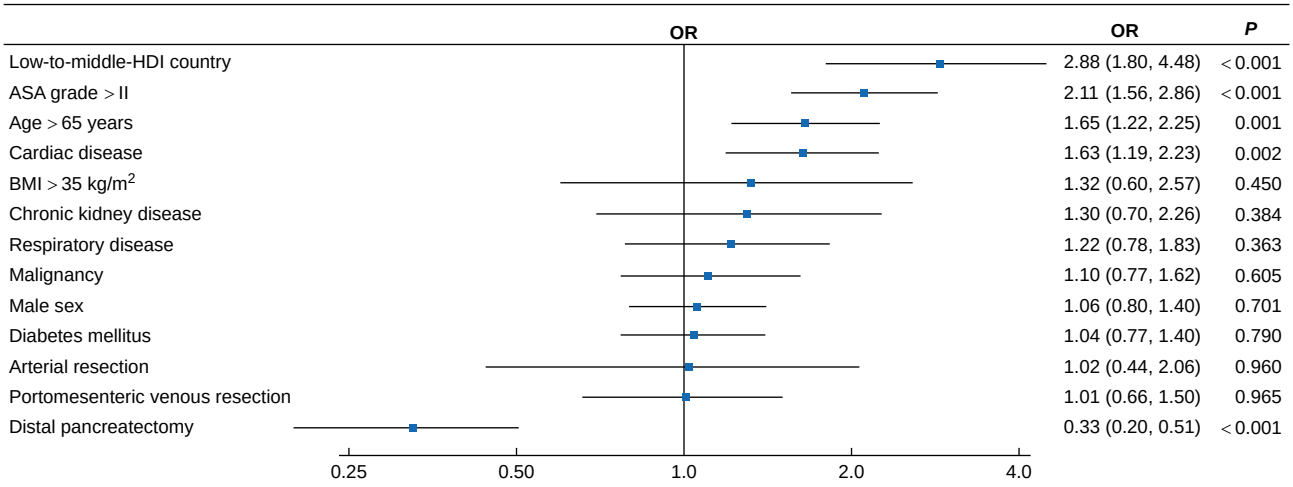


Fig. 2 Multivariable binary logistic regression analysis for 90-day mortality

ORs are shown with 95% confidence intervals. HDI, Human Development Index.

incomplete (R1) resection on histopathology, of those undergoing portomesenteric vein resection, only 20 of 392 (5 per cent) had a positive portal vein resection margin. The most frequent positive specific resection margins on histopathology were the posterior (214 of 1894), superior mesenteric vein (124 of 1894), and superior mesenteric (92 of 1894) margins.

Postoperative outcomes

Postoperative outcomes were recorded until hospital discharge and 90 days after operation (*Table 3*). Of all 4223 patients, 2901 (68.7 per cent) experienced a complication of any severity, 1873 (73.6 per cent) after pancreatoduodenectomy and 634 (60.8 per cent) after distal pancreatectomy. Major complication rates (Clavien–Dindo grade at least grade IIIa) were higher after pancreatoduodenectomy than distal pancreatectomy: 717 of 2554 (28 per cent) *versus* 203 of 1043 (20 per cent) ($P < 0.001$). The most frequent complications were pancreatic fistula (1053 of 4223, 24.9 per cent), infection (890 of 4223, 21.0 per cent), and delayed gastric emptying (800 of 4223, 18.9 per cent). The rate of major complications (Clavien–Dindo grade at least IIIa) was 25.8 per cent (1090 of 4223). The 90-day postoperative mortality rate was 5.4 per cent (229 of 4223) overall, 6.2 per cent (157 of 2554) after pancreatoduodenectomy and 1.9 per cent (20 of 1043) after distal pancreatectomy. The failure-to-rescue rate was 21.0 per cent (229 of 1090) overall. Specifically, however, it was 21.9 per cent (157 of 717) after pancreatoduodenectomy and 10.0 per cent (20 of 203) after distal pancreatectomy (*Table 3*).

Morbidity and mortality within Human Development Index groups

The HDI reflects the life expectancy, education levels, and income of different countries. Patient, disease, operation characteristics, and postoperative outcomes of patients among the three HDI groups are summarized in *Table S4*. Although the complexity of

pancreatic surgery was similar across HDI groups, postoperative morbidity, 90-day mortality, and failure-to-rescue rates differed (*Fig. 1*). Major complication rates (Clavien–Dindo grade at least IIIa) were 24.4 per cent (69 of 285) in low-to-middle-, 18.0 per cent (89 of 494) in high-, and 27.1 per cent (932 of 3444) in very high-HDI countries. Mortality rates were 9.8 per cent (28 of 285), 4.9 per cent (24 of 494), and 5.1 per cent (177 of 3444) respectively. The overall 90-day postoperative mortality rate was 5.4 per cent (229 of 4223), but was significantly higher in the low-to-middle-HDI group (adjusted OR 2.88, 95 per cent c.i. 1.80 to 4.48) (*Fig. 2*). The failure-to-rescue rate in the low-to-middle category was 41 per cent, twice that of the very high-HDI group (19 per cent) ($P < 0.001$).

Discussion

In this international, prospective 3-month snapshot study of 4223 patients, pancreatic surgery has been shown to be an established treatment modality worldwide. The PancreasGroup.org collaborative is a unique collaboration of pancreatic surgeons across countries of all HDI groups who have contributed to this seminal study investigating the global practice and outcomes of pancreatic surgery.

Reflecting its complexity, the minimally invasive approach remains rare for pancreatoduodenectomy worldwide. Similarly, distal pancreatectomy remains predominantly an open operation, despite wider support in the literature for minimally invasive approaches[19]. However, in this study, nearly one-tenth of distal pancreatectomies were undertaken using the robotic approach, which may well affect the prevalence of minimally invasive surgery in the field of pancreatic surgery in the future. Other examples of practice heterogeneity identified in this global cohort included stump closure technique in distal pancreatectomy and administration of enzyme supplementation. Interestingly, over 50 different stump closure combinations were noted. Over one-third of patients in this cohort did not receive pancreatic enzyme supplementation after surgery, even though the International Study Group on Pancreatic Surgery[20] has advised universal enzyme replacement therapy after pancreatic surgery.

Evidently, the predominant indication for pancreatic surgery is cancer. Of note, over one-fifth of patients with pancreatic ductal adenocarcinoma received neoadjuvant chemotherapy. This reflects the possibility of improving outcomes with neoadjuvant therapy and the ongoing expansion of the concept of resectability in pancreatic surgery[21–23]. With regard to adjuvant systemic therapy, only half of patients received adjuvant chemotherapy during the 3-month follow-up after surgery, with considerable discrepancy between very high-HDI and low-to-middle-HDI countries, a difference of 28 per cent. Adjuvant chemotherapy has shown to improve overall survival in patients with pancreatic cancer[24–26] and this difference, therefore, raises concerns regarding the treatment options available to patients in low-to-middle-HDI countries.

Pancreatoduodenectomy is the most commonly performed pancreatic operation, but it is far from being a standardized procedure. From initial descriptions tracing back to the late 1800s[27], followed by developments in the mid-1900s by Allen Oldfather Whipple[28], data in favour of different technique modifications continue to emerge. A lack of uniformity in surgical technique and postoperative management was expected as there is little high-quality evidence supporting the use of one technique or management strategy over another[29]. In the present cohort, there was a wide range of surgical and management strategies, reflecting the continued development of this complex operation as well as the lack of high-quality trials comparing techniques. Of note, although once rarely performed, vascular resections have become an integral part of pancreatic surgery[30]. More than 1 in 10 patients undergoing pancreatoduodenectomy also underwent portomesenteric venous resection. Arterial resections were performed in almost 3 per cent of operations; the disease would have been deemed unresectable in all these patients only a decade ago[31,32].

For meaningful comparison of outcomes, a novel complexity scoring system was developed that considers patient characteristics, pancreatic gland characteristics, and extent of resection, including vascular resection or resection extended to include additional organs. Globally, the major complication and surgical complexity rates after pancreatic surgery were comparable across centres in this study. This may reflect the fact that pancreatic surgery has become a specialist area of surgery globally as opposed to a branch of general surgery with possibly similar levels of surgical skills and training worldwide. Although the major complication and surgical complexity rates were similar, the postoperative 90-day mortality rate was higher in low-to-middle-HDI countries than in high- and very high-HDI countries. Optimizing perioperative management will potentially improve postoperative outcomes. This should be made a global priority in the field to decrease postoperative mortality, particularly in low-to-middle-HDI countries.

Postoperative death following a treatable complication has emerged as a focus for tackling inequalities in general surgical care in the past decade through the depiction of global surgery as a global health field[2]. Failure to rescue is defined by death after a treatable complication, and can be used as a measure of preventable deaths[33]. Here, death after pancreatic surgery in low-to-middle-HDI countries was found to be associated with higher failure-to-rescue rates. Although approximately two-thirds of patients experienced a complication of any severity, these were mostly low grade requiring no intervention or drug treatment only, among which pancreatic fistula, infection, and delayed gastric emptying were the most frequent. Although these are well recognized complications of pancreatic surgery, they can vary greatly in severity. Modifiable factors involved in the early recognition and management of complications after pancreatic surgery may affect failure-to-rescue rates. These factors involve the wider surgical ecosystem, including infrastructure together with hospital and governance workforce, which also played a role in the reduction of mortality observed after specialization[34]. Identifying the specific modifiable drivers of postoperative failure to rescue in pancreatic surgery and their management related to mortality ought to be the next priority in the field. In response to this, the IHPBA together with the PancreasGroup.org investigators have committed to collaborate further to face the global inequalities in pancreatic surgery.

The main strengths of this study are its wide geographical capture and richness of technique-specific and outcome data. Over 350 centres performing pancreatic surgery from low- to very high-HDI countries across all continents took part. This not only makes it the largest prospective global study looking at outcomes of pancreatic surgery, but also provides a focus on data from practice that is under-reported in the literature. The information provided in this study may contribute to identifying the reasons underlying complications, which could in turn lead to improved site-specific perioperative management guidelines. Details have been reported from preoperative management, including neoadjuvant chemotherapy, to postoperative care

through to 90-day outcomes in this study. This wealth of data points to specific areas in the care of patients undergoing pancreatic surgery that need further research and/or dissemination of information. Another important strength is the prospective design of this study. A snapshot representative of current global practice has been captured. Although a recruitment time frame of 3 months may appear brief and at risk of selection bias owing to seasonal variations, this study design was chosen to provide favourable conditions for the participation of centres in low-HDI countries. In requiring participating centres to include all consecutive pancreatic procedures during the chosen time frame, the authors also hoped to mitigate selective reporting.

Inherent limitations of this study relate to its global collaborative nature, and include the surveillance of prospective data reporting, adherence to the study protocol, and interpretation of data required for each patient. Participating centres were asked to follow the instructions laid out by PancreasGroup.org that included local data validation, but no independent monitoring was possible because of the scale of the study. This is, however, a recognized and accepted limitation of global surgery studies[35,36]. Online platforms were created to provide local investigators with adequate support to carry out the study. The PancreasGroup.org platform and electronic CRF included score calculators, unit convertors, and definitions to ensure uniformity of data capture. Although global recruitment, from all HDI countries, was encouraged, participation from very high-HDI countries was greatest. This may reflect a higher prevalence of pancreatic surgery practice in very high-HDI countries. Participation of certain institutions that initially registered their interest with PancreasGroup.org may also have been affected by the COVID-19 pandemic, or this may represent a true selection bias. Similarly, owing to the relatively smaller number of centres and patients submitted from low- and medium-HDI countries, such patients were grouped into one instead of two groups for the purpose of statistical analysis.

A potential limitation of this study pertains to the introduction and use of the complexity of pancreatic surgery score. Even though this score was formulated based on consistent clinical observations and analyses, it is currently in its inaugural phase of presentation in the literature. The parameters selected might still represent a subset of potential factors influencing outcomes. Although this data set encompasses wide geographical and institutional diversity, the authors recognize the need for external validation beyond the present study cohort. Plans are under way to carry out further validation of this score in non-participating institutions to better comprehend its robustness and generalizability.

Lastly, a perceived limitation of this study lies in the inherent variation in expertise across the centres that contributed data globally. Given the diverse range of institutions involved, from highly specialized centres with vast experience in pancreatic surgery to potentially less experienced regional hospitals, this study has demonstrated significant differences in surgical techniques, perioperative care, and postoperative management. These variations influenced the overall morbidity and mortality rates reported. Although this study has provided a comprehensive global perspective on outcomes after pancreatic surgery, it is essential to recognize that the benchmarks established by highly specialized centres might not be directly comparable to the broad range of outcomes observed in this study. However, the authors consider this a strength of this study as it captured the true morbidity and mortality of pancreatic surgery globally.

In conclusion, this is the first global study on pancreas surgery. Failure to rescue stands out as a key factor impacting the high postoperative mortality rates in low to middle HDI countries after pancreas surgery. Focusing on the heterogeneity in surgical approach, techniques, and postoperative management that we present, is a starting point to identify the key modifiable factors that drive failure to rescue. Further research is needed to characterize these modifiable risk factors. International Hepato-Pancreato-Biliary Association (IHPBA) and PancreasGroup.org collaboration task force will work together with the aim to tackle failure to rescue after pancreatic surgery worldwide.

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Disclosure

The authors declare no conflict of interest.

Supplementary material

Supplementary material is available at *BJS* online.

Data availability

Availability of data for secondary analysis is subject to approval by the Scientific and Management Committees. All requests will be evaluated based on the quality and validity of the proposed project, with decisions reached by majority consensus.

References

1. Meara JG, Leather AJ, Hagander L, Alkire BC, Alonso N, Ameh EA *et al.* Global surgery 2030: evidence and solutions for achieving health, welfare, and economic development. *Surgery* 2015;**158**:3–6

2. Dare AJ, Grimes CE, Gillies R, Greenberg SL, Hagander L, Meara JG *et al.* Global surgery: defining an emerging global health field. *Lancet* 2014;**384**:2245–2247
3. Ho CK, Kleeff J, Friess H, Buchler MW. Complications of pancreatic surgery. *HPB (Oxford)* 2005;**7**:99–108
4. Crist DW, Sitzmann JV, Cameron JL. Improved hospital morbidity, mortality, and survival after the Whipple procedure. *Ann Surg* 1987;**206**:358–365
5. Oguro S, Yoshimoto J, Imamura H, Ishizaki Y, Kawasaki S. Three hundred and sixty-eight consecutive pancreatico-duodenectomies with zero mortality. *J Hepatobiliary Pancreat Sci* 2017;**24**:226–234
6. Sanchez-Velazquez P, Muller X, Malleo G, Park JS, Hwang HK, Napoli N *et al.* Benchmarks in pancreatic surgery: a novel tool for unbiased outcome comparisons. *Ann Surg* 2019;**270**:211–218
7. La Torre M, Ramacciato G, Nigri G, Balducci G, Cavallini M, Rossi M *et al.* Post-operative morbidity and mortality in pancreatic surgery. The role of surgical Apgar score. *Pancreatology* 2013;**13**:175–179
8. Halloran CM, Ghaneh P, Bosonnet L, Hartley MN, Sutton R, Neoptolemos JP. Complications of pancreatic cancer resection. *Dig Surg* 2002;**19**:138–146
9. de Wilde RF, Besselink MG, van der Tweel I, de Hingh IH, van Eijck CH, Dejong CH *et al.* Impact of nationwide centralization of pancreaticoduodenectomy on hospital mortality. *Br J Surg* 2012;**99**:404–410
10. Hata T, Motoi F, Ishida M, Naitoh T, Katayose Y, Egawa S *et al.* Effect of hospital volume on surgical outcomes after pancreaticoduodenectomy: a systematic review and meta-analysis. *Ann Surg* 2016;**263**:664–672
11. Bhangu A, Kolias AG, Pinkney T, Hall NJ, Fitzgerald JE. Surgical research collaboratives in the UK. *Lancet* 2013;**382**:1091–1092
12. von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP *et al.* The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet* 2007;**370**:1453–1457
13. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 2004;**240**:205–213
14. Slankamenac K, Graf R, Barkun J, Puhan MA, Clavien PA. The comprehensive complication index: a novel continuous scale to measure surgical morbidity. *Ann Surg* 2013;**258**:1–7
15. Ghaferi AA, Birkmeyer JD, Dimick JB. Variation in hospital mortality associated with inpatient surgery. *N Engl J Med* 2009;**361**:1368–1375
16. PancreasGroup.org. *Case Report Forms 2021*. https://pancreasgroup.org/CRF (accessed 17 December 2021)
17. Chun YS, Pawlik TM, Vauthey JN. 8th Edition of the AJCC Cancer Staging Manual: pancreas and hepatobiliary cancers. *Ann Surg Oncol* 2018;**25**:845–847
18. United Nations Development Programme. *Human Development Reports 2020*. https://hdr.undp.org/data-center/human-development-index#/indicies/HDI (accessed 17 December 2022)
19. de Rooij T, van Hilst J, van Santvoort H, Boerma D, van den Boezem P, Daams F *et al.* Minimally invasive *versus* open distal pancreatectomy (LEOPARD): a multicenter patient-blinded randomized controlled trial. *Ann Surg* 2019;**269**:2–9
20. Gianotti L, Besselink MG, Sandini M, Hackert T, Conlon K, Gerritsen A *et al.* Nutritional support and therapy in pancreatic surgery: a position paper of the International Study Group on Pancreatic Surgery (ISGPS). *Surgery* 2018;**164**:1035–1048
21. Murphy JE, Wo JY, Ryan DP, Jiang W, Yeap BY, Drapek LC *et al.* Total neoadjuvant therapy with FOLFIRINOX followed by individualized chemoradiotherapy for borderline resectable pancreatic adenocarcinoma: a phase 2 clinical trial. *JAMA Oncol* 2018;**4**:963–969
22. Versteijne E, Vogel JA, Besselink MG, Busch ORC, Wilmink JW, Daams JG *et al.* Meta-analysis comparing upfront surgery with neoadjuvant treatment in patients with resectable or borderline resectable pancreatic cancer. *Br J Surg* 2018;**105**:946–958
23. Machairas N, Raptis DA, Velazquez PS, Sauvanet A, Rueda de Leon A, Oba A *et al.* The impact of neoadjuvant treatment on survival in patients undergoing pancreatoduodenectomy with concomitant portomesenteric venous resection: an international multicenter analysis. *Ann Surg* 2021;**274**:721–728
24. van Roessel S, van Veldhuisen E, Klompmaker S, Janssen QP, Abu Hilal M, Alseidi A *et al.* Evaluation of adjuvant chemotherapy in patients with resected pancreatic cancer after neoadjuvant FOLFIRINOX treatment. *JAMA Oncol* 2020;**6**:1733–1740
25. Conroy T, Hammel P, Hebbar M, Ben Abdelghani M, Wei AC, Raoul JL *et al.* FOLFIRINOX or gemcitabine as adjuvant therapy for pancreatic cancer. *N Engl J Med* 2018;**379**:2395–2406
26. Neoptolemos JP, Palmer DH, Ghaneh P, Psarelli EE, Valle JW, Halloran CM *et al.* Comparison of adjuvant gemcitabine and capecitabine with gemcitabine monotherapy in patients with resected pancreatic cancer (ESPAC-4): a multicentre, open-label, randomised, phase 3 trial. *Lancet* 2017;**389**:1011–1024
27. Are C, Dhir M, Ravipati L. History of pancreaticoduodenectomy: early misconceptions, initial milestones and the pioneers. *HPB (Oxford)* 2011;**13**:377–384
28. Whipple AO, Parsons WB, Mullins CR. Treatment of carcinoma of the ampulla of Vater. *Ann Surg* 1935;**102**:763–779
29. Halloran CM, Platt K, Gerard A, Polydoros F, O'Reilly DA, Gomez D *et al.* PANasta trial; Cattell Warren *versus* Blumgart techniques of panreatico-jejunostomy following pancreato-duodenectomy: study protocol for a randomized controlled trial. *Trials* 2016;**17**:30
30. Raptis DA, Sanchez-Velazquez P, Machairas N, Sauvanet A, Rueda de Leon A, Oba A *et al.* Defining benchmark outcomes for pancreatoduodenectomy with portomesenteric venous resection. *Ann Surg* 2020;**272**:731–737
31. Bockhorn M, Uzunoglu FG, Adham M, Imrie C, Milicevic M, Sandberg AA *et al.* Borderline resectable pancreatic cancer: a consensus statement by the International Study Group of Pancreatic Surgery (ISGPS). *Surgery* 2014;**155**:977–988
32. Del Chiaro M, Rangelova E, Halimi A, Ateeb Z, Scandavini C, Valente R *et al.* Pancreatectomy with arterial resection is superior to palliation in patients with borderline resectable or locally advanced pancreatic cancer. *HPB (Oxford)* 2019;**21**:219–225
33. Ahmad T, Bouwman RA, Grigoras I, Aldecoa C, Hofer C, Hoeft A *et al.* Use of failure-to-rescue to identify international variation in postoperative care in low-, middle- and high-income countries: a 7-day cohort study of elective surgery. *Br J Anaesth* 2017;**119**:258–266
34. Bachmann MO, Alderson D, Peters TJ, Bedford C, Edwards D, Wotton S *et al.* Influence of specialization on the management and outcome of patients with pancreatic cancer. *Br J Surg* 2003;**90**:171–177
35. GlobalSurg Collaborative. Mortality of emergency abdominal surgery in high-, middle- and low-income countries. *Br J Surg* 2016;**103**:971–988
36. GlobalSurg Collaborative. Surgical site infection after gastrointestinal surgery in high-income, middle-income, and low-income countries: a prospective, international, multicentre cohort study. *Lancet Infect Dis* 2018;**18**:516–525