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Minimally Invasive Distal Pancreatectomy: Greatest Benefit for the Frail

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Abstract

OBJECTIVE—The benefits of minimally invasive distal pancreatectomy (MIDP) over open surgery continue to be investigated. Frailty is a known predictor of postoperative outcome. We hypothesized that the benefit of minimally invasive distal pancreatectomy is greatest for the frailest of patients.

METHODS—Data from the pancreas-targeted National Surgical Quality Improvement Program (NSQIP) database for 2014 were reviewed. A modified frailty index (mFI) with 11 preoperative variables previously validated for use in NSQIP was used to determine the correlation between frailty and postoperative outcomes, including Clavien grade IV complications. Patients were classified into non-frail (mFI=0) or frail (mIF>0), in which they were sub-classified into mildly frail (mFI 1 or 2), or severely frail (mFI =3).

RESULTS—A total of 1,038 distal pancreatectomies (DP) were included in the analysis, of which 387 were minimally invasive (MIDP: laparoscopic: 285, robotic: 102), 558 open DP (ODP) and 93 MIDP converted to open (MIDPcODP: laparoscopic: 80, robotic: 13). More than 90% of patients had a mFI of 0 or 1 (mFI 0=473 (45.6%), 1=466 (44.9%), 2=94 (9.1%), and 3=5 (0.5%) respectively). Overall, 4.6% of patients experienced Clavien grade IV complications and 1.1% a mortality. Non-frail patients experienced a similar rate of grade IV Clavien complications with MIDP vs ODP vs MIDPcOP (2.3 vs. 2.3 vs. 4.9%; p=0.6), whereas frail patients (mFI>0) had a lower rate of complications with MIDP (2.4 vs. 8.3 vs. 11.5; p=0.007). Worsening frailty correlated with an increase in complications (non-frail: 2.5%; mildly frail: 6.3%; severely frail: 20%; p=0.005).

CONCLUSION—MIDP is associated with a lower risk of Clavien grade IV complications compared to ODP for frail patients, especially for benign disease. Thus, minimally invasive approach may mitigate risk in frail patients.

Keywords

frailty; minimally invasive; distal pancreatectomy; modified frailty index

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Introduction

By 2030, 70 million Americans will be older than 65 years and 5% will be octogenarians[1]. The median age of patients suffering from pancreas cancer is 70 years or more[2]. Even though pancreatectomies have been proven safe for patients older than 70 years[3], significant disparities have been noted in the elderly receiving appropriate surgical treatment for pancreatic cancer[4]. Therefore, more comprehensive assessments of peri-operative risk are needed.

Frailty is a multifaceted, age-related decrease in physiologic reserves, which thereby increases patient susceptibility to adverse events[5]. It correlates strongly with postoperative outcome in surgery patients[6, 7]. While there are multiple ways to assess frailty, one common method, is based on the frailty index (FI). The FI was developed by the Canadian Study of Health and Aging (CSHA), a 70-item scale which is based on the theory of "accumulating defects" and is known to correlate with survival[8–11]. Based on this, Velanovich et al[10] created a simplified 11-point modified frailty index (mFI) utilizing variables from the National Surgical Quality Improvement Program (NSQIP) which correlated with morbidity and mortality more strongly than age alone across multiple surgical specialties[12–15].

A recent NSQIP study on 13,020 patients who underwent either pancreaticoduodenectomy or distal pancreatectomy between 2005 and 2010, used mFI and found a stepwise increase of Clavien grade IV morbidity and mortality from non-frail to frail patients[16, 17]. However, the correlation between the type of surgical approach, minimally invasive versus open surgery, with morbidity and mortality was not assessed, as this information was not available for that time period. Minimally invasive surgery is associated with faster recovery and improved postoperative outcomes[18–20]. Likewise, there is increasing evidence that minimally invasive distal pancreatectomy is associated with improved peri-operative outcomes, and comparable oncologic outcomes compared to open distal pancreatectomy[18, 19]. The association of the minimally invasive approach in patients of different frailty states has not yet been studied. The recent introduction of the pancreas-targeted NSQIP module describes the method of surgical approach, yielding the opportunity to assess postoperative morbidity as a function of frailty in open versus minimally invasive surgery. We hypothesized that the benefit of minimally invasive distal pancreatectomy (MIDP) is more pronounced in frail patients.

Methods

Patient selection criteria and data collection

The National Surgical Quality Improvement Program (NSQIP) is the American College of Surgeons' quality improvement program, which prospectively collects nationwide, validated, outcomes-based data. This study used the recently developed pancreas-targeted NSQIP database, which includes variables related to pancreatectomy and data from 106 hospitals in the United States. Details about the methodology of NSQIP are available elsewhere[20]. The database contains de-identified data without protected health information and therefore local

Institutional Review Board (IRB) approval was not required for this study. Patients who underwent distal pancreatectomy were identified using the Current Procedural Terminology (CPT) code for distal pancreatectomy 48140 (distal pancreatectomy, with or without splenectomy, without pancreaticojejunostomy). We selected only elective procedures performed in adult patients. Procedures performed in an open, laparoscopic and robotic fashion were included. Hybrid procedures were excluded. Patients who underwent multivisceral resections other than splenectomy and cholecystectomy at the time of the DP were excluded.

Prospectively collected clinicopathologic, operative, and 30-day postoperative morbidity and mortality data were examined for the purpose of this study. Complications were graded using the Clavien-Dindo classification[17]. Our primary outcome was severe complications (Grade IV) as these are life-threatening and lead to organ dysfunction requiring ICU management and death (Grade V). The NSQIP variables, which are most consistent with grade IV complications are: septic shock, myocardial infarction, cardiac arrest, mechanical intubation greater than 48hrs, reintubation, pulmonary embolism, and renal dysfunction requiring dialysis[17]. The modified frailty index (mFI) was used to determine the correlation between frailty and postoperative morbidity and mortality. mFI was calculated by extrapolating its 11 variables from the corresponding NSQIP variables. The variables of the mFI and their distribution in the current patient cohort are illustrated in table 1. Patients were classified into non-frail (mFI =0) or frail (mFI >0), from which they were then sub-classified into mildly frail (mFI 1 or 2), or severely frail (mFI =3).

Statistical Analysis

Continuous variables are presented as median and range or mean and standard deviation. Categorical variables are presented as proportions. We assessed group differences using Fisher exact or Pearson x^2 test for categorical variables. Continuous variables were compared with the student's t test when the distribution was normal, or the Wilcoxon rank-sum test and Kruskal-Wallis test when the distribution was not normal. mFI was analyzed as a categorical variable. Statistical analysis was performed using SPSS Statistics v23 software (IBM Corp, Armonk, NY).

Results

Clinicopathologic Characteristics

A total of 1,038 distal pancreatectomies (DP) performed between January 1, 2014 and December 31, 2014 were analyzed, of which 480 (46.2%) were minimally invasive DP (MIDP, laparoscopic: 365, robotic: 115) and 558 (53.8%) were open DP (ODP).

Table 2 demonstrates the clinicopathologic and frailty status of all patients. The majority of patients were female (59.3%), of white race (77.6%) with ASA 3 (62.8%). The median age was 62 (range: 18-88 years). Malignancy was the most common indication for distal pancreatectomy (45.9%), whereas 10% of patients were operated on for pancreatitis. Grade IV and V (mortality) Clavien complications were 4.6% and 1.1% respectively. The overall incidence of pancreatic fistula was 17%.

Overall, there was no difference in the demographic characteristics and ASA status between MIDP and ODP. More malignant tumors were in the ODP group (Table 2). Similarly, between MIDP and ODP, there was no difference in the incidence of Grade IV major complications (3.5% versus 5.6% respectively; p=0.12), mortality (0.8% versus 1.3%, respectively; p=0.5), or the incidence of pancreatic fistula (19% versus 15.2%, respectively; p=0.11). The overall conversion rate for this series was 19.3% (MIDPcODP: laparoscopic: 21.9%, robotic: 11.3%).

More than 90% of patients had an mFI of 0 or 1 (mFI: 0,1,2,3 in 473 (45.6%), 466 (44.9%), 94 (9.1%), and 5 (0.5%) respectively). Table 1 shows the distribution of comorbidities based on the mFI. The most common comorbidities were hypertension requiring medical treatment (50.5%) and insulin-dependent diabetes mellitus (10.6%).

Frailty and Postoperative Outcome

Overall, the incidence of grade IV complications was 4.6%. Table 3 summarizes the distribution of grade IV complications in this cohort and according to frailty status. Frail patients experienced a higher incidence of grade IV complications compared to non-frail (6.4% versus 2.5%; p=0.003) and a tendency for higher mortality (frail: 1.6% versus non-frail: 0.4%; p=0.07). The degree of frailty correlated with the incidence of grade IV complications (non-frail: 2.5% versus mildly frail: 6.3% versus severely frail: 20%; p=0.005).

Table 4 illustrates a correlation of frailty, surgical modality and postoperative complications. Comparing the outcomes of MIDP versus ODP versus MIDPcOP for non-frail patients showed similar rates of Grade IV Clavien complications (2.3% versus 2.3% versus 4.9%; p=0.6), mortality (0.4% versus 0.6% versus 0%, respectively; p=0.87) and incidence of pancreatic fistula (19.4% versus 13.2% versus 17.1%; p=0.22).

Frail patients (mFI>0) had a lower rate of grade IV complications with MIDP versus ODP versus MIDPcOP (2.4% versus 8.3% versus 11.5%; p=0.007) and lower mortality (0% versus 2% versus 5.8%; p=0.009), whereas the incidence of pancreatic fistula was similar (17.5% versus 16.9% versus 25%; p=0.37). The length of stay was shorter with minimally invasive distal pancreatectomy for both the frail and non-frail (table 4).

Elderly

In total, 292 patients were 70 years old or more at the time of surgery (27.8% of all patients). There was no difference in the utilization of minimally invasive surgery for elderly versus younger patients (45.2% versus 46.6%, respectively; p=0.67). Overall, elderly patients did not experience a higher rate of grade IV complications (5.5% versus 4.3%; p=0.4) or mortality (1.4% versus 0.9%) compared to their younger counterparts. However, they did experienced a lower rate of Clavien IV complications with MIDP versus ODP or MIDPcODP (0% versus 8.8% versus 6.9%; p=0.009).

Discussion

The aging of the US population represents a multilevel challenge for the health care system and treating physicians. At present, the elderly often have limited access to appropriate cancer treatment and are often excluded from clinical trials[21]. Pancreatic surgery is not an exception to the above. Even though there are reports of safety in the elderly[3], pancreatic surgery is frequently underutilized[4]. Frailty is a strong predictor of postoperative outcome as it represents an expression of decreased physiologic reserve and increased multisystem deficits related to but distinct from the aging process.

In this report of elective distal pancreatectomies utilizing the pancreas module of the National Surgical Quality Improvement Program (NSQIP) of the American College of Surgeons, we found that with careful patient selection the vast majority of patients were non-frail or minimally frail. Frail patients had an increased incidence of grade 4 Clavien complications, which increased with worsening frailty. Minimally invasive distal pancreatectomy (MIDP) lowered this risk compared to open distal pancreatectomy (ODP) but this benefit was lost in the event of conversion. The elderly (age≥70), which constituted one third of this cohort had similarly decreased rates of major complications with MIDP.

Multiple prospective studies in surgical patients have shown a strong correlation between frailty and postoperative outcomes[22–25]. While aging is associated with some degree of physiologic decline, elderly patients represent a heterogeneous population in terms of physiologic reserves and age cannot be used as the sole determinant of eligibility for treatment. In this study we utilized the modified frailty index, which represents a version of the accumulated deficits model of frailty. Currently, two validated models of frailty are commonly used: the “phenotypic” model[26] and the “accumulating deficits” model. The frailty phenotype includes factors such as unintentional weight loss, subjective exhaustion, grip strength, walking speed and low physical activity. The accumulating deficits model which has been shown to predict morbidity and mortality in the elderly[27] is based on the assumption that accumulating comorbidity results in overall functional decline and uses tools such as the Canadian Study of Health and Aging Frailty Index (CSHA-FI)[9], a 70-variable tool. The mFI represents an 11-variable abbreviated expression of the latter and has been validated in multiple studies utilizing NSQIP data and diverse types of surgery patients. The mFI was found to be superior to age and American Society of Anesthesiologists’ classification, factors that are traditionally used in preoperative planning, for patients who underwent esophagectomy, gastrectomy, colectomy, pancreatic and liver surgery, cardiothoracic surgery, urologic and vascular surgery[12–15, 28]. Even though there are numerous different frailty indices, they seem to yield similar results as long as they measure variables related to health status[29]. Additionally, there are other commonly used ways to assess the effect of comorbidity on the postoperative and long term outcome, such as the Charlson Age Comorbidity Index (CACI). The CACI is calculated by weighing individual comorbidities and adding 1 point per decade to ages > 40 years, and it has been found to correlate with early mortality after surgery for pancreatic cancer[30]. However, it does not include the assessment of the functional status of the patient[31].

Frailty correlates strongly with the postoperative outcome after pancreatectomy. A NSQIP study on 13,020 patients who underwent either pancreaticoduodenectomy or distal pancreatectomy between 2005-2010, found that the modified frailty index predicted serious postoperative complications and death[16]. A stepwise increase of Clavien/Dindo grade 4 complications and mortality from nonfrail to frail patients was noted[16], however the mode of surgery, open or minimally invasive, was not available during that time period. Minimally invasive surgery is an ideal choice for frail patients as the physiologic insult of open surgery is greater in a patient with already limited reserves. The introduction of the NSQIP pancreas module created the opportunity to study the effects of open versus minimally invasive surgical approaches, as well as pancreas specific complications such as pancreatic fistula. A recent report on minimally invasive distal pancreatectomy utilizing the pancreas-targeted ACS-NSQIP database found that benign disease and BMI 30-40 were potential selection factors for MIDP. MIDP showed a trend for lower composite major morbidity, independent of patient risk factors[32]. In our report, after stratifying patients into non-frail and frail, there were fewer grade 4 Clavien complications for frail patients who underwent minimally invasive DP. The rates of pancreatic fistula remained similar, regardless of surgical approach or frailty status, as this is likely related more due to technical and pancreas related factors. Minimally invasive distal pancreatectomy is associated with improved perioperative outcomes in data from the National Inpatient Sample[18]. In addition, a recent Cochrane review on distal pancreatectomy for pancreatic ductal adenocarcinoma showed that minimally invasive DP had equivalent oncologic outcome to open with similar negative surgical margins, lymph node retrieval and overall survival, whereas it was associated with reduced blood loss and shorter hospital stay[19]. Despite the benefits of minimally invasive distal pancreatectomy, it remains underutilized[33]. Strong consideration should be given to minimally invasive approaches and frailty should be part of the preoperative evaluation and selection of the surgical approach for patients undergoing distal pancreatectomy.

Our study has several limitations. It represents a retrospective analysis of postoperative outcomes limited to 30 days, utilizing the mFI, which is a tool that still needs to be validated in prospective studies. However, the data are prospectively collected by trained dedicated personnel and the validity of mFI is being supported by numerous publications with consistent findings in diverse surgical populations. The relative few patients in the severely frail category (mFI=3) certainly represents a limitation and reflects good patient selection for surgery. Even though the mFI represents an abbreviated 11-variable version of the 70-element CSHA-FI tool, it has been shown that CSHA-FI can be modified to as few as 10 variables[29]. Inasmuch as the pancreas module of NSQIP represents a thorough database, there is no data on surgeon and hospital volume, nor technical details relative to postoperative outcome. High participation in NSQIP amongst centers of excellence limits the generalizability of our data. However, the use of NSQIP eliminates the issues with sample size, single institution and surgeon bias, which are significant problems in single institution studies constituting the majority of the literature.

Conclusion

In conclusion, minimally invasive distal pancreatectomy is associated with a decreased risk of major complications compared to open distal pancreatectomy for frail and elderly

patients, especially for benign disease. Conversion to an open procedure is related to a worse postoperative outcome. Identification of frail patients and referral to centers of excellence for minimally invasive surgery may improve postoperative outcomes. Frailty should be incorporated in future studies on pancreatic surgery.

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Disclosures

Dr. Yanghee Woo serves as Proctor and Course Head for Intuitive Surgical, is a Consultant for Ethicon and Verb Surgical, and serves as Surgeon Advisor for Titan Medical.

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Table 1

Modified Frailty Index (mFI). Variables and their distribution in 1038 distal pancreatectomy patients

mFI Variable	Points	n=1038 (%)
Functional health status before operation		
Totally dependent	1	1 (0.1)
Metabolic		
Insulin-dependent DM	1	110 (10.6)
Respiratory		
History of severe COPD or current pneumonia	1	36 (3.5)
Cardiovascular		
Congestive heart failure within 30d of surgery	1	4 (0.4)
MI within 6 mo of surgery	1	0
Previous PCI, cardiac surgery, or angina within 1 mo of surgery	1	0
HTN requiring medication	1	524 (50.5)
History of revascularization/amputation for PVD, or rest pain/gangrene	1	0
Neurologic		
History of TIA	1	0
CVA with deficit	1	0
Impaired sensorium	1	0

DM: diabetes mellitus, COPD: chronic obstructive pulmonary disease, d: days, MI: myocardial infarction, PCI: percutaneous coronary intervention, mo: month, HTN: hypertension, PVD: peripheral vascular disease, TIA: transient ischemic attack, CVA: cardiovascular accident

Table 2

Clinicopathologic and Frailty Characteristics of 1038 patients who underwent distal pancreatectomy

Variable	All patients n=1038 (%)	Open DP n=558 (%)	MIS DP n=480 (%)	p
Age, median (range), y	62 (18-88)	62 (18-88)	62 (20-88)	NS
BMI, mean (SD)	28.8 (6.5)	28.3 (6.2)	29.3 (6.7)	0.008
Gender, female	616 (59.3)	327 (58.6)	289 (60.2)	NS
Race, white	806 (77.6)	427 (76.5)	379 (79)	NS
Diabetes	256 (24.7)	150 (26.9)	106 (22)	NS
Smoking	185 (17.8)	106 (19)	79 (16.5)	
Hypertension	524 (50.5)	274 (49.1)	250 (52.1)	
ASA 3	652 (62.8)	348 (62.4)	304 (63.3)	NS
Chemotherapy	80 (7.7)	68 (12.2)	12 (2.5)	<0.001
Radiation	36 (3.5)	33 (5.9)	3 (0.6)	<0.001
Histopathology				
Malignancy	476 (45.9)	304 (54.5)	172 (35.8)	<0.001
Benign	389 (37.5)	165 (29.6)	224 (46.7)	
Pancreatitis	104 (10)	45 (8.1)	104 (12.3)	
Other/unspecified	69 (6.6)	44 (7.9)	25 (5.2)	
mFI				NS
0	473 (45.6)	257 (46.1)	216 (45)	
1	466 (44.9)	244 (43.7)	222 (46.3)	
2	94 (9.1)	53 (9.5)	41 (8.5)	
3	5 (0.5)	4 (0.7)	1 (0.2)	
Operative time, mean, (SD), min	228 (103)	230 (111)	224 (93)	NS
Return to OR	34 (3.3)	22 (3.9)	12 (2.5)	NS
Blood transfusion (<72hr)	100 (9.6)	76 (13.6)	24 (5)	<0.001
Grade IV Clavien	48 (4.6)	17 (3.5)	31 (5.6)	NS
Mortality	11 (1.1)	4 (0.8)	7 (1.3)	NS
Pancreatic Fistula	176 (17)	91 (19)	85 (15.2)	NS
Length of Stay, mean, (SD), d	6.6 (7.3)	7.4	5.6	<0.001

Open DP: open distal pancreatectomy, MIS DP: minimally invasive distal pancreatectomy, y: years, ASA: American Society of Anesthesiologists, mFI: modified Frailty Index, NS: not significant, OR: operating room, d: days

Table 3

Distribution of grade 4 Clavien Complications in 1038 distal pancreatectomy patients according to frailty status

Complication	All patients n=1038 (%)	Non-Frail n=473 (%)	Frail n=565 (%)	p
Grade 4 Clavien	48 (4.6)	12 (2.5)	26 (6.4)	0.003
Mortality	11 (1.1)	2 (0.4)	9 (1.6)	0.07
Specific grade 4 Clavien complication				
Intubation greater than 48 hours	18 (1.7)	3 (0.6)	15 (2.7)	0.01
Reintubation	21 (2)	6 (1.3)	15 (2.7)	NS
Septic Shock	17 (1.6)	2 (0.4)	15 (2.7)	0.005
Postoperative hemodialysis	8 (0.8)	2 (0.4)	6 (1.1)	NS
Pulmonary Embolism	14 (1.3)	5 (1.1)	9 (1.6)	NS
Cardiac Arrest	5 (0.5)	0	5 (0.5)	0.04
Myocardial Infarction	7 (0.7)	1 (0.2)	6 (1.1)	NS

NS: not significant

Table 4

Frailty and Postoperative Outcome in 1038 distal pancreatectomy patients according to surgical modality (Open DP: open distal pancreatectomy, MIDP: minimally invasive distal pancreatectomy, MIDPcODP: minimally invasive distal pancreatectomy converted to open distal pancreatectomy)

Variable	MIS DP	Open DP	MISODP	p
Non-frail (N=473)	n=175 (%)	n=257 (%)	n=41 (%)	
Clavien 4	4 (2.3)	6 (2.3)	2 (4.9)	NS
Mortality	1 (0.4)	1 (0.6)	0 (0)	NS
Pancreatic fistula	34 (19.4)	34 (13.2)	7 (17.1)	NS
Length of stay, mean, d	4.9	6.4	6.7	<0.001
Frail (N=565)	n=212 (%)	n=301 (%)	n=52 (%)	
Clavien 4	5 (2.4)	25 (8.3)	6 (11.5)	0.007
Mortality	0 (0)	6 (2)	3 (5.8)	0.009
Pancreatic fistula	37 (17.5)	51 (16.9)	13 (25)	NS
Length of stay, mean, d	5.6	8.2	7.5	0.007

NS: not significant, d: days