National Pancreatic Fistula Rates after Minimally Invasive Pancreaticoduodenectomy: A NSQIP Analysis

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BACKGROUND: There is a substantial learning curve associated with minimally invasive pancreaticoduodenectomy (MIPD). We sought to determine if national MIPD pancreatic fistula rates are decreasing with time.

STUDY DESIGN: All patients undergoing elective MIPD and accrued into the pancreatectomy-targeted NSQIP database between 2014 and 2017 were included in the study. Trends in MIPD outcomes by year were examined using Cochran-Armitage and Mann-Kendall tests for trend. Multivariable logistic regression was used to assess for an independent association between increasing year of operation and pancreatic fistula.

RESULTS: There were 1,096 patients who underwent MIPD between 2014 and 2017. There was a significant trend toward decreasing pancreatic fistula rates (23.6% vs 19.2% vs 14.9% vs 12.7%, $p < 0.01$) and clinically relevant pancreatic fistula rates (18.3% vs 15.4% vs 11.1% vs 9.1%, $p < 0.01$) by increasing year. In multivariable analysis, increasing year of operation was independently protective against pancreatic fistula (odds ratio [OR] 0.76 per year, $p < 0.01$) and clinically relevant pancreatic fistula (OR 0.73 per year, $p < 0.01$). Patients without pancreas ducts < 3 mm or soft pancreas gland texture experienced a significant decreasing trend in pancreatic fistula rates (23.7% vs 13.2% vs 10.3% vs 8.0%, $p < 0.01$) and clinically relevant pancreatic fistula rates (18.3% vs 9.1% vs 5.2% vs 6.0%, $p < 0.01$), respectively, by increasing year. However, there was not a significant trend in pancreatic fistula rate or clinically relevant fistula rate among patients having either pancreas ducts < 3 mm or soft gland texture.

CONCLUSIONS: National MIPD pancreatic fistula rates are improving with time. A major contributing factor for this finding is better outcomes in patients who are at lower risk of pancreatic fistula, which could be a reflection of evolving minimally invasive anastomotic techniques. (J Am Coll Surg 2019;229:192−199. © 2019 by the American College of Surgeons. Published by Elsevier Inc. All rights reserved.)

Minimally invasive pancreaticoduodenectomy (MIPD), including robotic-assisted and totally laparoscopic pancreaticoduodenectomy, has a significant learning curve,[1-3] and MIPD requires highly advanced minimally invasive surgical skills coupled with a thorough knowledge of pancreatic surgery. The "Achilles heel" of pancreaticoduodenectomy is pancreatic fistula, which is a major driver of morbidity and mortality.[4,5] Accordingly, some studies have shown MIPD to be associated with increased rates of pancreatic fistulas compared with open pancreaticoduodenectomy (OPD).[6-9] However, there is controversy regarding these findings because other studies have

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Abbreviations and Acronyms

MIPD = minimally invasive pancreaticoduodenectomy
OPD = open pancreaticoduodenectomy
OR = odds ratio
SSI = surgical site infection

demonstrated that MIPD is associated with decreased complications, operative blood loss, and length of stay.[10-12] The learning curve for MIPD could be a major contributor to such discrepancies.

The American College of Surgeons National Surgical Quality Improvement Program (NSQIP) is a methodically rigorous and robust method of complication gathering, which is performed by trained reviewers.[13] The NSQIP pancreatectomy-targeted dataset participant use file (PUF) includes cases accrued since 2014, and tracks defined, pancreatectomy-specific variables and outcomes.[14] Therefore, pancreatectomy-targeted NSQIP could provide invaluable information regarding the progress of MIPD at the national level, and shed light on whether MIPD outcomes are improving.

This study sought to examine whether national MIPD pancreatic fistula rates are improving with time. We compared outcomes for patients in the pancreatectomy-targeted NSQIP database undergoing MIPD in 2014, 2015, 2016, and 2017 to determine whether the rate of pancreatic fistula is decreasing nationally with time. We hypothesized that national pancreatic fistula rates after MIPD would decrease with time. Because anastomoses involving larger pancreatic ducts and more firm pancreas gland texture (ie low fistula risk) are learned more quickly than those involving small pancreatic ducts or soft pancreas gland texture (ie high fistula risk), we also hypothesized that a decrease in national pancreatic fistula rates would be driven largely by a decrease in pancreatic fistula rates in low risk glands.

METHODS

Study design

This was a retrospective study that included patients undergoing elective MIPD and accrued to data collection at 142 total hospitals using the 2014 to 2017 pancreatectomy-targeted NSQIP database.[14] The NSQIP database is a quality improvement database that collects national preoperative and postoperative data through 30 days after surgery.[13,15] The NSQIP database is maintained by certified clinical reviewers and undergoes quality auditing, as previously described.[13]

Patient population

All patients undergoing MIPD (defined as laparoscopic and robotic pancreaticoduodenectomy, including open-assisted and open conversion) in the 2014 to 2017 pancreatectomy-targeted ACS NSQIP databases were identified using CPT codes (48150, 48152, 48153, and 48154) and included. Patients who underwent nonelective and hybrid procedures were excluded, as done previously (Fig. 1).[16,17] Patients undergoing elective OPD were also identified and used as a comparison group, when assessing overall trends in national outcomes. The basic NSQIP participant user files for 2014 to 2017 were merged with the pancreas-targeted NSQIP user files for each respective year. Patient outcomes were compared based on whether MIPD was performed in 2014, 2015, 2016, or 2017.

Outcomes

Complications included superficial incisional surgical site infection (SSI), deep incisional SSI, organ space SSI, wound dehiscence, unplanned intubation, pulmonary embolism, ventilator > 48 hours, progressive renal insufficiency, acute renal failure, urinary tract infection, stroke/cerebrovascular accident, cardiac arrest requiring CPR, myocardial infarction, blood transfusions, deep venous thrombosis, sepsis, septic shock, return to operating room (OR), still in hospital after 30 days, pneumonia, delayed gastric emptying, and pancreatic fistula. Pancreatic fistula was defined by NSQIP as persistent drainage (a drain output of any measurable volume of fluid on or after postoperative day 3) of amylase-rich fluid (an amylase content greater than 3 times the serum amylase activity) and 1 of the following 3 criteria: drain continued longer than 7 days; percutaneous drainage performed; or reoperation performed.[18] Alternatively, pancreatic fistula was also present if a clinical diagnosis of pancreatic fistula was made by an attending surgeon and 1 of the following 4 criteria: drain continued longer than 7 days; spontaneous wound drainage; percutaneous drainage performed; reoperation.[18] In 2016, the definition of pancreatic fistula was slightly modified to also include any patients with persistent drainage of amylase-rich fluid or an attending diagnosis of pancreatic fistula in the setting of patients being made NPO with total parenteral nutrition.[19] Clinically relevant pancreatic fistula was defined as the presence of a fistula in addition to 1 of the following: a drain in place longer than 21 days, a hospital length of stay of at least 14 days, organ space SSI, postoperative percutaneous drain placement, reoperation, sepsis, shock, or single and multisystem organ failure (respiratory or renal failure), as has been done previously using this database.[20] Multivisceral resection was defined as MIPD with concomitant small bowel, colon, or liver resection.

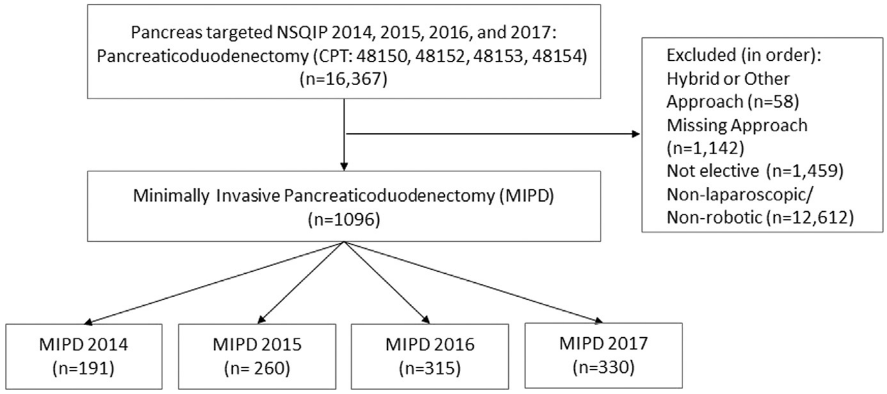

Figure 1. CONSORT diagram.

Statistical analyses

Covariates were compared between MIPD patients by year using chi-square test for categorical variables and 1-way ANOVA test for continuous variables. Trends in MIPD outcomes by year were examined using Cochran-Armitage test for trend for categorical outcomes and Mann-Kendall test for trend for continuous variables. Multivariable logistic regression was used to examine the association between increasing year of operation with pancreatic fistula and clinically relevant pancreatic fistula. All p values were 2-sided, and a value of $p < 0.05$ was considered statistically different. All statistical models were performed using SAS version 9.4 (SAS Inc).

RESULTS

In total, 13,708 patients underwent elective MIPD or OPD and were accrued into NSQIP for the years 2014, 2015, 2016, and 2017. Of these, 1,096 were MIPD (8.0%). Five hundred thirty-five (48.8%) of MIPDs were robotic. Of patients who underwent MIPD, 191 (17.4%) were in 2014, 260 (23.7%) were in 2015, 315 (28.7%) were in 2016, and 330 (30.1%) were in 2017. When comparing MIPD patients from different years, MIPD patients were less likely to undergo vascular resection (18.3% in 2014 vs 16.5% in 2015 vs 10.2% in 2016 vs 11.8% in 2017, p = 0.022) and multivisceral resection (4.2% in 2014 vs 1.2% in 2015 vs 1.0% in 2016 vs 1.8% in 2017, p = 0.047) than during the later years (Table 1). However, MIPD patients were more likely to undergo robotic resection in the later years (42.4% in 2014 vs 43.5% in 2015 vs 56.8% in 2016 vs 49.1% in 2017, p = 0.003).

When testing for a trend in MIPD pancreatic fistula rates, there was a significant decrease in pancreatic fistula rates (23.6% in 2014 vs 19.2% in 2015 vs 14.9% in 2016 vs 12.7% in 2017, p = 0.001) and clinically relevant pancreatic fistula rates (18.3% in 2014 vs 15.4% in 2015 vs 11.1% in 2016 vs 9.1% in 2017, p = 0.001) with increasing year of operation (Fig. 1). By comparison, there was no significant trend in pancreatic fistula rate (17.4% in 2014 vs 18.1% in 2015 vs 17.3% in 2016 vs 17.4% in 2017, p = 0.743) or clinically relevant pancreatic fistula rate (13.3% in 2014 vs 14.2% in 2015 vs 13.5% in 2016 vs 14.0% in 2017, p = 0.679) by year among patients undergoing elective OPD with increasing year (Fig. 2). There was not a significant trend by year in any of the other outcomes examined among MIPD patients, except for a trend toward lower rates of cardiac arrest requiring CPR with increasing year (2.1 in 2014 vs 1.9% in 2015 vs 0.3% in 2016 vs 0.6% in 2017, p = 0.041) (eTable 1, online only). In a multivariable analysis, increasing year of operation was independently protective against pancreatic fistula (odds ratio [OR] 0.73, p = 0.001) and clinically relevant pancreatic fistula (OR 0.76, p = 0.001) among MIPD patients (Table 2).

Other covariates that were independently associated with pancreatic fistula after MIPD in multivariable analysis besides increasing year of operation, included T3 and T4 malignant tumors (OR 0.55, p = 0.025), open assisted/conversion (OR 2.16, p = 0.001), soft pancreas gland texture (OR 2.26, p = 0.001), and neoadjuvant chemotherapy (OR 0.39, p = 0.007). Other covariates independently associated with clinically relevant pancreatic fistula after MIPD in multivariable analysis besides increasing year of operation included male sex (OR 1.78, p = 0.004), T3 and T4 malignant tumors (OR 0.54, p = 0.038), open assisted/conversion (OR 2.48, p = 0.001), and nonhard pancreas gland texture (soft [OR 2.85, p = 0.001] intermediate [OR 2.64, p = 0.020], and unknown [OR 2.15, p = 0.028] pancreas gland texture).

One potential explanation for improved MIPD outcomes with time is that minimally invasive pancreatic anastomotic techniques improved, which could potentially explain the decreased rate of pancreatic fistula with

Table 1. Characteristics of Patients Undergoing Minimally Invasive Pancreaticoduodenectomy by Year (n = 1,096)

Characteristic	2014 (n = 191)	2015 (n = 260)	2016 (n = 315)	2017 (n = 330)	p Value*
Age, y, mean (SD)	64.2 (11.0)	62.7 (12.6)	64.3 (11.8)	65.4 (11.5)	0.063
Sex, n (%)					0.838
Male	106 (55.5)	134 (51.5)	165 (52.4)	171 (51.8)	
Female	85 (44.5)	126 (48.5)	150 (47.6)	159 (48.2)	
Race, n (%)					0.278
White	162 (84.8)	219 (84.2)	252 (80.0)	263 (79.7)	
Nonwhite	29 (15.2)	41 (15.8)	60 (20.0)	67 (20.3)	
BMI, kg/m^2, mean (SD)	28.5 (7.0)	27.9 (5.7)	27.5 (6.2)	27.7 (5.3)	0.278
Comorbidity, n (%)					
Dyspnea	9 (4.7)	11 (4.2)	12 (3.8)	16 (4.9)	0.923
Diabetes	41 (21.5)	60 (23.1)	68 (21.6)	85 (25.8)	0.573
Obstructive jaundice	78 (40.8)	96 (36.9)	106 (33.7)	109 (33.0)	0.266
Weight loss	16 (8.4)	29 (11.2)	31 (9.8)	33 (10.0)	0.813
ASA class ≥ 3	150 (78.5)	194 (74.6)	247 (78.4)	239 (72.4)	0.242
Pathology, n (%)					0.146
Benign lesion < 5 cm	23 (12.0)	39 (15.0)	44 (14.0)	42 (12.7)	
Benign lesion > 5 cm	7 (3.7)	6 (2.3)	9 (2.9)	14 (4.2)	
Chronic pancreatitis	3 (1.6)	15 (5.8)	7 (2.2)	5 (1.5)	
T0–T2, malignant	38 (19.9)	62 (23.9)	74 (23.5)	70 (21.2)	
T3–T4 malignant	107 (56.0)	130 (50.0)	169 (53.7)	183 (55.5)	
Unknown	13 (6.8)	8 (3.1)	12 (3.8)	16 (4.9)	
Operative variable, n (%)					
Operative drain	181 (94.8)	245 (94.2)	307 (97.5)	320 (97.0)	0.137
Vascular resection	35 (18.3)	43 (16.5)	32 (10.2)	39 (11.8)	0.022
Multivisceral resection	8 (4.2)	3 (1.2)	3 (1.0)	6 (1.8)	0.047
Robotic-assisted	81 (42.4)	113 (43.5)	179 (56.8)	162 (49.1)	0.003
Open assisted/conversion	81 (42.4)	95 (36.5)	113 (35.9)	135 (40.9)	0.339
Gland texture, n (%)					0.058
Soft	80 (41.9)	93 (35.8)	142 (45.1)	131 (39.7)	
Intermediate	11 (5.8)	14 (5.4)	34 (10.8)	24 (7.3)	
Hard	57 (29.4)	83 (31.9)	75 (23.8)	97 (29.4)	
Unknown	43 (22.5)	70 (26.9)	64 (20.3)	78 (23.6)	
Pancreatic duct size, n (%)					0.196
<3 mm	40 (20.9)	73 (28.1)	89 (28.3)	86 (26.1)	
3–6 mm	74 (38.7)	85 (32.7)	127 (40.3)	137 (41.5)	
>6 mm	31 (16.2)	35 (13.5)	41 (13.0)	44 (13.3)	
Unknown	46 (24.1)	67 (25.8)	58 (18.4)	63 (19.1)	
Neoadjuvant therapy, n (%)					
Neoadjuvant chemotherapy	34 (17.8)	48 (18.5)	59 (18.7)	80 (24.2)	0.176
Neoadjuvant radiation	15 (7.9)	13 (5.0)	14 (4.4)	25 (7.6)	0.228

*p Values are by chi-square test (categorical variables) or ANOVA (continuous variables).
ASA, American Society of Anesthesiologists.

time. As has been previously demonstrated, the 2 risk factors most strongly and consistently associated with an increased risk of pancreatic fistula after pancreaticoduodenectomy are the presence of a small pancreatic duct and/or soft pancreas gland texture.[20-22] Patients having MIPD were dichotomized into high and low risk for pancreatic fistula based on pancreatic duct size and pancreas gland texture. Patients were classified as high fistula risk if they had a pancreatic duct diameter < 3 mm (ie smallest pancreatectomy-targeted NSQIP pancreatic duct category) or a soft pancreas gland texture and underwent pancreatic anastomosis (2014, n = 88; 2015, n = 122;

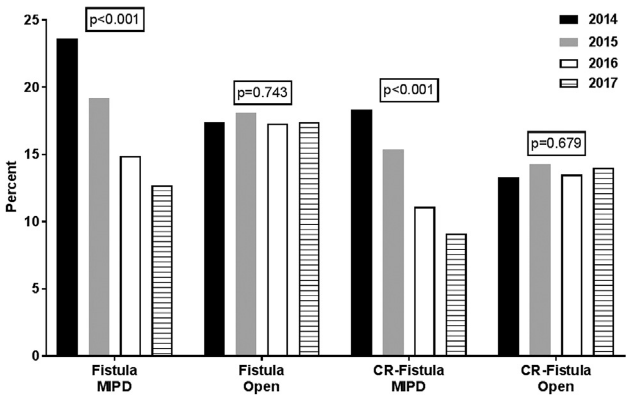

Figure 2. Trends in postoperative pancreatic fistula rates after minimally invasive pancreaticoduodenectomy (MIPD) and open pancreaticoduodenectomy (OPD) in 2014 (MIPD, n = 191; OPD, n = 2,593), 2015 (MIPD, n = 260; OPD, n = 3,042), 2016 (MIPD, n = 315; OPD = 3,430), and 2017 (MIPD, n = 330; OPD, n = 3,547). The p value is for Cochran-Armitage test for trend. CR, clinically relevant.

2016, n = 166; 2017, n = 153). Patients were classified as low risk if they did not have a pancreatic duct diameter < 3 mm, did not have soft pancreas gland texture, and underwent pancreatic anastomosis (2014, n = 93; 2015, n = 121; 2016, n = 136; and 2017, n = 151).

Among high pancreatic fistula risk patients (ie pancreatic duct size < 3 mm or soft pancreas gland texture), there was not a statistically significant trend associated with pancreatic fistula rate (23.9% in 2014 vs 27.1% in 2015 vs 19.3% in 2016 vs 19.0%, p = 0.148) or clinically relevant pancreatic fistula (18.2% in 2014 vs 23.8% in 2015 vs 16.3% in 2016 vs 13.1% in 2017, p = 0.086) with time (Fig. 3). However, there was a significant trend associated with decreasing pancreatic fistula rate (23.7% in 2014 vs 13.2% in 2015 vs 10.3% in 2016 vs 8.0%, p = 0.001), and clinically relevant pancreatic fistula rate (18.3% in 2014 vs 9.1% in 2015 vs 5.2% in 2016 vs 6.0% in 2017, p = 0.001) with increasing year among patients in the low pancreatic fistula risk group (ie excluding pancreatic ducts < 3 mm and soft pancreas gland texture).

DISCUSSION

Pancreatic fistula is the major driver of morbidity and mortality in pancreaticoduodenectomy. The rate of pancreatic fistula in patients undergoing MIPD within the 2014 to 2017 pancreatectomy-targeted NSQIP database decreased with increasing year. This finding could indicate that national MIPD outcomes are improving with time, which has important implications because this operation has a substantial learning curve. Reported MIPD outcomes are highly dependent on where surgeons are located on their individual learning curves.[3,23] Understanding national trends in MIPD outcomes is critical to ensure that patient outcomes are not being compromised at the expense of disseminating a new technique.

Pancreatic reconstruction in MIPD is among the most technically challenging anastomoses in all of minimally invasive surgery, and experience in both pancreatic surgery and minimally invasive suturing are of paramount importance.[1] Anastomoses involving small pancreatic ducts or soft pancreas glands leak not infrequently, despite technique.[21,22,24] However, anastomoses involving larger pancreatic ducts and more firm pancreas glands are less likely to leak and here, technique and experience could play a larger role in preventing fistula formation. In our subgroup analysis, we found that the improvement in outcomes in MIPD patients was largely attributable to an improved pancreatic fistula rate in patients without small pancreatic ducts and without soft pancreas gland texture. Supporting this conclusion, there was no statistically significant trend toward decreased pancreatic fistula rates among patients having either small ducts or soft glands. We suspect that as surgeons gain more experience with MIPD, the anastomoses that are at lower risk for leak will be less likely to do so; anastomoses at higher risk for leak will take longer to master and may still be prone to higher rates of fistula formation for some time. It has previously been suggested that laparoscopic pancreaticoduodenectomy should be performed only in patients at low risk of pancreatic fistula.[9] It seems logical that surgeons would first master minimally invasive pancreatic anastomoses at lower risk of pancreatic fistula before perfecting anastomoses in patients at higher risk for pancreatic fistula. Perhaps, with more time and a higher number of patients, there will also be a significant decreasing trend in pancreatic fistula rates in patients with small pancreatic ducts and soft pancreas gland texture as well.

Other than increasing year of operation, we found that larger malignant tumors (ie T3 and T4) and neoadjuvant chemotherapy were protective against both pancreatic fistula and clinically relevant pancreatic fistula. We suspect these 2 variables could be related to gland firmness and pancreatic duct size because patients with larger malignant tumors are more likely to have pancreatic duct obstruction and gland fibrosis, and patients who receive neoadjuvant chemotherapy likely had larger malignant tumors before therapy. We also found that open assistance/conversion and soft pancreas gland texture were independently associated with increased risk of pancreatic fistula and clinically relevant fistula. We surmise that conversion/open assistance may, in some cases, reflect the difficulty of pancreatic anastomoses, which could explain the association with increased risk of pancreatic fistula.

Table 2. Multivariable Analysis of Factors Associated with Pancreatic Fistula after Minimally Invasive Pancreaticoduodenectomy (n = 1,096)

	Clinically relevant pancreatic fistula		Any pancreatic fistula	
Characteristic	**OR (95% CI)**	**p Value**	**OR (95% CI)**	**p Value**
Age	1.00 (0.98−1.01)	0.702	0.99 (0.98−1.01)	0.396
Sex				
Female	[reference]	[reference]	[reference]	[reference]
Male	1.78 (1.20−2.63)	0.004	1.38 (0.98−1.94)	0.067
Race				
White	[reference]	[reference]	[reference]	[reference]
Nonwhite	0.78 (0.46−1.33)	0.362	0.78 (0.49−1.25)	0.306
BMI, kg/m^2	0.99 (0.96−1.02)	0.559	1.00 (0.97−1.03)	0.969
Comorbidity				
Dyspnea	0.87 (0.34−2.21)	0.771	0.89 (0.39−2.04)	0.786
Diabetes	0.89 (0.55−1.43)	0.625	0.96 (0.63−1.46)	0.833
Obstructive jaundice	1.18 (0.76−1.85)	0.468	1.23 (0.83−1.82)	0.314
Weight loss	0.52 (0.24−1.14)	0.103	1.02 (0.56−1.83)	0.958
ASA class ≥ 3	1.05 (0.66−1.65)	0.844	1.06 (0.70−1.59)	0.793
Pathology				
Benign lesion < 5 cm	[reference]	[reference]	[reference]	[reference]
Benign lesion > 5 cm	0.55 (0.17−1.77)	0.316	0.50 (0.17−1.43)	0.195
Chronic pancreatitis	0.95 (0.42−2.14)	0.895	0.71 (0.33−1.53)	0.384
T0−T2, malignant	0.86 (0.48−1.52)	0.595	0.86 (0.51−1.44)	0.569
T3−T4 malignant	0.54 (0.30−0.97)	0.038	0.55 (0.33−1.53)	0.025
Unknown	1.24 (0.54−2.83)	0.613	1.17 (0.54−2.52)	0.685
Operative variable				
Operative drain	3.35 (0.77−14.54)	0.107	5.03 (1.16−21.68)	0.030
Vascular resection	0.75 (0.40−1.38)	0.350	0.83 (0.48−1.41)	0.485
Multivisceral resection	1.38 (0.37−5.13)	0.627	0.90 (0.25−3.28)	0.871
Robotic-assisted	1.21 (0.79−1.84)	0.385	1.07 (0.74−1.56)	0.714
Open assisted/conversion	2.48 (1.63−3.79)	0.001	2.16 (1.48−3.14)	0.001
Gland texture				
Soft	2.85 (1.59−5.11)	0.001	2.26 (1.38−3.70)	0.001
Intermediate	2.64 (1.17−5.95)	0.020	1.69 (0.80−3.55)	0.168
Hard	[reference]	[reference]	[reference]	[reference]
Unknown	2.15 (1.08−4.27)	0.028	1.75 (0.98−3.14)	0.061
Pancreatic duct size				
<3 mm	1.80 (0.88−3.71)	0.110	1.50 (0.81−2.80)	0.198
3−6 mm	1.23 (0.61−2.48)	0.570	1.05 (0.58−1.92)	0.863
>6 mm	[reference]	[reference]	[reference]	[reference]
Unknown	1.12 (0.51−2.46)	0.780	0.97 (0.50−1.92)	0.938
Neoadjuvant therapy				
Neoadjuvant chemotherapy	0.56 (0.28−1.15)	0.115	0.39 (0.19−0.77)	0.007
Neoadjuvant radiation	1.88 (0.67−5.27)	0.230	1.54 (0.57−4.19)	0.396
Increasing year of operation	0.73 (0.61−0.87)	0.001	0.76 (0.65−0.89)	0.001

ASA, American Society of Anesthesiologists; OR, odds ratio.

Soft pancreas gland texture has previously been identified as a strong predictor of increased pancreatic fistula risk.[4,21,22,24] Although MIPD patients were more likely to undergo robotic resection in the later years, robotic assistance was not independently associated with reduced pancreatic fistula rate in multivariable analysis.

The MIPD operation is still in its infancy, and comparisons with OPD must take this into account. The field of

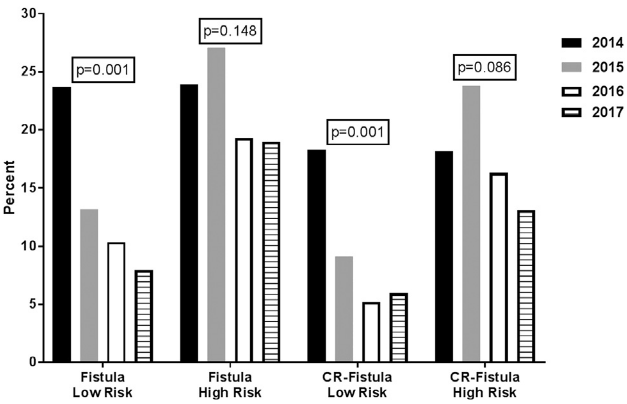

Figure 3. Trends in postoperative pancreatic fistula rates by year after minimally invasive pancreaticoduodenectomy among patients with low risk (excluding pancreatic duct < 3 mm and soft pancreas gland texture) vs high risk (pancreatic duct < 3 mm or soft pancreas gland texture) of pancreatic fistula. Low risk: 2014, n = 93; 2015, n = 121; 2016, n = 136; 2017, n = 151. High risk: 2014, n = 88; 2015, n = 122; 2016, n = 166; 2017, n = 153. The p values are for Cochran-Armitage test for trend. CR, clinically relevant.

pancreas surgery has about 80 years of consistent experience with OPD.[25] During this time, we have seen the mortality rate go from Allen Oldfather Whipple's rate of 33% to 1% to 2% by surgeons at high volume centers, yet pancreatic fistulas remain a vexing problem.[25-27] The first MIPD was reported in 1994,[28] but it was largely abandoned until the early 2000s, when minimally invasive techniques, especially intracorporal suturing, had improved to the point at which this operation was more technically feasible. Whether or not MIPD is truly associated with better outcomes compared with OPD will take more time and experience to determine. The decreasing trend in pancreatic fistula rates associated with MIPD is encouraging, but MIPD should continue to be performed by appropriately trained pancreatic surgeons at high volume centers, and its outcomes studied closely.

The benefit of MIPD compared with OPD is controversial. A large multicenter, international study from Europe suggested that MIPD is associated with increased pancreatic fistula rates, and these differences appear to be driven by technique.[7] Furthermore, a randomized study (LEOPARD-2) from the Netherlands comparing laparoscopic with open PD, was prematurely stopped, due to a nonstatistically significant trend toward higher mortality in the laparoscopic group.[6] However, another randomized trial (PADULAP) from Spain, compared laparoscopic to open PD, and demonstrated decreased severe complication rates as well as decreased length of stay in the laparoscopic group.[12] It is imperative that surgeons work together to improve MIPD outcomes and make the results reproducible worldwide.

This study has several limitations. First, we were unable to investigate individual surgeon and hospital volume effects, let alone track these over time. This would undoubtedly be important given the importance of surgeon and hospital volume in MIPD patient outcomes.[29,30] The NSQIP is often conducted based on a systematic sampling algorithm, though hospitals can dedicate resources to complete case accrual if desired, and there is the possibility that sampling error played into the observed differences. However, we did not observe a significant trend in pancreatic fistula rates by year among OPD patients. Furthermore, the improved outcomes in MIPD were largely driven by improved outcomes in patients at lower risk of pancreatic fistula. We believe this provides a plausible explanation for improvements in MIPD techniques, rather than merely random sampling error. Perhaps, more patients from hospitals with better MIPD outcomes were progressively included in each year of the database. Regardless of this possibility, the findings of this study would still be important because this would reflect the national dissemination of this procedure.

The NSQIP database does include some patients with missing covariate values; most pertinent are duct size and gland texture. We adjusted for this in our multivariable analysis, but nevertheless, this could add some variability to the outcomes. In 2016, the definition of pancreatic fistula was slightly modified to also include any patients with persistent drainage of amylase-rich fluid or an attending diagnosis of pancreatic fistula in the setting of patients being made NPO with total parenteral nutrition. However, this change in definition did not affect the rate of pancreatic fistula in 2016 and 2017 OPD patients compared with the previous 2 years, and if anything, would have increased the rate of pancreatic fistula among 2016 and 2017 MIPD patients, which was not the case.

CONCLUSIONS

In conclusion, there was a significant trend toward decreasing pancreatic fistula rates with increasing year of operation in patients undergoing MIPD at NSQIP participating institutions and accrued into the pancreatectomy-targeted NSQIP database. This could indicate that national MIPD outcomes are improving with time. A major component of this finding was better MIPD outcomes in patients with larger pancreatic ducts and more firm pancreas gland texture, which could be a reflection of still developing minimally invasive anastomotic techniques. Outcomes of MIPD should continue to be closely tracked and frequently analyzed as this operation is disseminated.

Author Contributions

Study conception and design: Panni, Sanford
Acquisition of data: Panni, Guerra, Sanford
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Drafting of manuscript: Panni, Guerra, Hall, Sanford
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eTable 1. Trends in Postoperative Outcomes of Patients Undergoing Minimally Invasive Pancreaticoduodenectomy by Year (n = 1,096)

Complication	2014 (n = 191)	2015 (n = 260)	2016 (n = 315)	2017 (n = 330)	p Value*
Superficial incisional SSI, n (%)	14 (7.3)	12 (4.6)	18 (5.7)	20 (6.1)	0.831
Deep incisional SSI, n (%)	1 (0.5)	6 (2.3)	3 (1.0)	2 (0.6)	0.485
Organ space SSI, n (%)	24 (12.6)	39 (15.0)	43 (13.7)	40 (12.1)	0.479
Wound dehiscence, n (%)	0 (0)	5 (1.9)	1 (0.3)	1 (0.3)	0.479
Unplanned intubation, n (%)	8 (4.2)	13 (5.0)	12 (3.8)	15 (4.6)	0.963
Pulmonary embolism, n (%)	4 (2.1)	4 (1.5)	6 (1.9)	8 (2.4)	0.650
Ventilator > 48 h, n (%)	5 (2.6)	12 (4.6)	8 (2.5)	13 (3.9)	0.780
Progressive renal insufficiency, n (%)	1 (0.5)	0	0	3 (0.9)	0.319
Acute renal failure, n (%)	1 (0.5)	3 (1.2)	2 (0.6)	5 (1.5)	0.377
Urinary tract infection, n (%)	6 (3.1)	9 (3.5)	12 (3.8)	3 (0.9)	0.103
Stroke/CVA, n (%)	1 (0.5)	2 (0.8)	0	1 (0.3)	0.386
Cardiac arrest requiring CPR, n (%)	4 (2.1)	5 (1.9)	1 (0.3)	2 (0.6)	0.041
Myocardial infarction, n (%)	1 (0.5)	1 (0.4)	1 (0.3)	1 (0.3)	0.688
Blood transfusion, n (%)	31 (16.2)	36 (13.9)	34 (10.8)	51 (15.5)	0.762
DVT, n (%)	8 (4.2)	5 (1.9)	8 (2.5)	11 (3.3)	0.882
Sepsis, n (%)	18 (9.4)	18 (6.9)	19 (6.0)	20 (6.1)	0.159
Septic shock, n (%)	5 (2.6)	8 (3.1)	12 (3.8)	10 (3.0)	0.754
Return to the OR, n (%)	13 (6.8)	19 (7.3)	16 (5.1)	25 (7.6)	0.930
Still in hospital after 30 days, n (%)	6 (3.1)	12 (4.6)	7 (2.2)	11 (3.3)	0.664
Pneumonia, n (%)	7 (3.7)	4 (1.5)	6 (1.9)	8 (2.4)	0.587
Delayed gastric emptying, n (%)	34 (17.8)	42 (16.2)	49 (15.6)	56 (17.0)	0.851
Pancreatic fistula, n (%)	45 (23.6)	50 (19.2)	47 (14.9)	42 (12.7)	0.001
Clinically relevant pancreatic fistula, n (%)	35 (18.3)	40 (15.4)	35 (11.1)	30 (9.1)	0.001
Any complication, n (%)	105 (55.0)	123 (47.3)	144 (45.7)	153 (46.4)	0.086
30-d mortality, n (%)	5 (2.6)	6 (2.3)	1 (0.3)	6 (1.8)	0.281
30-d readmission, n (%)	41 (21.5)	51 (19.6)	62 (19.7)	64 (19.4)	0.625
Length of hospital stay, d, mean (SD)	10.9 (9.3)	9.9 (8.8)	8.2 (14.6)	9.5 (12.1)	0.069

*p Values for categorical outcomes are for Cochran-Armitage test for trend. p Values for continuous variables are for Mann-Kendall test for trend.
DVT, deep venous thrombosis; OR, operating room; SSI, surgical site infection.