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Niccolò Napoli[1], MD, PhD, FEBS, Greta Donisi[2,3], MD, Emanuele F. Kauffmann[1], MD, PhD, FEBS, Michael Ginesini[1], MD, Mohammad Abu Hilal[4], MD, Gianluca Baiocchi[5], MD, Umberto Bracale[6], MD, Alberto Brolese[7], MD, Giovanni Butturini[8], MD, Roberto Coppola[9], MD, Andrea Coratti[10], MD, Raffaele Dalla Valle[11], MD, Fabrizio Di Benedetto[12], MD, Giorgio Ercolani[13], MD, Giovanni Ferrari[14], MD, Gianluca Garulli[15], MD, Elio Jovine[16], MD, FACS, Michele Mazzola[14] MD, Riccardo Memeo[17], MD, Carlo Molino[18], MD, Luca Moraldi[19], MD, Luca Morelli[20], MD, FACS, Roberto Salvia[21], MD, Giovanni D. Tebala[22], MD, FACS, FRCS, Vincenzo Tondolo[23], MD, Roberto Ivan Troisi[24], MD, Massimo Giuseppe Viola[25], MD, Marco Vivarelli[26], MD, Alessandro Zerbi[2,3], MD, Ugo Boggi[1], MD, FEBS

Institutions:

(1)Division of General and Transplant Surgery, University of Pisa, Pisa, Italy.
(2)Department of Biomedical Sciences, Humanitas University, Pieve Emanuele, Milan, Italy.
(3)IRCCS Istituto Clinico Humanitas, Rozzano, Milan, Italy.
(4)Department of General Surgery, Istituto Ospedaliero Fondazione Poliambulanza, Brescia, Italy
(5)Division of General Surgery, ASST Cremona, Cremona, Italy and Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy

(6)Department Clinical Medicine and Surgery, Federico II University of Naples, Naples, Italy
(7)Department of General Surgery and Hepato-Pancreato-Biliary (HPB) Unit-APSS, Trento, Italy.
(8)Divisione di Chirurgia Epato-bilio-Pancreatica Ospedale P. Pederzoli, Peschiera del Garda, Verona, Italy
(9)Fondazione Campus Biomedico University School of Medicine, Rome, Italy
(10) Department of General and Urgent Surgery, USL Toscana Sud Est, Misericordia Hospital, School of Robotic Surgery, Grosseto, Italy
(11) Programma di Chirurgia Oncologica ad indirizzo epato-bilio-pancreatico, Azienda Ospedaliero-Universitaria di Parma, Parma, Italy
(12) Unit of Hepato-Pancreato-Biliary Surgery and Liver Transplantation, University of Modena and Reggio Emilia, Modena, Italy
(13) Unit of General Surgery, Morgagni-Pierantoni Hospital in Forlì, Department of Medical and Surgical Sciences – University of Bologna, Bologna, Italy
(14) Department of Oncological and Minimally Invasive Surgery, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy
(15) General Surgery Unit, Infermi Hospital, Rimini, Italy
(16) Alma Mater Studiorum, University of Bologna and IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy
(17) Department of Hepato-Pancreatic-Biliary Surgery, "F. Miulli" General Regional Hospital, Acquaviva Delle Fonti, Department of Medicine and Surgery, LUM University, Casamassima, Bari, Italy
(18) UOC Chirurgia Generale I ad alta specializzazione Pancreatica, AORN A. Cardarelli, Naples, Italy
(19) Division of Hepato-Biliary-Pancreatic Surgery, Azienda Ospedaliero Universitaria Careggi, Florence, Italy
(20) General Surgery Unit, Department of Translational Research and New Technologies in Medicine and Surgery, University of Pisa, Pisa, Italy
(21) Department of Surgery, Pancreas Institute, Verona University Hospital, Verona, Italy
(22) Department of Digestive and Emergency Surgery, S. Maria Hospital Trust, Terni, Italy
(23) Università Cattolica del Sacro Cuore, Ospedale Isola Tiberina - Gemelli Isola, Rome, Italy

(24) Department of Clinical Medicine and Surgery, Division of HBP, Minimally Invasive and Robotic Surgery Transplantation Center, Federico II University Hospital, Naples, Italy
(25) Department of General Surgery, Ospedale Cardinale G. Panico, Tricase (LE), Italy
(26) Division of Hepatobiliary, Pancreatic, and Transplantation Surgery, Polytechnic University of Marche, Ospedali Riuniti delle Marche, Ancona, Italy

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Corresponding author: Ugo Boggi, M.D., F.E.B.S.; Address: Via Savi 10, 56126 Pisa (PI), Italy; E-mail: u.boggi@med.unipi.it.

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Roberto Salvia is one of the leaders of the ISGPS that developed the complexity score for MIPD that this manuscript aimed to validate.
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ABSTRACT

Objective: To validate the ISGPS complexity grading system for minimally invasive pancreaticoduodenectomy (MIPD).

Background: Although concerns about patient safety persist, MIPD is gaining popularity. The ISGPS recently introduced a difficulty grading system to improve patient selection by aligning procedural complexity with surgeon and center expertise.

Methods: Data from MIPD cases reported in the IGOMIPS registry (October 2019–February 2024) were analyzed, with severe postoperative complications as the primary outcome. Logistic regression was used to identify risk factors for complications.

Results: Of the 771 MIPD cases, 426 (55.3%) were analyzed. A pancreatic duct size ≤3 mm was the only significant risk factor for severe complications (OR=2.22, p=0.0001). Most cases (n=255; 59.9%) were classified as grade C complexity, whereas 22 (5.1%) were classified as grade A. Severe postoperative complications increased with complexity (grade A, 31.8%; grade B, 36.3%; grade C, 48.6%; p=0.0091). For grade A complexity, the outcomes were consistent across surgeons and centers. Grade B outcomes were similar between grade B and C centers but superior to grade A centers. In grade C cases, outcomes were comparable between grade A and B centers, with improvements at grade C centers. Grade A ISGPS experience correlated strongly with mismatches between planned and performed procedures (grade A, 15.0%; grade B, 3.0%; grade C, 3.1%; p<0.0001), including total pancreatectomy (grade A, 11.5%; grade B, 1.2%; grade C, 3.1%; p=0.0005).

Conclusions: The ISGPS complexity grading system effectively predicted MIPD outcomes, supporting better patient selection and alignment of complexity with surgical expertise.

INTRODUCTION

Pancreatoduodenectomy (PD) remains technically challenging. Despite advancements, outcomes of open PD remain suboptimal, with many patients experiencing severe postoperative complications[1,2]. minimally invasive PD (MIPD) has recently emerged as a viable alternative in select cases[3-4]. However, concerns regarding patient safety and oncologic efficacy have arisen[5,6], prompting critical discussions on patient selection[7], surgeon training[8], and the steep learning curve associated with this procedure[9]. In this evolving context, a standardized difficulty grading system is necessary to align patient selection with institutional experience, ensuring both safety and optimized outcomes.

Two difficulty grading systems have recently been introduced: one specific to robotic PD (PD-ROBOSCORE) and another designed for broader use in all MIPD cases [10,11], the latter developed by the International Study Group for Pancreatic Surgery (ISGPS). The ISGPS system classifies difficulty based on patient-, surgeon-, and center-related factors using an A-B-C grading framework. Patient-related factors included anatomical considerations (such as the main pancreatic and bile duct diameters), tumor characteristics (such as vascular involvement), and conditional factors (e.g., BMI $\geq$30 kg/m² or prior complex upper abdominal surgery). In this system, grade A reflects the absence of risk factors, grade B indicates the presence of one risk factor, and grade C indicates multiple risk factors or vascular involvement. Similarly, this grading applies to surgeons (A: <40 cases; B: 41-79 cases; C: $\geq$80 cases) and centers (A: <10 cases; B: 10-30 cases; C: >30 cases), based on overall and annual case volumes.

Based on the ISGPS score, surgeons and centers classified as level A should manage MIPD in patients with grade A complexity. Surgeons and centers at level B are suitable for handling patients with grades A and B, whereas those at level C can manage patients of any complexity grade.

Although the ISGPS grading system is based on a literature review and expert consensus, it is yet to be clinically validated. This study aimed to validate the ISGPS score using data from the Italian prospective observational registry on pancreatic surgery (IGOMIPS)[12,13].

METHODS

The IGOMIPS registry (https://www.yoursuite.it/IGOMIPS/) is a prospective Italian database tracking operative and 90-day postoperative outcomes of minimally invasive pancreatic resections based on an intention-to-treat approach (i.e., procedures are declared the day before surgery). Furthermore, it records the consecutive case numbers per surgeon and center, including cases performed before the establishment of the registry. Launched in 2019 following Ethics Committee approval at the Humanitas Institute (authorization 2167), it is registered with the Registry of Patient Registries (https://www.ahrq.gov/ropr/index.html). Additional approval was obtained from the local Ethics Committees at the participating centers[12,13]. This study followed the Declaration of Helsinki and adhered to STROBE guidelines[14,15].

Study Design

The IGOMIPS registry was queried for MIPD procedures performed between October 1, 2019, and February 2, 2024. Patients with complete data were included in the study. Procedures were categorized as A, B, and C based on the ISGPS classification, and outcomes were compared across surgeons and centers. The primary outcome was the incidence of severe postoperative complications (> grade 2 on the Clavien-Dindo scale)[16]. Predictors of severe postoperative complications were evaluated using a logistic regression analysis. Pancreas-specific complications were classified according to ISGPS definitions[17-20]. Validation of the ISGPS grading system was based on the hypothesis that outcomes for grade A procedures should be similar regardless of surgeon or center experience. For grade B procedures, outcomes were expected to improve with more experienced surgeons and centers (categories B and C), whereas for grade C procedures, category C surgeons and centers were anticipated to outperform those in categories A and B.

Variables for ISGPS Score Calculation

While the IGOMIPS registry provided more data than required for the ISGPS, two parameters were not prospectively recorded: common bile duct diameter and vascular contact. Consequently, patients without a prior cholecystectomy or ongoing biliary obstruction were classified as having a thin bile duct. Patients who underwent vascular resection were assumed to have vascular contacts. Additional procedural data and information on the surgeon and center experience were collected. Center volume was calculated based on the median annual volume during the study period, and the surgeon and center categories were assigned using the lower value, as per the ISGPS guidelines.

Statistical Methods

Nominal variables were reported as frequencies and percentages, while continuous variables were expressed as mean ± standard deviation (SD) for normally distributed data or median with interquartile range (IQR) for non-normally distributed data, as determined using the Shapiro-Wilk test.

Procedure complexity was validated by comparing intraoperative and postoperative outcomes across different difficulty levels, while center experience was validated by comparing outcomes across varying experience levels. For patient selection validation, the outcomes were stratified by procedural complexity and center experience.

Continuous variables were compared using the Wilcoxon rank-sum test for non-normally distributed data or t-tests and ANOVA for normally distributed data, according to the results of the skewness analysis for each variable. Welch's analysis of variance was applied to detect unequal variances using Levene's test. Categorical variables were compared using the Cochran–Armitage test for trends and Pearson's chi-square test or Fisher's exact test for pairwise comparisons. To reduce the risk of a type I error in multiple comparisons, Bonferroni correction was applied where necessary.

Logistic regression was used to estimate the risk of severe complications with odds ratios (OR) and interquartile ranges (IQR) provided as risk estimates. Both univariate and multivariate logistic regression analyses were performed to identify the predictors of severe postoperative complications. Sensitivity analyses were conducted to assess the incidence of postoperative complications, excluding the learning curve effect (defined as a center experience of fewer than 40 cases) and separately evaluating outcomes for laparoscopic and robotic MIPD[21].

Statistical significance was set at p<0.05, with a threshold of p<0.0167 for pairwise comparisons (after the Bonferroni correction). All analyses were performed using JMP Pro 17 and R Studio 2024.04.2, using the ggplot2 package for visualization.

RESULTS

During the study period, 2,257 minimally invasive pancreatic resections were reported in the IGOMIPS registry from 37 Italian centers. MIPD was planned in 816 patients (36.2%), and the procedure was completed in 770 patients (94.4%). An additional MIPD was performed in a patient who was initially scheduled for transduodenal ampullectomy. MIPD was performed at 25 IGOMIPS centers (67.5%), with a median number of reported MIPD per center of 14 (IQR: 5 – 37.5). Seven centers reported laparoscopic MIPD (28.0%), 5 reported both laparoscopic and robotic MIPD (20.0%), and 13 reported robotic MIPD (52.0%).

The MIPD cohort consisted of 546 robotic MIPD cases (70.8%) and 225 laparoscopic MIPD cases (19.2%). In the first year, 115 MIPD cases were enrolled in the registry, with a relatively balanced distribution between robotic (52 cases, 45.2%) and laparoscopic procedures (63 cases, 54.8%). In contrast, in the final year, 147 MIPD cases were recorded, of which 140 (95.2%) were robotic and seven (4.8%) were laparoscopic. The shift toward robotic surgery became more pronounced over time, with a deflection point identified in Case 357, after which there was a significantly lower probability of MIPD being performed laparoscopically (AUC = 0.76146; p < 0.0001).

The reasons for not proceeding with the planned MIPD included the discovery of distant metastases (8 patients; 1.0%) and the decision to perform a different type of pancreatic resection in 38 patients (32/808; 3.9%), distal pancreatectomy in 2 patients (0.2%), total pancreatectomy in 28 patients (3.5%), and other pancreatic resections in 8 patients (1%). Ultimately, 771 MIPDs were performed, and owing to missing data, 426 of these procedures were analyzed in this study. The study flowchart is shown in Supplementary Figure 1, Supplemental Digital Content 1, http://links.lww.com/SLA/F365. Preoperative characteristics and outcomes are presented in Table 1.

Analysis of preoperative parameters identified a pancreatic duct diameter ≤3 mm as the only independent risk factor for developing severe postoperative complications (OR= 2.24 [1.51-3.35], p<0.0001).

Validation of the ISGPS Complexity Grading System

Table 2 presents the application of complexity scores to the IGOMIPS cohort. Table 3 provides additional baseline characteristics and relevant outcomes. Most MIPD in the IGOMIPS registry were classified as grade C (255/426; 59.9%), whereas a small minority were classified as A (22/426; 5.1%). Conversely, the majority of cases were managed by surgeon-center experience levels equivalent to ISGPS grades A (170/426; 39.9%) and B (161/426; 37.8%), with a small proportion of procedures performed by grade C surgeons at grade C centers (95/426; 22.3%). The distribution of surgical experience was relatively balanced across the population, with grade A at 144/426 (33.8%), grade B at 128/426 (30.0%), and grade C at 154/426 (36.2%). In contrast, there was a significant difference in the distribution of center experience levels: Grade A centers accounted for 129/426 (30.3%), grade B for 202/426 (47.4%), and grade C for 95/426 (22.3%). Notably, grade C procedures were frequently performed by grade A centers (29.0%) or grade A surgeons (35.1%).

An increase in procedural complexity was significantly associated with a higher frequency of difficult factors, except for instances of previous complicated abdominal surgery. Interestingly, grade C complexity was correlated with a lower incidence of a hard pancreatic stump (18.1% vs. 40.9% and 43.3% for grades A and B, respectively). The incidence of severe postoperative complications increased progressively from grade A to C, with rates of 31.8%, 36.3%, and 48.6%, respectively. Although postoperative mortality did not reach statistical significance, no deaths occurred in grade A MIPD, whereas mortality exceeded 7% in grades B and C.

Grade C procedures were associated with younger patients, fewer ASA IV cases, and greater reliance on laparoscopy over robotic approaches. Despite the higher complexity, approximately 40% of grade C procedures are performed by grade A or grade A surgeons. This mismatch may contribute to the higher rates of severe postoperative complications, postoperative pancreatic fistula (POPF), grade C POPF, abdominal fluid collection, and necessity for percutaneous drainage in grade C procedures.

Procedure difficulty was not associated with length of hospital stay.

Validation of the ISGPS Surgeon and Center Experience Classification System

Table 4 summarizes the preoperative characteristics and outcomes based on surgeon and center experience. Table 5 provides additional baseline characteristics and relevant outcomes. MIPD in patients with vascular tumor contact was more frequent among those treated by grade C surgeons and centers. However, no significant differences were observed across experience levels regarding prior complicated abdominal surgery or an elevated BMI. Notably, the proportion of patients with a small pancreatic duct was lower at grade C experience levels, whereas the proportion of patients with small bile ducts remained consistent across the ISGPS experience levels.

Patients treated by grade C surgeons demonstrated improved overall outcomes, including lower rates of severe postoperative complications, POPF, biliary leaks, postoperative hemorrhage (PPH), and reoperations. They also had a higher number of lymph nodes.

Surgeon and center experience were not associated with length of hospital stay.

Validation of the ISGPS Patient Selection System

Preoperative characteristics and outcomes, categorized by ISGPS experience level and stratified by procedural complexity, are presented in Supplementary Tables 1-3, Supplemental Digital Content 1, http://links.lww.com/SLA/F365. Figure 1 illustrates the risk of severe postoperative complications based on center experience and procedural complexity.

For grade A complexity, no significant differences in outcomes were observed across centers. Notably, there were no instances of 90-day mortality, grade C POPF, or biliary fistula.

For grade B complexity, the outcomes were comparable between grade B and C centers. However, procedures conducted at grade C centers resulted in fewer severe complications, lower 90-day mortality, reduced PPH rates, and fewer reoperations, along with improved POPF and conversion rates. Surgeries at grade B centers also demonstrated less blood loss and lower conversion rates than those at grade A centers.

For grade C complexity, the outcomes were similar between grade A and B centers. However, grade C centers exhibited fewer severe complications, lower rates of all grades of POPF, and decreased PPH. A higher proportion of patients experienced no postoperative complications in grade C centers.

Impact of ISGPS Experience Level on Mismatch Between Planned and Performed Pancreatic Resections

The ISGPS experience level was strongly correlated with the concordance between the planned and performed procedures. A different procedure than that declared the day before surgery was carried out for 30 out of 200 patients (15.0%) at the grade A ISGPS experience level, and for 5 out of 116 (3.0%) and 3 out of 98 (3.1%) patients with grade B and C ISGPS experience levels, respectively ($p < 0.0001$). The need to convert MIPD into total pancreatectomy was also associated with the ISGPS experience level, with grade A in 23 out of 200 (11.5%), grade B in 2 out of 166 (1.2%), and grade C in 3 out of 98 (3.1%) patients ($p = 0.0005$). It is noteworthy that differences in the need for either a procedure other than MIPD or specifically a total pancreatectomy were significant between grade A ISGPS experience level and grade B/C, but not between grade B and C experience levels.

Sensitivity Analyses

To exclude the impact of the feasibility learning curve on the incidence of severe postoperative complications, the first 40 MIPD cases per center were excluded from the analysis. Based on this criterion, 17 of 25 centers (68.0%) did not complete the feasibility learning curve when they enrolled their first case in the IGOMIPS registry. Four of these centers (23.6%) completed the learning curve during their participation in the registry. After excluding cases performed before reaching this time point, the incidence of severe postoperative complications increased with procedural complexity (Grade A 27.8%; Grade B, 30.1%; and Grade C, 45.5%; $p = 0.0138$).

To assess the impact of surgical technique on the incidence of severe postoperative complications, the outcomes of laparoscopic and robotic MIPD were analyzed separately. An improvement in the rate of severe postoperative complications was observed for robotic

MIPD (Grade A 26.3%; Grade B, 31.8%; Grade C, 42.3%; p = 0.0138), but not for laparoscopic MIPD (Grade A 66.7%; Grade B, 48.7%; Grade C, 60.9%; p = 0.3383). This discrepancy may explain the shift from laparoscopic to robotic MIPD observed in our registry.

DISCUSSION

ISGPS recently introduced a complexity grading system for MIPD to standardize and promote the safe adoption of this approach. This system is based on the well-established literature and incorporates factors strongly associated with procedural difficulty [11]. Although prospective studies are ideal for validation, data from the prospective IGOMIPS registry (2019–2023) enable a timely, albeit retrospective, assessment of its clinical utility. This analysis also provides insights into potential refinements of the scoring system based on real-world outcomes.

This study validated the ability of the ISGPS score to predict MIPD outcomes based on procedural complexity. This highlights the importance of aligning surgeons and centers' experience with procedural complexity to minimize complications and improve outcomes. Although high-experience centers (grade C) performed better overall, the higher rates of severe complications in grade C procedures performed at grade A centers suggest that training and procedure selection should be optimized for more complex cases.

Notably, 4% of patients scheduled for MIPD underwent a different procedure, often total pancreatectomy. While total pancreatectomy eliminates the risks associated with POPF, it presents unique challenges in a minimally invasive setting[22-24]. The need for total pancreatectomy may reflect an unfavorable tumor location or more advanced disease, requiring technical modifications. Centers pursuing MIPD should be prepared for alternative procedures and have the flexibility to adjust them intraoperatively.

The ISGPS is not the only grading system for MIPD complexity. The PD-ROBOSCORE, developed specifically for robotic PD, focuses on procedural difficulty without accounting for surgeon or center experience[10]. PD-ROBOSCORE includes six parameters, three of which overlap with the ISGPS: high BMI, small pancreatic duct, and vascular tumor contact. However, PD-ROBOSCORE emphasizes anatomical challenges, such as uncinate process tumors and variant hepatic arteries, while the ISGPS score includes previous complicated abdominal surgery and small bile ducts. Despite these differences, both systems underscore the complexity of MIPD[10,11].

Among all ISGPS parameters, a small pancreatic duct size was a predictor of severe postoperative complications in the IGOMIPS registry. Remarkably, despite the fact that 40% of grade C procedures were performed by grade A or grade A centers, grade C MIPD at grade C centers had lower rates of severe complications, emphasizing the importance of both individual and institutional experience in complex cases.

Severe postoperative complications are pivotal outcomes in PD, as they prolong hospital stays[25], increase costs and mortality rates[25,26], delay or prevent adjuvant oncologic treatments[27], and adversely affect overall and disease-free survival[28]. Although the search for an ideal outcome metric in PD continues and holistic scoring systems are being proposed[29], the reduction of postoperative complications remains the cornerstone of successful pancreatic surgery.

In the IGOMIPS registry, MIPD did not significantly reduce the incidence of severe postoperative complications compared with the rates typically seen with open PD. These findings align with those of two recent randomized controlled trials that compared MIPD with open PD[30,31]. However, outcomes markedly improved when MIPD was performed by expert surgeons at high-volume centers, underscoring the importance of both surgeon and center volumes.

Interestingly, the relevance of previous complicated upper abdominal surgery as a difficulty parameter may be overstated, as 0.2% of the patients met this criterion. Surgeons may view this condition as a contraindication rather than a challenge for MIPD, reflecting improved patient selection.

Patient selection remains critical, particularly with regard to duct size. A high proportion of MIPDs were performed on patients with small pancreatic and bile ducts, which poses significant technical challenges. In a minimally invasive setting, these challenges are amplified, with some cases appearing straightforward during resection but proving difficult during reconstruction[32].

Vein resection and reconstruction increase the risk of severe complications in open PD;[33], data on vascular resections in MIPD are limited. Although many centers consider this a contraindication for MIPD, recent studies have shown its feasibility at high-volume centers in select patients[34,35]. The new REDISCOVER guidelines and 2023 international consensus guidelines on robotic pancreatic surgery support minimally invasive approaches for borderline resectable cases, emphasizing patient selection and surgeon experience[36-38]. The high conversion rates, particularly for cases involving vein resection, highlight the increased complexity of MIPD[30].

This study found that 5% of MIPD cases were classified as low complexity. While this highlights the critical role of patient selection, it also raises the question of how many 'easy' cases can truly be identified in PD, a procedure inherently complex by nature. This consideration likely extends to open PD as well, where poor outcomes have consistently been linked to low-volume centers, often regarded as a comprehensive quality metric[39]. Thus, the debate on MIPD complexity may also apply to open PD, potentially revealing outcome-related factors beyond the volume.

Laparoscopy is more frequently used in grade C procedures. This may be due to the early adoption of laparoscopic MIPD, resulting in some surgeons being more comfortable with laparoscopy than with robotics in complex cases, or due to limited access to robotic systems. Additionally, the lack of specialized robotic tools for efficient dissection may have contributed to this, as such tools are more readily available for laparoscopy. It is also possible that some surgeons were unaware of the complexity of MIPD because of the absence of a complexity score. This aligns with the finding that less experienced centers often handle a higher proportion of complex cases, while more experienced centers tend to select easier cases, as seen in the validation of the PD-ROBOSCORE[10]. Ultimately, as surgeons complete their learning curve, the proportion of difficult cases decreases across all centers, indicating that mastering MIPD involves not only technical skills, but also refining patient selection. This reflects the principle that the clinical benefits of minimally invasive surgery decrease with the complexity of the procedures.

Over time, the use of laparoscopy has gradually decreased in the IGOMIPS registry, as already shown in the E-MIPS registry[40]. While there is no definitive evidence that robotic assistance improves MIPD outcomes and concerns persist regarding costs and accessibility, the clinical implementation trends show that robotic assistance was preferred by Italian surgeons[40,41].

This study did not demonstrate a reduction in hospital stay length based on procedural difficulty or surgeon/center experience, despite the higher rates of severe postoperative complications in grade C procedures and fewer complications in grade C centers. Several factors may explain the contradictory findings. First, while enhanced recovery after surgery protocols can reduce hospital stay, their use in the IGOMIPS registry is not mandatory[42]. Second, hospital stay lengths can vary geographically. For instance, a study found a fourfold difference in stay length after pancreatectomy between the USA and Japan, with Italian hospitals—mostly public—reporting lengths similar to Japan[43,44]. Third, most pancreatic resections in Italy are centralized in select centers and require long-distance travel for patients upon discharge. Finally, a mismatch between procedure difficulty and surgeon/center expertise may have obscured the impact of ISGPS score on hospital stay duration.

This study had several limitations. The bile duct size and vascular tumor contact were not prospectively recorded in the IGOMIPS registry. Although small bile ducts are linked to difficult anastomosis and vascular tumor contact with vascular resections, surrogate markers were used to estimate these factors. Additionally, being part of a registry may have led some centers to broaden MIPD indications to increase patient enrollment, contributing to the observed high-complexity cases. As a result, the final validation of the ISGPS complexity grading system will require prospective studies explicitly designed for this purpose. While such studies might yield more selective findings compared to the broader scope of registry-based analyses, they will provide critical insights into the true clinical utility of MIPD. These insights will be pivotal in ensuring the continued safe and effective global implementation of MIPD. In fact, given the growing demand for minimally invasive pancreatic surgery, the inherent complexity of MIPD necessitates a cautious and evidence-based approach. In this context, the progressive adoption of increasingly complex cases should be guided by the acquisition of both practical skills and cognitive knowledge to ensure optimal patient outcomes.

In conclusion, this study provides the first clinical validation of the ISGPS complexity score for MIPD. Although further refinements are likely to be experienced as the system grows, the

ISGPS score represents a vital tool for promoting safe MIPD adoption and enabling meaningful comparisons between centers and techniques, including open PD.

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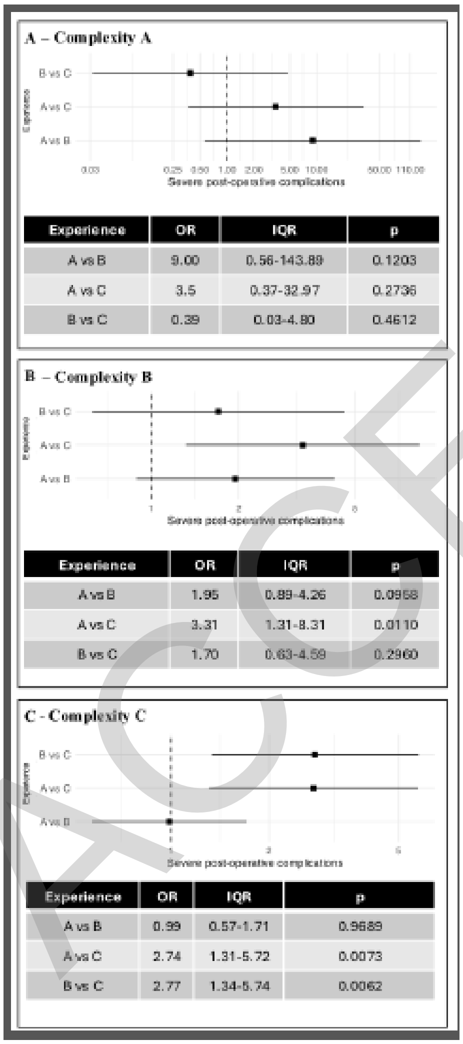
Figure 1. Risk of development of severe post-operative complication based on different grade of experience, stratified by procedure complexity. 1A) Complexity A, experience based on specific annual volume. 1B) Complexity A, experience based on median annual volume. 1A) Complexity B, experience based on specific annual volume. 1A) Complexity B, experience based on median annual volume. 1A) Complexity C, experience based on specific annual volume. 1A) Complexity C, experience based on median annual volume.



Experience	OR	IQR	p
A vs B	9.00	0.56-143.89	0.1203
A vs C	3.5	0.37-32.97	0.2736
B vs C	0.39	0.03-4.80	0.4612

Experience	OR	IQR	p
A vs B	1.95	0.89-4.26	0.0958
A vs C	3.31	1.31-8.31	0.0110
B vs C	1.70	0.63-4.59	0.2960

Experience	OR	IQR	p
A vs B	0.99	0.57-1.71	0.9689
A vs C	2.74	1.31-5.72	0.0073
B vs C	2.77	1.34-5.74	0.0062

Table 1 – Preoperative characteristics and outcomes of MIPD in the IGOMIPS registry.

	Results
Age, median (IQR), years	69 (61-75)
Male gender, n (%)	236 (55.4%)
Body mass index (BMI) Median (IQR), kg/m^2 ≥30 kg/m^2, n (%)	24.5 (22.5-27) 38 (8.9%)
ASA score, n (%) I II III IV >II	22 (5.2%) 209 (49.1%) 189 (44.4%) 6 (1.4%) 195 (45.8%)
Previous upper abdominal surgery, n (%)	156 (36.6%)
Previous complex upper abdominal surgery, n (%)	1 (0.2%)
Pre-operative oncology treatments, n (%) Chemotherapy Radiotherapy	22 (5.2%) 3 (0.7%)
Tumor vascular contact, n (%)	32 (7.5%)
Main pancreatic duct diameter ≤3 mm, n (%)*	235 (55.4%)
Common bile duct diameter ≤5 mm, n (%)	377 (88.4%)
ISGPS complexity grading system, n (%) Grade A Grade B Grade C	22 (5.2%) 149 (35.0%) 255 (59.9%)
ISGPS experience scoring system, n (%) Grade A Grade B Grade C	170 (39.9%) 161 (37.8%) 95 (22.3%)
Approach, n (%) Laparoscopy Hybrid laparoscopy All laparoscopic approaches Robotic	107 (25.1%) 22 (5.2%) 129 (30.3%) 297 (69.7%)
Operative time, mean±SD, min	505.7±109.8
Blood loss, median (IQR), mL	200 (100-300)
Blood transfusion, median (IQR), mL	0 (0-0)
Conversion, n (%) Due to intraoperative complications All reasons	7 (1.6%) 35 (8.4%)
Firm pancreatic stump, n (%)	297 (72.1%)
Pancreatic anastomosis, n (%) Pancreatojejunostomy Pancreatogastrostomy Duct occlusion	400 (94.5%) 18 (4.3%) 5 (1.2%)
Length of hospital stay, median (IQR), days	16 (10-27)
Postoperative complications, n (%) None Grade 1 Grade 2 Grade 3a Grade 3b Grade 4a Grade 4b	47 (11.0%) 58 (13.6%) 143 (33.6%) 82 (19.2%) 38 (8.9%) 21 (4.9%) 7 (1.6%)

Grade 5 Grade >2	30 (7.0%) 185 (43.4%)
Failure-to-rescue, n (%)	30 (16.4%)
Post-operative pancreatic fistula, n (%) Biochemical leak Grade B/C Grade C	51 (12.0%) 108 (25.4%) 23 (5.4%)
Biliary leak, n (%)	40 (9.4%)
Intestinal leak, n (%)	16 (3.8%)
Chyle leak, n (%)	24 (5.6%)
Delayed gastric emptying, n (%) Grade B/C All grades	72 (16.9%) 105 (24.6%)
Post-pancreatectomy hemorrhage, n (%)	84 (19.7%)
Drained abdominal fluid collections, n (%)	86 (20.2%)
Reoperation, n (%)	65 (15.3%)
Tumor type, n (%) Malignant tumor* PDAC*	355 (88.8%) 162 (40.5%)
Lymph nodes, median (IQR) Examined* Positive*	24 (17-34) 2 (1-5)

*Data missing on 2 cases for main pancreatic duct size, 26 cases for tumor type, on 44 cases for examined lymph nodes, and 8 cases for positive nodes; BMI: Body Mass Index; PDAC: Pancreatic Ductal Adenocarcinoma

Table 2 –ISGPS complexity scoring in the IGOMIPS registry

	Complexity Scoring			
	Grade A (n= 22)	**Grade B** (n= 149)	**Grade C** (n= 255)	**p**
ISGPS complexity parameters, n (%)				
Main pancreatic duct diameter ≤3 mm*	0	14 (9.4%)	221 (87.4%)	**<0.0001**
Common bile duct diameter ≤5 mm	0	135 (90.6%)	242 (94.9%)	**<0.0001**
Tumor vascular contact	0	0	32 (12.6%)	**<0.0001**
BMI≥30 kg/m^2	0	0	38 (14.9%)	**<0.0001**
Previous complex upper abdominal surgery	0	0	1 (0.4%)	0.4440
ISGPS experience scoring system, n (%)				
Grade A	5 (22.7%)	65 (43.6%)	100 (39.2%)	0.7360
Grade B	7 (31.8%)	47 (31.5%)	107 (42.0%)	**0.0440**
Grade C	10 (45.5%)	37 (24.8%)	48 (18.8%)	**0.0061**
ISGPS center classification				
Grade A	2 (9.1%)	53 (35.6%)	74 (29.0%)	0.7972
Grade B	10 (45.5%)	59 (39.6%)	133 (52.2%)	**0.0404**
Grade C	10 (45.5%)	37 (24.8%)	48 (18.8%)	**0.0061**
ISGPS surgeon classification				
Grade A	4 (18.2%)	50 (33.6%)	90 (35.3%)	0.2108
Grade B	6 (27.3%)	42 (28.2%)	80 (31.4%)	0.4766
Grade C	12 (54.6%)	57 (38.3%)	85 (33.3%)	0.0560
ISGPS center and surgeon classification, n (%)				
Center A	(n=2)	(n=53)	(n=74)	
Surgeon A	1 (50.0%)	38 (71.7%)	64 (86.5%)	**0.0217**
Surgeon B	1 (50.0%)	14 (26.4%)	8 (10.8%)	**0.0108**
Surgeon C	0	1 (1.9%)	2 (2.7%)	0.7181
Center B	(n=10)	(n=59)	(n=26)	
Surgeon A	3 (30.0%)	12 (20.3%)	26 (19.6%)	0.5538
Surgeon B	5 (50.0%)	28 (47.5%)	72 (54.1%)	0.4573
Surgeon C	2 (20.0%)	19 (32.2%)	35 (26.3%)	0.7661
Center C	(n=10)	(n=37)	(n=48)	
Surgeon A	0	0	0	NA
Surgeon B	0	0	0	NA
Surgeon C	10 (100.0%)	37 (100.0%)	48 (100.0%)	NA

***** Data missing on 2 cases for main pancreatic duct size; **Bold= significant p**

Table 3. Additional relevant baseline characteristics and main outcomes based on ISGPS complexity scoring in the IGOMIPS registry

	Complexity Scoring			
	Grade A (n= 22)	**Grade B** (n= 149)	**Grade C** (n= 255)	**p**
Age, median (IQR), years	73.5 (67-79)	72 (64-77)	67 (57-74)	**<0.0001**
Male gender, n (%)	13 (59.1%)	85 (57.1%)	138 (54.1%)	0.5021
BMI, median (IQR), kg/m^2	25 (22.6-26)	24.2 (22.2-26.2)	24.6 (22.6-27.6)	0.0870
ASA score, n (%) I	0	6 (4.0%)	16 (6.3%)	0.1427
II	7 (31.8%)	74 (49.7%)	128 (50.2%)	0.2740
III	14 (63.6%)	65 (43.6%)	110 (43.1%)	0.2249
IV	1 (4.6%)	4 (2.7%)	1 (0.4%)	**0.0228**
>II	15 (68.2%)	69 (46.3%)	111(43.5%)	0.0803
Pre-operative oncology treatments, n (%) Chemotherapy Radiotherapy	0 0	7 (4.7%) 2 (1.3%)	15 (5.9%) 1 (0.4%)	0.2729 0.5309
Approach, n (%) Laparoscopy Hybrid laparoscopy All laparoscopic approaches Robotic	 3 (13.6%) 0 3 (13.6%) 19 (86.4%)	 36 (24.2%) 3 (2%) 39 (26.2%) 110 (73.8%)	 68 (26.7%) 19 (7.5%) 87 (34.1%) 168 (65.9%)	 0.2220 **0.0100** **0.0167** **0.0167**
Operative time, mean±SD, min	482±23.4	499.4±9	511.4±6.9	0.3337
Blood loss, median (IQR), mL	200 (100-325)	177.5 (100-337.5)	200 (100-300)	0.8483
Blood transfusion, median (IQR), mL	0 (0-0)	0 (0-0)	0 (0-0)	0.2575
Conversion, n (%) Due to intraoperative complications All reasons	 0 0	 2 (1.3%) 13 (9.1%)	 5 (2%) 22 (8.8%)	 0.4512 0.4166
Firm pancreatic stump, n (%)	9 (40.9%)	61 (43.3%)	45 (18.1%)	**<0.0001**
Pancreatic anastomosis, n (%) Pancreatojejunostomy Pancreatogastrostomy Duct occlusion	 22 (100%) 0 (0%) 0 (0%)	 142 (96%) 4 (2.7%) 2 (1.4%)	 236 (93.3%) 14 (5.5%) 3 (1.2%)	 0.1085 0.0904 0.8381
Length of hospital stay, median (IQR), days	15 (10-31.3)	14 (10-23)	17.5 (11-29)	0.1575
Postoperative complications, n (%) None Grade 1 Grade 2 Grade 3a Grade 3b Grade 4a Grade 4b Grade 5 > Grade 2	3 (13.6%) 2 (9.1%) 10 (45.5%) 4 (18.2%) 2 (9.1%) 1 (4.6%) 0 0 7 (31.8%)	23 (15.4%) 24 (16.1%) 51 (34.2%) 24 (16.1%) 12 (8.1%) 4 (2.7%) 0 11 (7.4%) 54 (36.3%)	21 (8.2%) 32 (12.6%) 82 (32.2%) 54 (21.2%) 24 (9.4%) 16 (6.3%) 7 (2.8%) 19 (7.5%) 124 (48.6%)	**0.0443** 0.6812 0.2820 0.2854 0.7272 0.1844 **0.0414** 0.4075 **0.0091**
Failure-to-rescue, n (%)	0	11 (21.2%)	19 (15.3%)	0.9482

Post-operative pancreatic fistula, n (%) Biochemical leak Grade B/C Grade C	2 (9.1%) 3 (13.6%) 0	23 (15.4%) 26 (17.5%) 4 (2.7%)	49 (19.2%) 79 (31.0%) 19 (7.5%)	0.1590 **0.0015** **0.0202**
Biliary leak, n (%)	0	15 (10.1%)	25 (9.8%)	0.3815
Intestinal leak, n (%)	1 (4.6%)	5 (3.4%)	10 (3.92%)	0.9148
Chyle leak, n (%)	1 (4.6%)	6 (4%)	17 (6.7%)	0.3082
Delayed gastric emptying, n (%) Grade B/C All grades	5 (22.7%) 7 (31.8%)	19 (12.8%) 30 (20.1%)	48 (18.8%) 68 (26.7%)	0.4297 0.4981
Post-pancreatectomy hemorrhage, n (%)	4 (18.2%)	26 (17.5%)	54 (21.2%)	0.4045
Abdominal fluid collections, n (%) Drained All	3 (13.6%) 7 (31.8%)	21 (14.1%) 43 (28.9%)	62 (24.3%) 102 (40%)	**0.0148** **0.0429**
Reoperation, n (%)	2 (9.1%)	20 (13.4%)	43 (16.9%)	0.2154
Tumor type, n (%) Malignant tumor* PDAC*	20 (100%) 11 (55%)	120 (87%) 67 (48.6%)	215 (88.8%) 84 (34.7%)	0.5865 **0.0035**
Lymph nodes, median (IQR) Examined* Positive*	29.5 (22.3-36.8) 6 (2-8)	23 (17-34) 2 (1-5)	23 (17-32) 2 (0-4)	0.0899 **0.0303**

***** Data missing on 26 cases for tumor type, on 44 cases on number of examined lymph nodes, and on 8 cases for positive; BMI: Body Mass Index; PDAC: Pancreatic Ductal Adenocarcinoma; **Bold= significant p**

Table 4– ISGPS experience scoring system in the IGOMIPS registry

	Experience Scoring						
	Grade A	**Grade B**	**Grade C**	**p**	**pAB**	**pAC**	**pBC**
ISGPS complexity parameters, n (%)							
Main pancreatic duct diameter ≤3 mm*****	98 (57.7%)	105 (65.2%)	32 (34.4%)	**0.0029**	0.1575	**0.0003**	**<0.0001**
Common bile duct diameter ≤5 mm	153 (90.0%)	148 (91.9%)	76 (80.0%)	**0.0358**	0.5419	0.0227	**0.0053**
Tumor vascular contact	12 (7.1%)	2 (1.2%)	18 (19.0%)	**0.0054**	**0.0116**	**0.0034**	**<0.0001**
BMI ≥30 kg/m^2	11 (6.5%)	23 (14.3%)	4 (4.2%)	0.9454	0.0192	0.5835	**0.0112**
Previous complex upper abdominal surgery	0	0	1 (1.1%)	0.1256	NA	0.3585	0.3711
ISGPS center classification							
Grade A	129 (75.9%)	0	0	**<0.0001**	**<0.0001**	**<0.0001**	NA
Grade B	41 (24.1%)	161 (100.0%)	0	0.4926	**<0.0001**	**<0.0001**	**<0.0001**
Grade C	0	0	95 (100.0%)	**<0.0001**	NA	**<0.0001**	**<0.0001**
ISGPS surgeon classification							
Grade A	144 (84.7%)	0	0	**<0.0001**	**<0.0001**	**<0.0001**	NA
Grade B	23 (13.5%)	105 (65.2%)	0	0.9491	**<0.0001**	**<0.0001**	**<0.0001**
Grade C	3 (1.8%)	56 (34.8%)	95 (100.0%)	**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**
ISGPS center and surgeon classification, n (%)							
Center A	(n=129)	(n=0)	(n=0)				
Surgeon A	103 (79.8%)	0	0	NA	NA	NA	NA
Surgeon B	23 (17.8%)	0	0	NA	NA	NA	NA

Surgeon C	3 (2.3%)	0	0	NA	NA	NA	NA
Center B	(n=41)	(n=161)	(n=0)				
Surgeon A	41 (100.0%)	0	0	**<0.0001**	**<0.0001**	NA	NA
Surgeon B	0	105 (65.2%)	0	**<0.0001**	**<0.0001**	NA	NA
Surgeon C	0	56 (34.8%)	0	**<0.0001**	**<0.0001**	NA	NA
Center C	(n=0)	(n=0)	(n=95)				
Surgeon A	0	0	0	NA	NA	NA	NA
Surgeon B	0	0	0	NA	NA	NA	NA
Surgeon C	0	0	95 (100.0%)	NA	NA	NA	NA

***** Data missing on 2 cases for main pancreatic duct size; **Bold= significant p**

Table 5 Additional relevant baseline characteristics and main outcomes based on ISGPS experience scoring system in the IGOMIPS registry.

	Experience Scoring						
	Grade A	**Grade B**	**Grade C**	**p**	**pAB**	**pAC**	**pBC**
Age, median (IQR), years	69 (60.8-75)	70 (61-76.5)	67 (61-74)	0.1710	0.4212	0.2411	0.0574
Male gender, n (%)	92 (54.1%)	90 (55.9%)	54 (56.8%)	0.6527	0.7445	0.6689	0.8834
BMI, median (IQR), kg/m^2	24.1 (22.2-26.3)	25.4 (23.2-27.8)	24.2 (22.3-26.6)	**0.0019**	**0.0008**	0.6084	**0.0146**
ASA score, n (%)							
I	9 (5.3%)	12 (7.5%)	1 (1.1%)	0.2399	0.4205	0.1012	0.0351
II	95 (55.9%)	90 (55.9%)	24 (25.3%)	**<0.0001**	0.9973	**<0.0001**	**<0.0001**
III	64 (37.7%)	56 (34.8%)	69 (72.6%)	**<0.0001**	0.5879	**<0.0001**	**<0.0001**
IV	2 (1.2%)	3 (1.9%)	1 (1.1%)	0.9760	0.6774	1.0000	1.0000
>II	66 (38.8%)	59 (36.7%)	70 (73.7%)	**<0.0001**	0.6829	**<0.0001**	**<0.0001**
Pre-operative oncology treatments, n (%)							
Chemotherapy	12 (7.1%)	4 (2.5%)	6 (6.3%)	0.5448	0.0715	0.8177	0.1805
Radiotherapy	1 (0.6%)	2 (1.2%)	0	0.7222	0.6139	1.0000	0.5314
Approach, n (%)							
Laparoscopy	41 (24.1%)	66 (41%)	0	**0.0013**	**0.0010**	**<0.0001**	**<0.0001**
Hybrid laparoscopy	14 (8.2%)	8 (5%)	0	**0.0039**	0.2331	**0.0027**	0.0275
All laparoscopic approaches	55 (32.4%)	74 (46%)	0	**<0.0001**	**0.0112**	**<0.0001**	**<0.0001**
Robotic	115 (67.7%)	87 (54%)	95 (100%)	**<0.0001**	**0.0112**	**<0.0001**	**<0.0001**
Operative time, mean±SD, min	513±8.2	474.4±8.4	546.1±11	**<0.0001**	**0.0021**	0.0199	**<0.0001**
Blood loss, median (IQR), mL	200 (100-387.5)	200 (150-300)	150 (100-300)	**0.0033**	0.8501	**0.0025**	**0.0019**
Blood transfusion, median (IQR), mL	0 (0-0)	0 (0-0)	0 (0-0)	**0.0030**	**0.0006**	0.3985	0.0232
Conversion, n (%)							
Due to intraoperative complications	4 (2.4%)	3 (1.9%)	0	0.1701	1.0000	0.3002	0.2971
All reasons	26 (15.4%)	8 (5%)	1 (1.2%)	**<0.0001**	**0.0019**	**0.0002**	0.1678

Firm pancreatic stump, n (%)	41 (24.9%)	112 (72.3%)	31 (33.7%)	0.1387	0.5566	0.1300	0.3234
Pancreatic anastomosis							
Pancreatico-jejunostomy	148 (87.6%)	161 (100%)	91 (97.9%)	**<0.0001**	**<0.0001**	**0.0051**	0.1331
Pancreatico-gastrostomy	16 (9.5%)	0	2 (2.2%)	**0.0007**	**<0.0001**	0.0380	0.1331
Duct occlusion	5 (3%)	0	0	**0.0160**	0.0610	0.1644	NA
Length of hospital stay, median (IQR), days	15 (10-26)	17 (10-29)	18 (11-25.5)	0.3804	0.2813	0.2096	0.7943
Postoperative complications, n (%)							
None	0	0	47 (49.5%)	**<0.0001**	NA	**<0.0001**	**<0.0001**
Grade 1	32 (18.8%)	20 (12.4%)	6 (6.3%)	**0.0037**	0.1310	**0.0053**	0.1374
Grade 2	51 (30%)	68 (42.2%)	24 (25.3%)	0.8077	0.0204	0.4117	**0.0063**
Grade 3a	38 (22.4%)	34 (21.1%)	10 (10.5%)	**0.0302**	0.7855	**0.0165**	0.0300
Grade 3b	24 (14.1%)	9 (5.6%)	5 (5.3%)	**0.0065**	**0.0096**	0.0384	1.0000
Grade 4a	8 (4.7%)	12 (7.5%)	1 (1.1%)	0.3363	0.2944	0.1637	0.0351
Grade 4b	3 (1.8%)	4 (2.5%)	0	0.3809	0.7170	0.5550	0.3000
Grade 5	14 (8.2%)	14 (8.7%)	2 (2.1%)	0.0980	0.8804	0.0582	0.0578
> Grade 2	87 (51.2%)	73 (45.3%)	25 (26.3%)	**0.0002**	0.2883	**<0.0001**	**0.0025**
Failure-to-rescue, n (%)	14 (16.5%)	14 (19.2%)	2 (8%)	0.5386	0.6568	0.5182	0.3458
Post-operative pancreatic fistula, n (%)							
Biochemical leak	29 (17.1%)	41 (25.5%)	4 (4.2%)	**0.0464**	0.0612	**0.0018**	**<0.0001**
Grade B/C	51 (30%)	42 (26.1%)	15 (15.8%)	**0.0139**	0.4286	**0.0103**	0.0557
Grade C	15 (8.8%)	7 (4.3%)	1 (1.1%)	**0.0055**	0.1023	**0.0129**	0.2645
Biliary leak, n (%)	24 (14.1%)	13 (8.1%)	3 (3.2%)	**0.0026**	0.0812	**0.0050**	0.1801
Intestinal leak, n (%)	4 (2.4%)	11 (6.8%)	1 (1.1%)	0.9516	0.0643	0.6574	0.0355
Chyle leak, n (%)	12 (7.1%)	9 (5.6%)	3 (3.2%)	0.1919	0.5838	0.2693	0.5435
Delayed gastric emptying, n (%)							
Grade B/C	25 (14.7%)	34 (21.1%)	13 (13.7%)	0.9095	0.1276	0.8200	0.1378
All grades	36 (21.2%)	53 (32.9%)	16 (16.8%)	0.8248	**0.0160**	0.3942	**0.0051**
Post-pancreatectomy hemorrhage, n (%)	41 (24.1%)	37 (23%)	6 (6.3%)	**0.0014**	0.8076	**0.0002**	**0.0006**

Abdominal fluid collections, n (%) Drained abdominal fluid collection All abdominal fluid collection	43 (25.3%) 67 (39.4%)	27 (16.8%) 53 (32.9%)	16 (16.8%) 32 (33.7%)	0.0626 0.2784	0.0577 0.2194	0.1127 0.3553	0.9881 0.9001
Reoperation, n (%)	36 (21.2%)	22 (13.7%)	7 (7.4%)	**0.0021**	0.0724	**0.0035**	0.1247
Tumor type, n (%) Malignant tumor* PDAC*	148 (87.1%) 67 (39.4%)	144 (90%) 58 (36.3%)	63 (90%) 37 (52.9%)	0.4183 0.1446	0.4029 0.5540	0.5252 0.0561	1.0000 0.0186
Lymph nodes, median (IQR) Examined* Positive*	23 (17-33) 1 (0-4)	20 (16-26) 1 (0-3)	38 (29-48.5) 3.5 (1-6)	**<0.0001** **<0.0001**	**0.0031** 0.5740	**<0.0001** **<0.0001**	**<0.0001** **<0.0001**

***** Data missing on 26 cases for tumor type, on 44 cases on number of examined lymph nodes, and on 8 cases for positive; BMI: Body Mass Index; PDAC: Pancreatic Ductal Adenocarcinoma; **Bold= significant p**