

Comparative Analysis of Outcomes of Distal Pancreatectomy with or without Splenectomy Using the National Inpatient Sample

Hassan Aziz¹, Mazhar Khalil¹, Bellal Joseph¹, Evan Ong², Taylor S Riall¹, Tun Jie¹

¹Division of Hepatopancreaticobiliary Surgery, Department of Surgery, Banner University Medical Center, Tucson, AZ

²Division of Surgical Oncology, Department of Surgery, Swedish Medical Center, Seattle, WA

ABSTRACT

Background Recent literature has advocated splenic preservation during distal pancreatectomy. However, no national analysis to date assessed the differences in outcomes between patients who underwent distal pancreatectomy with a concomitant splenectomy and patients who underwent distal pancreatectomy with a splenic preservation. **Materials and Methods** We performed a retrospective analysis of Nationwide Inpatient Sample database of patients who underwent distal pancreatectomy from 2004 until 2011(8 years). Patients were categorized into two groups: Distal pancreatectomy with splenectomy and distal pancreatectomy with splenic preservation. **Results** A total of 10,925 patients underwent distal pancreatectomy over the 8-year study period. 76.4% (n = 8,352) of the patients underwent Distal pancreatectomy with splenectomy. On multivariate regression analysis, age (OR [95%CI]: 1.02 [1.1-1.2]), female gender (OR [95%CI]: 1.8 [1.2-2.7]), malignant disease (OR [95%CI]: 1.8[1.0-3.05]), and weekend admission (OR [95% CI]: 3.7[2.3-6.1]) were predictors of mortality. Teaching status of the hospital (OR [95%CI]: 0.6 [0.4-0.9]) and distal pancreatectomy with splenectomy (OR [95%CI]: 0.5 [0.3-0.8]) were associated with decreased odds of mortality. **Conclusion** In this nationwide database analysis, distal pancreatectomy with splenic preservation was found to be independently associated with higher mortality rates when compared to distal pancreatectomy with splenectomy.

INTRODUCTION

Distal pancreatectomy for both benign and malignant disease in the tail of the pancreas has traditionally included splenectomy as an integral part of the procedure [1]. In recent years, many authors proposed a less invasive procedure, with preservation of the spleen in place of splenectomy [2]. This surgical procedure is called distal pancreatectomy with splenic preservation (DPSP). DPSP was initially described in 1943 by Mallet-Guy and Vachon [3]. In 1988 Warshaw described an alternative technique for splenic preservation during distal pancreatectomy. The spleen is perfused by preserving the short gastric vessels and the splenic vessels are divided with the pancreas [4].

The clinical outcomes data comparing DPSP and DPS is not well described in literature and is often conflicting [5]. Majority of the studies published on this topic are either retrospective analyses of case series or are based

on individual institutional experiences [6]. It is believed that patients with splenectomy are at a potential risk for infection because the spleen is known to be the largest aggregation of the lymphoid tissue in the body [7]. Shoup *et al.* reported that DPSP was associated with fewer perioperative complications and shorter hospital stay [7]. Conversely, Holdsworth *et al.* in a collective critical review of the literature, did not find frequency of infections or postoperative complications to be increased as a result of splenectomy [8]. Similarly, Martin *et al.* and Montorsi *et al.* have reported a significantly higher incidence of pancreatic leaks following DPSP [9, 10].

Overall, the role of splenic preservation in distal pancreatectomy has been debated, but the data was insufficient to formulate definitive conclusions [4, 5]. The aim of this study was to assess the differences in mortality rates after DPSP and DPS using a nationwide sample. Secondary outcome was to assess the predictors of mortality in patients undergoing distal pancreatectomy.

METHODS

Data Source

We performed an 8 year (2004-2011) retrospective analysis of National Inpatient Sample (NIS) database. NIS is the largest all-payer publically available database, maintained by the Healthcare Cost and Utilization Project (HCUP). NIS database incorporates 20% stratified sample of discharge data reported from over 1,000 hospitals

Received March 01st, 2016 - Accepted April 10th, 2016

Keywords Pancreatectomy

Abbreviations DPS Distal pancreatectomy with splenectomy; DPSP distal pancreatectomy with splenic preservation; NIS Nationwide Inpatient Sample

Correspondence Hassan Aziz

Division of HepatoPancreaticobiliary Surgery,
Department of Surgery, Banner University - Tucson, AZ
1501 N. Campbell Ave, PO Box 245072
Tucson, AZ, 85724-5072

Phone + (520) 626-4409

E-mail haziz@surgery.arizona.edu

across 44 states in the United States, representing 95% of the population. Weighted sampling technique allows for national estimates of different diagnoses and procedures. The database includes over 100 clinical and non-clinical data points encompassing patient demographics, admission profiles, in-hospital diagnoses and procedures, complications, socioeconomic factors, total charges, length of stay, and hospital profiles. This study was exempt from IRB approval since NIH data had been de-identified and no new patient was enrolled, making the consent requirement inapplicable.

Study Population

We included the data for all adult discharged between 2004 and 2011 who underwent distal pancreatectomy. Distal pancreatectomy was identified using International Classification of Diseases, Ninth Revision, Clinical Modification procedural codes 52.52 and 52.59. We excluded all patient records with either missing diagnosis information or missing surgical procedure information.

We divided our population into two groups: distal pancreatectomy with splenectomy (DPS) and distal pancreatectomy with a splenic preservation (DPSP). DPS category was created by applying ICD-9 procedural codes concurrently for both distal pancreatectomy (52.52 and 52.59) and splenectomy (41.5 and 41.53), while DPSP category included ICD-9 procedural codes for distal pancreatectomy (52.52 and 52.59) only.

Variables Collected and Definitions

We abstracted NIH data on demographics (age, race, and gender), mode of presentation (elective vs. non-elective), insurance status, teaching status of the hospital, location of the hospital (urban vs. rural), weekend admission, Charlson Comorbidity Index (CCI), indications for surgery, operative approach, complications, mortality, length of stay, and total charges.

CCI is a measure of comorbidities burden. The index was calculated by assigning a score to each comorbidity and incorporating all of the resulting scores into a weighted formula to obtain the final CCI.

We divided indications for surgery into three categories: inflammatory diseases, benign neoplastic diseases, and malignant neoplastic diseases. Inflammatory disorders were defined as acute and chronic pancreatitis (577.0 and 577.1), cyst and pseudocyst (577.2), and other specified and unspecified disorders of pancreas (577.8 and 577.9). Benign and malignant neoplastic disorders were identified using ICD-9 diagnosis codes for benign neoplasm of pancreas (211.6) and malignant neoplasm of pancreas (157.0-157.4 and 157.8-157.9).

Operative approach was defined as either open or minimally invasive surgery. Minimally invasive surgery was defined as either laparoscopic (54.21) or robotic assisted (17.41-17.44 and 17.49).

Complications were identified primarily using the ICD-9 diagnosis codes. In some instances procedural codes were

also used to identify procedures as surrogates for certain complications. We grouped our complications into wound complications, bleeding complications, reoperations, infectious complications, thromboembolic complications, end-organ dysfunction, and major complications.

Wound complications were defined as seroma that required a drainage procedure (998.13), non-healing surgical wound (998.83), persistent postoperative fistula (998.6), disruption of wound (998.3), disruption of internal surgical wound (998.31), or disruption of external surgical wound (998.32).

Bleeding complications were defined as post-surgical hematoma (998.11), hemorrhage (4590), or post-operative blood transfusions - transfusion of whole blood (99.03), packed red blood cells (PRBC) (99.04), platelets (99.05), or plasma (99.07).

Re-operation was defined as a return to the operating room for disruption of surgical wound (998.30, 998.31, or 998.32), post-surgical hematoma (998.11), or abdominal abscess (567.22). We further included ICD-9 procedure code (540) for drainage of extra or retroperitoneal abscess.

Infectious complications were defined as postoperative infection (998.5), other postoperative infection (998.59), infected postoperative seroma (998.51), abdominal abscess (567.22), percutaneous drainage of abscess (5491), drainage of extra or retroperitoneal abscess (540), urinary tract infection (599.0), sepsis (995.91 and 995.92), or pneumonia (507, 480.0-480.9, 481, 482.0-482.9, 483.0-483.8, 485, 486).

End organ dysfunction was defined as respiratory failure, continuous invasive mechanical ventilation for 96 hours or more, acute renal failure, need for hemodialysis, myocardial infarction, or cardiac arrest.

Outcomes

Our primary outcome measure was the difference in in-hospital mortality rates between DPSP and DPS. Our secondary outcome measures were rates of in-hospital complications, hospital length of stay, total charges, and failure to rescue in distal pancreatectomy. We defined failure to rescue (FTR) as mortality after developing a major complication.

Statistical Analysis

To account for the missing data on patient demographics, insurance status, location and teaching status of the hospital, we performed a missing value analysis. The original data was analyzed for random missing data points using little's MCAR test and the data were treated as missing at random. We imputed the missing data using multiple imputations technique. The procedure for multiple imputations was the Markov Chain Monte Carlo method (MCMC). The MCMC method refers to a collection of methods for simulating random draws from nonstandard distributions. All data presentations and statistical analyses were performed after addressing the missing data.

The data were presented as means (standard deviations) for continuous variables and as proportions for categorical variables. We performed χ^2 to compare the values for categorical variables and student's t-test for continuous descriptive variables. To assess the association of different factors with mortality, we conducted a multivariate binary logistic regression following a univariate logistic regression analysis. We included all the factors that were significantly associated with mortality on univariate analysis into our multivariate model. The significance for univariate analysis was set at $p \leq 0.2$ and for all other analyses it was set at $p \leq 0.05$. We used Statistical Package for Social Sciences V.20 (SPSS Inc. Armonk, NY) for the statistical analyses.

RESULTS

A total of 10,925 patients underwent distal pancreatectomy over the eight year study period. Mean age of the population was 56.5 (SD 17.1) years, 54.4% of the patients were female, and 76.4% of the patients underwent DPS.

An overwhelming majority of the population underwent surgery at a teaching hospital (75.6%). A majority of hospitals where surgery took place were urban (95%). The patients in DPS group were more likely to undergo surgery as an elective case (74.4% vs. 70%), at a non-teaching (25% vs. 21%) urban hospital (95.6% vs. 93.9%) compared to patients undergoing DPSP. There were significant differences in the indications of surgery with malignant diseases more likely to require DPS (29% vs. 14%, $p < 0.001$) while patients with benign diseases were more likely to undergo DPSP (55% vs. 42%, $p < 0.001$). **Table 1** describes the comparison of basic demographics between the groups.

Overall 42.6% of the population developed in-hospital complications. Bleeding complications (24%) followed by the infectious complications (20%) were among the most common categories of complications. The rate of complications was significantly higher in DPSP group compared to DPS group (44% vs. 38%, $p = 0.01$). The patients in DPS group were more likely to develop post-operative bleeding complications (26% vs. 19%, $p < 0.001$), but less likely to develop wound complications (1.9% vs. 2.6%, $p = 0.019$) and post-operative infectious complications (19.6% vs. 21.9%, $p = 0.012$) in general, and sepsis (4.1% vs. 7.9%, $p < 0.001$) in particular. **Table 2** provides the detailed comparison of outcomes between the two study groups.

Overall mortality in our population was 3.5%. DPS group had lower mortality (3.2% vs. 4.3%, $p = 0.008$) and failure to rescue rate (2.9% vs. 4.2%, $p = 0.002$) compared to DPSP group. On analysis of hospital length of stay and total charges, DPS group had shorter hospital length of stay (11.5 (SD 12.8) days vs. 13.7 (SD 17.5) days, $p < 0.001$), and less total hospital charges (\$100,869 (SD \$127,226) vs. \$117,820 (SD \$165,133), $p < 0.001$) compared to DPSP.

Predictors of Mortality

Univariate analysis assessed for factors associated with mortality after distal pancreatectomy. Age, female gender,

malignant disease as an indication of surgery, insurance status of the patient, teaching status of the hospital, weekend admission, CCI, and DPS showed statistically significant association with mortality ($p < 0.05$). **Table 3** provides the details of univariate analysis.

On multivariate regression analysis, after controlling for all the significant factors from univariate analysis, age (OR [95%CI]: 1.02 [1.004-1.03], $p < 0.001$), female gender (OR [95%CI]: 1.8 [1.2-2.7], $p < 0.001$), malignant disease as indication for surgery (OR [95%CI]: 1.802 [1.06-3.05], $p = 0.003$), and weekend admission (OR [95% CI]: 3.7 [2.3-6.1], $p < 0.001$) were associated with increased odds of mortality. Teaching status of the hospital (OR [95%CI]: 0.6 [0.4-0.9], $p = 0.011$) and DPS (OR [95%CI]: 0.5 [0.3-0.8], $p = 0.025$) were associated with decreased odds of mortality. **Table 4** provides the details of multivariate regression analysis.

DISCUSSION

In this nationwide data analysis of patients who underwent distal pancreatectomy; we found that distal pancreatectomy with splenic preservation was associated with higher rates of infectious complications and higher mortality rates compared to patients undergoing a concomitant splenectomy with distal pancreatectomy. We found that older age, female gender, and diagnosis of malignancy were predictors of mortality in patients undergoing distal pancreatectomy, while distal pancreatectomy with splenectomy and teaching status of a hospital were associated with increased rate of survival. We also found hospital length of stay to be shorter and hospital cost to be lower in patients who underwent distal pancreatectomy with splenectomy.

Benoist *et al.* analyzed 40 patients undergoing distal pancreatectomy for indications other than chronic pancreatitis. Pancreatic resection with splenectomy turned out to have a lower morbidity rate, as pancreatic complications such as fistula and sub phrenic abscess occurred more frequently in patients after spleen-conserving surgery [11]. Similar to our results, Aldridge and Williamson reported lower complication rates in DPS (24%) compared with SPDP (20%) patients [12]. Shoup *et al.* published their experience in a retrospective review of 125 patients who underwent either SPDP or DPS for benign disease. Contrary to our results, they reported higher rates of postoperative complications, including infectious complications, in the DPS group [7]. Rodriguez *et al.* in a retrospective study of 259 patients who underwent distal pancreatectomy, with or without splenectomy, showed less blood loss (300 mL vs. 500 mL) in patients undergoing DPSP [13]. In our study, we also found increased rate of bleeding complications and increased need for blood transfusions in patients undergoing splenectomy in comparison to spleen-preserving distal pancreatectomy patients.

We found higher mortality rates and failure to rescue rates in patients undergoing DPSP. Higher failure to rescue rates can partially explain higher mortality rates observed

Table 1. Demographics.

Variable	Total Population N=10,925	DPS N=8352	DPSP N=2573	p-value
Age, mean (SD)	56.5 (17.1)	57 (16.4)	53.3 (19.1)	0.1
Gender (female)	5951 (54.4%)	4510 (54%)	1441 (56%)	0.1
Race				0.65
White	7850 (71.8%)	6013 (72%)	1837 (71.4%)	
Black	1328 (12.2%)	1027 (12.3%)	301 (11.7%)	
Hispanic	1015 (9.3%)	768 (9.2%)	247 (9.6%)	
Other	732 (6.7%)	544 (6.5%)	188 (7.3%)	
Insurance Status				<0.001
Private	5052 (46.3%)	3745 (45%)	1307 (50.8%)	
Medicare	3988 (36.6%)	3172 (38.1%)	242 (9.4%)	
Medicaid	968 (8.9%)	726 (8.7%)	316 (9.6%)	
Self-Pay	610 (4.4%)	375 (4.5%)	110 (4.3%)	
Weekend admission	732(6.7%)	543 (6.5%)	189 (7.3%)	0.13
Teaching hospital	8256 (75.6%)	6239 (74.7%)	2017 (78.4%)	0.03
Urban location	10400 (95.2%)	7984 (95.6%)	2416 (93.9%)	0.04
Elective admission	8020(73.4%)	6214 (74.4%)	1806 (70.2%)	<0.001
Indications for surgery				
Benign Diseases	4889 (44.8%)	3482 (41.7%)	1407 (54.7%)	<0.001
Inflammatory	3392(31%)	2397 (28.7%)	995 (38.7%)	<0.001
Benign neoplastic	1785(16.3%)	1296 (15.5%)	489 (19%)	<0.001
Malignant Diseases	2810(25.7%)	2439 (29.2%)	371 (14.4%)	<0.001
Surgical Approach				
MIDP	836 (6%)	526 (6.3%)	157 (6.1%)	0.78
Laparoscopy	546 (5%)	440 (5.3%)	106 (4.1%)	0.02
Robotic	137 (1.3%)	86 (1%)	51 (2%)	<0.001
CCL, mean (SD)	1.92 (2.45)	2.07 (2.53)	1.45 (2.53)	<0.001

MIDP minimally invasive distal pancreatectomy

Table 2. Outcomes.

Variable	Total Population N=10,925	DPS N=8,352	DPSP N=2,573	p-value
Complications				
Wound	226 (2.1%)	158 (1.9%)	68 (2.6%)	0.019
Bleeding	2629 (24.1%)	2140 (26%)	489 (19%)	<0.001
Reoperation	465 (4.3%)	359 (4.3%)	106 (4.1%)	0.69
Infectious	2204 (20.2%)	1640 (19.6%)	564 (21.9%)	0.012
UTI	615 (5.6%)	472(5.7%)	143 (5.6%)	0.85
Sepsis	543 (5%)	341 (4.1%)	202 (7.9%)	<0.001
Pneumonia	714 (6.5%)	547 (6.5%)	167(6.5%)	0.91
Thromboembolic complications				
Stroke	17 (0.2%)	12 (0.1%)	5 (0.2%)	0.56
VTE/PE	82 (0.8%)	64 (0.8%)	18 (0.7%)	0.73
End Organ Dysfunction				
Respiratory	821 (7.5%)	589 (7.1%)	232 (9%)	0.001
Renal	741 (6.8%)	523 (6.3%)	218 (8.5%)	<0.001
MI/Cardiac arrest	91 (0.8%)	69 (0.8%)	22 (0.9%)	0.8
Mortality	385 (3.5%)	276 (3.3%)	109 (4.2%)	0.008
Failure to rescue	352 (3.2%)	245 (2.9%)	107(4.2%)	0.002
Hospital Length of stay, days, mean (SD)	12 (14)	11.5 (12.8)	13.7 (17.5)	<0.001
Total charges, \$, mean (SD)	104869(137301)	100869(127226)	117820(165133)	<0.001

in this group. To our knowledge, this is the first study to highlight a difference that exists in mortality and failure to rescue rates between two groups. In order to fully assess the influence of splenectomy on survival after distal and total pancreatectomy, future studies including larger series of patients are required. The concept of failure to rescue has been extensively described in literature in patients undergoing pancreatic resection. Ghaferi *et al.* identified teaching hospital settings and increased nurse-to-patient ratios to be significantly associated with lower failure to

rescue rates after pancreatectomy [14]. We believe that clarifying physician, patient, and caregiver goals of care by qualitative techniques also provides insight into differences in management of complications within this group of patients and can help reduce the rates of failure to rescue.

We found a longer hospital length of stay in patients undergoing DPSP. In a series of 235 patients, Lillemoe *et al.* did not identify any differences in morbidity, mortality, operative time or blood loss when comparing SPDP with DPS patients [15]. They, nonetheless, did report an

Table 3. Univariate regression analysis for factors associated with mortality.

	Unadjusted OR [95% CI]	p-Value
Age	1 [1.1-1.2]	<0.001
Female	2 [1.6-2.4]	<0.001
Race		0.348
White	0.5[0.3-1.1]	0.047
Black	0.7[0.4-1.2]	0.303
Hispanic	0.6[0.3-1.2]	0.196
Other	0.7[0.3-1.5]	0.391
Minimally Invasive approach	2.8[1.4-5.4]	0.002
Malignant Disease	1.4[1.1-1.9]	0.003
Urban location	0.6[0.2-1.8]	0.415
Insurance type		<0.001
Medicare	1.6[0.8-3.1]	0.143
Medicaid	1.5[0.7-3.1]	0.207
Private	0.7 [0.408-1.513]	0.413
Self-pay	3.7[1.3-10.7]	0.014
Weekend admission	3.4[2.6-4.4]	<0.001
CCI	1.04 [1.01-1.09]	0.016
DP with splenectomy	0.7 [0.6-0.9]	0.025
Teaching hospital	0.6 [0.4-0.8]	0.011

Table 4. Multivariate regression analysis for factors associated with mortality.

	Adjusted OR [95% CI]	p-Value
Age	1.02 [1.004-1.03]	0.012
Female	1.8 [1.2-2.7]	0.001
Minimally Invasive approach	2.8[0.6-11.8]	0.145
Malignant Disease	1.8[1.06-3.0]	0.029
Insurance type		0.26
Medicare	1.2[0.6-2.7]	0.493
Medicaid	0.6[0.3-1.1]	0.113
Private	1.1[0.5-2.7]	0.674
Self-pay	3.3[0.9-11.0]	0.057
Weekend admission	3.7[2.343-6.112]	<0.001
CCI	1.03 [0.9-1.1]	0.437
DPS	0.5 [0.3-0.8]	0.009
Teaching hospital	0.6 [0.4-0.9]	0.017

unexplained longer hospital stay among DPSP patients. One plausible explanation for longer hospital length of stay in DPSP group can be higher complication rates. The same finding can also explain higher costs in DPSP group, as addressing developing complications can lead to additional resource use, longer hospital stays, and intensive monitoring. This finding carries important implications in current times, as healthcare system faces severe economic burdens. Further research into outcomes and more detailed cost analysis of two procedures can delineate the future of distal pancreatectomy.

We also found that weekend admission was predictive of adverse outcomes in this subset of patients. This association has been well defined in literature in patients with renal failure, heart disease, and acute surgical conditions. This study is the first one to highlight this association with distal pancreatectomy. We also found an association between teaching status of the hospital and better clinical outcomes. Several studies have demonstrated that hospitals with a high

volume of pancreatic resections are more likely to have the systematic clinical support to successfully treat these complex patients [16].

The results of this study should be interpreted in the context of its limitations. Firstly, this study is a retrospective analysis of an administrative database. Secondly, the quality of the data is limited by the coding recorded at the individual patient level. Likewise, NIS limits diagnosis and procedures to 25 codes and 15 codes, respectively. Taking this together, we may be missing critical data that was either not coded at all or coded beyond the scope of the NIS. For example, the database cannot account for procedure-specific complications such as leaks or fistulas. We are also unable to account for institution-specific factors that may present additional confounding variables affecting the results of this analysis. Furthermore, a limitation of ICD-9 codes relates to the severity of disease. While some diseases such as diabetes have unique ICD-9 codes for sequelae of the primary disease, this is not always the case. Finally, we have no data concerning mortality or complications after the discharge. Furthermore, re-admissions data is not recorded in the NIS and cannot be added to this analysis.

Conclusion

In this nationwide analysis of data we found DPSP to be associated with higher complication rates and higher mortality rates compared to DPS. The difference in mortality rates remained significant after multivariate analysis was performed and the effect of other confounding variables was taken into account.

Conflict of interests

There is no conflict of interests.

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