Original Article

Factors leading to pancreatic resection in patients with pancreatic cancer: a national perspective

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Background: Resection is the only option for potential cure in pancreatic cancer. Patients admitted for resection may have the procedure deferred during their hospitalization. We aim to identify factors that lead pancreatic cancer patients to undergo resection.

Methods: An analysis utilizing the Nationwide Inpatient Sample (NIS) database, 2003–2009. Study population included adults (≥18 years) with pancreatic cancer who underwent either pancreatic resection or other interventions. Surgeon volume classified based on the median into low and high-volume surgeon.

Results: Eleven thousand three hundred and sixty-five patients were included; 68.0% underwent pancreatic resection, while 32.0% had other interventions. The majority of patients resected were <60 years old, female, with higher annual household income (P<0.05 for all). Patients with Medicaid coverage and comorbidity scores ≥2 were least likely to undergo pancreatic resection. Resection was more likely for high-volume surgeons, high-volume hospitals and teaching hospitals (P<0.05 for all). Those managed by high-volume surgeons were at a lower risk of postoperative complications, lower mortality, shorter hospital stay, and lower healthcare costs (P<0.05 for all).

Conclusions: Patients' insurance type and economic status are significantly associated with their ability to achieve pancreatic resection. Surgeon experience and hospital volumes were also significantly associated with pancreatic resection, clinical and economic outcomes.

Keywords: Pancreatic cancer; pancreatic resection; surgeon volume; patient factors and pancreatic resection; Nationwide Inpatient Sample (NIS)

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Introduction

Pancreatic cancer is the fourth leading cause of cancer related death in the United States today (1). With 2015 estimated incidence and mortality rates of 48,960 and 40,560 respectively and a reported 5-year survival rate of 7.2% after diagnosis, pancreatic malignancy remains one of the most challenging and lethal cancers (2). Resection, though technically complex, remains the only option for potential cure (3). Though post resection mortality continues to decrease, morbidity remains high with reported rates from 30–50% (4-9).

Potential cure and/or long-term survival correlate with stage and potential resectability. Determination of resectability is contingent upon its relationship to nearby vascular structures and evidence of metastasis (10). Although it is important to evaluate tumor characteristics to determine resectability and to predict outcomes and survival, it is equally important to consider patient and hospital-specific factors (11). These can, not only contribute to post-resection survival, but may also play a role in

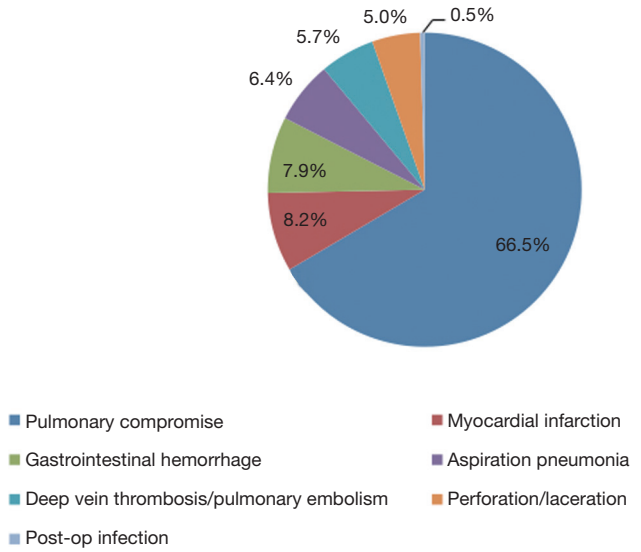

Figure 1 Postoperative complications identified in study patient population, identified through the Nationwide Inpatient Sample database 2003–2009.

patients' ability to achieve surgical resection (3,12,13).

Using the Nationwide Inpatient Sample (NIS) database, we aim determine if patient-specific characteristics (patient demographics, economic factors, payers of health services and comorbidities) and hospital-specific factors (surgeon volume, hospital volume, hospital teaching status) were associated with pancreatic resection for pancreatic cancer.

Methods

The study is a cross-sectional analysis using the NIS database for the years 2003–2009. NIS is part of the Healthcare Cost and Utilization Project (HCUP), sponsored by the Agency for Healthcare Research and Quality (AHRQ). This is the largest all-payer inpatient care database that is publicly available in the United States. It contains data from approximately 8 million hospital stays from about 1,000 hospitals sampled to approximate a 20% stratified sample of U.S. community hospitals (14). The NIS database consists of publicly available de-identified data that is exempt from the approval of the Institutional Review Board. International Classification of Disease, 9th Revision (ICD-9) was used in defining the diagnoses and procedures of interest.

The study population included adult (≥18 years) patients who were electively admitted with a primary diagnosis of pancreatic cancer (ICD-9: 157). Then based on the primary surgical procedure the study population was divided into those who underwent pancreatic resection (ICD-9: 52.5, 52.51, 52.52, 52.53, 52.59, 52.6, 52.7) or those who underwent abdominal procedures other than pancreatic resection.

The primary objective of this study was to assess patients' characteristics and clinical factors association with pancreatic resection. Those factors included (I) patients' demographics: age (<45, 45–65, >65 years), and gender; (II) economic factors: annual household income (≤ national median, > national median) (15), and main payer of health service (Medicare, Medicaid, private insurance, self-pay, no charge, other); (III) clinical factors: a modification of the Charlson Comorbidity Index Score (CCIS) (score: 0–1, ≥2) (16); and surgeon volume, classified based on the number of surgeries performed by each surgeon per year, subsequently, categorized based on the median into low-volume surgeons group (1–5 surgeries/year) and high-volume surgeons group (≥6 surgeries/year); (IV) hospital characteristics: hospital volume, classified based on the number of surgeries performed in each hospital per year, subsequently, categorized based on the median into low-volume hospitals group (1–17 surgeries/year) and high-volume surgeons group (≥18 surgeries/year), and hospital teaching status (non-teaching, teaching).

The secondary objective was to assess post-pancreatectomy outcomes in relation to surgeon volume in the sub-population of patients who underwent pancreatic resection. Those outcomes included: (I) postoperative complications, classified as the presence or absence of one or more of pulmonary, cardiovascular, gastrointestinal, infectious, or procedural complications (*Figure 1*) (17); (II) in-hospital death; (III) length of stay (LOS), classified based on the 75th percentile into short stay (≤14 days) and long stay (>14 days); and (IV) cost of health services per case, adjusted for the inflation rate to reflect 2015 U.S. dollar values, and classified based on the 75th percentile into low cost (≤$41,564.67) and high cost (>$41,564.67).

Other secondary independent factors that were assessed for their confounding included: race (white, black, Hispanic, Asian/Pacific Islander, Native American, other) and type of pancreatectomy (partial, total, and Whipple procedure). All variable were checked for completeness, subjects with missing values were eliminated. However, surgeon volume was only available for 5,438 subjects, those without surgeon volume were not dropped from the whole study; instead models that included surgeon volume as the main factor were performed in a smaller sample size and annotated

accordingly in the tables of this manuscript.

Statistical analysis used weighted data reflecting the national estimate. The records' weights are available in the NIS data and calculated based on the stratification variables that were used in sampling methodology. These variables are hospital geographic region, urban/rural location, teaching status, bed-size, and ownership (14).

Cross-tabulation and Chi-square test were used to examine the association between each of the independent factors and the outcomes of interest. Factors with significant association were considered confounders and were included in multivariate logistic regression models. Multivariate logistic regression models were used to calculate the odds ratio (OR) and 95% confidence interval (CI). Significance level was set as (α =0.05). All data analyses were performed using SAS 9.3 for Windows (SAS Institute Inc., Cary, NC, USA).

Results

A total of 11,365 discharge records were included (*Table 1*). Pancreatic resection was performed in 7,707 (68.0%) subjects, while the remaining 3,658 (32.0%) underwent procedures other than pancreatectomy (*Table 2*). The mean age of the study population was 65.5±0.1 years old. Whites made up 81.4% of the study sample and the majority had Medicare as health insurance (52.1%). Female and male each represented approximately half of the study population. In regard to the type of pancreatectomy, Whipple procedure was the most performed operation (68.6%), while partial and total pancreatectomies formed 27.0% and 4.3% respectively. Postoperative complications were reported in 1,344 (11.8%) patients (*Figures 1,2*), and 378 (3.3%) died during their hospital stay. The average LOS was 11.2±0.2 days, and the average cost of health services per case was $32,510.00±843.41.

Younger patients (<60 years) and females with pancreatic malignancy were more likely to undergo pancreatic resection (P<0.05 each) (*Table 3*). Contrarily, pancreatic cancer patients with household income below the national median and those with Medicaid coverage were less likely to have pancreatectomy (P<0.01 each). Patients with two or more comorbidities were also less likely to undergo pancreatectomy (OR: 0.74, 95% CI: 0.67–0.82, P<0.001) (*Table 3*).

High-volume surgeons performed more pancreatic resections for pancreatic cancer compared to low-volume surgeons (OR: 1.33, 95% CI: 1.11–1.59, P=0.002). Similarly, pancreatic resections were more prevalent in high-volume hospitals than low-volume hospitals (OR: 1.73, 95% CI: 1.50–1.99, P<0.001). Furthermore, teaching hospitals had a higher rate of pancreatic cancer resection than non-teaching hospitals (OR: 1.36, 95% CI: 1.17–1.57, P<0.001).

In the subpopulation of patients who underwent pancreatectomy, high-volume surgeons were more likely to perform a Whipple procedure than low-volume surgeons (OR: 1.37, 95% CI: 1.05–1.80, P=0.021). Patients who underwent pancreatic surgery by high-volume surgeons had a lower postoperative complications risk (10.4% *vs.* 18.1%, P<0.001), and lower mortality risk (2.1% *vs.* 4.8%, P=0.008) (*Table 4*). Additionally, surgeries performed by high-volume surgeons associated with a shorter hospital stay and lower healthcare cost (P<0.05 for all).

Discussion

With reported mortality rates upwards of 7% in some series, a plethora of studies have evaluated patient-specific factors that affect outcomes after pancreatic resection (4,5,7). Demographics, socioeconomic status (SES) and other patient-specific factors such as comorbidities play a significant role in post-resection outcomes. Ragulin-Coyne *et al.* (4) developed a risk score estimating in-hospital mortality after pancreatectomy. Age >80, having multiple comorbidities, and having had multiple operations for pancreatitis were factors most predictive of mortality after pancreatectomy. These factors, along with resection for non-benign disease, have been attributed to increased postoperative complication rates (7).

SES is associated with outcome differentials in pancreatic cancer patients (5,18). Lim *et al.* (11) in a review of 396 patients undergoing resection for pancreatic cancer demonstrated a difference in post resection survival for individuals above the median household income level (11). Similarly, our results demonstrated an advantage towards high SES. There is very limited data in the literature addressing this important issue. We conducted our study using the large NIS database to further investigate the association between SES and pancreatic resection. We found individuals above the national median household income were more likely to achieve pancreatic resection when compared to those below the national median.

For the first time, our analysis significantly demonstrates patient age (<60), female sex, and household income above the national median as patient-specific factors most associated with undergoing pancreatic resection. Patients

Table 1 Descriptive statistics of study population

Factor	All cases (N=11,365)	Pancreatic resection		P[a]
		Performed (N=7,707)	Not-performed (N=3,658)	
Age (yr), %				<0.001
<45	4.2	5.0	2.7	
45–65	42.3	42.4	42.1	
>65	53.5	52.7	55.3	
Gender, %				0.007
Male	51.0	50.1	52.8	
Female	49.0	49.9	47.2	
Race, %				0.290
White	81.4	81.5	81.0	
Black	7.7	7.5	8.1	
Hispanic	6.2	6.2	6.2	
Asian/Pacific Islander	2.5	2.6	2.3	
Native American	0.3	0.4	0.1	
Other	2.0	1.9	2.2	
Household income, %				<0.001
≤ National median	44.8	43.4	47.8	
> National median	55.2	56.6	52.2	
Service payer, %				<0.001
Medicare	52.1	51.2	53.9	
Medicaid	4.3	4.0	4.8	
Private	39.9	41.3	37.1	
Self-pay	1.8	1.6	2.3	
No charge	0.2	0.3	0.2	
Other	1.7	1.6	1.7	
CCIS, %				<0.001
Low: 0–1	65.8	68.3	60.4	
High: ≥2	34.2	31.7	39.6	
Pancreatectomy type, %				NA
Partial	27.0	27.0	NA	
Total	4.3	4.3	NA	
Whipple	68.6	68.6	NA	
Surgeon volume (surgeries/yr), %				<0.001
Low: 1–5	50.3	45.3	60.6	
High: ≥6	49.7	54.7	39.4	
Postoperative complications, %				<0.001
None	88.2	86.0	92.8	
One or more	11.8	14.0	7.2	
Length of stay (days), %				<0.001
≤14	79.7	76.1	87.4	
>14	20.3	23.9	12.6	
In-hospital mortality, %				0.420
No	96.7	96.6	96.9	
Yes	3.3	3.4	3.1	
Hospital volume (surgeries/yr), %				<0.001
Low: 1–17	51.1	45.9	62.2	
High: ≥18	48.9	54.1	37.8	
Hospital teaching status, %				<0.001
Non-teaching	20.1	16.9	26.7	
Teaching	79.9	83.1	73.3	
Cost of health services, %				<0.001
≤$41,564.67	80.7	75.0	92.7	
>$41,564.67	19.3	25.0	7.3	

[a], Chi-square test. CCIS, Charlson comorbidity index score; NA, not applicable; yr, year.

with Medicaid coverage and a Charlson comorbidity score ≥2 were least likely to undergo pancreatic resection.

Zell *et al.* (19), in their review of 17,326 patients with pancreatic cancer from the California Cancer Registry in 2007, addressed pancreatic resection. By dividing patients into quintiles based on their SES, they were able to demonstrate increasing quintiles were associated with several treatment modalities such as surgery, chemotherapy and radiation (19). Cress *et al.* (20) in a comparable review also concluded that patients of low SES are less likely to undergo pancreatic resection, which may negatively affect survival.

Table 2 Codes of the primary procedures of patients with pancreatic cancer and did not undergo pancreatic resection

Code	Definition
44.38	Laparoscopic gastroenterostomy
44.39	Gastroenterostomy NEC
45.01	Duodenal incision
45.14	Close small bowel biopsy
45.33	Local excision small bowel NEC
45.73	Right hemicolectomy
45.74	Transverse colon resection
45.75	Left hemicolectomy
45.76	Sigmoidectomy
45.91	Small-to-small bowel anastomosis
46.32	Percutaneous endoscopic jejunostomy
46.39	Enterostomy NEC
50.12	Open liver biopsy
50.14	Laparoscopic liver biopsy
50.19	Hepatic diagnostic procedure NEC
50.22	Partial hepatectomy
51.13	Open biliary tract biopsy
51.21	Partial cholecystectomy
51.22	(Total) cholecystectomy
51.23	Laparoscopic cholecystectomy
51.32	Gallbladder-to-intestine anastomosis
51.34	Gallbladder-to-stomach anastomosis
51.36	Choledochoenterostomy
51.37	Hepatic duct-gastrointestinal anastomosis
51.39	Bile duct anastomosis NEC
51.49	Incision obstructed bile duct NEC
51.51	Common duct exploration
51.59	Bile duct incision NEC
51.63	Common duct excision NEC
51.69	Bile duct excision NEC
51.79	Bile duct repair NEC
51.82	Pancreatic sphincterotomy
51.83	Pancreatic sphincteroplasty
51.99	Biliary tract operation NEC
52.12	Open pancreatic biopsy
53.49	Umbilical hernia repair NEC
53.61	Incisional hernia repair-graft
54.0	Abdominal wall incision
54.11	Exploratory laparotomy
54.19	Laparotomy NEC
54.21	Laparoscopy
54.22	Abdominal wall biopsy
54.23	Peritoneal biopsy
54.24	Closed intra-and mass biopsy
54.25	Peritoneal lavage
54.59	Other lysis abdominal adhesion
87.53	Intraoperative cholangiogram
87.54	Cholangiogram NEC

NEC, not elsewhere classified.

Case volume as it relates to outcomes has been considered in the literature since the 1970s (21). Many studies have indicated a relationship between surgeon and/or hospital volume and mortality, complication rate, LOS, hospital costs, and resection rates in pancreatic surgery (12,22-29). Our analysis shows high-volume surgeons performed more pancreatectomies for pancreatic cancer compared to low-volume surgeons. More specifically, pancreaticoduodenectomy was more likely to be performed by high-volume surgeons when compared to low-volume surgeons. Pancreatectomy for pancreatic cancer was more prevalent and more likely to be performed in high-volume hospitals.

In several large series reviews, high volume surgeons have been shown to improve outcomes in complex procedures (30,31). Eppsteiner *et al.* (23) reviewed 3,581 patients undergoing pancreatic resection from 1998–2005 using the NIS database. They determined that high-volume surgeons (≥5 surgeries/year) experienced a significant reduction in in-hospital mortality when compared to low-volume surgeons (2.6% *vs.* 6.7%). Similar findings were demonstrated in a database review of 91,241 patients by Nathan *et al.* (25). Surgeons performing a high volume of pancreatic resections were strongly associated with decreased in-hospital

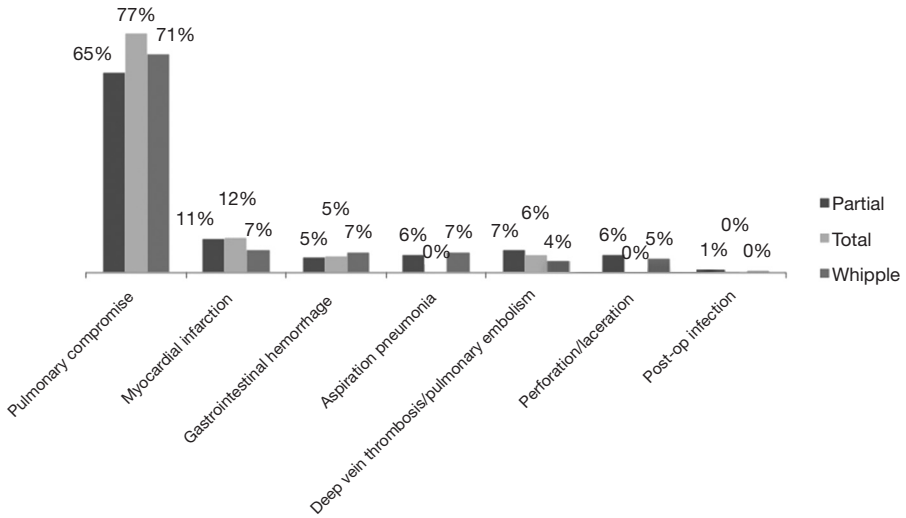

Figure 2 Postoperative complication risk by type of pancreatectomy performed for pancreatic cancer.

Table 3 The adjusted odds ratio of undergoing pancreatic resection for pancreatic cancer

Factor	% pancreatic resection	aOR[a]	95% CI	P
Age (yr)				
<45	79.8	Reference	–	–
45–65	68.1	0.56	0.44–0.72	<0.001
>65	66.9	0.55	0.43–0.71	<0.001
Gender				
Male	66.8	Reference	–	–
Female	69.2	1.10	1.02–1.19	0.019
Household income				
≤ National median	65.8	Reference	–	–
> National median	69.7	1.15	1.05–1.25	0.002
Service payer				
Private	70.2	Reference	–	–
Medicare	66.8	0.95	0.84–1.08	0.450
Medicaid	63.8	0.74	0.60–0.92	0.007
Self-pay	60.1	0.67	0.47–0.96	0.028
CCIS				
Low: 0–1	70.6	Reference	–	–
High: ≥2	63.0	0.74	0.67–0.82	<0.001
Surgeon volume (surgeries/yr)[b]				
Low: 1–5	60.2	Reference	–	–
High: ≥6	73.8	1.33	1.11–1.59	0.002
Hospital volume (surgeries/yr)				
Low: 1–17	61.0	Reference	–	–
High: ≥18	75.2	1.73	1.50–1.99	<0.001
Hospital teaching status				
Non-teaching	57.3	Reference	–	–
Teaching	70.6	1.36	1.17–1.57	<0.001

[a], the model includes: age, gender, household income, service payer, Charlson comorbidity index score, hospital volume, and hospital teaching status (N=11,365); [b], the model includes surgeon volume in addition to the above factors. The sample size for this model is (N=5,438). aOR, adjusted odds ratio; CI, confidence interval; CCIS, Charlson comorbidity index score; yr, year.

mortality, even after adjustment for hospital volume (25). Our findings were in line with the previously stated studies. High-volume surgeons had decreased post-resection complication and mortality. Moreover, shorter hospital stay and lower healthcare cost was associated with cases performed by high-volume surgeons.

Table 4 The risk of selected post-pancreatectomy outcomes in relation to surgeon volume (SV)

Outcome	Volume	% outcome	aOR[a]	95% CI	P
One or more postoperative complications	Low SV	18.1	Reference	–	–
	High SV	10.4	0.60	0.47–0.77	<0.001
In hospital mortality	Low SV	4.8	Reference	–	–
	High SV	2.1	0.56	0.37–0.86	0.008
Length of stay >14 days	Low SV	31.7	Reference	–	–
	High SV	19.1	0.52	0.43–0.63	<0.001
Cost of health services >$41,564.67	Low SV	26.1	Reference	–	–
	High SV	20.2	0.66	0.47–0.92	0.015

[a], the model includes: age, gender, household income, service payer, Charlson comorbidity index score, type of pancreatectomy, surgeon volume, hospital volume, and hospital teaching status (N=5,438). aOR, adjusted odds ratio; CI, confidence interval.

Regarding hospital volume, we demonstrate that pancreatectomy is more prevalent and more likely to be performed in high-volume hospitals when compared to low-volume hospitals. This has also been described by Gooiker *et al.* (29) showing an increase in resection rates from 10.7% to 15.3% after regionalization of pancreatic resections in the Netherlands. They also display a small but significant increase in overall survival for high-volume hospitals compared to low/mid-volume centers. Others attribute superior outcomes in cancer surgery to hospital volume (12,22,26,27). Sosa *et al.* (32) conclude pancreatic cancer patients treated by resection or palliative procedure benefit from referral to high-volume center citing decreased in-hospital mortality rates, LOS, and hospital charges for services.

Our current study is limited by the administrative nature of the database and the cross-sectional design. Additionally, it is limited by having information on patients during their hospital stay only and there is a lack of follow-up for mortality or other complications that could develop after hospital discharge. The study has several strengths represented by the long study period, large sample size, and the application of a weighted analysis that reflects more accurate estimates at the national level. These national estimates warrant replication of this study be performed using different and more sophisticated resources.

With resection being the only option for potential cure and long-term survival in pancreatic cancer treatment, it is important we understand factors associated with pancreatic resection. For the first time, we have successfully described both patient-specific and hospital-specific factors that make patients more likely to undergo pancreatic resection for pancreatic cancer. We have demonstrated that patients of lower SES and patients with Medicaid health coverage are significantly less likely to undergo pancreatic resection for a diagnosis of pancreatic cancer. Factors increasing the likelihood of pancreatic resection include age <60, female gender, and higher household income. We have also shown that those patients cared for by high-volume surgeons were more likely to achieve resection for their disease, at a lower risk of postoperative complications, had lower mortality rates, experienced shorter hospital stays, and lower healthcare costs.

It is likely patients of low SES are receiving care at low volume hospitals by low volume surgeons where costs for health services are higher and disease-based outcomes are inferior. As a healthcare provider caring for pancreatic cancer patients, it is important to be aware of patient-specific and hospital specific factors associated with pancreatic resection. One cannot overlook the effect these factors have on patients' ability to receive the best care and ultimately affect the course of their disease.

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Footnote

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

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