Perioperative Mortality for Pancreatectomy

A National Perspective

James T. McPhee, MD, Joshua S. Hill, MD,* Giles F. Whalen, MD,**
Maksim Zayaruzny, MD, MPH, Demetrius E. Litwin, MD, MBA,* Mary E. Sullivan, MS,**
Frederick A. Anderson, PhD,† and Jennifer F. Tseng, MD**

Objective: To analyze in-hospital mortality after pancreatectomy using a large national database.

Summary and Background Data: Pancreatic resections, including pancreaticoduodenectomy, distal pancreatectomy, and total pancreatectomy, remain the only potentially curative interventions for pancreatic cancer. The goal of this study was to define factors affecting outcomes after pancreatectomy for neoplasm.

Methods: A retrospective analysis was performed using all patients undergoing pancreatic resections for neoplastic disease identified from the Nationwide Inpatient Sample from 1998 to 2003. Crude in-hospital mortality was analyzed by χ^2. A multivariable model was constructed to adjust for age, sex, hospital teaching status, hospital surgical volume, year of resection, payer status, and selected comorbid conditions.

Results: In all, 279,445 patient discharges were identified with a primary diagnosis of pancreatic neoplasm. A total of 39,463 (14%) patients underwent resection during that hospitalization. In-hospital mortality was 5.9% with a significant decrease from 7.8% to 4.6% from 1998 to 2003 by trend analysis ($P < 0.0001$). Resections done at low (<5 procedures/year)- and medium (5–18/year)-volume centers had higher mortality compared with those at high (>18/year)-volume centers (low-volume odds ratio = 3.3; 95% confidence interval, 2.3–4.; medium-volume, odds ratio = 2.1; 95% confidence interval, 1.5–3.0). The proportion of procedures performed at high volume centers increased from 30% to 39% over the 6-year time period ($P < 0.0001$) by trend test.

Conclusions: This large observational study demonstrates an improvement in operative mortality for patients undergoing pancreatectomy for neoplastic disease from 1998 to 2003. In addition, a greater proportion of pancreatectomies were performed at high-volume centers in 2003. The regionalization of pancreatic surgery may have partially contributed to the observed decrease in mortality rates.

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Pancreatic cancer remains the fourth leading cause of cancer deaths overall in the United States, killing an estimated 31,800 people in 2005.[1] A number of single-institution and single-state reports have described an improvement in perioperative mortality in the 1980s and 1990s for high-risk cancer resections, including pancreaticoduodenectomy (PD).[2–4] In the state of Maryland, concurrent with a move toward statewide regionalization of PD, a decrease in perioperative mortality was described over an 11-year span.[2]

In contrast, in 2002, a national study based on the Medicare Provider Analysis and Review database evaluated trends in operative outcomes over time for high-risk procedures.[5] This study, which included PD, concluded that no significant improvement in perioperative mortality was found for the years 1994 to 1999 for PD. While previous studies have focused on resections of the pancreatic head, there is a paucity of national data focused on distal pancreatectomy and total pancreatectomy for neoplastic disease. Several studies evaluating surgical outcomes are limited by number of subjects or by single-institutional design.[6–10]

The inverse relationship between mortality and hospital surgical volume for high-risk procedures, including major cancer resections, has been demonstrated in prior studies over the past several years.[11–17] Researchers working in collaboration with organizations such as the Leapfrog Group have proposed that patient lives can be saved by the enforcement of volume criteria.[18] This information is readily available to the consumer (www.leapfroggroup.org).[19]

In the current work, we sought to analyze the national picture on perioperative mortality for pancreatic resection, including PD, distal pancreatectomy, and total pancreatectomy, for all neoplastic disease including all periampullary cancers as well as benign neoplastic disease. If perioperative mortality for major pancreatic resection has declined, a portion of this decline might be attributable to a change in referral patterns, with a greater percentage of procedures being performed at higher-volume centers.

From the *Department of Surgery and †Center for Outcomes Research, University of Massachusetts Medical School, Worcester, MA.

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Reprints: Jennifer F. Tseng, MD, University of Massachusetts Medical School, UMass Memorial Medical Center, 119 Belmont Street, Swift House, Worcester, MA 01605-2982. E-mail: tsengj@ummhc.org.

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MATERIALS AND METHODS

Database

To evaluate trends in pancreatic resection for neoplastic disease at the national level, we used the Nationwide Inpatient Sample (NIS) for the years 1998 to 2003, inclusive. The NIS is the largest national all-payer hospital inpatient care database in the United States. Data exist for approximately 7 million hospital discharges per year from a stratified sample of 20% of nonfederal U.S. community hospitals from participating states (n = 37 in 2003), including academic and specialty hospitals.[20] The NIS is supported by the Healthcare Cost and Utilization Project and contains all-payer discharge information for 100% of patient discharges from participating hospitals. It contains hospital level information obtained from a direct link to the American Hospital Association's annual survey of hospitals, which includes hospital type (teaching/nonteaching) and geographic region (Northeast, West, South, Midwest as defined by the U.S. Census Bureau). A weighting strategy is implemented by the NIS to allow population-based estimates to be drawn at the national level. Sampled hospitals are given appropriate weights based on the number of hospitals they represent in the database for a given year.[20] All statistical analyses were performed based on these survey weights; therefore, all data provided in the results represent weighted frequencies.

Diagnosis Codes

The primary measured outcome for this study was in-hospital mortality. Mortality was defined as death from any cause prior to discharge regardless of time from operation. To identify all patient discharges with the principal diagnosis of pancreatic neoplasm, including benign lesions, we used selected codes from the International Classification of Diseases Ninth Revision Clinical Modification (ICD-9-CM).[21] We limited the initial cohort to those patients undergoing pancreatectomy based on the ICD-9 procedure codes for pancreatic resections (Table 1).

Volume Analysis

To evaluate hospital surgical volume, we categorized the hospitals as low volume (average <5 pancreatic resections/year over the years analyzed), medium volume (average 5–18 resections/year), or high volume (average >18 resections/year). These procedure volume numbers were selected to obtain 3 volume groups of approximately equal sizes for purposes of comparison prior to any volume–outcome data analyses, a technique previously described by other authors.[12]

Statistical Analysis

All data were analyzed using the advanced survey procedures in SAS version 9.1 (SAS Institute, Cary, NC). Univariate analyses of categorical variables were performed using Rao-Scott χ^2 tests, with a P value <0.05 considered statistically significant. All pancreatic resections were first evaluated in aggregate form, and then separate univariate analyses were performed to evaluate PD, distal pancreatectomy, and total pancreatectomy. Proximal pancreatectomy was thought to include heterogeneous operations (eg, PD, duodenum-sparing pancreatectomy); thus, a separate analysis was not included. Trend analyses were performed using the Mantel-Haenszel χ^2 test. A multivariable logistic regression was constructed with in-hospital mortality as the dependent variable. Independent variables included patient age group (<50, 50–69, ≥70 years), sex, race, and year of resection. Additionally, various comorbid medical conditions were included in the analyses from previously established comorbidity software for use with national datasets (congestive heart failure, chronic lung disease, valvular heart disease, renal failure, diabetes mellitus, liver disease, obesity, and peripheral vascular disease).[22] Certain hospital level characteristics, including calculated surgical volume, geographic region (as described above), and teaching status, were also evaluated as independent variables.

TABLE 1. ICD-9 CM Diagnostic and Procedural Codes

Diagnostic Code	Diagnosis	Procedural Code	Procedure
152.0	Malignancy of duodenum	52.6	Pancreatectomy (total) with synchronous duodenectomy
156.1	Malignancy of extrahepatic bile ducts	52.7	Pancreaticoduodenectomy, radical (one-stage) (two-stage)
156.2	Periampullary malignancy	52.51	Proximal pancreatectomy (head) (with part of body) (with synchronous duodenectomy)
156.8	Unspecified bile duct malignancy	52.52	Distal pancreatectomy (tail) (with part of body)
157.0	Malignancy of pancreatic head	52.53	Radical/subtotal pancreatectomy
157.1	Malignancy of pancreatic body	52.59	Pancreatectomy/pancreaticoduodenectomy partial NEC
157.2	Malignancy of pancreatic tail	52.51	Proximal pancreatectomy (head) (with part of body) (with synchronous duodenectomy)
157.3	Malignancy of pancreatic ducts	52.52	Distal pancreatectomy (tail) (with part of body)
157.8	Malignancy of neck, contiguous sites, ectopic tissue	52.53	Radical/subtotal pancreatectomy
157.9	Malignant primary of pancreas	52.59	Pancreatectomy/pancreaticoduodenectomy partial NEC
211.6	Benign neoplasm of pancreas		
235.5	Pancreatic neoplasm of uncertain behavior		
230.9	Malignant neoplasm in situ		
239.0	Unspecified pancreatic neoplasm		

TABLE 2. Patient and Hospital Characteristics for All Pancreatic Resections for Neoplasm (1998–2003): Results of Univariate Analysis of Mortality Included

Factor	Overall No. (%)	Mortality Rate (%)	P
No. patients (weighted)	39,463 (100)	5.9	NA
Age (yr)			<0.0001
Mean (SEM)	64.1 (0.19)		
<50	5392 (13.7)	1.8	
50–69	18,390 (46.6)	4.7	
≥70	15,652 (39.7)	8.8	
Sex			<0.0001
F	20,329 (51.6)	4.4	
M	19,082 (48.4)	7.5	
Race			0.02
White	23,596 (79.6)	5.8	
Nonwhite	6066 (20.4)	5.7	
Year of resection			0.044
1998	4893 (12.4)	7.8	
1999	6362 (16.1)	4.8	
2000	5688 (14.4)	6.7	
2001	6609 (16.8)	6.4	
2002	7525 (19.1)	6.0	
2003	8346 (21.1)	4.6	
Diagnosis type			<0.0001
Periampullary malignancy	24,725 (62.7)	6.7	
Benign/unspecified	6943 (17.6)	3.5	
Malignancy of body/tail	3807 (9.7)	4.8	
Biliary tract neoplasm	1823 (4.6)	7.8	
Ductal malignancy	802 (2.0)	8.8	
Metastatic disease	703 (1.8)	3.5	
Islet cell neoplasm	619 (1.6)	1.3	
Procedure type			0.0002
Pancreaticoduodenectomy	27,289 (72.3)	6.6	
Distal pancreatectomy	7872 (20.8)	3.5	
Total pancreatectomy	1399 (3.7)	8.3	
Other	1201 (3.2)	5.4	
Comorbid conditions			
Other/none	23,642 (57.2)	NA	NA
Diabetes mellitus	7728 (19.6)	4.3	0.003
Chronic lung disease	4465 (11.3)	8.6	0.0002
Congestive heart failure	1657 (4.2)	16.7	<0.0001
Valvular heart disease	1409 (3.6)	7.3	0.36
Liver disease	1083 (2.7)	10.9	0.002
Obesity	883 (2.2)	1.1	0.006
Peripheral vascular disease	690 (1.8)	12.7	0.002
Renal failure	395 (1.0)	36.1	<0.0001
Payer status			0.39
Private/HMO	35,924 (91.3)	6.0	
Medicaid/self-pay/other	3416 (8.7)	5.2	
Hospital type			<0.0001
Teaching	28,351 (71.9)	4.5	
Nonteaching	11,068 (28.1)	9.5	
Hospital geographic region			0.06
Northeast	8694 (22.1)	5.0	
Midwest	9605 (24.4)	5.1	
South	13,323 (33.8)	7.2	
West	7801 (19.8)	5.6	
Hospital surgical vol.			<0.0001
Low (<5/yr)	13,575 (34.4)	9.2	
Medium (5–18/yr)	13,047 (33.1)	5.9	
High (>18/yr)	12,802 (32.5)	2.4	

NA indicates not applicable.

Unadjusted and adjusted odds ratios were calculated to determine the effects of the identified covariates on the outcome measure of perioperative mortality.

Patient race was evaluated by univariate analysis and was initially included in the logistic regression. However, due to a prohibitive amount of missing data, race was ultimately excluded from the multivariate analysis.

RESULTS

Demographics

During the sampled time frame 1998 to 2003, 279,445 patient discharges occurred for the principal diagnosis of pancreatic neoplasm. Overall, 39,463 (14%) patients underwent pancreatic resection during that hospitalization, for an average of 6600 resections per year. Of the operative cohort, 52% were female. The mean age for all patients was 69 years (range, 18–103 years) while the mean age for operative patients was 64 years (range, 18–93 years). Patient characteristics, including the univariate analysis of mortality, are shown in Table 2. Of patients who underwent resection, 63% had operations for malignancy of the pancreatic head, neck, or periampullary region. Table 3 includes the breakdown of patient characteristics by hospital volume strata, including procedure type and medical comorbidities.

Univariate Analysis

For all resected patients, the crude in-hospital mortality rate was 5.9%. The Mantel-Haenszel test for linear association, which included all of the studied years, revealed that the mortality decrease over time from 7.8% in 1998 to 4.6% in 2003 was a significant trend ($P < 0.0001$) (Fig. 1). Mortality was higher for males than for females ($P < 0.0001$). In addition, in-hospital mortality increased with older patient age ($P < 0.0001$). Institutional annual surgical volume inversely correlated with mortality in the univariate analysis. The highest-volume centers (>18 resections/year) had a mortality of 2.5% compared with medium-volume centers (5–18 resections/year) and low-volume centers (<5 resections/year), which had overall mortality rates of 5.9% and 9.2%, respectively ($P < 0.0001$). This inverse relationship of decreasing mortality with increasing volume was also significant by the trend test ($P < 0.0001$) (Table 2).

Multivariable Analysis

Using a multivariable logistic regression model, independent predictors of in-hospital mortality were evaluated. A hospital's annual surgical volume was highly predictive of

in-hospital mortality. Compared with the high-volume centers (>18 resections/year), the low-volume centers (<5 resections/year) had 3.3 times higher likelihood of death in the hospital (95% confidence interval [CI], 2.3–4.8), while the medium-volume centers (5–18 resections/year) had odds ratio of death of 2.1 (95% CI, 1.5–3.0) compared with high-volume centers ($P < 0.0001$). Patient factors that were significantly predictive of in-hospital mortality included male sex ($P < 0.0001$), older age ($P < 0.0001$), and certain comorbid medical conditions, including renal failure ($P < 0.0001$), congestive heart failure ($P < 0.0001$), and a history of liver disease ($P = 0.003$) (Table 4; Fig. 2).

Overall, the year of resection, when evaluated as a continuous variable, was not independently predictive of a difference in mortality ($P = 0.11$). However, when evaluated as a categorical variable, which included all of the studied years; the year 1998, when directly compared with the year 2003, demonstrated an adjusted odds ratio of mortality of 1.49 (95% CI, 1.04–2.13). The remainder of the years when compared with 2003 did not demonstrate a significant value. Payer status ($P = 0.10$), obesity ($P = 0.11$), chronic lung disease ($P = 0.34$), and valvular heart disease ($P = 0.63$) also were not independently predictive of in-hospital mortality in the adjusted logistic regression model.

To assess whether practice and referral patterns to higher-volume centers could explain a portion of the observed decrease in perioperative mortality rates, the percentage of cases performed over time in the different volume designated hospitals was evaluated. In 1998, 30% of resections were performed at high-volume centers; and in 2003, 39% of pancreatic resections were performed at high-volume centers. This increasing percentage of cases performed at high-volume centers over time was significant by the trend test ($P < 0.0001$) (Fig. 3).

Using the overall mortality rates for patients at high-, medium-, and low-volume centers, we calculated the expected change in mortality from 1998 to 2003 based on this shift from low- to high-volume centers. This predicted a change in mortality of 0.8% from 1998 to 2003, which accounts for approximately one fourth of the observed change of 3.3% in our cohort, indicating that, to some degree (approximately 25%), this shift to higher-volume centers has contributed to the observed decrease in mortality rate.

Mortality by Procedure

Separate univariate analyses were performed for PD, distal pancreatectomy, and total pancreatectomy for neoplastic disease. The results of these univariate analyses can be found in Table 5. PD was the most frequent procedure performed (72%). The overall perioperative mortality rate was 6.6%. By the trend test, there was a significant decrease in mortality from 8.2% in 1998 to 5.5% by 2003 ($P = 0.003$). The mortality rate was higher for men compared with women (8.2% vs. 4.8%, $P < 0.0001$), as well as the oldest patient

TABLE 3. Hospital Characteristics for All Pancreatic Resections for Neoplasm by Volume Designations

	Low (<5/year)	Medium (5–18/year)	High (>18/year)	Overall	*P*
No. (%) hospitals	1356 (78)	321 (18.4)	66 (3.8)	1743	NA
No. patients*	13,575	13,047	12,802	39,463	0.94
Age (yr) [mean (SEM)]	64.9 (0.23)	64.1 (0.25)	63.3 (0.25)	64.1 (0.14)	<0.0001
Age groups					0.003
<50 yr (%)	12.5	13.8	14.8	13.7	
50–69 yr (%)	44.8	46.5	48.7	46.6	
≥70 yr (%)	42.7	39.7	36.5	39.7	
Sex					0.09
M (%)	46.6	49.3	49.5	48.4	
F (%)	53.4	50.7	50.5	51.6	
Procedure type (%)					0.02
Pancreaticoduodenectomy	68.4	74.0	74.6	72.3	
Distal pancreatectomy	24.6	19.4	18.4	20.8	
Total pancreatectomy	3.8	3.5	3.8	3.7	
Other	3.2	3.5	3.2	3.2	
Comorbid conditions (%)					
Other/none	51.4	46.1	41.4	46.4	NA
Diabetes	20.4	19.8	18.4	19.6	0.23
Chronic lung disease	14.1	10.7	9.0	11.3	<0.0001
Congestive heart failure	5.9	3.8	2.9	4.2	<0.0001
Valvular heart disease	3.3	3.6	3.8	3.6	0.66
Liver disease	2.4	2.7	3.2	2.7	0.38
Obesity	2.3	2.5	1.9	2.2	0.37
Peripheral vascular disease	1.7	1.9	1.7	1.8	0.84
Renal failure	1.3	1.1	0.51	1.0	0.004

*Weighted frequency.
NA indicates not applicable.

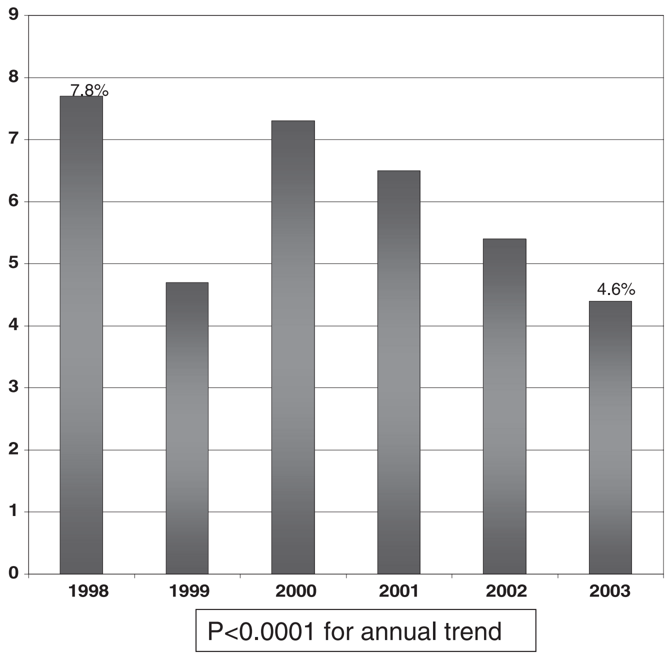

FIGURE 1. The in-hospital mortality rate (%) for all pancreatic resections for neoplasm from 1998 to 2003. The decrease over time was a significant trend ($P < 0.0001$).

group (≥70 years) compared with the youngest group (<50 years) (9.5% vs. 2.6%, $P < 0.0001$). The lowest-volume pancreatic surgery centers had significantly higher mortality rates compared with the highest-volume centers (11.1% vs. 2.7%, $P < 0.0001$).

Distal pancreatectomy was the second most common procedure performed (21%). This had the lowest overall mortality rate of all studied resection types (3.5%). Mortality rate was significantly higher for men (4.9% vs. 2.8%, $P = 0.029$), older patients (patients ≥70 years, 6.5% vs. patients <50 years, 0.3%, $P < 0.0001$), and patients undergoing operations at the lowest-volume centers (5.1% vs. 0.43% for high-volume centers, $P < 0.0001$) (Table 5).

Total pancreatectomy was the least common procedure (3.7%). These patients had the highest overall perioperative mortality at 8.3%, a factor that did not significantly vary by hospital volume ($P = 0.85$). A patient's sex did not significantly influence mortality, ($P = 0.42$). The youngest patient group (age <50 years) did not have a significantly lower in-hospital mortality compared with the older patient groups (age 50–70 and age >70 years) (3.0% vs. 9.6% and 8.3%, respectively, $P = 0.49$).

DISCUSSION

In this study, we have demonstrated that pancreatic resections for neoplastic disease remain operations that are associated with significant perioperative mortality in the current era. We found an overall in-hospital mortality rate of 5.9% for all pancreatic resections for neoplastic disease. This rate has significantly decreased over time. In-hospital mortality decreased from 7.8% in 1998 to 4.6% by 2003. After pancreatectomy, in-hospital mortality correlated inversely with volume; the high-volume centers had a crude mortality rate of 2.4% compared with 9.2% for the low-volume group. After multivariable analysis, a hospital's annual surgical volume, remained strongly associated with in-hospital mortality, with the low-volume centers having odds ratio of death of 3.3 compared with the high-volume centers. Intriguingly, our data suggest that increasing regionalization of these high-risk operations may have contributed in part to the observed improvement in outcome and that approximately one fourth of the observed decrease in mortality may be attributable to more pancreatectomies being performed at high-volume centers. Older patients, males, and individuals with medical comorbidities had higher perioperative mortality for pancreatic resection.

Our results, with an overall mortality of 5.9%, compare favorably with previously published reports, which are largely limited to resections involving the pancreatic head. Our overall PD in-hospital mortality rate of 6.6% for 27,323 PDs shows a substantial decrease from that reported in previous national surveys, which typically report values of >10%[5,15] up to 14%.[11] Of note, the NIS is an all-payer database and includes all adult patients, in contrast to studies using other databases, which may be limited to patients 65 years of age or older.[5,13,15] Additionally, the current work reports in-hospital mortality rates as opposed to 30-day mortality rates.[5,13]

In our study, mortality rates differed according to the type of pancreatic resection performed. PD was the most frequent procedure performed, and the overall in-hospital mortality rate for the 27,323 patients by weighted analysis undergoing PD was 6.6%. In analyzing risk factors by type of procedure, we found that men had significantly higher mortality rates compared with women for PD (8.2% vs. 4.8%). Because of the paucity of published national data on in-hospital mortality for distal pancreatectomy and total pancreatectomy for neoplastic disease, these procedures were evaluated as separate analyses. The observed in-hospital mortality rate for distal pancreatectomy in 7876 patients was 3.5%. Considerable variability exists in the literature, with perioperative mortality rates for distal pancreatectomy ranging from 0% to 21%.[6–9] These prior studies are generally limited by total number due to single-institution or case series. Total pancreatectomy for neoplasm is a rarely performed procedure; indeed, some authors have questioned it as a viable treatment option for malignancy due to its poor overall survival despite its technical feasibility.[10] No specific national benchmark was identified for the purposes of comparison to our study, which found an overall mortality rate after total pancreatectomy of 8.3%; however, in smaller series, the perioperative mortality rate ranges from 3% to 28%.[10,23] In the current work, the relatively small number of patients undergoing total pancreatectomy (n = 1399) limited the significance of comparisons made between groups as seen in the observed differences in mortality rates between the low-volume (9.6%) and high-volume (7.2%) groups ($P = 0.85$).

In the literature, conflicting data exist regarding an improvement in perioperative mortality over time for PD. Goodney et al, using the Medicare Provider Analysis and Review database from 1994 to 1999, found no significant improvement in mortality for pancreatectomy over a 6-year

TABLE 4. Logistic Regression of In-Hospital Mortality (Unadjusted and Adjusted)

Factor	Odds Ratio (Unadjusted)	95% Confidence Interval	Odds Ratio (Adjusted)	95% Confidence Interval
Patient sex				
Men (vs. women)	1.76	1.45–2.13	1.63	1.32–2.00
Age groups (yr)				
≥70 (vs. <50)	5.38	3.40–8.51	4.43	2.68–7.30
≥70 (vs. 50–69)	1.97	1.63–2.39	1.83	1.48–2.28
Year of resection				
1998 (vs. 2003)	1.76	1.14–2.72	1.49	1.04–2.13
1999 (vs.2003)	1.06	0.74–1.53	1.02	0.71–1.46
2000 (vs. 2003)	1.51	1.04–2.20	1.35	0.95–1.91
2001 (vs. 2003)	1.42	0.96–2.10	1.31	0.91–1.90
2002 (vs. 2003)	1.34	0.93–1.95	1.37	0.97–1.94
Insurance type				
Medicaid/self-pay (vs. Medicare/private)	0.86	0.60–1.22	1.19	0.81–1.75
Procedure Type				
Distal pancreatectomy (vs. pancreaticoduodenectomy)	0.52	0.39–0.69	0.57	0.42–0.77
Total pancreatectomy (vs. pancreaticoduodenectomy)	1.28	0.80–2.06	1.39	0.86–2.25
Comorbidities				
Diabetes mellitus (vs. none)	0.66	0.51–0.87	0.59	0.45–0.79
Chronic lung disease (vs. none)	1.59	1.24–2.04	1.17	0.90–1.53
Valvular heart disease (vs. none)	1.27	0.76–2.11	0.90	0.53–1.52
Congestive heart failure (vs. none)			2.45	1.73–3.49
Liver disease (vs. none)	2.01	1.28–3.16	2.07	1.30–3.29
Obesity (vs. none)	3.51	2.58–4.78	0.32	0.08–1.28
Peripheral vascular disease (vs. none)	2.37	1.35–4.15	2.18	1.24–3.82
Renal failure (vs. none)	9.53	5.95–15.3	7.09	4.03–12.5
Hospital surgical vol.				
Low (vs. high)	4.12	3.04–5.58	3.33	2.33–4.75
Medium (vs. high)	2.53	1.84–3.48	2.14	1.52–3.01
Hospital teaching status				
Nonteaching (vs. teaching)	2.24	1.79–2.81	1.25	0.97–1.62

period, with the mortality rate remaining greater than 10% over the duration of the study.[5] This may reflect in part a difference in patient case-mix between the databases. In

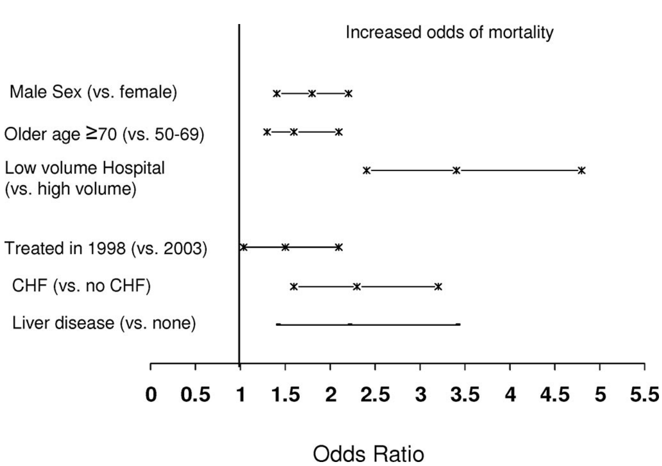

FIGURE 2. The multivariable logistic regression for in-hospital mortality following pancreatic resection for neoplasm. Data are adjusted odds ratios with 95% confidence intervals.

addition, the current series, which covers the years 1998 to 2003, may better capture a national trend toward the regionalization of high-risk surgery. The decreasing mortality rate over time for PD seen in this study is comparable to the findings by Gordon et al with data from the state of Maryland demonstrating a decrease in perioperative mortality over a 12-year period concurrent with the regionalization of pancreatic surgery to high-volume centers.[2] In addition, Kotwall et al, in their NIS-based analysis, identified a progressive decrease in mortality from 1988 through 1995, although the mortality rate in 1995 was still greater than 8%,[11] in contrast to the 5.9% seen in our study from 1998 to 2003. The fact that the decreased mortality rate seen in the current study was not uniformly linear indicates that other confounding factors may exist, such as hospital sampling variability and coding inaccuracies, despite the rigorous sampling methodology used by the NIS.[20]

With administrative databases, the difficulty of accurately assessing patient case-mix, including severity of comorbid disease, and distinguishing preexisting comorbidity from postoperative complications, is well documented.[24,25] In this study, these limitations certainly apply. We have no

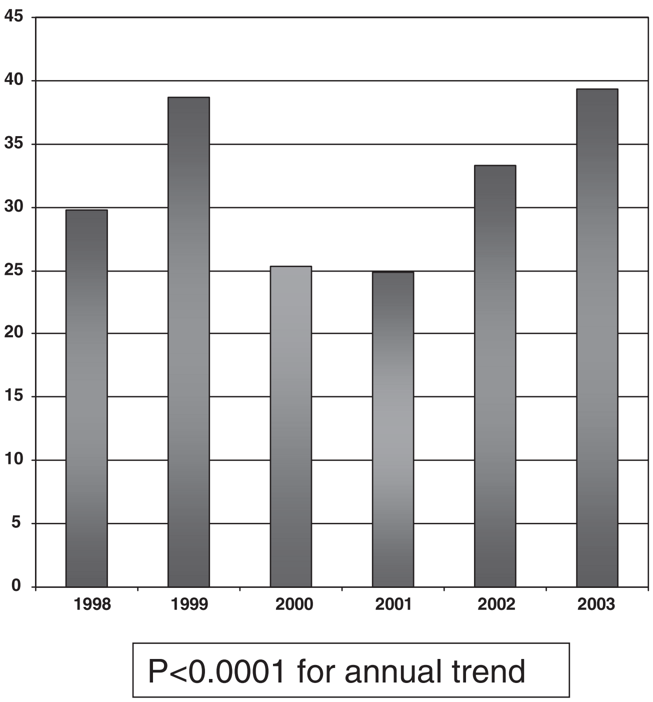

FIGURE 3. The percentage of pancreatic resections for neoplasm performed at high volume centers from 1998 to 2003. The shift over time was a significant trend ($P < 0.0001$).

information on stage of disease or patient preoperative performance status; however, other reports have concluded that patient level characteristics probably do not account for observed mortality outcomes across hospital volume strata.[12,15,16] Likewise, certain patient demographic information such as race was excluded from the final multivariable regression due to a prohibitive amount of missing data, which is a known limitation of administrative datasets. As noted above, the current work looks at the outcome measure of in-hospital mortality. This may reflect a lower mortality rate compared with studies utilizing 30-day mortality rates, especially if patients are being discharged from the hospital prior to their death. Other outcomes such as more comprehensive 30-day and long-term mortality data as well as postoperative morbidity and complications, including reoperation, pancreatic leak rates, and hospital readmission, are crucial in evaluating performance across hospital surgical volume strata in addition to trends over time.

The reasons for a decrease in perioperative mortality for pancreatic resection over time are multifactorial. Our data suggest that a modest proportion (≈25%) may be attributable to a shift of high-risk procedures to higher-volume centers with demonstrated superior outcomes. It should be noted that at the lowest-volume centers, which had the most room for improvement, a substantial decrease in perioperative mortality also occurred over time. We can speculate about a referral bias where the higher-risk patients or the more difficult resections were referred to higher-volume centers; however, the mean patient age and comorbidity profiles were similar across the volume designations. Other factors may include improvements in patient selection over time, the development of diagnostic modalities for more accurate preoperative staging, advances in perioperative care, and the presence of clinical pathways for pancreatic surgery.[26,27] These and other factors warrant further investigation.

TABLE 5. Univariate Analyses of Mortality for Pancreaticoduodenectomy, Distal Pancreatectomy, and Total Pancreatectomy

	Pancreaticoduodenectomy		Distal Pancreatectomy		Total Pancreatectomy	
Factor	**Mortality (%)**	***P***	**Mortality (%)**	***P***	**Mortality (%)**	***P***
Overall	6.6	NA	3.5	NA	8.3	NA
Sex		<0.0001		0.029		0.42
M	8.2		4.9		7.0	
F	4.8		2.8		9.8	
Age (yr)		<0.0001		<0.0001		0.49
<50	2.6		0.3		3.0	
50–69	4.8		3.0		9.6	
≥70	9.5		6.5		8.3	
Year of resection		0.003 (trend)		0.007 (trend)		0.039 (trend)
1998	8.2		3.1		17.1	
1999	5.4		3.5		4.1	
2000	7.3		5.2		12.2	
2001	7.0		4.6		5.2	
2002	6.7		3.7		8.9	
2003	5.5		1.6		6.4	
Hospital surgical vol.		<0.0001		<0.0001		0.85
Low (<5/yr)	11.1		5.1		9.6	
Medium (5–18/yr)	6.2		4.3		8.0	
High (>18 yr)	2.7		.43		7.2	

NA indicates not applicable.

One factor that deserves future consideration is the concrete definition of a "high volume center" for pancreatectomy in practice. In the current and previous works based on nationally abstracted data, the cutoff points used to create volume designations are predicated by statistical necessity, ie, maintaining equally sized patient groups for the purposes of comparison, therefore yielding varying "high-volume" definitions based on the dataset, patient population, or years of study. Of note, the Leapfrog Group, in reporting to consumers and payers alike, on their website (www.leapfroggroup.org),[19] requires ≥11 pancreatic resections/year for an institution to obtain "full-credit" for pancreatectomy.

We have added to the growing body of evidence that patients are more likely to survive the postoperative period for pancreatic resection at high-volume hospitals. Other authors have demonstrated that, beyond in-hospital mortality, long-term survival is also improved through treatment at high-volume centers.[28] In the current era, the only possibility of cure for a pancreatic neoplasm involves surgical resection.[29] Actuarial 5-year survival for pancreatic adenocarcinoma after PD remains only 18% in the most experienced of hands.[30] These facts emphasize the need to minimize perioperative mortality to improve patients' chances at long-term survival. A critical controllable step for decreasing a patient's risk of mortality in the management of pancreatic cancer is the referral to a high-volume pancreatic surgery center.

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