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A Comparative Analysis of Open Versus Minimally Invasive Pancreatoduodenectomies

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ABSTRACT

Background and Objectives: Pancreatoduodenectomy (PD) has been associated with significant morbidity and mortality. To reduce morbidity, minimally invasive pancreatoduodenectomies (MIPD) have become more prevalent. We aimed to compare short-term survival and complications for open (OPD) versus MIPD and to assess the relationship between operative approach and operative time on outcomes.

Methods: Patients undergoing PD between 2017 and 2020 were identified within the National Surgical Quality Improvement Program (NSQIP). The primary outcome was operative time, and the secondary outcomes were death at 30 days, reoperation, readmission, and NSQIP-identified 30-day postoperative complications. A multivariable logistic regression was performed.

Results: A total of 14 977 PDs were performed from 2017 to 2020. MIPD increased from less than 8% of pancreatoduodenectomies performed in 2017 to over 10% of PD by 2020. Of the MIPD cohort, 62% were robotic, and 38% were laparoscopic, with robotic surgery becoming most prevalent by the end of the study period. MIPD was associated with significantly longer operative times than OPD ($p < 0.01$). MIPD was associated with decreased odds of postoperative bleeding and surgical site infection ($p < 0.01$), but higher odds of death at 30 days.

Conclusions: MIPD has been shown to have improved postoperative outcomes compared to OPD but is associated with longer operative times, which can be associated with increased complications.

1 | Introduction

Pancreatoduodenectomy (PD) has been associated with significant morbidity and mortality [1, 2]. While the centralization of PD to specialized centers, as well as improved surgical techniques and aftercare, have significantly reduced the mortality associated with the operation, postoperative morbidity remains high [2–5]. To reduce the morbidity of major operations such as this, there has been a shift in the surgical community toward minimally invasive surgery (MIS) [6]. Minimally invasive distal pancreatectomies are the preferred approach for most lesions of the body and tail of the pancreas [7, 8]. Utilization of MIS for distal pancreatectomy is consistently four to five times that of use for PD (50% vs. 10%) [7].

The benefits of MIS are well-established with some specialty groups considering them as the standard of care [6]. However, PD is a complex surgical procedure with a steep learning curve, and the adoption of a minimally invasive approach for PD has been slower [9]. The increased use of robotic surgery has also gained popularity in recent years, leading to further debate about which minimally invasive approach is better for outcomes.

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The objectives of this study are to (1) compare overall operative time for open versus minimally invasive PD, (2) compare 30-day mortality and complication outcomes for open versus minimally invasive PD, with minimally invasive approach further stratified into robotic and laparoscopic approaches, and (3) to assess the relationship between operative approach and operative length on these outcomes. We hypothesize that overall MIPD and OPD will be equivalent, and that operative time, regardless of approach, will have the most significant impact on outcomes.

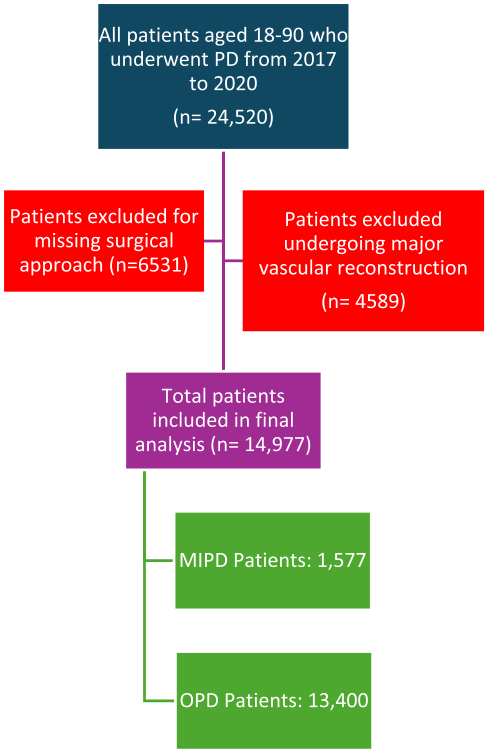

FIGURE 1 | Inclusion criteria for study cohort.

2 | Methods

A retrospective cohort analysis of the American College of Surgeons National Surgical Quality Improvement Program (ASC NSQIP) Pancreatectomy Procedure Target Data File was conducted. The years 2017–2020 were included in the study. The ACS NSQIP is a program that collects data on over 150 variables, including preoperative information and risk factors, intraoperative variables, and 30-day postoperative outcomes [10]. The pancreas procedure targeted data file abstracts data on preoperative, postoperative, and intraoperative variables following pancreatectomies [10, 11]. The Northwestern IRB classified this study as exempt from review because it uses pre-existing de-identified data.

2.1 | Eligibility Criteria

All patients aged 18–90 who underwent a PD at NSQIP reporting hospitals were included (Figure 1). The total number of patients who underwent PD at reporting hospitals was 25 795. Patients were excluded if the surgical approach was missing (open vs. minimally invasive) ($n = 4303$), and patients with missing histologic or staging information were also excluded ($n = 2738$). Any patients who underwent major vascular reconstruction were excluded ($n = 3777$). The total number of patients ultimately included in this study for analysis was 14 977.

TABLE 1 | Patient cohort characteristics and bivariate analysis (overall $N = 14\,977$).

Patient characteristics	Overall	Open surgery ($n = 13\,400$)	Minimally invasive technique ($n = 1577$)
Age (years)			
Mean ± SD	65 ± 11.5	65 ± 11.5	65 ± 11.6
Range	18–90	18–90	18–90
Sex, *n* (%)			
Male	8031 (53.6)	7221 (53.9)	810 (51.4)
Female	6943 (46.4)	6176 (46.1)	767 (48.6)
Surgery year, *n* (%)**			
2017	3610 (24.1)	3288 (24.5)	322 (20.4)
2018	3594 (24.0)	3259 (24.3)	335 (21.2)
2019	3945 (26.4)	3478 (26.0)	467 (29.6)
2020	3825 (25.5)	3372 (25.2)	453 (28.7)
Race, *n* (%)**			
Non-Hispanic White	10 421 (69.6)	9294 (69.4)	1127 (71.5)
Non-Hispanic Black	1183 (7.9)	1058 (7.9)	125 (7.9)
Hispanic	768 (5.1)	717 (5.4)	51 (3.2)

(Continues)

TABLE 1 | (Continued)

Patient characteristics	Overall	Open surgery ($n = 13\,400$)	Minimally invasive technique ($n = 1577$)
Asian	720 (4.8)	620 (4.6)	100 (6.3)
AI/AN/NH/PI	52 (0.4)	48 (0.4)	4 (0.3)
Other/unknown	1830 (12.2)	1660 (12.4)	170 (10.8)
Diabetes, *n* (%)			
None	10 946 (73.1)	9783 (73.0)	1163 (73.8)
NIDDM	2026 (13.5)	1812 (13.5)	224 (14.2)
IDDM	2002 (13.4)	1802 (13.5)	190 (12.1)
Smoker, *n* (%)*	2473 (16.5)	2241 (16.7)	232 (14.7)
COPD, *n* (%)	591 (4.0)	51 (3.2)	540 (4.0)
Hypertension, *n* (%)	7919 (53.0)	7071 (52.8)	848 (53.8)
Preoperative albumin < 3, *n* (%)	2306 (15.4)	2135 (15.9)	171 (10.9)
ASA class, *n* (%)**			
1–2	2990 (20.0)	2601 (19.4)	389 (24.7)
3	10 868 (72.6)	9753 (72.8)	1113 (70.7)
4–5	1116 (7.5)	1043 (7.8)	73 (4.6)
BMI (kg/m^2)			
Mean ± SD	26.91 ± 6	26.86 ± 6	27.27 ± 5.8
Range	16–66	18–66	16–62
Histologic subtype, *n* (%)**			
Adenocarcinoma	6725 (46.6)	6164 (47.7)	561 (37.1)
Benign/other histology	7704 (53.4)	6752 (52.3)	952 (62.9)
Stage of disease (for adenocarcinoma, benign and unknown excluded)			
Stage 0	189 (1.9)	176 (2.0)	13 (1.2)
Stage IA	1441 (14.3)	1264 (14.0)	177 (16.5)
Stage IB	1628 (16.1)	1450 (16.1)	178 (16.6)
Stage IIA	1230 (12.2)	1120 (12.4)	110 (10.2)
Stage IIB	3688 (36.6)	3279 (36.4)	409 (38.1)
Stage III	1367 (13.6)	1221 (13.6)	146 (13.6)
Stage IV	260 (2.6)	246 (2.7)	14 (1.3)
Unknown stage	285 (2.8)	258 (2.8)	27 (2.5)
Received neoadjuvant therapy (includes chemo and radiation), *n* (%)	2848 (26.0)	2614 (26.2)	234 (23.6)
Surgical characteristics			
Operative drain placement, *n* (%)			
No	1469 (9.8)	1424 (10.6)	45 (2.6)
Yes	13 505 (90.2)	11 973 (89.4)	1532 (97.2)
Operative time (min), *n* (%)**			
Mean ± SD	364.15 ± 119	356.46 ± 117	429.43 ± 118
Range	4–1245 min	4–1245	60–1110
Hospital stay characteristics			
Length of hospital stay**			

(Continues)

TABLE 1 | (Continued)

Patient characteristics	Overall	Open surgery ($n = 13\,400$)	Minimally invasive technique ($n = 1577$)
Average ± SD	9.51 ± 6	9.56 ± 6	9.10 ± 6
Median	7 days	8 days	7 days
Range	0–90	0–90	0–70
Return to OR*			
No	14 163 (94.6)	12 697 (94.7)	1466 (93.0)
Yes	811 (5.4)	700 (5.2)	111 (7.0)
Readmission in 30 days*			
No readmission	12 382 (82.7)	11 111 (83.0)	1271 (81.00)
Readmitted in 30 days	2592 (17.3)	2286 (17.1)	306 (19.4)
30-day mortality*			
No	14 739 (98.4)	13 196 (98.5)	1543 (97.8)
Yes	235 (1.6)	201 (1.5)	34 (2.2)
Death POD0			
No	14 970 (99.9)	13 393 (99.9)	1577 (100.00)
Yes	4 (0.03)	4 (0.03)	0 (0.00)
Prolonged hospital stay (longer than 30 days)			
No	14 493 (96.8)	12 973 (96.8)	1520 (96.4)
Yes	481 (3.2)	424 (3.2)	57 (3.6)
Discharge destination			
Home discharge	13 062 (87.5)	11 670 (89.3)	1392 (90.7)
Skilled care facility	840 (5.8)	755 (5.8)	85 (5.5)
Rehab facility	492 (3.4)	462 (3.5)	30 (2.0)
Hospice/expired/ama/other	205 (1.4)	178 (1.4)	27 (1.8)
Postoperative complications			
Venous thromboembolism			
DVT	362 (2.4)	318 (2.4)	44 (2.8)
Pulmonary embolism	186 (1.2)	159 (1.2)	27 (1.7)
Pancreatic fistula, *n* (%)	2314 (15.5)	2082 (15.5)	232 (14.7)
Delayed gastric emptying, *n* (%)	2204 (15.1)	1972 (15.1)	232 (15.1)
Superficial Incisional Surgical site infection, *n* (%)**	1 (0.01)	1 (0.01)	0 (0.00)
Deep incisional surgical site infection, *n* (%)	27 (0.2)	24 (0.2)	3 (0.2)
Organ space surgical site infection, *n* (%)	29 (0.2)	23 (0.2)	3 (0.2)
Bleeding complications**			
No intra or post op transfusions required	12 783 (85.4)	11 395 (85.1)	1388 (88.0)
POD0 bleeding	1526 (10.2)	1397 (10.4)	129 (8.2)
Bleeding POD1-3	662 (4.4)	603 (4.5)	59 (3.7)
Bleeding POD4 or later	3 (0.02)	2 (0.01)	1 (0.1)

*$p < 0.05$;
**$p < 0.01$.

2.2 | Independent Variable and Covariates

The primary independent variable is the surgical approach, categorized as open or minimally invasive PD. For this study, the primary independent variable was coded as the initial intended surgical approach. Any surgical approach that began as open was coded as such, and any surgical approach that began as minimally invasive was coded as such, regardless of whether the procedure was converted to open. Given the known impact of operative time on surgical outcomes, an interaction term was created combining the variables of time and operative approach, to allow for further evaluation of the interplay and mutual influence between these two factors. Using the designations of short (surgeries lasting less than 8 h) and long (surgeries lasting longer than 8 h), based on median operative time, four categories were created: MIPD short, MIPD long, OPD Short, OPD long.

Patient characteristics, medical history, preoperative information, and oncologic characteristics were included in the final statistical analysis. These covariates included age, sex, race/ethnicity, BMI, ASA class, smoking history, presence of hypertension, COPD, diabetes, and hypoalbuminemia (Table 1). Age was coded as both a continuous variable and an ordinal variable, BMI and ASA class were coded as ordinal variables and hypertension, COPD, diabetes, smoking status, and hypoalbuminemia were coded as binary variables. Race/ethnicity was coded as an unordered categorical variable, with non-Hispanic white patients as the reference category as it is the predominant patient population for the disease [12].

For BMI and ASA class, "normal BMI" and ASA 1–2 were used as the reference categories for statistical analysis. Each of these variables was chosen because they have been previously identified as characteristics that not only impact operative morbidity and mortality but also increase the odds of postoperative complications and, therefore, could be confounders [1, 2, 13, 14]. Oncologic variables included in the model were receipt of neoadjuvant therapy (chemotherapy or radiation therapy), stage of disease (when appropriate), and pancreatic histology. Receipt of neoadjuvant therapy was coded as binary (received either chemotherapy or radiation therapy or did not receive therapy), and pancreatic histology was coded as either "adenocarcinoma" or "non-adenocarcinoma/benign/other."

2.3 | Outcomes

The primary outcome for this study was operative time. Operative time was coded as both a continuous variable as an outcome and a ranked ordinal variable as a covariate. Length of stay was coded as a continuous variable. Other secondary outcome variables included return to OR, readmission, and the following complications: death at 30 days, postoperative bleeding, venous thromboembolism, delayed gastric emptying, postoperative pancreatic fistula, and surgical site infection. Any bleeding events requiring transfusion or intervention in the postoperative course were included as "bleeding event," all postoperative surgical site infections were grouped into one variable, including superficial and deep incisional infection as well as organ space infection. Both the presence of deep venous thrombosis and pulmonary embolism were included as "VTE."

2.4 | Statistical Analysis

An initial chi-square analysis for categorical variables was performed to determine significant relationships between predictor variables and individual outcome variables (Table 2). Continuous variables, including hospital length of stay and operative time, were compared using the Kruskall–Wallis test. Two separate regression models were run with the primary independent variable (operative approach), additionally one separate regression model was run for the secondary independent variables (operative/time categories). All models were weighted using propensity scoring to adjust for significant differences in OPD and MIPD sample sizes [15].

For the primary independent variable (operative approach) the first model for the primary outcome was a multivariable

TABLE 2 | Multivariable linear regression of factors related to increased operative time.

	Operative time	
Covariate	**Coefficient [95% CI]**	***p***
Operative approach		
Open PD	1	Ref
MIPD		
All	70.9 [64.7, 77.1]	< 0.01
Robotic	67.7 [60.2, 75.3]	< 0.01
Laparoscopic	71.6 [61.4, 81.7]	< 0.01
Sex		
Male	1	Ref
Female	−29.1 [−32.8, −25.3]	< 0.01
Smoking status		
Non-smoker	1	Ref
Active smoker	5.12 [−0.04, 10.3]	0.052
COPD status		
No COPD	1	Ref
COPD	−3.18 [−13.1, 6.7]	0.528
ASA class		
1–2	1	Ref
3	1.22 [−3.6, 6.1]	0.615
4–5	13.5 [5.2, 21.8]	< 0.01
BMI		
< 25	1	Ref
25–30	27.3 [23.4, 31.2]	< 0.01
> 30	11.8 [−22.4, 45.9]	0.499
Operative year		
2017	1	Ref
2018	6.3 [0.92, 11.7]	0.02
2019	12.0 [6.5, 12.5]	< 0.01
2020	15.3 [9.4, 21.1]	< 0.01
Pancreas histology		
Adenocarcinoma	1	Ref
Benign/other	−12.2 [−18.5, −5.6]	< 0.01

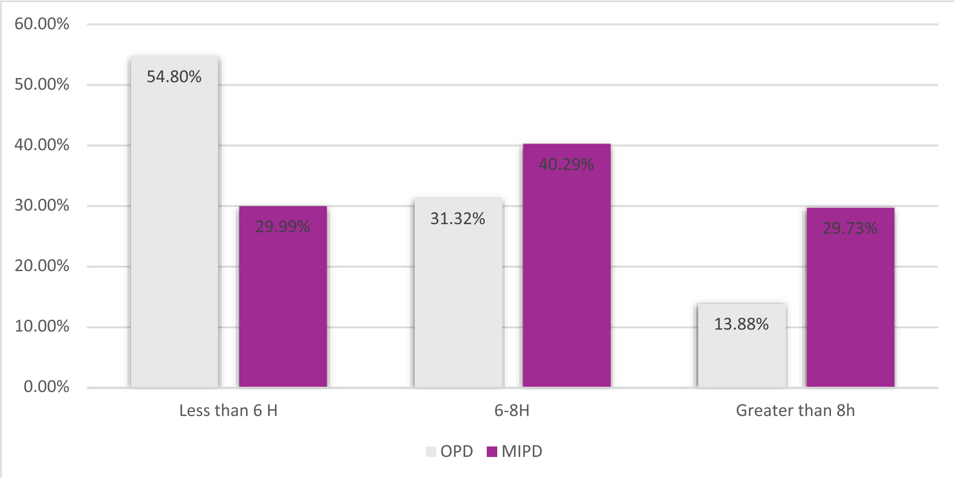

FIGURE 2 | Percent operative approach by operative length (hours).

linear regression, and secondary outcomes was a multivariable logistic regression. Coefficients and odds ratios were reported respectively, with p-values less than 0.05 considered significant. Both models included the same predictor variables (Figure 2).

For the second statistical analysis utilizing the interaction term of time and operative approach, a Poisson regression with robust variance estimates was used [16]. The outcome variables in this model included the postoperative complications, previously described. The Poisson regression was chosen given the rates of complications for each combined category were greater than 15%–20%, and there was concern that a logistic regression with odds ratios would not appropriately correlate with the relative risk of the outcome [16]. Relative risks with p-values less than 0.05 were considered significant. Statistical analysis was conducted via STATA v.17.0 (StataCorp, College Station, TX).

3 | Results

Between 2017 and 2020, a total of 14,977 pancreatoduodenectomies (PD) were performed at 706 hospitals, with 1577 (10.5%) adopting a minimally invasive approach (MIPD). MIPD increased from less than 8% of pancreatoduodenectomies performed from 2017 to 2018 to over 10% of the operative approach for PD by 2020. Of the MIPD cohort, 62% were robotic, and 38% were laparoscopic procedures, with robotic surgery becoming most prevalent toward the end of the study period (73% of MIS and 8.6% of all procedures by 2020).

The overall cohort was predominantly non-Hispanic White (70%) 47% female with a mean age of 65 years old, with similar sociodemographic characteristics and comorbid conditions between MIPD and open pancreatoduodenectomy (OPD) groups (Table 1**)**. In terms of histology, OPD cases had malignant pathology 75% of the time, while only 63% of MIPD cases were for malignancy. Operative time analysis revealed that 54.8% of OPD cases were less than 6 h, compared to only 30% of MIPD cases. The average length of stay was 9.5 days for OPD and 9.1 days for MIPD (median 8 vs. 7) ($p < 0.001$).

Bivariate analysis of postoperative complications (Table 1**)** highlighted higher rates for MIPD in return to the operating room (7 vs. 5%), 30-day readmission (19 vs. 17%), and operations lasting longer than 8 h (30 vs. 14%) ($p < 0.01$). The death rate at 30 days was 2.16% for MIPD and 1.5% for OPD ($p = 0.047$). Notably, OPD showed higher rates of surgical site infections (2.52% vs. 0.91%, $p < 0.01$) and bleeding events (14.4% vs. 11.5%, $p < 0.01$). Despite less malignant pathology, MIPD exhibited no difference in fistula rate or delayed gastric emptying compared to OPD.

In an adjusted propensity score weighted linear regression model (Table 2), MIPD overall was associated with an 80-min increase in median operative time compared to OPD. When delineating laparoscopic and robotic approaches compared to open PD, laparoscopic PD, and robotic PD were associated with a 72-min and 67-min increase in median operative time, respectively ($p < 0.01$).

When comparing open PD to laparoscopic and robotic PD (Table 3) there were no significant differences in odds of bleeding, surgical site infection, VTE, pancreatic fistula, reoperation, or readmission for laparoscopic surgery compared to OPD. Robotic surgery was associated with 50% decreased odds of bleeding and 80% decreased odds of surgical site infection but increased odds of VTE, return to the OR, and readmission compared to OPD ($p < 0.01$ for all).

In an adjusted Poisson regression with robust variances (Table 4) using the combined time and approach categories, with the reference category as short MIPD operations (< 8 h), long MIPD operations (> 8 h) had a 190% increased risk of return to OR. There was no significant difference in risk of returning to OR for either open category compared to MIPD short operations. Compared to MIPD/Short operation, OPD/short, MIPD/long, and OPD/long operations all had increased risk of bleeding events, postoperative pancreatic fistulas, postoperative surgical site infections, and delayed gastric emptying. MIPD/Long operations had a 219% increased risk of VTE compared to MIPD/short. There was no statistically significant increased risk for open long or short operations for VTE.

TABLE 3 | Multivariable logistic regression of odds of developing postoperative complication based on operative approach.

		Odds ratio [95% CI]						
Covariate		**Death at 30 days**	**Return to OR**	**Readmission in 30 days**	**VTE**	**Bleeding event**	**Postoperative pancreatic fistula**	**Postoperative Surgical Site Infection**
Operative approach								
Open PD		1 (REF)						
MIPD	All	1.53 [1.05, 2.24]**	1.43 [1.13, 1.80]**	1.12 [0.97, 1.28]	1.07 [0.79, 1.43]	0.68 [0.58, 0.51]**	0.79 [0.68, 0.94]**	0.32 [0.19, 0.55]**
	Robotic	1.15 [0.68, 1.93]	1.35 [1.04, 1.80]*	1.21 [1.03, 1.43]*	1.25 [0.88, 1.75]	0.52 [0.41, 0.65]**	0.69 [0.56, 0.85]**	0.21 [0.09, 0.47] **
	Lap	1.71 [0.96, 3.04]	1.35 [0.93, 1.97	0.93 0.73, 1.18]	0.82 [0.47, 1.41]	1.03 [0.80, 1.32]	0.81 [0.62, 1.05]	0.52 [0.25, 1.07]
Operative time								
Less than 6 h		1 (REF)						
6–8 h		1.16 [0.87, 1.56]	0.97 [0.81, 1.17]	1.06 [0.96, 1.17]	1.22 [0.98, 1.52]	1.59 [1.42, 1.77]**	1.06 [0.95, 1.18]	1.43 [1.12, 1.84]*
Greater than 8 h		1.07 [0.76, 1.57]	1.21 [0.97, 1.50]	1.17 [1.03, 1.34]*	1.65 [1.27, 2.13]**	2.28 [2.00, 2.61]**	1.24 [1.09, 1.42]**	1.91 [1.42, 2.56]**
Sex								
Male		1 (REF)						
Female		0.63 [0.47, 0.83] **	0.69 [0.59, 0.82]**	0.84 [0.77, 0.92]**	0.93 [0.77, 1.13]	1.16 [1.05, 1.29]**	0.78 [0.71, 0.86]**	0.69 [0.55, 0.87]*
Smoking status								
Non-smoker		1 (REF)						
Active smoker		0.88 [0.59, 1.91]	0.99 [0.79, 1.24]	1.03 [0.92, 1.16]	0.82 [0.62, 1.09]	0.91 [0.78, 1.03]	0.92 [0.81, 1.05]	1.02 [0.76, 1.38]
COPD status								
No COPD		1 (REF)						
COPD		2.04 [1.25, 3.31]**	1.29 [0.89, 1.87]	1.58 [1.29, 1.94]**	1.11 [0.64, 1.71]	1.23 [0.98, 1.55]	1.30 [1.02, 1.64]*	1.65 [1.05, 2.61]*
ASA class								
1–2		1 (REF)						
3		1.46 [0.96, 2.22]	1.2 [0.97, 1.50]	1.10 [0.98, 1.23]	0.98 [0.77, 1.26]	1.91 [1.65, 2.22]**	0.88 [0.78, 0.99]*	1.18 [0.87, 1.59]
4–5		2.07 [1.19, 3.57]**	0.85 [0.60, 1.23]	0.91 [0.74, 1.11]	0.88 [0.57, 1.36]	3.42 [2.78, 4.19]**	0.72 [0.58, 0.89]**	1.22 [0.76, 1.94]
BMI								
< 25		1	1	1	1	1	1	1
25–30		1.22 [0.92, 1.62]	1.09 [0.93, 1.29]	1.11 [0.98, 1.23]	1.23 [1.01, 1.51]*	0.78 [0.71, 0.86]**	1.71 [1.53, 1.89]**	1.05 [0.83, 1.32]
> 30		1.98 [0.45, 8.7]	1.35 [0.41, 4.47]	1.05 [0.44, 2.53]	1.71 [0.41, 7.27]	0.52 [0.22, 1.26]	1.84 [0.84, 4.10]	1
Operative year								
2017		1 (REF)						

(Continues)

TABLE 3 | (Continued)

Covariate	Odds ratio [95% CI]						
	Death at 30 days	Return to OR	Readmission in 30 days	VTE	Bleeding event	Postoperative pancreatic fistula	Postoperative Surgical Site Infection
2018	1.06 [0.72, 1.58]	0.75 [0.59, 0.93]**	1.19 [1.05, 1.33]**	0.82 [0.62, 1.07]	0.95 [0.84, 1.09]	0.69 [0.61, 0.79]**	0.89 [0.65, 1.21]
2019	1.27 [0.76, 1.64]	0.67 [0.54, 0.83]**	1.13 [1.00, 1.28]*	0.87 [0.68, 1.13]	0.97 [0.85, 1.11]	0.71 [0.62, 0.81]**	0.97 [0.73, 1.31]
2020	1.39 [0.96, 2.01]	0.77 [0.62, 0.95]*	1.18 [1.04, 1.33]**	0.87 [0.67, 1.12]	0.99 [0.87, 1.11]	0.73 [0.65, 0.84]**	0.79 [0.59, 1.09]
Histology							
Adenocarcinoma				1 (REF)			
Benign/other	1.10 [0.81, 1.49]	1.24 [1.05, 1.45]**	1.30 [1.19, 1.42]**	1.51 [1.24, 1.84]**	0.96 [0.87, 1.06]	2.03 [1.83, 2.24]**	1.31 [1.05, 1.63]*

*$p < 0.05$;
**$p < 0.01$.

4 | Discussion

This study highlights the impact of operative time on operative outcomes. Overall postoperative complications were similar between OPD and MIPD, if not higher for OPD. However, this benefit of a minimally invasive approach significantly decreases as operative time increased. This is taken in conjunction with the fact that, on average, MIPD took over an hour longer than OPD, even when accounting for conversion to open procedure, regardless of whether the approach was laparoscopic or robotic. Fadi et al. found similar results in their comparison of OPD versus MIPD—the benefits of a minimally invasive approach decreased significantly as operative time increased [17].

Our hypothesis was that MIPD and OPD would be equivalent, but that operative time would significantly impact the benefits of MIPD compared to OPD, including blood loss and VTE risk. To better understand the relationship between approach and operative time, combined time/approach categories were created. This demonstrated a significant increase in the risk of VTE, bleeding, pancreatic fistulas, surgical site infections, and delayed gastric emptying for long operations compared to short operations. For MIPD, the risk of VTE increased by 200% when the operation took longer than 8 h. This decreasing benefit of the MIS approach as operative time increases is likely secondary to provider experience, operating room infrastructure, and patient selection [18, 19].

This effect is dissimilar from other cancers, such as colon cancer and esophageal cancer, and robotic approaches to rectal cancer—where the benefits of a minimally invasive approach are preserved compared to open approaches, despite increased operative time [17, 20].

Given that conversions were coded as their intended procedure and not excluded or coded as "open," this could account for some of the increased rates of complications as conversions lengthen the operative time. Unplanned intraoperative conversions have worse outcomes than completed MIPD and upfront OPD [17]. However, MIPD has an associated conversion rate of almost 40% in the literature [21]. In our analysis, 61.3% of MIS operations were converted to open. While many of the increased complication rates could be accounted for by the inclusion of cases that were converted to open, the fact that MIPD had a greater than 60% risk of conversion means this is an important potential risk to be aware of when undertaking the minimally invasive approach. Understanding the risk of both conversion and increased complication rates for prolonged operative time associated with MIPD –is important to consider when attempting this approach [18, 22].

4.1 | Limitations

There are several limitations to our study. First, with all retrospective analyses, it is only possible to assess correlation, not causation. Additionally, conversions were not excluded in our original analysis, they were analyzed separately in a post-hoc analysis to determine their impact on our findings. However, conversions are known to lengthen operative time and increase

TABLE 4 | Modified Poisson regression with robust variances of relative risk of developing postoperative complications.

	Complication						
	RR [95% CI]						
Characteristic	**Return to OR**	**Readmission in 30 days**	**VTE**	**Bleeding event**	**Postop pancreatic fistula**	**Surgical site infection**	**DGE**
Operative time and approach							
MIS short				1 (REF)			
Open short	1.10 [0.70, 1.75]	1.03 [0.84, 1.26]	1.25 [0.69, 2.27]	1.06 [1.03, 1.10]**	1.67 [1.24, 2.24]**	3.29 [1.65, 4.76]**	0.97 [0.96, 0.99]**
MIS long	2.92 [1.66, 5.13]**	1.33 [0.99, 1.79]	3.19 [1.54, 6.62]**	1.10 [1.03, 1.16]**	1.86 [1.26, 2.76]**	2.81 [1.05, 3.24]**	0.93 [0.89, 0.96]**
Open long	0.98 [0.56, 1.71]	1.07 [0.84, 1.37]	1.52 [0.77, 2.98]	1.20 [1.15, 1.26]**	1.78 [1.28, 2.47]**	5.73 [1.11, 6.78]**	0.95 [0.94, 0.97]**
Sex							
Male				1 (REF)			
Female	0.72 [0.61, 0.83]*	0.87 [0.81, 0.93]*	0.91 [0.75, 1.08]	1.02 [1.01, 1.03]*	0.81 [0.74, 0.87]**	0.66 [0.53, 0.83]**	1.02 [1.01, 1.03]*
Smoking status							
Non-smoker				1 (REF)			
Active Smoker	0.96 [0.78, 1.17]	1.05 [0.96, 1.15]	0.78 [0.59, 1.02]	0.98 [0.96, 0.99]*	0.95 [0.85, 1.05]	1.02 [0.77, 1.35	1.02 [1.01, 1.02]**
COPD diagnosis							
No COPD				1 (REF)			
Yes COPD	1.29 [0.92, 1.82]	1.42 [1.21, 1.65]*	1.09 [0.69, 1.76]	1.03 [0.99, 1.06]	1.23 [1.02, 1.48]**	1.67 [1.08, 2.60]*	0.97 [0.95, 0.98]*
ASA class							
1–2				1 (REF)			
3	1.21 [0.99, 1.48]	1.06 [0.97, 1.16]	1.05 [0.83, 1.32]	1.07 [1.06, 1.09]**	0.89 [0.81, 0.98]**	1.26 [0.94, 1.68]	0.98 [0.98, 0.99]**
4–5	0.87 [0.61, 1.25]	0.89 [0.76, 1.07]	0.96 [0.63, 1.46]	1.17 [1.13, 1.21]**	0.75 [0.63, 0.89]**	1.34 [0.85, 2.11]	0.99 [0.98, 1.01]
BMI							
< 25				1 (REF)			
25-30	1.08 [0.93, 1.27]	1.11 [1.03, 1.19]*	1.25 [1.02, 1.52]*	0.97 [0.95, 0.98]**	1.58 [1.45, 1.73]**	1.07 [0.86, 1.34]	0.99 [0.98, 0.99]*
> 30	1.22 [0.41, 3.69]	1.03 [0.49, 2.14]	1.63 [0.40, 6.55]	0.91 [0.81, 1.03]	1.66 [0.88, 3.11]	0.02 [0.01, 0.03]**	1.01 [0.95, 1.06]
Operative year							
2017				1 (REF)			
2018	0.76 [0.62, 0.93]**	1.16 [1.04, 1.28]*	0.83 [0.64, 1.08]	0.99 [0.97, 1.01]	0.75 [1.45, 1.73]	0.90 [0.67, 1.22]	1.01 [0.99, 1.02]
2019	0.68 [0.56, 0.84]**	1.12 [1.04, 1.28]*	0.88 [0.68, 1.13]	1.01 [0.98, 1.02]	0.76 [0.68, 0.84]	0.98 [0.74, 1.31	1.00 [0.99, 1.01]

(Continues)

TABLE 4 | (Continued)

	Complication						
	RR [95% CI]						
Characteristic	**Return to OR**	**Readmission in 30 days**	**VTE**	**Bleeding event**	**Postop pancreatic fistula**	**Surgical site infection**	**DGE**
2020	0.78 [0.64, 0.95]**	1.15 [1.04, 1.27]**	0.88 [0.68, 1.14]	1.00 [0.98, 1.02]	0.78 [0.69, 0.87]	0.81 [0.59, 1.08]	1.01 [0.99, 1.02]
Pancreas histology							
Adenocarcinoma				1 (REF)			
Benign or other	1.22 [1.05, 1.42]*	1.25 [1.17, 1.35]**	1.44 [1.19, 1.74]**	0.99 [0.98, 1.01]	1.83 [1.68, 1.99]**	1.23 [0.99, 1.52]	0.98 [0.97, 0.98]**

*$p < 0.04$;
**$p < 0.01$.

rates of complications, which is why the post-hoc analysis was performed. Additionally, despite propensity score weighting, there was significantly smaller sample size of MIPD compared to OPD.

While many of our findings are statistically significant, it is important to consider that the absolute difference in number of outcomes for many of the variables is very small, so clinically, some findings may not be significant.

Finally, robotic procedures, specifically, were more recently introduced and therefore have a learning curve associated with the procedure. Data from years after 2020 may show improvement in various minimally invasive techniques as those learning curves decrease, however the data available at the time of this study was only to 2020.

5 | Conclusion

While MIPD is a safe approach which may serve to decrease some of the significant morbidity associated with PD, MIPD is associated with longer operative times, which can also be associated with increased complications for cases over 8 h. This highlights the importance of patient selection and utilization of experienced centers.

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Conflicts of Interest

Dr David Bentrem is Editor in Chief of *Journal of Surgical Oncology*. The remaining authors have nothing to disclose.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

References

1. C. J. Yeo, J. L. Cameron, T. A. Sohn, et al., "Six Hundred Fifty Consecutive Pancreaticoduodenectomies in the 1990s: Pathology, Complications, and Outcomes," *Annals of Surgery* 226, no. 3 (September 1997): 248–260, discussion 257–260, https://doi.org/10.1097/00000658-199709000-00004.

2. S. A. M. Karim, K. S. Abdulla, Q. H. Abdulkarim, and F. H. Rahim, "The Outcomes and Complications of Pancreaticoduodenectomy (Whipple Procedure): Cross Sectional Study," *International Journal of Surgery* 52 (April 2018): 383–387, https://doi.org/10.1016/j.ijsu.2018.01.041.

3. P. C. Conroy, L. Calthorpe, J. A. Lin, et al., "Determining Hospital Volume Threshold for Safety of Minimally Invasive Pancreaticoduodenectomy: A Contemporary Cutpoint Analysis," *Annals of Surgical Oncology* 29, no. 3 (March 2022): 1566–1574, https://doi.org/10.1245/s10434-021-10984-1.

4. D. W. Crist, J. V. Sitzmann, and J. L. Cameron, "Improved Hospital Morbidity, Mortality, and Survival After the Whipple Procedure,"

Annals of Surgery 206, no. 3 (September 1987): 358–365, https://doi.org/10.1097/00000658-198709000-00014.

5. “Safety in Numbers: Hospital Performance on Leapfrog's Surgical Volume Standard Based on Results of the 2019 Leapfrog Hospital Survey,” Leapfrog, 2020, https://www.leapfroggroup.org/sites/default/files/Files/Leapfrog%20Report%20on%20Safe%20Surgical%20Volumes%202020.pdf.

6. C. Correa-Gallego, H. E. Dinkelspiel, I. Sulimanoff, et al., “Minimally-Invasive vs Open Pancreaticoduodenectomy: Systematic Review and Meta-Analysis,” *Journal of the American College of Surgeons* 218, no. 1 (January 2014): 129–139, https://doi.org/10.1016/j.jamcollsurg.2013.09.005.

7. Q. Chen, K. Merath, F. Bagante, et al., “A Comparison of Open and Minimally Invasive Surgery for Hepatic and Pancreatic Resections Among the Medicare Population,” *Journal of Gastrointestinal Surgery* 22, no. 12 (December 2018): 2088–2096, https://doi.org/10.1007/s11605-018-3883-x.

8. J. van Hilst, N. de Graaf, M. Abu Hilal, and M. G. Besselink, “The Landmark Series: Minimally Invasive Pancreatic Resection,” *Annals of Surgical Oncology* 28, no. 3 (March 2021): 1447–1456, https://doi.org/10.1245/s10434-020-09335-3.

9. K. S. Chan, Z. K. Wang, N. Syn, and B. K. P. Goh, “Learning Curve of Laparoscopic and Robotic Pancreas Resections: A Systematic Review,” *Surgery* 170, no. 1 (July 2021): 194–206, https://doi.org/10.1016/j.surg.2020.11.046.

10. “ACS NSQIP Operations Manual: Variables and Definitions,” ACS, 2020.

11. User Guide for the 2020 ACS NSQIP Participant User Data File (PUF), https://www.facs.org/media/yaol5yoj/nsqip_puf_userguide_2020.pdf.

12. R. L. Siegel, K. D. Miller, and A. Jemal, “Cancer Statistics, 2018,” *CA: A Cancer Journal for Clinicians* 68, no. 1 (January 2018): 7–30, https://doi.org/10.3322/caac.21442.

13. Y. You, I. W. Han, D. W. Choi, et al., “Nomogram for Predicting Postoperative Pancreatic Fistula,” *HPB* 21, no. 11 (November 2019): 1436–1445, https://doi.org/10.1016/j.hpb.2019.03.351.

14. R. Simon, “Complications After Pancreaticoduodenectomy,” *Surgical Clinics of North America* 101, no. 5 (October 2021): 865–874, https://doi.org/10.1016/j.suc.2021.06.011.

15. P. C. Austin and E. A. Stuart, “Estimating the Effect of Treatment on Binary Outcomes Using Full Matching on the Propensity Score,” *Statistical Methods in Medical Research* 26, no. 6 (December 2017): 2505–2525, https://doi.org/10.1177/0962280215601134.

16. G. Zou, “A Modified Poisson Regression Approach to Prospective Studies With Binary Data,” *American Journal of Epidemiology* 159, no. 7 (April 2004): 702–706, https://doi.org/10.1093/aje/kwh090.

17. M. D. Williams, A. R. Bhama, S. Naffouje, et al., “Effect of Operative Time on Outcomes of Minimally Invasive Versus Open Pancreatoduodenectomy,” *Journal of Gastrointestinal Surgery* 27, no. 1 (January 2023): 93–104, https://doi.org/10.1007/s11605-022-05504-9.

18. H. Topal, R. Aerts, A. Laenen, et al., “Survival After Minimally Invasive vs Open Surgery for Pancreatic Adenocarcinoma,” *JAMA Network Open* 5, no. 12 (December 2022): e2248147, https://doi.org/10.1001/jamanetworkopen.2022.48147.

19. R. J. Torphy, C. Friedman, A. Halpern, et al., “Comparing Short-Term and Oncologic Outcomes of Minimally Invasive Versus Open Pancreaticoduodenectomy Across Low and High Volume Centers,” *Annals of Surgery* 270, no. 6 (December 2019): 1147–1155, https://doi.org/10.1097/SLA.0000000000002810.

20. E. Duchalais, N. Machairas, S. R. Kelley, et al., “Does Prolonged Operative Time Impact Postoperative Morbidity in Patients Undergoing Robotic-Assisted Rectal Resection for Cancer?,” *Surgical Endoscopy* 32, no. 8 (August 2018): 3659–3666, https://doi.org/10.1007/s00464-018-6098-z.

21. G. P. Wright and A. H. Zureikat, “Development of Minimally Invasive Pancreatic Surgery: An Evidence-Based Systematic Review of Laparoscopic Versus Robotic Approaches,” *Journal of Gastrointestinal Surgery* 20, no. 9 (September 2016): 1658–1665, https://doi.org/10.1007/s11605-016-3204-1.

22. Z. Zhao, Z. Yin, Z. Hang, G. Ji, Q. Feng, and Q. Zhao, “A Systemic Review and an Updated Meta-Analysis: Minimally Invasive vs Open Pancreaticoduodenectomy,” *Scientific Reports* 7, no. 1 (May 2017): 2220, https://doi.org/10.1038/s41598-017-02488-4.