Incidence and risk factors for post-operative mortality, hospitalization, and readmission rates following pancreatic cancer resection

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Background: The only potentially curative approach for pancreatic cancer is surgical resection, but this technically challenging procedure carries risks for postoperative morbidities and mortality. This study of a large, contemporary national database illustrates incidences of, and risk factors for, post-procedural mortality, prolonged hospital stay, and 30-day readmission.

Methods: From the National Cancer Database (NCDB), stage I–III pancreatic adenocarcinomas were identified [2004–2015]. Surgical techniques included pancreaticoduodenectomy, partial pancreatectomy (selective removal of the pancreatic body/tail), total pancreatectomy (removal of the entire pancreas) with or without subtotal resection of the duodenum and/or stomach, and extended pancreatectomy. Predictors of 30/90-day post-operative mortality, 30-day readmission rates, and prolonged hospital stay (>17 days per receiver operating curve analysis) were identified via multivariable logistic regression.

Results: Overall, 24,798 patients were analyzed (median age of 66). The majority of cases were T3 (47%), N0 (65%), pancreatic head lesions (83%), and treated with pancreaticoduodenectomy (57%). Only 16% received neoadjuvant therapy. Overall unadjusted risk of 30- and 90-day mortality ranged from 1.3–2.5% and 4.1–7.1%, respectively, depending on extent of surgery. Independent predictors of 30-/90-day mortality included preoperative therapy, increasing age, higher comorbidity score, lower income, case volume, and more extensive surgery. Similar findings were demonstrated regarding prolonged hospital stay and 30-day readmission. Age ≥70 was most associated with 30-day mortality, whereas age ≥60 was most associated with 90-day mortality and prolonged hospital stay.

Conclusions: Quantitation of incidences and risk factors for postoperative outcomes following resection for pancreatic cancer is essential for judicious patient selection and shared decision-making between providers and patients.

Keywords: Pancreatic cancer; Whipple; pancreaticoduodenectomy; pancreatectomy

Introduction

Pancreatic cancer is a highly lethal malignancy affecting over 50,000 patients each year in the United States (1). To date, surgery remains the only potentially curative option for pancreatic cancer (2). However, due to a high proportion of patients presenting at advanced stages, only 15–20% of patients ultimately end up being eligible for surgery (3). The most common oncologic surgery is pancreaticoduodenectomy, which is a technically complicated, high-risk procedure. The best outcomes following the procedure have been reported at high-volume centers, with mortality rates in the 3–5% range (4,5). Generally speaking, guidelines define resectability along a continuum based on involvement of nearby normal structures and vasculature, as well as presence or absence of metastatic disease (6,7). In addition, patient comorbidities, physician bias, and other socioeconomic factors play a role in whether or not surgical resection is offered or attempted, as well as outcomes thereof (8). With that in mind, we sought to use the National Cancer Database (NCDB) to examine 30-day and 90-day post-operative mortality following contemporary pancreatic cancer surgery across the United States, as well as evaluate predictors for worse outcomes.

Methods

The NCDB is overseen by the American College of Surgeons and the Commission on Cancer and encompasses an estimated 70% of annual newly diagnosed cancer cases in the United States. The American College of Surgeons and the Commission on Cancer have not verified and are not responsible for the analytic or statistical methodology employed, or the conclusions drawn from these data by the investigator. Given its retrospective nature and de-identified dataset, this study was exempt from institutional review board approval. We queried the NCDB from 2004–2015 for patients with stage 1–3 adenocarcinoma of the pancreas treated surgically with at least 30 days of follow up. *Figure 1* is a CONSORT diagram outlining all inclusion and exclusion criteria.

Surgery is coded in the NCDB based on degree of pancreatic removal and gastroduodenal resection. These were grouped into categories of pancreaticoduodenectomy, partial pancreatectomy (e.g., selective removal of the pancreatic body or tail with or without other organs such as the spleen), total pancreatectomy (removal of the entire pancreas) with or without subtotal resection of the duodenum and/or stomach, and extended pancreatectomy. Of note, the definition of extended pancreatectomy is more difficult to ascertain because it has utilized various definitions in relation to resection of adjacent organs (e.g., colon) with or without arterial and/or venous structures (9). Although a more unified definition was proposed in mid-2014 (10), it is unlikely that most patients herein were defined by the unified terminology because a minority of patients in the NCDB were treated in 2014–2015.

The NCDB contains various patient-related and socioeconomic factors ranging from race, median household income, type of insurance, gender, age, education level, distance from treatment facility, and comorbidity score. Race was simplified into 3 categories: Caucasian, African American, or other. The Charlson/Deyo comorbidity index (a widely used scale) was recorded and quantified the degree of comorbidities in the patient population (11). Age was broken up into 5 groups; <50, 50–59, 60–69, 70–79, and ≥80. Socioeconomic data in the patients' residence census tract were divided into quartiles based upon the percentage of persons with less than a high school education and median household income based on zip code of residence. Facility type was grouped according to the Commission on Cancer accreditation category (community cancer center, comprehensive community cancer center, and academic/research program). Locations were described based on data provided by the US Department of Agriculture Economic Research Service. Insurance status is documented in the NCDB as it appears on the admission page.

Statistical methodology for this study mirrored analogous impactful publications in other neoplasms (12). Data were analyzed using Medcalc Version 18 (Ostend, Belgium). Summary statistics are presented for discrete variables. Sociodemographic, treatment, and tumor characteristics were first tabulated. Multivariable logistic regression was done to identify predictors of 30-day mortality, 90-day mortality, readmission within 30 days of surgery, and prolonged hospital stay (defined as >17 days based on receiver operator curve analysis). Number of pancreatic surgeries per year was calculated by tabluting the number of times, a facility ID was listed in the dataset, and then dividing that sum by the number of years. That value was then split into quartiles to create 4 different groups of surgical volume. Adjusted hazard ratios and 95% confidence intervals are reported, using an alpha level of 0.05 to indicate statistical significance.
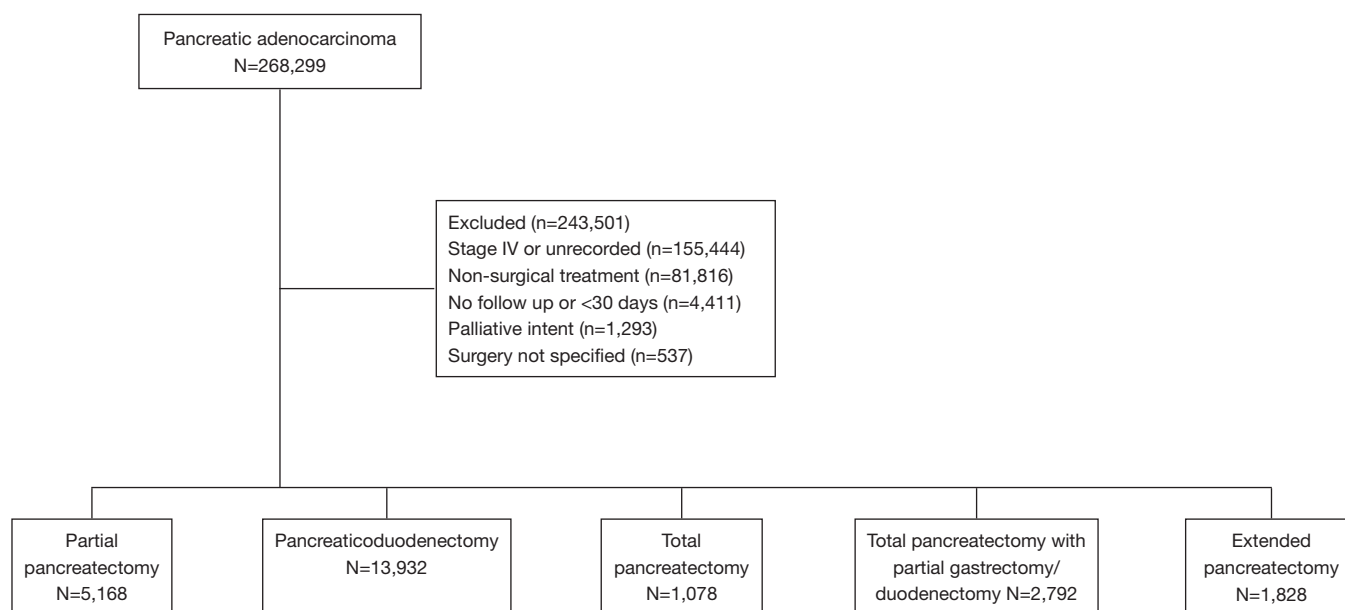
Figure 1 CONSORT diagram.

Results

Using the above eligibility criteria, we identified 24,798 patients with pancreatic adenocarcinoma treated surgically. *Table 1* outlines baseline patient characteristics for the entire cohort. Briefly, the majority were lesions of the pancreatic head (83%), stage T3 (47%), N0 (65%), and treated with pancreaticoduodenectomy (57%). The median age across the cohort was 66 [40–90]. Eighty-three percent of patients were treated without any neoadjuvant therapy; 7% and 9% received neoadjuvant chemotherapy or chemoradiation, respectively. The median radiation dose in that subset was 50 Gy (interquartile range, 45–50.4 Gy) in 28 fractions (interquartile range, 25–28 fractions). The median time from diagnosis to surgery was 21 days (interquartile range, 6–47 days). Median follow up for the entire cohort was 20 months (range, 1–155).

The global rate of 30-day and 90-day post-operative mortality was 1.7% and 5%, respectively. On multivariable analysis, predictors of 30-day mortality included preoperative therapy, increasing age, higher comorbidity score, lower income, lower case volume, and type of surgery (total pancreatectomy with duodenal/gastric resection, or extended pancreatectomy) (*Table 2*). Ninety day mortality was associated with preoperative therapy, increasing age, higher comorbidity score, higher T stage, lower case volume, and type of surgery (total pancreatectomy with

duodenal/gastric resection, or extended pancreatectomy) (*Table 2*).

The median hospital stay was 9 days (interquartile range, 7–13 days). Receiver operating curve analysis identified 17 days as indicative of higher mortality, and was thus used to define a prolonged hospital course (*Figure S1*). The global rate of patients experiencing hospitalization >17 days was 14% for the entire cohort. Multivariable analysis identified the following to associate with prolonged hospital stay: increasing age, lower education, lower income, non-Caucasian race, lower case volume, and more extensive surgery (i.e., techniques involving bowel removal) (*Table 3*). We also looked at readmission rates, and across all 24,798 patients 32% ended up with a readmission. On multivariable analysis, similar variables to those for prolonged hospital stay predicted for 30-day readmission (*Table 3*).

We also calculated absolute rates of 30- and 90-day mortality for each age group by surgical approach (*Table 4*). Post-operative mortality increased across all age groups (*Figure 2*) and also by extent of surgery [with a dip for the oldest group or patients and extended pancreatectomy (likely owing to small sample sizes)] (*Figure 3*). Age ≥70 was most associated with 30-day mortality, whereas age ≥60 was most associated with 90-day mortality and prolonged hospital stay. Mortality rates peaked at 30 and 90 days for the oldest

Table 1 Patient characteristics (n=24,798)

Characteristics	No. [%]
Sex	
Male	12,738 [51]
Female	12,060 [49]
Race	
White	21,535 [87]
African American	2,219 [9]
Other	1,044 [4]
Comorbidity score	
0	16,523 [67]
1	6,579 [27]
≥2	1,696 [6]
Insurance	
Not insured	595 [2]
Private payer	9,626 [39]
Government	14,306 [58]
Unrecorded	271 [1]
Education %	
≥29	3,551 [15]
20 to 28.9	5,985 [26]
14 to 19.9	8,197 [34]
<14	6,652 [25]
Treatment facility type	
Community cancer program	850 [3]
Comprehensive community cancer program	6,794 [28]
Academic/research program	16,942 [69]
Treatment facility location	
Metro	19,833 [83]
Urban	3,548 [15]
Rural	471 [2]
Income, US dollars	
<30,000	3,694 [15]
30,000 to 35,000	5,509 [23]
35,000 to 45,999	6,601 [27]

Table 1 (*Continued*)

Table 1 (*Continued*)

Characteristics	No. [%]
>46,000	8,576 [35]
Distance to treatment facility, miles	
≤10 miles	11,990 [51]
>10 miles	11,604 [49]
Age distribution, years	
<50	1,621 [7]
51–59	5,041 [20]
60–69	8,385 [34]
70–79	7,487 [30]
≥80	2,264 [9]
Year of diagnosis	
2004–2006	2,894 [12]
2007–2009	5,973 [24]
2010–2012	9,050 [36]
2013–2015	6,881 [28]
Anatomic site	
Pancreatic head	20,662 [83]
Pancreatic body	875 [4]
Pancreatic tail	1,031 [4]
Pancreas, NOS	2,230 [9]
T stage	
1	3,476 [14]
2	8,513 [34]
3	11,587 [47]
4	1,221 [5]
N stage	
Nx	1,145 [5]
N0	16,119 [65]
N1	7,534 [30]
Grade	
Well differentiated	2,060 [8]
Moderately differentiated	11,465 [46]
Poorly differentiated	8,371 [34]

Table 1 (*Continued*)

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Table 1 (*Continued*)

Characteristics	No. [%]
Not recorded	2,902 [12]
Surgery	
Partial pancreatectomy	5,168 [21]
Pancreaticoduodenectomy	13,932 [57]
Total pancreatectomy	1,078 [4]
Total pancreatectomy with partial gastrectomy/duodenectomy	2,792 [11]
Extended pancreatectomy	1,828 [7]
Preoperative treatment	
None	20,638 [83]
Chemotherapy	1,613 [7]
Chemotherapy and radiation	2,459 [9]
Radiation	88 [1]
Case volume (per year)	
1–2	5,838 [25]
3–6	5,405 [23]
7–14	5,889 [25]
>14	6,489 [27]

group of patients treated with a total pancreatectomy with partial gastrectomy (7.08% and 13.27%, respectively).

Discussion

This study of a large, contemporary national database illustrates incidences of, and risk factors for, post-procedural mortality, along with those for prolonged hospital stay and 30-day readmission. Although resection is the only potentially curative option for pancreatic cancer, quantitation of incidences and risk factors for these outcomes is essential for judicious patient selection and shared decision-making between providers and patients. Data presented from the current analysis shows an acceptably low 30-day and 90-day mortality risk, mirroring existing studies (10-13). As expected, the risk of mortality increased with advancing age, in some cases eclipsing 10%. However, this must also be contextualized with the case volume and extent of surgery, which also were powerful predictors of postoperative outcomes. Other interesting findings include the potential protective nature

of "other race" in this series, although we must admit that represents a heterogeneous population and was only 5% of our cohort allowing for possible bias. Additionally, older year of diagnosis/treatment and anatomic site predicted for prolonged hospital stay, likely showing an increase in surgical expertise and technology over time, as well as highlighting the increased difficulty of surgery on non-head lesions.

The increased mortality with neoadjuvant therapy may be from other disease features not captured in the NCDB, as opposed to a treatment-related detriment. Systematic analyses of prospective data have failed to numerically associate neoadjuvant chemotherapy or chemoradiation with worse postoperative complications or mortality (13). However, chemotherapy utilization has historically been singlet or doublet therapy, whereas multi-agent chemotherapy is expected to rise in the near future (14). The use of stereotactic body radiation therapy in the neoadjuvant setting has also increased, which requires further longitudinal assessment of complications, especially as related to technical planning parameters (15).

There are also data from single institutions as well as national databases to appropriately consent patients regarding potential post-operative risks. A large series from Memorial Sloan Kettering examined outcomes in close to 600 patients treated surgically between 2001 and 2009. In that series the rate of high grade complications (≥ grade 3) was 22% and 90-day mortality was excellent at 3.7%. High grade complications were not associated with any detriment to survival (16). The group from University of North Carolina used the Nationwide Inpatient Sample database to examine outcomes (specifically in-hospital mortality) in close to 25,000 patients treated with pancreaticoduodenectomy between 1988 and 1995 (17). The in-hospital mortality rate using that data was higher, 11%, in urban teaching hospitals. Granted, the number of procedures per year in their dataset was only 2–3 per year for teaching hospitals (i.e., significantly lower than the data cited above using a cutoff of 25 cases/year to define high volume). Another series used data from Veterans Affairs (VA) hospital systems and compared outcomes to those patients treated in the private sector with pancreatectomy (18). In total, over 1,000 patients were included, with VA patients having worse performance status and comorbidities. In terms of 30-day mortality, the rate was 6.4% in the VA system compared to 3.8% in the private sector (P=0.0015). Lastly, a more limited analysis of the NCDB from 2007–2010 examined 30-day and 90-day mortality

Table 2 Hazard ratios for 30-day and 90-day post-operative mortality

Characteristic	30-day post op mortality		90-day post op mortality	
	Hazard ratio (95% CI)	P	Hazard ratio (95% CI)	P
Preoperative treatment				
None	Reference		Reference	
Chemotherapy	1.70 (1.16–2.50)	0.0068	1.09 (0.84–1.42)	0.5015
Chemoradiation	1.98 (1.45–2.70)	<0.0001	1.56 (1.28–1.89)	<0.0001
Radiation	8.12 (3.80–17.37)	<0.0001	5.77 (3.32–10.03)	<0.0001
Age, years				
<50	Reference		Reference	
51–59	0.98 (0.53–1.83)	0.9563	1.10 (0.75–1.61)	0.6344
60–69	1.50 (0.84–2.70)	0.1733	1.86 (1.29–2.67)	0.0008
70–79	2.19 (1.21–3.99)	0.0102	2.55 (1.76–3.69)	<0.0001
≥80	2.86 (1.51–5.44)	0.0013	3.8 (2.58–5.63)	<0.0001
Comorbidity score				
0	Reference		Reference	
1	0.94 (0.74–1.20)	0.6325	0.99 (0.86–1.14)	0.8894
≥2	2.02 (1.50–2.73)	<0.0001	1.71 (1.41–2.06)	<0.0001
Facility type				
Community cancer program	Reference		Reference	
Comprehensive community cancer program	0.76 (0.44–1.29)	0.3072	1.15 (0.81–1.63)	0.4464
Academic/research program	0.98 (0.56–1.72)	0.9546	1.42 (0.99–2.04)	0.0548
Grade				
Well differentiated	Reference		Reference	
Moderately differentiated	1.10 (0.74–1.62)	0.6458	1.15 (0.90–1.47)	0.2537
Poorly differentiated	1.13 (0.76–1.70)	0.5438	1.50 (1.17–1.91)	0.0012
Education, %				
≥29	Reference		Reference	
20–28.9	0.87 (0.63–1.19)	0.3780	0.97 (0.80–1.17)	0.7291
14–19.9	0.91 (0.65–1.29)	0.5970	0.87 (0.71–1.06)	0.1616
<14	0.90 (0.60–1.36)	0.6219	0.72 (0.56–0.92)	0.0081
Income, USD				
<30,000	Reference		Reference	
30,000–35,000	0.83 (0.60–1.14)	0.2448	1.04 (0.86–1.26)	0.7031
35,000–45,999	0.69 (0.48–0.98)	0.0380	0.86 (0.70–1.06)	0.1614
>46,000	0.58 (0.39–0.88)	0.0098	0.83 (0.65–1.05)	0.1223

Table 2 (*Continued*)

Table 2 (*Continued*)

Characteristic	30-day post op mortality		90-day post op mortality	
	Hazard ratio (95% CI)	P	Hazard ratio (95% CI)	P
Insurance				
None	Reference		Reference	
Private	1.10 (0.48–2.54)	0.8199	0.67 (0.45–1.00)	0.0483
Government	1.41 (0.61–3.25)	0.4162	0.92 (0.62–1.37)	0.6780
Location				
Metropolitan	Reference		Reference	
Urban	0.80 (0.59–1.10)	0.1719	0.84 (0.70–1.02)	0.0733
Rural	0.81 (0.40–1.63)	0.5563	1.01 (0.68–1.50)	0.9652
Race				
Caucasian	Reference		Reference	
African American	0.99 (0.69–1.43)	0.9732	1.09 (0.89–1.34)	0.3876
Other	0.46 (0.21–0.97)	0.0419	0.70 (0.49–0.99)	0.0454
Sex				
Male	Reference		Reference	
Female	0.89 (0.73–1.09)	0.2773	0.92 (0.82–1.04)	0.1712
N stage				
N0	Reference		Reference	
N1	0.91 (0.72–1.15)	0.4422	1.03 (0.90–1.18)	0.6782
NX	0.74 (0.43–1.28)	0.2882	1.04 (0.79–1.37)	0.7939
T stage				
T1	Reference		Reference	
T2	1.11 (0.79–1.56)	0.5403	1.09 (0.89–1.33)	0.4211
T3	1.15 (0.82–1.61)	0.4214	1.23 (1.01–1.50)	0.0397
T4	1.63 (0.99–2.66)	0.0526	1.78 (1.32–2.39)	0.0001
Surgery type				
Partial pancreatectomy	Reference		Reference	
Pancreaticoduodenectomy	1.12 (0.84–1.48)	0.4448	1.13 (0.96–1.32)	0.1519
Total pancreatectomy	1.16 (0.66–2.03)	0.6041	1.04 (0.74–1.45)	0.8276
Total pancreatectomy with partial gastrectomy/duodenectomy	1.76 (1.24–2.50)	0.0015	1.57 (1.27–1.93)	<0.0001
Extended pancreatectomy	1.50 (1.00–2.26)	0.0515	1.57 (1.24–1.99)	0.0002

Table 2 (*Continued*)

Table 2 (*Continued*)

Characteristic	30-day post op mortality		90-day post op mortality	
	Hazard ratio (95% CI)	P	Hazard ratio (95% CI)	P
Year of treatment				
2004–2006	Reference		Reference	
2007–2009	0.89 (0.62–1.27)	0.5200	0.94 (0.76–1.15)	0.5325
2010–2012	0.93 (0.67–1.30)	0.6812	0.86 (0.71–1.05)	0.1384
2013–2015	0.78 (0.55–1.12)	0.1779	0.79 (0.64–0.97)	0.0245
Tumor site				
Pancreas head	Reference		Reference	
Pancreas body	0.88 (0.50–1.57)	0.6745	1.05 (0.76–1.44)	0.7760
Pancreas tail	0.77 (0.43–1.40)	0.3988	1.05 (0.78–1.42)	0.7379
Pancreas, NOS	1.12 (0.80–1.57)	0.4983	1.06 (0.87–1.30)	0.5636
Distance				
≤18 miles	Reference		Reference	
>18 miles	1.23 (0.97–1.57)	0.0830	1.07 (0.93–1.24)	0.3166
Case volume (per year)				
0–2	Reference		Reference	
3–6	0.78 (0.57–1.06)	0.1087	0.91 (0.76–1.08)	0.2617
7–14	0.84 (0.60–1.16)	0.2931	0.69 (0.57–0.85)	0.0003
>14	0.52 (0.36–0.75)	0.0004	0.58 (0.47–0.72	<0.0001

Table 3 Multivariable logistic regression for readmission and prolonged hospital stay

Characteristic	Readmission within 30 days		Hospital stay >17 days	
	Odds ratio (95% CI)	P	Odds ratio (95% CI)	P
Preoperative treatment				
None	Reference		Reference	
Chemotherapy	0.84 (0.67–1.06)	0.1498	0.71 (0.58–0.86)	0.0007
Chemoradiation	1.17 (0.98–1.39)	0.0875	0.99 (0.85–1.15)	0.9139
Radiation	1.15 (0.53–2.52)	0.7205	1.63 (0.90–2.95)	0.1062
Age, years				
<50	Reference		Reference	
51–59	1.04 (0.82–1.32)	0.7751	1.13 (0.92–1.40)	0.2489
60–69	0.88 (0.70–1.12)	0.2955	1.40 (1.14–1.72)	0.0012
70–79	0.93 (0.73–1.19)	0.5703	1.64 (1.32–2.03)	<0.0001
≥80	1.03 (0.78–1.36)	0.8480	2.10 (1.66–2.65)	<0.0001

Table 3 (*Continued*)

Table 3 (*Continued*)

Characteristic	Readmission within 30 days		Hospital stay >17 days	
	Odds ratio (95% CI)	P	Odds ratio (95% CI)	P
Comorbidity score				
0	Reference		Reference	
1	1.13 (1.01–1.27)	0.0292	0.92 (0.84–1.00)	0.0617
≥2	1.31 (1.09–1.57)	0.0035	1.14 (0.98–1.32)	0.0828
Facility type				
Community cancer program	Reference		Reference	
Comprehensive community cancer program	1.53 (1.06–2.20)	0.0231	0.92 (0.73–1.16)	0.4691
Academic/research program	1.64 (1.13–2.37)	0.0097	0.94 (0.74–1.20)	0.6276
Grade				
Well differentiated	Reference		Reference	
Moderately differentiated	0.89 (0.75–1.07)	0.2134	1.01 (0.87–1.16)	0.9226
Poorly differentiated	0.92 (0.77–1.11)	0.3800	0.97 (0.83–1.12)	0.6776
Education, %				
≥29	Reference		Reference	
20–28.9	1.17 (0.98–1.39)	0.0846	0.95 (0.83–1.08)	0.4207
14–19.9	1.13 (0.93–1.36)	0.2143	0.98 (0.85–1.12)	0.7198
<14	1.16 (0.94–1.44)	0.1689	0.83 (0.71–0.98)	0.0294
Income, USD				
<30,000	Reference		Reference	
30,000–35,000	1.00 (0.84–1.20)	0.9658	0.94 (0.82–1.07)	0.3452
35,000–45,999	0.98 (0.81–1.18)	0.8320	0.81 (0.70–0.93)	0.0037
>46,000	1.00 (0.81–1.23)	0.9809	0.81 (0.69–0.95)	0.0092
Insurance				
None	Reference		Reference	
Private	1.08 (0.76–1.55)	0.6584	0.84 (0.65–1.07)	0.1612
Government	1.33 (0.93–1.92)	0.1220	0.96 (0.74–1.23)	0.7239
Location				
Metropolitan	Reference		Reference	
Urban	1.15 (0.98–1.35)	0.0897	0.95 (0.83–1.08)	0.4050
Rural	1.31 (0.93–1.86)	0.1237	0.84 (0.62–1.13)	0.2497
Race				
Caucasian	Reference		Reference	
African American	0.97 (0.81–1.17)	0.7683	1.20 (1.05–1.37)	0.0085
Other	1.02 (0.80–1.31)	0.8707	1.38 (1.15–1.65)	0.0005

Table 3 (*Continued*)

Table 3 (*Continued*)

Characteristic	Readmission within 30 days		Hospital stay >17 days	
	Odds ratio (95% CI)	P	Odds ratio (95% CI)	P
Sex				
Male	Reference		Reference	
Female	0.95 (0.86–1.05)	0.3028	0.93 (0.86–1.00)	0.0559
N stage				
N0	Reference		Reference	
N1	0.88 (0.78–0.99)	0.0321	0.85 (0.78–0.94)	0.0008
NX	0.90 (0.70–1.15)	0.3892	1.04 (0.87–1.25)	0.6639
T stage				
T1	Reference		Reference	
T2	1.05 (0.90–1.23)	0.5449	1.05 (0.93–1.18)	0.4584
T3	1.02 (0.87–1.19)	0.8020	1.05 (0.93–1.19)	0.4000
T4	1.14 (0.87–1.49)	0.3585	1.22 (0.97–1.51)	0.0975
Surgery type				
Partial pancreatectomy	Reference		Reference	
Pancreaticoduodenectomy	0.84 (0.74–0.95)	0.0059	1.20 (1.08–1.33)	0.0009
Total pancreatectomy	0.71 (0.54–0.95)	0.0191	1.00 (0.79–1.26)	0.9709
Total pancreatectomy with partial gastrectomy/duodenectomy	0.96 (0.81–1.15)	0.6708	1.37 (1.19–1.58)	<0.0001
Extended pancreatectomy	1.01 (0.83–1.24)	0.8966	1.22 (1.03–1.44)	0.0206
Year of treatment				
2004–2006	Reference		Reference	
2007–2009	1.06 (0.88–1.26)	0.5383	0.99 (0.86–1.13)	0.8326
2010–2012	1.00 (0.84–1.18)	0.9693	0.85 (0.75–0.96)	0.0119
2013–2015	0.88 (0.73–1.05)	0.1531	0.70 (0.61–0.80)	<0.0001
Tumor site				
Pancreas head	Reference		Reference	
Pancreas body	0.99 (0.76–1.30)	0.9596	0.67 (0.52–0.86)	0.0015
Pancreas tail	1.18 (0.93–1.49)	0.1788	0.49 (0.38–0.63)	<0.0001
Pancreas, NOS	0.98 (0.82–1.18)	0.8672	0.88 (0.76–1.02)	0.0853
Distance				
≤18 miles	Reference		Reference	
>18 miles	0.89 (0.79–1.00)	0.0442	0.89 (0.81–0.98)	0.0208
Case volume (per year)				
0–2	Reference		Reference	
3–6	1.23 (1.05–1.44)	0.0091	0.91 (0.81–1.02)	0.0987
7–14	1.07 (0.90–1.27)	0.4547	0.72 (0.64–0.83)	<0.0001
>14	1.19 (0.99–1.42)	0.0571	0.60 (0.52–0.69)	<0.0001

Table 4 Unadjusted absolute mortality estimates at 30 days and 90 days post-surgery by age

| Age (years)	Outcome	Partial pancreatectomy		Pancreaticoduodenectomy		Total pancreatectomy		Total pancreatectomy with partial gastrectomy/duodenectomy		Extended pancreatectomy	
		No.	%	No.	%	No.	%	No.	%	No.	%
30-day post-op mortality											
All	Alive	5,100	98.68	13,711	98.41	1,060	98.33	2,721	97.46	1,789	97.87
	Dead	68	1.32	221	1.59	18	1.67	71	2.54	39	2.13
<50	Alive	315	99.05	906	99.02	75	100.00	187	99.47	122	97.60
	Dead	3	0.95	9	0.98	0	0.00	1	0.53	3	2.40
50–59	Alive	993	99.20	2,837	99.27	211	98.14	575	98.12	377	98.95
	Dead	8	0.80	21	0.73	4	1.86	11	1.88	4	1.05
60–69	Alive	1,733	99.08	4,635	98.41	361	98.90	962	98.26	570	97.94
	Dead	16	0.92	75	1.59	4	1.10	17	1.74	12	2.06
70–79	Alive	1,573	98.25	4,073	97.86	326	97.89	787	96.80	559	96.71
	Dead	28	1.75	89	2.14	7	2.11	26	3.20	19	3.29
≥80	Alive	486	97.39	1,260	97.90	87	96.67	210	92.92	161	99.38
	Dead	13	2.61	27	2.10	3	3.33	16	7.08	1	0.62
90-day post-op mortality											
All	Alive	4,941	95.81	13,211	95.05	1,023	95.34	2,602	93.42	1,697	92.88
	Dead	216	4.19	688	4.95	50	4.67	183	6.58	130	7.12
<50	Alive	311	98.10	890	97.69	72	96.00	183	98.39	119	95.20
	Dead	6	1.90	21	2.31	3	4.00	3	1.61	6	4.80
50–59	Alive	366	96.06	2,783	97.48	208	96.74	563	96.08	366	96.06
	Dead	15	3.94	72	2.52	7	3.26	23	3.92	15	3.94
60–69	Alive	534	91.91	4,493	95.64	347	95.07	923	94.38	534	91.91
	Dead	47	8.09	205	4.36	18	4.93	55	5.62	47	8.09
70–79	Alive	524	90.66	3,878	93.36	313	94.85	737	91.10	524	90.66
	Dead	54	9.34	276	6.64	17	5.15	72	8.90	54	9.34
≥80	Alive	154	95.06	1,167	91.10	83	94.32	196	86.73	154	95.06
	Dead	8	4.94	114	8.90	5	5.68	30	13.27	8	4.94
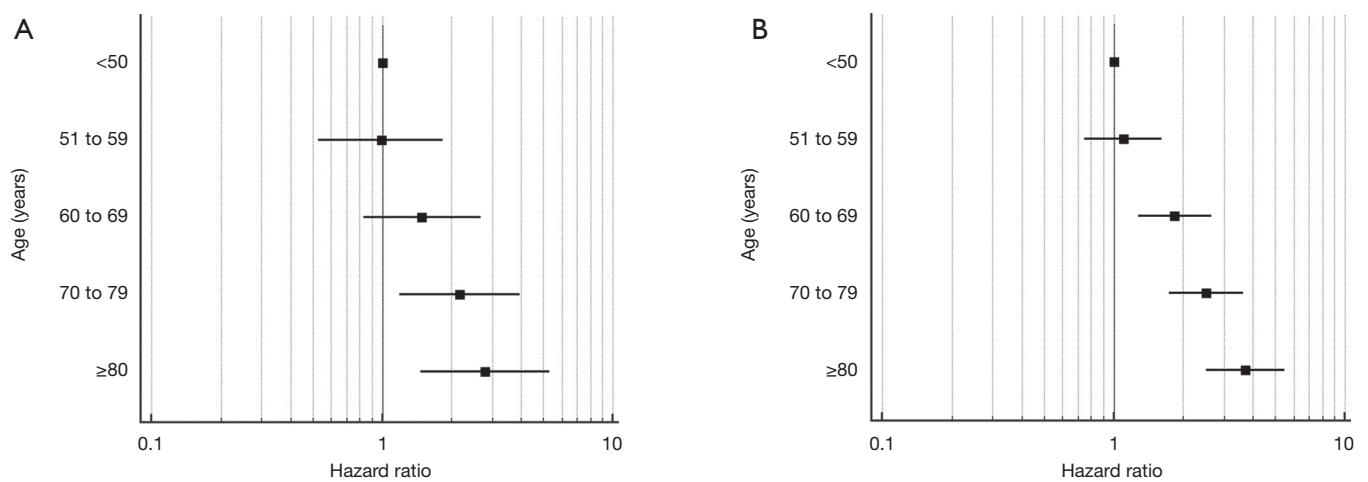
Figure 2 30-day (A) and 90-day (B) mortality rate hazard ratios by patient age.
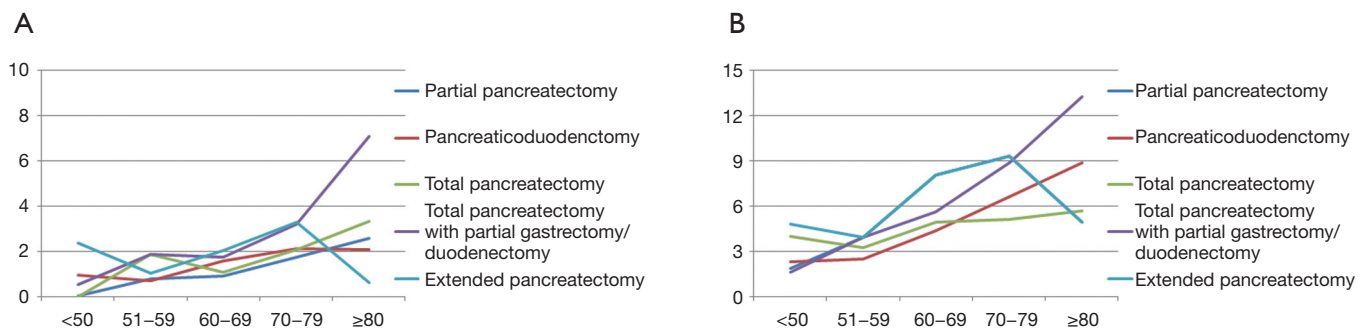

Figure 3 Absolute rates (%) of 30-day (A) and 90-day (B) mortality by age and type of surgery.

following pancreatectomy (19). That study included over 21,000 patients revealing an overall 30 day mortality rate of 3.7%, which doubled to 7.4% at 90 days. Predictors for increased mortality included older age, government insurance, lower income, lower hospital volume, and higher comorbidity score.

Surgical technique also has the potential to play a role in post-operative outcomes. A relatively recent, small, randomized study (32 patients in each arm) from India directly compared a laparoscopic approach to traditional open pancreaticoduodenectomy (20). There was less blood loss and shorter hospital stay with the minimally invasive approach, with similar complication rate. The group from Memorial Sloan Kettering performed an earlier meta-analysis of 6 studies with over 500 patients comparing laparoscopic and open approaches (21). The findings of that study were that minimally invasive pancreaticoduodenectomy was a feasible approach with

likely less blood loss and shorter hospital stay, keeping in mind possible selection bias as all the included studies were retrospective in nature. In the recent past, a robotic approach has been utilized with increasing frequency as well, with proposed advantages being positioning, better visualization, and increased dexterity. A multi institutional analysis reviewed outcomes in over 1,000 patients, of which 211 were treated with a robotic pancreaticoduodenectomy (22). Within that cohort, operative times were longer, but blood loss and major complications were reduced. Length of stay, readmission, and 90 day mortality were not associated with operative approach. Likewise, operative approach was not a predictor of margin status or extent of nodal dissection. The NCDB (2010–2012 version) has also been utilized to compare open approaches to minimally invasive approaches for pancreaticoduodenectomy (23). That particular analysis showed shorter length of stay, more margin-negative resections, and quicker time to adjuvant systemic

therapy using a minimally invasive approach. There was no difference in survival based on operative technique. We also considered looking into surgical technique (open/laparoscopic/robotic) for the present analysis, and if it played any role in outcomes, but that data was not captured until 2010 (and only sparingly so thereafter).

The limitations of the current study include its retrospective nature and inherent selection bias. It is important to note however that unlike the majority of NCDB studies, much of the selection bias is mitigated since overall survival is not the main endpoint. The NCDB does not code completely for lack of or presence of vascular involvement which affect surgical outcomes and technique for pancreatic cancer, but since T4 by definition denotes vascular involvement; this may be an adequate surrogate. There are also no data captured on specific chemotherapy agents or number of cycles delivered. More specific toxicity and morbidity data is also lacking in the NCDB, which is also important to consider in the post-operative setting. Lastly, nuances of procedures are also not captured by the NCDB (e.g., pylorus preservation techniques, portal vein reconstructions, etc.).

Conclusions

This study of a large, contemporary national database illustrates incidences of, and risk factors for, post-procedural mortality, along with those for prolonged hospital stay and 30-day readmission. Although resection is the only potentially curative option for pancreatic cancer, quantitation of incidences and risk factors for these outcomes is essential for judicious patient selection and shared decision-making between providers and patients.

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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Discharge days associated
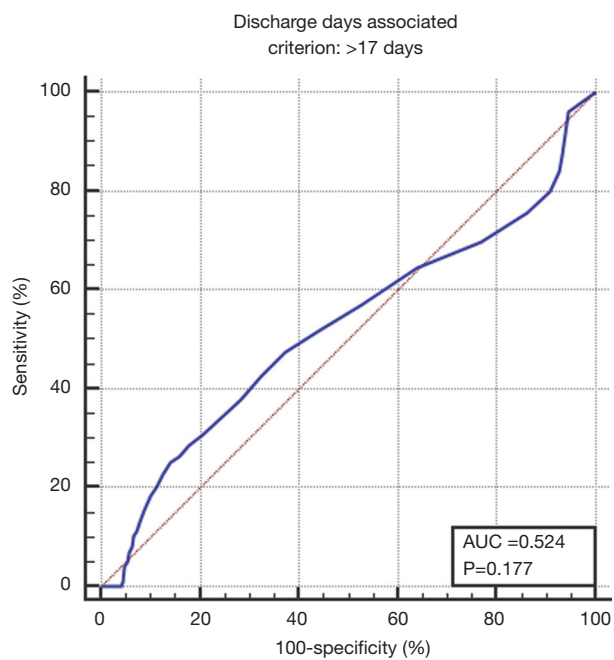criterion: >17 days

AUC =0.524
P=0.177

Figure S1 Receiver operating characteristic (ROC) curve analysis showing correlation of days to discharge with outcome (17 days identified as the cutoff).