Published in final edited form as:

J Gastrointest Surg. 2014 March ; 18(3): 512–522. doi:10.1007/s11605-013-2399-7.

Impact of Cardiac Comorbidity on Early Outcomes after Pancreatic Resection

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Abstract

Background—In patients undergoing pancreatic resection (PR), identification of subgroups at increased risk for postoperative complications can allow focused interventions that may improve outcomes.

Study Design—Patients undergoing PR from 2005–2010 were selected from the American College of Surgeons National Surgical Quality Improvement Program database and categorized as having any history of cardiac disease (angina, congestive heart failure (CHF), myocardial infarction (MI), cardiac stent, or bypass) or as having acute cardiac disease (symptoms of CHF or angina within 30 days or MI within 6 months). These variables were utilized to examine the relationship between cardiac disease and outcomes after PR.

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Presented at Pancreas Club (May 17th, 2013) in Orlando, FL

Results—The rate of serious complications and perioperative mortality in patients with any history of cardiac disease vs. those without was 34 vs. 24 % ($p < 0.001$) and 4.5 vs. 2.0 % ($p < 0.001$), respectively, and in patients with acute cardiac disease compared to patients without was 37 vs. 25 % ($p < 0.001$) and 8.6 vs. 2.2 % ($p < 0.001$), respectively. In multivariate analysis, the two cardiac disease variables remained associated with mortality.

Conclusions—In patients undergoing PR, cardiac disease is a significant risk factor for adverse outcomes. These observations are critical for meaningful informed consent in patients considering pancreatectomy.

Keywords

Pancreatic resection; Pancreatic surgery; Cardiac disease; American College of Surgeons National Surgical Quality Improvement Program; Surgical outcomes

Introduction

Pancreatic resection (PR) encompasses a number of challenging procedures such as pancreaticoduodenectomy (PD) and distal pancreatectomy that historically have been associated with significant rates of morbidity and mortality.^{1, 2} Due largely to improvements in perioperative care, early mortality after PR is now uncommon (approximately 1–3 %), but the rates of serious postoperative complications remain high (30–50 %).^{3–9}

Previous studies have identified risk factors that influence perioperative outcomes after PR. These patient, provider, procedure, and disease-related factors include patient comorbidities, surgeon and hospital procedure volume, type of procedure, and the underlying pathology. Enhanced imaging modalities have allowed improved characterization of disease and, in combination with more stringent criteria for operative patient selection, have also contributed toward decreased mortality rates.^{1, 2, 10–15}

In an earlier analysis of predictors of poor outcome after PD using data from the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP), postoperative cardiac complications such as myocardial infarction and cardiac arrest were associated with a high rate of 30-day mortality (66 %). Preoperative cardiac comorbidities such as coronary artery disease and congestive heart failure demonstrated potential association with morbidity and mortality after PD (significant via univariate analysis).¹⁶

The purpose of the present study was to further explore the association between cardiac comorbid illness and adverse outcomes after PR. We examined acute and chronic cardiac disease separately. Our goal was to provide information to aid preoperative risk assessment, which is crucial for both meaningful informed consent discussions and to select high-risk individuals for perioperative interventions designed to improve outcomes.

Material and Methods

Database

We conducted a retrospective cohort study utilizing data from the ACS NSQIP Participant Use Data Files from the years 2005–2010, collected from over 250 community and academic hospitals across the USA. At each ACS NSQIP participating site, a surgical clinical reviewer records information on 240 precisely defined clinical variables, including patient demographics, comorbidities, operative factors, and 30-day postoperative complications and mortality. Details regarding the procedure sampling and data collection process as well as variable definitions are available on the ACS NSQIP website.¹⁷

Inclusion and Exclusion Criteria

Patients undergoing PR procedure were identified using Current Procedure Terminology (CPT) codes and included in the study. The following procedures were included: distal pancreatectomy (CPT codes 48140, 48145, and 48146) and pancreaticoduodenectomy (CPT codes 48150, 48152, 48153, and 48154).

We excluded atypical and high-risk patients with the following characteristics: comatose, ventilator-dependent, septic shock, disseminated cancer, American Society of Anesthesiology (ASA) class V or VI, and emergency operation.

Patient Variables

Demographics, comorbidities, preoperative lab values, and postoperative outcomes (mortality and postoperative complications) were evaluated. Age, gender, and race comprised the demographic data. Comorbid conditions and clinical factors included body mass index, diabetes, smoking, alcohol use, dyspnea, do-not-resuscitate status, functional status (independent, partially dependent, or totally dependent) prior to surgery, chronic obstructive pulmonary disease, pneumonia, ascites, esophageal varices, congestive heart failure (CHF), history of myocardial infarct (MI), history of percutaneous coronary intervention (PCI), previous cardiac surgery, angina, hypertension, prior procedure for vascular disease, rest pain, acute renal failure, dialysis, impaired sensorium, coma, hemiplegia, transient ischemic attack, stroke with or without neurologic deficit, central nervous system tumor, paraplegia, quadriplegia, disseminated cancer, wound infection, steroid use, significant weight loss in the previous 6 months, bleeding disorders, preoperative blood transfusion, chemotherapy for malignancy within 30 days, radiation therapy for cancer within 90 days, pregnancy, and prior operation within 30 days.

Lab values collected were serum sodium, blood urea nitrogen, creatinine, albumin, total bilirubin, aspartate aminotransferase, alkaline phosphatase, white blood cell count, hematocrit, platelet count, and international normalized ratio.

Postoperative Outcomes

Postoperative outcomes consisted of 30-day mortality and serious complications. Serious complications included respiratory complications (pneumonia, unplanned reintubation, and prolonged mechanical ventilation >48 h postoperatively), neurologic complications (stroke

and coma >24 h postoperatively), abscess (deep and organ space surgical site infection), cardiac complications (MI or cardiac arrest), renal failure, dehiscence, sepsis and septic shock, venous thromboembolism, and hemorrhage requiring transfusion. The following complications were excluded from the definition of serious complications: superficial surgical site infection, urinary tract infection, and peripheral nerve injury. Other outcomes that were examined included prolonged length of hospital stay (defined as greater than or equal to 75th percentile in days for that procedure category) and the frequency of reoperation within the first 30 days.

Definition of Cardiac Disease

We created two explanatory variables to analyze the association between cardiac disease and perioperative outcomes after PR. The variable “history of cardiac disease” encompassed CHF onset or exacerbation in 30 days prior to surgery, history of angina within 1 month of surgery, MI in 6 months prior to surgery, and history of percutaneous coronary intervention or major cardiac surgery. “Acute cardiac disease” included a subset of the previous group and was defined as CHF onset or exacerbation in the prior 30 days, angina within 1 month, or MI within 6 months.

Statistical Analysis

Preoperative cardiac disease was initially examined for association with demographics, preoperative health status, and comorbidities using Pearson's chi-square or Fisher's exact test and Wilcoxon rank-sum test as appropriate. Similarly, the relationships between risk factors, serious postoperative complications, and 30-day mortality were also evaluated. A multiple logistic regression analysis was performed to determine the influence of various factors on mortality after pancreatic resection and the corresponding adjusted odds ratios and 95 % confidence intervals were calculated. Only variables with $p < 0.20$ were incorporated into the multivariable model. To avoid over-fitting the model, Spearman's correlation was computed for each pair of variables. For any pairs of variables with a correlation $\rho > 0.40$, the variable of greater significance in the univariate analysis was selected for inclusion into the final model. The goodness-of-fit for the model was assessed by Hosmer–Lemeshow test. Any lab variables with >20 % missing values and characteristic variables representing <1 % of the study population were excluded from the analysis. All analyses were conducted using SAS 9.2 (SAS Institute, Cary, NC) software. A p value <0.05 was considered statistically significant in two-tailed statistical tests.

Results

Patient Characteristics

A total of 13,021 patients underwent PR (approximately 2/3 PD and 1/3 distal pancreatectomy) and otherwise met the inclusion criteria for the study. Of these, 1435 individuals (11.0 %) had any history of cardiac disease, while 139 (1.1 %) had recent acute cardiac disease. Compared to the group of patients without cardiac disease, patients with history of cardiac disease were older, more likely to be male, and had more medical comorbidities (Table 1).

Outcomes

Of the 13,021 patients who underwent PR, 3,253 (25 %) had a serious complication, and 297 (2.3 %) died within 30 days of surgery. The most common serious complications were sepsis (13.6 %), abscess (12.0 %), and respiratory complications (8.9 %) (Table 2). A total of 825 patients (6.3 %) required reoperation in 30 days.

The overall rate of cardiac complications (acute MI or cardiac arrest) was 1.6 %. In these patients who suffered a cardiac complication, the 30-day mortality rate was 39 % compared to 0.7 % in those without a cardiac complication. The rate of cardiac complications in patients with any history of cardiac disease was 3.8 % compared to 1.3 % with no cardiac comorbidities ($p < 0.001$). For patients with a recent history of acute cardiac disease, the rate of cardiac complications was 7.9 vs. 1.5 % in patients without cardiac comorbidities ($p < 0.001$) (Table 3).

In addition, patients with cardiac disease had higher rates of serious complications and mortality after PR via univariate analysis. History of cardiac disease and acute cardiac disease were associated with a 1.6-fold and 1.8-fold increase in serious complications and a 2.3-fold and 4.2-fold increase in mortality, respectively.

Predictors of Mortality

In univariate analysis, older age, male gender, and a number of comorbid conditions, including the two cardiac risk variables, history of cardiac disease, and acute cardiac disease, were associated with the 30-day mortality (Table 4). We then constructed a multivariable model of mortality. After controlling for potential confounders, any history of cardiac disease and acute cardiac disease were both significant predictors of mortality, with adjusted odds ratios (OR) of 1.45 and 2.07, respectively (Table 5). Additional significant predictors of the 30-day mortality after pancreatic resection included older age, dependent functional status, dyspnea, increased ASA class, hypoalbuminemia, and elevated serum creatinine.

On subgroup analysis of patients undergoing PD ($n = 8736$), 1,015 (11.6 %) patients had a history of cardiac disease, while 92 (1.1 %) had acute cardiac disease. Postoperative mortality was 2.9 % in this group with serious complications occurring in 27.2 %. Acute cardiac disease and any history of cardiac disease were associated with increased morbidity (OR=1.66, $p < 0.001$ and OR=1.65, $p < 0.001$, respectively) and mortality (OR=4.74, $p < 0.001$ and OR=2.71, $p < 0.001$, respectively) after PD compared to those without cardiac disease. After controlling for potential confounders, acute cardiac disease remained a significant predictor of mortality with adjusted OR of 2.39 ($p = 0.01$), while any history of disease approached significance with adjusted OR of 1.34 ($p = 0.078$). Additional factors associated with the 30-day mortality after PD include increasing age, dependent functional status, dyspnea, hypertension requiring medication, steroid use, and increased ASA (table not shown).

Discussion

Pancreatic resection (PR) is associated with high rates of morbidity. In a previous study on early outcomes after PD based upon ACS NSQIP data, we found that patients who had cardiac comorbid conditions such as congestive heart failure and coronary artery disease had increased frequencies of serious complications and mortality on univariate analysis.¹⁶ In the current study, we further analyzed the associations between preexisting cardiac disease and postoperative serious complications and mortality in patients undergoing PR, as well as a subgroup analysis of patients undergoing PD.

On subgroup analysis of patients undergoing PD, we found a similar frequency of history of cardiac disease and acute exacerbation/onset of cardiac disease compared to the overall population. Mortality rate in the patients undergoing PD was elevated compared to the overall population (2.9 vs 2.3 %), but this was not an unexpected finding. A previous investigation found an association between CAD and mortality after PD that did not remain significant in the multivariate model.¹⁶ In our study, we found that patients with acute cardiac disease had significantly increased risk of mortality compared to those without cardiac disease (adjusted OR, 2.39; $p=0.01$). The discrepancy in our findings vs. the earlier study is likely attributable to the larger patient population ($n=8736$ vs $n=4945$) which increases the power of the study.

In our multi-institutional sample of over 13,000 patients who underwent PR, one in four suffered a serious complication, and 2.3 % died within 30 days. We examined two cardiac disease-related variables, history of cardiac disease (including history of cardiac revascularization), and acute cardiac disease (e.g., recent MI or symptoms of CHF). The frequencies of these factors were 11 and 1.1 %, respectively. Univariate analysis demonstrated that any history of cardiac disease and acute cardiac disease were both associated with the 30-day mortality, serious complications including postoperative MI and cardiac arrest, and prolonged length of stay. The rate of serious complications and perioperative mortality in patients with any history of cardiac disease vs. those without was 33.9 vs. 23.9 % ($p<0.001$) and 4.5 vs. 2.0 % ($p<0.001$), respectively. The rate of serious complications and perioperative death in patients with acute cardiac disease compared to patients without was 37.4 vs. 24.9 % ($p<0.001$) and 8.6 vs. 2.2 % ($p<0.001$), respectively. In multivariate analysis, after controlling for potential confounders, the two cardiac disease variables remained predictors of mortality.

De la Fuente and colleagues¹⁸ utilized the ACS NSQIP database to determine preoperative and intraoperative variables corresponding with poor outcome in patients undergoing PD. While age (>80 vs <80 years) was the main explanatory variable, coronary artery disease (defined as history of MI within 6 months, previous PCI or major cardiac procedure, and angina within 30 days of operation) was among the statistically significant determinants associated with mortality and complications after PD. In another analysis utilizing the ACS NSQIP database, preoperative variables that significantly impacted postoperative outcome were incorporated into a risk calculator to predict mortality, serious morbidity, and overall morbidity after pancreatic resection. Coronary artery disease was one of the determinants of increased risk and deemed an important predictive variable associated with worse

postoperative outcome.¹⁹ DeOliveira and colleagues²⁰ also noted the impact of cardiac comorbid disease when evaluating surgical complications after pancreatic surgery. In this investigation, the focus was to introduce a novel grading system for complications in patients undergoing pancreatic surgery that may be translatable and easily reproducible and possibly serve as an outcomes measure. Included was an evaluation of risk factors for development of these complications. The only risk factor that remained significant on multivariate analysis for overall complications and complication severity was history of cardiovascular disease. Concordant with our study, it appears evident that patients with cardiac comorbidities are at higher risk for postoperative mortality and complications after pancreatic resection. As quality of surgical care is increasingly scrutinized and surrogate measures have included mortality, postoperative complications, and even hospital/surgeon volume, it is important to appropriately delineate preoperative risk both for patient discussion as well as for comparisons of quality outcome.²¹

Improved patient outcomes with increasing expertise and operative volume have consistently been demonstrated for more than 10 years.^{14, 22} In a study by van Heek and colleagues¹ when evaluating patients undergoing pancreatic resection in Netherlands, hospital mortality rates varied between 13.8 and 16.5 % in hospitals performing less than five PRs per year; this was in comparison to mortality of 0 to 3.5 % in hospitals performing more than 24 PRs per year.⁵ Birkmeyer and colleagues²² examined the mortality associated with six major cardiac operations and eight major cancer resection operations. PR was included among the fourteen procedures, and low-volume hospitals performed two or fewer, while high-volume hospitals performed 16 or greater PRs per year. Absolute mortality risk reduction of 12.5 % for PR (3.8 vs 16.3 %, a 4.3-fold increase) as well as risk reduction in each of the other 13 operative categories supported the volume-outcome effect. Similar results were obtained by Brennan and colleagues¹⁴ when evaluating mortality in major cancer operations in high-volume centers vs. low-volume centers. An absolute risk reduction in mortality in patients undergoing PR was 7.1 % (12.9 vs 5.8 %, $p = 0.004$). Considering that patients with acute cardiac disease in the current study demonstrated a 2.1-fold increased risk for mortality, performing PR in these high-risk patients at centers other than high-volume institutions will likely result in suboptimal patient outcomes.

The strength of this investigation derives from utilization of data from a large number of patients and using prospectively collected morbidity and mortality data from a nationally prominent and validated dataset. However, there are limitations which should be considered when interpreting this study. Although the explanatory variables were derived from NSQIP variables which included precisely defined cardiac comorbidities, other conventional cardiac risk factors such as hypertension and peripheral vascular disease were not incorporated into the cardiac disease explanatory variables. While greater than 80 % of the patients with any history of cardiac disease or acute cardiac disease also had hypertension, and peripheral vascular disease was more prevalent in patients with cardiac disease than those without, the purpose of the study was to evaluate patients with cardiac end-organ dysfunction undergoing PR. Another limitation is consequent to the format of the dataset. It was impossible to obtain information regarding preoperative evaluation and risk optimization, specifically in the patients with any history of cardiac disease. Unfortunately, preoperative assessment and

preparation for operative intervention varies widely between institutions. Standardization of patient preparation prior to PR could eliminate variability in results due to preoperative clinical approach. A third confine is the duration of data collection: NSQIP collects data for 30 days postoperatively. While this is meant to capture immediate postoperative morbidity and mortality, a more comprehensive dataset could include a longer follow-up, perhaps including inhospital morbidity and mortality, or data collected over longer time duration (e.g., 3 months). To demonstrate this, a study evaluating rates of pancreatic fistula (PF) after PR found that the mean hospital stay was 19 days, with a range of 6–118 days.²³ In another study investigating patients undergoing pancreatic resection for suspected malignancy, 30-day mortality was 4.7 % compared to 9.5 % for inhospital mortality, which occurred out to 48 days.²⁴ Thus, although 30 days is an accepted interval for follow-up, it likely does not reflect the clinically relevant data for complex operations of this type, in which associated morbidity and mortality can occur after 30 days. A fourth limitation is NSQIP's definitions for the complications that commonly affect patients after PR, including delayed gastric emptying (DGE) and PF. Current variables would not capture the incidence of DGE (unless as a direct consequence of organ space SSI, etc.) which can result in increased duration of hospitalization, increased costs, and decreased quality of life, and occurs in 19–57 % of patients undergoing PR.²⁵ Although it is likely that the grade B/C PF were captured in the dataset as “organ space surgical site infection,” this broad definition will not capture some ISGPF grade A fistulae that contributes to the overall complication rate. Distinction of this complication will be incorporated into subsequent NSQIP datasets as a postoperative variable. As specified within the Participant Use Data Files for NSQIP, approximately 10–15 % of patients did not have all preoperative labs drawn. While this may not significantly alter outcomes in patients with and without cardiac disease, it may influence the accuracy of the multivariable model incorporating these labs. Finally, the Participant Use Data Files did not allow for evaluation of volume-outcome relationships as data provided was an aggregate of pancreatic resections from all institutions.

Conclusion

Irrespective of these limitations, the aim of this study was to identify whether a history of cardiac disease or acute exacerbation of cardiac disease correlated with negative patient outcomes. We found that acute cardiac disease, as defined by CHF onset/exacerbation within 30 days of surgery, history of angina in 1 month before surgery, and history of MI 6 months prior to surgery, was associated with a 2.1-fold increase in mortality compared to those without an acute exacerbation via multivariate analysis. Any history of cardiac disease resulted in a 1.45-fold increase in mortality after PR via multivariate analysis. The implication of these findings are that patients who present for evaluation of pancreatic resection with concomitant history of cardiac disease or acute changes in cardiovascular status would benefit from referral to a high-volume center familiar with these complex operations and with full access to pre- and postoperative cardiologists and critical care. Proficiency with surgical procedure, experienced surgical staff, and recognition of early postoperative warning signs are essential to decrease the risk of death. Modern techniques and improved medical management have allowed for greater survival, even in patients with significant comorbidities. Consequently, PR is more commonly being performed on older

patients with associated comorbidities which can impact patient outcomes. Preoperative informed consent should include discussions regarding the putative additional risk.

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Table 1Characteristics of patients ($n=13,021$) who received pancreatic resection

Characteristic	n (%)	History of cardiac disease		p value	Acute cardiac disease		p value
		Presence ($n = 1,435$)	Absence ($n = 11,586$)		Presence ($n = 139$)	Absence ($n = 12,882$)	
Demographics							
Age				<0.0001*			<0.0001*
<50	2,177 (16.7)	47 (3.3)	2,130 (18.4)		4 (2.9)	2,173 (16.9)	
50–59	2,766 (21.2)	160 (11.2)	2,606 (22.5)		19 (13.7)	2,747 (21.3)	
60–69	3,720 (28.6)	459 (32.0)	3,261 (28.2)		46 (33.2)	3,674 (28.5)	
70–79	3,283 (25.2)	568 (39.6)	2,715 (23.4)		52 (37.4)	3,231 (25.2)	
80	1,075 (8.3)	201 (14.0)	874 (7.5)		18 (13.0)	1,057 (8.2)	
Gender				<0.0001*			<0.0014*
Male	6,259 (48.1)	1,063 (74.1)	5,196 (44.9)		88 (63.3)	6,171 (47.9)	
Female	6,741 (51.8)	371 (25.9)	6,370 (55.0)		51 (36.7)	6,690 (51.9)	
Missing	21 (0.1)	1 (0.1)	20 (0.2)		0 (0)	21 (0.2)	
Race				<0.0001*			0.715
White	10,010 (76.9)	1,187 (82.7)	8,823 (76.2)		108 (77.7)	9,902 (76.9)	
Black	1,057 (8.1)	66 (4.6)	991 (8.6)		13 (9.4)	1,044 (8.1)	
Other	1,954 (15.0)	182 (12.7)	1,772 (15.3)		18 (13.0)	1,936 (15.0)	
Preoperative health status and comorbidities							
Distribution of BMI ^a classification 2				<0.0001*			0.296
Underweight	405 (3.1)	29 (2.0)	376 (3.2)		4 (2.9)	401 (3.1)	
Normal weight	4,594 (35.3)	448 (31.2)	4,146 (35.8)		41 (29.5)	4,553 (35.3)	
Overweight	4,463 (34.3)	583 (40.6)	3,880 (33.5)		48 (34.5)	4,415 (34.3)	
Obese	3,442 (26.4)	364 (25.4)	3,078 (26.6)		43 (30.9)	3,399 (26.4)	
Missing	117 (0.9)	11 (0.8)	106 (0.9)		3 (2.2)	114 (0.9)	
Diabetes mellitus	2,433 (18.7)	474 (33.0)	1,959 (16.9)	<0.0001*	41 (29.5)	2,392 (18.6)	0.001*
Current smoker	2,838 (21.8)	314 (21.9)	2,524 (21.8)	0.94	36 (25.9)	2,802 (21.8)	0.24
Alcohol user (>2 drinks/day in 2 weeks)	397 (3.0)	41 (2.9)	356 (3.1)	0.97	8 (5.8)	389 (3.0)	0.08
Functional status prior to surgery	333 (2.6)	72 (5.0)	261 (2.3)	<0.0001*	20 (14.4)	313 (2.4)	<0.0001*
COPD ^b	566 (4.4)	127 (8.9)	439 (3.8)	<0.0001*	19 (13.7)	547 (4.3)	<0.0001*
Dyspnea	1,146 (8.8)	225 (15.7)	921 (7.9)	<0.0001*	45 (32.4)	1,101 (8.6)	<0.0001*
Hypertension requiring medication	6,760 (51.9)	1,169 (81.5)	5,591 (48.3)	<0.0001*	112 (80.6)	6,648 (51.6)	<0.0001*
Peripheral vascular disease	176 (1.4)	65 (4.5)	111 (1.0)	<0.0001*	10 (7.2)	166 (1.3)	<0.0001*
Neurologic event/disease	641 (4.9)	157 (10.9)	484 (4.2)	<0.0001*	17 (12.2)	624 (4.8)	<0.0001*
Steroid use	244 (1.9)	41 (2.9)	203 (1.8)	0.004*	4 (2.9)	240 (1.9)	0.33
Bleeding disorder	351 (2.7)	101 (7.0)	250 (2.2)	<0.0001*	15 (10.8)	336 (2.6)	<0.0001*
Chemotherapy within 30 days	209 (1.6)	17 (1.2)	192 (1.7)	0.18	2 (1.4)	207 (1.6)	1.000
Radiation therapy within 90 days	285 (2.2)	33 (2.3)	252 (2.2)	0.76	3 (2.2)	282 (2.2)	1.000

Characteristic	<i>n</i> (%)	History of cardiac disease		<i>p</i> value	Acute cardiac disease		<i>p</i> value
Other major op 30 days prior to surgery	176 (1.4)	27 (1.9)	149 (1.3)	0.18	5 (3.6)	171 (1.3)	0.041*
NSQIP risk score, mean (SD) ^c							
NSQIP probability of morbidity	0.31 (1.5)	0.397 (0.14)	0.300 (1.60)	<0.0001*	0.439 (0.18)	0.309 (1.5)	<0.0001*
NSQIP probability of mortality	0.024 (0.04)	0.041 (0.05)	0.022 (0.036)	<0.0001*	0.058 (0.08)	0.023 (0.04)	<0.0001*
ASA ^d class				<0.0001*			
No disturbance	192 (1.5)	5 (0.4)	187 (1.61)		0 (0)	192 (1.5)	
Mild disturbance	4,214 (32.4)	110 (7.7)	4,104 (35.4)		14 (10.1)	4,200 (32.6)	
Severe disturbance	8,046 (61.8)	1,143 (79.7)	6,903 (59.6)		99 (71.2)	7,947 (61.7)	
Life-threatening disturbance	560 (4.3)	175 (12.2)	385 (3.3)		26 (18.7)	534 (4.2)	
Missing	9 (0.1)	2 (0.1)	7 (0.1)		0.0	9 (0)	

*
 $p < 0.05$ (denotes statistical significance)

^a Body mass index (calculated as kilograms per square meter)

^b Chronic obstructive pulmonary disease

^c Standard deviation

^d American Society of Anesthesiologist

Table 2

Frequency of 30-day adverse outcomes in 13,021 subjects who received pancreatic resection stratified by return to OR and mortality

Adverse outcome	Reoperation (<i>n</i> =825 (+)/ <i>n</i> =12,196 (-))				Mortality (<i>n</i> =297 (+)/ <i>n</i> =12,724 (-))				Total <i>n</i> (%)
	Presence	Absence	Odds ratio	<i>p</i> value	Presence	Absence	Odds Ratio	<i>p</i> value	
Postoperative mortality	125 (15.15)	172 (1.41)	12.48	<0.0001*	NA	NA	NA	NA	297 (2.3)
Reoperation	NA	NA	NA	NA	125 (42.09)	700 (5.50)	12.48	<0.0001*	825 (6.3)
Any complication	659 (79.88)	3,564 (29.22)	9.62	<0.0001*	256 (86.20)	3,967 (31.18)	13.78	<0.0001*	4,223 (32.4)
Any serious complication	631 (76.48)	2,622 (21.50)	11.88	<0.0001*	255 (85.86)	2,998 (23.56)	19.70	<0.0001*	3,253 (25)
Prolonged length of stay	427 (51.76)	1,989(16.31)	5.51	<0.0001*	91 (30.64)	2,325 (18.27)	1.98	<0.0001*	2,416 (18.6)
Sepsis/septic shock	409 (49.58)	1,356 (11.12)	7.86	<0.0001*	152 (51.18)	1,613 (12.68)	7.22	<0.0001*	1,765 (13.6)
Abscess	336 (40.73)	1,233 (10.11)	6.11	<0.0001*	66 (22.22)	1,503 (11.81)	2.13	<0.0001*	1,569 (12)
Respiratory complication	371 (44.97)	786 (6.44)	11.86	<0.0001*	204 (68.69)	953 (7.49)	27.09	<0.0001*	1,157 (8.9)
Wound infection	107 (12.97)	984 (8.07)	1.70	<0.0001*	17 (5.72)	1,074 (8.44)	0.66	0.095	1,091 (8.4)
Urinary tract infection	67 (8.12)	600 (4.92)	1.71	<0.0001*	16 (5.39)	651 (5.12)	1.05	0.834	667 (5.1)
Neurologic complication	59 (7.15)	582 (4.77)	1.54	0.0022*	27 (9.09)	614 (4.83)	1.97	0.0008*	641 (4.9)
VTE ^a	40 (4.85)	199 (1.63)	3.07	<0.0001*	17 (5.72)	222 (1.74)	3.42	<0.0001*	239 (1.8)
Renal failure	85 (10.30)	127 (1.04)	10.92	<0.0001*	65 (21.89)	147 (1.16)	23.97	<0.0001*	212 (1.6)
Dehiscence	116 (14.06)	87 (0.71)	22.77	<0.0001*	11 (3.70)	192 (1.51)	2.51	0.0025*	203 (1.6)
MI/Cardiac arrest	59 (7.15)	143 (1.17)	6.49	<0.0001*	115 (38.72)	87 (0.68)	91.78	<0.0001*	202 (1.6)
Hemorrhage transfusion	78 (9.45)	54 (0.44)	23.48	<0.0001*	28 (9.43)	104 (0.82)	12.63	<0.0001*	132 (1.0)
Graft/prosthesis/FF	8 (0.97)	5 (0.04)	23.87	<0.0001*	3 (1.01)	10 (0.08)	12.97	<0.0001*	13 (0.1)
Peripheral nerve injury	1 (0.12)	6 (0.05)	2.47	0.388	0 (0)	7 (0.06)	NA	0.686	7 (0.1)

* *p* <0.05 (denotes statistical significance)

^aVenous thromboembolism

Table 3

Frequency of 30-day adverse outcomes in 13,021 subjects who received pancreatic resection stratified by cardiac risk factors

Adverse outcome	History of cardiac disease (<i>n</i> =1,435 (+)/ <i>n</i> =11,586 (-))				Acute cardiac disease (<i>n</i> =139(+)/ <i>n</i> =12,882(-))			
	Presence	Absence	Odds ratio	<i>p</i> value	Presence	Absence	Odds ratio	<i>p</i> value
Postoperative mortality	65 (4.53)	232 (2.00)	2.32	<0.0001*	12 (8.63)	285 (2.21)	4.18	<0.0001*
Reoperation	111 (7.74)	714 (6.16)	1.28	0.021*	10 (7.20)	815 (6.30)	1.15	0.676
Any complication	600 (41.81)	3,623 (31.27)	1.58	<0.0001*	65 (46.8)	4,158 (32.3)	1.84	0.0003*
Any serious complication	486 (33.87)	2,767 (23.88)	1.63	<0.0001*	52 (37.4)	3,201 (24.9)	1.81	0.0007*
Prolonged length of stay	333 (23.21)	2,083 (17.98)	1.37	<0.0001*	45 (32.4)	2,371 (18.4)	2.12	<0.0001*
Sepsis/septic shock	270 (18.82)	1,495 (12.90)	1.56	<0.0001*	20 (14.4)	1,745 (13.6)	1.07	0.773
Abscess	200 (13.94)	1,369 (11.82)	1.21	0.020*	22 (15.8)	1,547 (12.0)	1.38	0.169
Respiratory complication	220 (15.33)	937 (8.09)	2.05	<0.0001*	30 (21.6)	1,127 (8.80)	2.87	<0.0001*
Wound infection	147 (10.24)	944 (8.15)	1.29	0.007*	14 (10.1)	1,077 (8.40)	1.23	0.469
Urinary tract infection	65 (4.53)	602 (5.20)	0.87	0.280	10 (7.20)	657 (5.10)	1.44	0.265
Neurologic complication	157 (10.94)	484 (4.18)	2.82	<0.0001*	17 (12.2)	624 (4.80)	2.74	<0.0001*
VTE ^a	35 (2.44)	204 (1.76)	1.39	0.071	5 (3.60)	234 (1.80)	2.02	0.120
Renal failure	49 (3.41)	163 (1.41)	2.48	<0.0001*	6 (4.30)	206 (1.60)	2.78	0.012*
Dehiscence	35 (2.44)	168 (1.45)	1.70	0.004*	3 (2.20)	200 (1.60)	1.40	0.566
MI/cardiac arrest	54 (3.76)	148 (1.28)	3.02	<0.0001*	11 (7.90)	191 (1.50)	5.71	<0.0001*
Hemorrhage requiring transfusion	15 (1.05)	117 (1.01)	1.04	0.899	3 (2.20)	129 (1.00)	2.18	0.176
Graft/prosthesis/FF	1 (0.07)	12 (0.10)	0.67	1.000	0	13 (0.10)	NA	1.000
Peripheral nerve injury	1 (0.07)	6 (0.05)	1.35	0.559	0	7 (0.10)	NA	1.000

* *p* <0.05 (denotes statistical significance)

^aVenous thromboembolism

Table 4

Patient preoperative characteristics and correlation with postoperative complications or mortality

Characteristic	<i>n</i> (%)	Serious complication (<i>n</i> =3253) Univariate Analysis <i>p</i> value	30-Day mortality (<i>n</i> =297) Univariate Analysis <i>p</i> value
Demographics			
Age		<0.0001*	<0.0001*
<50	2,177 (16.7)		
50–59	2,766 (21.2)		
60–69	3,720 (28.6)		
70–79	3,283 (25.2)		
80	1,075 (8.26)		
Gender		<0.0001*	0.049*
Male	6,259 (48.1)		
Female	6,741 (51.8)		
Missing	21 (0.1)		
Race		0.099	0.183
White	10,010 (76.9)		
Black	1,057 (8.1)		
Other	1,954 (15)		
Preoperative health status and comorbidities			
Distribution of BMI ^a classification		<0.0001*	0.677
Underweight	405 (3.11)		
Normal weight	4,594 (35.28)		
Overweight	4,463 (34.28)		
Obese	3,442 (26.43)		
Missing	117 (0.90)		
Diabetes mellitus	2,433 (18.7)	0.007*	0.0004*
Current smoker	2,838 (21.8)	0.204	0.095
Alcohol user (>2 drinks/day in 2 weeks)	397 (3.0)	0.007*	0.178
Functional status prior to surgery	333 (2.6)	<0.0001*	<0.0001*
COPD ^b	566 (4.4)	<0.0001*	0.004*
Dyspnea	1,146 (8.8)	<0.0001*	<0.0001*
Hypertension requiring medication	6,760 (51.9)	<0.0001*	<0.0001*
Peripheral vascular disease	176 (1.4)	<0.0001*	0.007*
Neurologic event/disease	641 (4.9)	0.0002*	0.0008*
Steroid use	244 (1.9)	<0.0001*	0.005*
Bleeding disorder	351 (2.7)	<0.0001*	0.148
Chemotherapy within 30 days	209 (1.6)	0.351	0.636
Radiation therapy within 90 days	285 (2.19)	0.121	0.160

Characteristic	<i>n</i> (%)	Serious complication (<i>n</i> =3253) Univariate Analysis <i>p</i> value	30-Day mortality (<i>n</i> =297) Univariate Analysis <i>p</i> value
Other major operation within 30 days prior to surgery	176 (1.4)	0.128	0.128
NSQIP risk score, mean (SD) ^c			
NSQIP probability of morbidity	0.31 (1.51)	<0.0001 [*]	<0.0001 [*]
NSQIP probability of mortality	0.024 (0.039)	<0.0001 [*]	<0.0001 [*]
History of cardiac disease	1,435 (11.0)	<0.0001 [*]	<0.0001 [*]
Acute cardiac disease	139 (1.07)	0.0007 [*]	<0.0001 [*]
ASA ^d class		<0.001 [*]	<0.001 [*]
No disturbance	192 (1.5)		
Mild disturbance	4,214 (32.4)		
Severe disturbance	8,046 (61.8)		
Life-threatening disturbance	560 (4.3)		
Missing	9 (0.1)		

^{*} *p* <0.05 (denotes statistical significance)

^a Body mass index (calculated as kilogram per square meter)

^b Chronic obstructive pulmonary disease

^c Standard deviation

^d American society of anesthesiologist

Table 5

Multivariate logistic regression for 30-day mortality - core variables + history of cardiac disease (A) or acute cardiac disease (B)

Demographics	Adjusted odds ratio	95 % CI	Wald chi-square <i>p</i> value
Characteristic			
A			
Age		<0.0001	
<50	Ref	Ref	Ref
50–59	1.87	(1.043, 3.359)	0.036
60–69	2.43	(1.405, 4.202)	0.002
70–79	3.55	(2.062, 6.115)	<0.0001
80	4.88	(2.718, 8.778)	<0.0001
Preoperative health status and comorbidities			
Functional status prior to surgery	2.89	(1.908, 4.389)	<0.0001
Dyspnea	1.57	(1.127, 2.184)	0.008
History of cardiac disease	1.45	(1.068, 1.960)	0.017
Acute cardiac disease	NA	NA	NA
Major cardiac procedure	NA	NA	NA
ASA ^a class			0.001
No disturbance	Ref	Ref	Ref
Mild disturbance	1.20	(0.161, 8.903)	0.861
Severe disturbance	2.52	(0.345, 18.36)	0.363
Life-threatening disturbance	3.19	(0.422, 24.14)	0.261
Preoperative laboratory value			
Serum albumin (g/dL)			
<3	1.62	(1.200, 2.185)	0.0016
>3	Ref	Ref	Ref
Serum creatinine (mg/dL)			
1.2	Ref	Ref	Ref
>1.2	1.67	(1.221, 2.291)	0.001
B			
Age			<0.0001
<50	Ref	Ref	Ref
50–59	1.88	(1.046, 3.368)	0.035
60–69	2.49	(1.441, 4.303)	0.001
70–79	3.70	(2.154, 6.359)	<0.0001
80	5.16	(2.879, 9.239)	<0.0001
Preoperative health status and comorbidities			
Functional status prior to surgery	2.85	(1.873, 4.332)	<0.0001
Dyspnea	1.56	(1.119, 2.175)	0.009
History of cardiac disease	NA	NA	NA
Acute cardiac disease	2.07	(1.090, 3.920)	0.026

Demographics	Adjusted odds ratio	95 % CI	Wald chi-square <i>p</i> value
Major cardiac procedure	1.45	(1.061, 1.969)	0.0195
ASA ^a class			0.008
No disturbance	Ref	Ref	Ref
Mild disturbance	1.20	(0.161,8.924)	0.859
Severe disturbance	2.52	(0.345,18.37)	0.363
Life-threatening disturbance	3.25	(0.429,24.54)	0.254
Preoperative laboratory value			
Serum albumin (g/dL)			
<3	1.61	(1.192, 2.172)	0.0019
>3	Ref	Ref	Ref
Serum creatinine (mg/dL)			
1.2	Ref	Ref	Ref
>1.2	1.69	(1.231, 2.312)	0.001

^a American Society of Anesthesiologist