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ORIGINAL SCIENTIFIC REPORT

Opportunity Lost? Diagnostic Laparoscopy in Patients with Pancreatic Cancer in the National Surgical Quality Improvement Program Database

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Abstract

Background Routine preoperative staging in pancreas cancer is controversial. We sought to evaluate the rates of diagnostic laparoscopy (DLAP) for pancreatic cancer.

Methods We queried the National Surgical Quality Improvement Program for patients with pancreas cancer (2005–2013) and compared groups who underwent DLAP, exploratory laparotomy (XLAP), pancreas resection (RSXN) or therapeutic bypass (THBP). We compared demographics, comorbidities, postoperative complications, 30-day mortality (Chi-square $P < 0.05$) and trends over time (R^2 0–1).

Results We identified 17,138 patients (RSXN 81.8%, XLAP 16.5%, THBP 8.2%, and DLAP 12.9%), with some having multiple CPT codes. Only 10.3% (n = 1432) of RSXN patients underwent DLAP prior to resection. XLAP occurred in 49.5% of non-RSXN patients, of whom 67.1% had no other operation. The percentage of patients undergoing RSXN increased 20.3% over time (R^2 0.81), while DLAP decreased 52.6% (R^2 0.92). XLAP patients without other operations decreased from 4.2 to 2.4%, although not linearly (R^2 0.31). Only 10.3% of XLAP had a diagnostic laparoscopy as well, leaving nearly 90% of these patients with an exploratory laparotomy without RSXN or THBP.

Discussion Diagnostic laparoscopy for pancreas malignancy is becoming less common but could benefit a subset of patients who undergo open exploration without resection or therapeutic bypass.

Introduction

Pancreatic cancer is the fourth leading cause of cancer death in the USA, with an overall 5-year survival rate of 5% [1]. The only definitive treatment for pancreas cancer remains surgical resection with pancreaticoduodenectomy. However, only 10–20% of those with pancreatic cancer undergo curative resection. This is primarily due to locally advanced disease, disseminated disease, or patient comorbidities, which preclude resection. As such, preoperative staging is imperative for appropriate patient selection prior to operative intervention.

Computerized tomography (CT) is routinely performed for pancreatic cancer staging. Enhanced resolution of helical CT has led to improved diagnosis and staging for pancreatic cancer [2–5]. However, despite advances in imaging and clinical staging to determine overall resectability, CT continues to underestimate the extent of small liver metastases and peritoneal deposits (<5–8 mm) [6–8]. Given this, a subset of pancreatic cancer patients

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with seemingly localized disease on imaging subsequently undergoes unnecessary laparotomy without curative resection. The use of diagnostic laparoscopy (DLAP) to assess resectability prior to laparotomy for curative resection is well documented [4]. However, many surgeons proceed directly to laparotomy without DLAP, resulting in decreased use of diagnostic laparoscopy [2, 7].

Rates of diagnostic laparoscopy and staging in pancreatic cancer remain controversial. In an attempt to better evaluate trends in DLAP for pancreas cancer staging, we queried the National Surgical Quality Improvement Program (NSQIP) to analyze the rates of diagnostic laparoscopy and laparotomy without resection (XLAP) for surgical patients with a pancreatic cancer diagnosis over time.

Methods

NSQIP is a national collaborative of over 680 North American academic and community hospitals with the goal of improving outcomes in surgical patients. The large, validated, multicenter database is composed of data on 135 variables, including preoperative, intraoperative and postoperative outcomes for patients undergoing major inpatient and outpatient surgical procedures. These data are collected prospectively by each center's clinical abstractors. This study was approved by the Boston University School of Medicine Institutional Review Board. Informed consent was not required.

The NSQIP database was queried for patients with a diagnosis of pancreatic cancer from 2005 to 2013. Patients were classified into groups based upon the type of surgical intervention. These included diagnostic laparoscopy (DLAP), laparotomy without resection (XLAP), pancreas resection (RSXN) or therapeutic biliary and/or gastroduodenal bypass (THBP). DLAP patients were further stratified into those in whom a biopsy was performed (DLAP+) and those who did not undergo biopsy (DLAP−), but may have undergone brushings or washings at the time of the procedure.

Comparisons were based on demographics, comorbidities, postoperative complications and 30-day mortality (Chi-square $P < 0.05$) as well as trends over time (R^2 0–1). Outcomes involved comparison among DLAP (DLAP+ and DLAP−), XLAP, RSXN, and THBP. A second subgroup analysis evaluated outcomes of DLAP alone versus DLAP and RSXN. Data analyses were performed using SAS v.9.3 software (SAS Institute Inc, Cary, NC).

Results

Demographic characteristics

The study cohort consisted of 17,138 patients with pancreatic cancer who underwent surgical intervention. RSXN occurred in 81.8% of patients, while 16.5% underwent XLAP, 8.2% underwent THBP, and 12.9% underwent DLAP (DLAP+ 8.4% and DLAP− 4.5%), with some patients undergoing more than one operation. Demographic characteristics and comorbidities for this cohort can be found in Table 1. The most common comorbidities were diabetes mellitus and hypertension. When compared to other groups, DLAP patients were more likely to have CHF, while THBP patients were more likely to have had preoperative weight loss and undergone preoperative chemotherapy. DLAP patients, who did not undergo resection, were more likely to have had preoperative weight loss and severe COPD as compared to DLAP with resection. RSXN patients were more likely to have diabetes mellitus or hypertension (Table 2).

Operative data

Definitive surgical resection was performed in 81.8% of patients (n = 14,017). Among RSXN patients, only 10.3% had DLAP prior to resection (DLAP− 2%, DLAP+ 8.3%). Of the DLAP̄ patients, 38.4% had no other operation within 30 days. Of the 18.2% of patients (n = 3121) who did not have a definitive resection of their pancreatic cancer, 24.8% underwent DLAP, 42% (n = 1311) underwent THBP operations and 33.2% (n = 1036) were XLAP patients who had no other operation. In fact, out of all patients who underwent XLAP (n = 1155), only 10.3% (n = 119) had a diagnostic laparoscopy as well, leaving nearly 90% of these patients with an exploratory laparotomy without pancreatic resection or therapeutic bypass.

Operative outcomes

Wound complications, including wound dehiscence and wound infections, urinary tract infections, and deep venous thromboembolism, were significantly less common with DLAP when compared to XLAP, RSXN, and THBP (Table 3). Thirty-day mortality was significantly lower for RSXN (Table 3). The aforementioned factors were significantly less common with DLAP alone when compared to DLAP with RSXN, and there was no difference in the 30-day mortality (Table 4).

Table 1 Comparison of baseline characteristics in patients with operative intervention for pancreas cancer in the National Surgical Quality Improvement Program (NSQIP) database (2005–2013)

	DLAP	XLAP	RSXN	THBP	*P* value
Age > 65 (%)	44.18	48.14	49.15	50.18	0.140
Sex (% male)	56.48	53.68	50.92	55.12	0.001
Preoperative weight loss (>10%/6 mol%)	27.91	23.38	18.38	34.85	<0.001
Race/ethnicity (%)					
Hispanic, white	0	0.44	1.62	0.65	0.090
Black (non-hispanic)	5.83	10.22	7.36	10.97	
White (non-hispanic)	91.26	83.11	85.60	82.26	
Hispanic, color unknown	0.97	4.44	2.39	3.55	
Other	1.94	1.78	2.99	2.58	
ASA class ≥ 3	72.97	78.04	72.66	83.65	<0.001
Preoperative smoker (within 1 year %)	22.42	23.46	20.13	23.85	0.001
Preoperative chemotherapy (%)	6.16	6.37	4.42	6.91	<0.001
Diabetes requiring medication (%)	27.25	32.73	27.42	30.94	<0.001
Renal failure on dialysis (%)	0.22	0.43	0.29	0.57	0.306
CHF (within 30 days) (%)	1.10	0.95	0.29	0.35	<.001
Severe COPD (%)	3.96	5.19	4.87	4.97	0.775
MI (within 6 months) (%)	0.29	0.69	0.24	0.37	0.118
PVD (%)	1.17	0.93	1.30	1.38	0.802
TIA (%)	2.64	2.89	2.35	2.67	0.718
Hypertension requiring medication (%)	49.45	57.66	56.14	57.98	0.010

Other American Indian, Alaskan Native, Asian, or Pacific Islander, *ASA* American Society of Anesthesiologists, *CHF* congestive heart failure, *COPD* chronic obstructive pulmonary disease, *MI* myocardial infarction, *PVD* peripheral vascular disease, *TIA* transient ischemic attack, *DLAP* diagnostic laparoscopy, *XLAP* exploratory laparotomy, *RSXN* pancreatic resection, *THBP* therapeutic gastric and/or biliary bypass

Trends over time

The percentage of patients undergoing RSXN increased 20.3% over time (R^2 0.81), while DLAP decreased by 52.6% (R^2 0.92) (Fig. 1). Patients undergoing XLAP without other operations decreased from 4.2 to 2.4%, although not in a linear fashion (R^2 0.31).

Discussion

Surgical resection is the only definitive treatment for pancreatic cancer. Accurate tumor staging in patients with pancreatic cancer is imperative to determine those with resectable disease who would benefit from surgical resection. Historically, patients were often staged both radiographically with preoperative imaging, and surgically with subsequent staging laparoscopy. However, with advancements in multi-detector CT imaging, the radiographic ability to detect metastatic or locally advanced pancreas cancer is improving. In a study by Howard et al. [5], helical CT was reported to be 63% sensitive, 77% specific and overall 86% accurate in determining resectability for pancreatic cancer. In addition, Soriano et al. determined CT to have 73% accuracy in accessing the extent of the primary tumor, 74% accuracy in determining local–regional extension, 83% accuracy in identifying vascular invasion, 88% accuracy in identifying distant metastasis, and 83% overall accuracy in determining tumor resectability [3].

Despite these improvements in preoperative imaging, radiographically occult metastases or local–regional advanced disease remain as high as 20% [4]. Valls et al. determined helical CT was unable to identify small peritoneal or hepatic metastases, and thus many argue that laparoscopy continues to play a critical role in pancreas cancer staging [9–12]. For example, Beenen et al. reported that 16% of patients undergoing staging laparoscopy prior to intervention were found to have metastatic disease [13]. In addition, studies show that utilizing staging laparoscopy to identify this subset of patients with occult metastasis can result in decreased postoperative pain, a shorter hospital stay, a higher likelihood of undergoing systemic therapy, and a lower overall cost [13–16]. The role of diagnostic laparoscopy has been demonstrated to have benefit in hepatobiliary malignancies as well, with D'Angelica et al.

Table 2 Comparison of baseline characteristics in patients undergoing laparoscopy with or without resection for pancreas cancer in the National Surgical Quality Improvement Program (NSQIP) database (2005–2013)

	DLAP	DLAP with RSXN	*P* value
Age > 65 (%)	44.18	50.55	0.09
Sex (% male)	56.48	52.73	0.32
Preoperative weight loss (>10%/6 mol%)	27.91	19.64	0.01
Race/ethnicity (%)			
Black (non-hispanic)	5.83	11.3	0.35
White (non-hispanic)	91.26	88.71	
Hispanic, color unknown	0.97	0	
Other	1.94	0	
ASA class ≥ 3	72.97	72.36	0.86
Preoperative smoker (within 1 year) (%)	22.42	23.64	0.70
Preoperative chemotherapy (%)			
Diabetes requiring medication (%)	27.25	31.64	0.04
Renal failure on dialysis (%)	0.22	0.36	0.72
CHF (within 30 days) (%)	1.1	0	0.08
Severe COPD (%)	3.96	7.27	0.05
MI (within 6 months) (%)	0.29	0	0.48
PVD (%)	1.17	2.33	0.32
TIA (%)	2.64	2.91	0.86
Hypertension requiring medication (%)	49.45	58.18	0.02

ASA American Society of Anesthesiologists, *CHF* congestive heart failure, *COPD* chronic obstructive pulmonary disease, *MI* myocardial infarction, *PVD* peripheral vascular disease, *TIA* transient ischemic attack, *DLAP* diagnostic laparoscopy, *XLAP* exploratory laparotomy, *RSXN* pancreatic resection, *THBP* therapeutic gastric and/or biliary bypass

Table 3 Comparison of postoperative outcomes in patients with operative intervention for pancreas cancer in the National Surgical Quality Improvement Program (NSQIP) database (2005–2013)

	DLAP	XLAP	RSXN	THBP	*P* value
30-day mortality (%)	5.05	6.53	2.50	6.20	<0.0001
Emergency procedure (%)	1.10	4.59	0.74	2.13	<0.0001
Wound dehiscence (%)	0.22	0.87	1.50	1.06	0.03
Deep surgical site infection (%)	0.44	1.90	9.07	4.83	<0.0001
Superficial surgical site infection (%)	0.44	2.16	8.25	7.95	<0.0001
Urinary tract infection (%)	1.10	2.16	4.57	3.83	<0.0001
Pulmonary embolism (%)	0.88	1.21	1.12	1.35	0.82
DVT/thrombophlebitis (%)	0.66	1.65	2.36	2.20	0.03
Readmission within 30 days (%)	7.70	16.33	14.63	18.13	0.35
Acute renal failure (%)	0	0.43	0.14	0.28	0.07
Reoperation (%)	2.44	4.52	5.52	4.24	0.70
Unplanned return to the OR (%)	7.70	5.11	5.74	4.83	0.10

DVT Deep venous thromboembolism, *DLAP* diagnostic laparoscopy, *XLAP* exploratory laparotomy, *RSXN* pancreatic resection, *THBP* therapeutic gastric and/or biliary bypass

[17] finding that diagnostic laparoscopy prevented laparotomy in 1 in 5 patients in that population while reducing length of stay and morbidity. It has also been shown to be cost-effective in pancreatic malignancy [15], which strengthens the argument in favor of diagnostic laparoscopy for these patients. A Cochran review suggested that the use of diagnostic laparoscopy would save unnecessary laparotomy in up to 21 out of 100 patients in whom pancreatic resection was planned for curative intent [18]. In our study, we found that the use of diagnostic

Table 4 Comparison of postoperative outcomes in patients undergoing laparoscopy with or without resection for pancreas cancer in the National Surgical Quality Improvement Program (NSQIP) database (2005–2013)

	DLAP	DLAP with RSXN	*P* value
30-day mortality (%)	5.05	2.90	0.16
Emergency procedure (%)	1.10	0.73	0.62
Wound dehiscence (%)	0.22	3.27	0.0006
Deep surgical site infection (%)	0.44	7.27	<0.0001
Superficial surgical site infection (%)	0.44	12.00	<0.0001
Urinary tract infection (%)	1.10	3.27	0.04
Pulmonary embolism (%)	0.88	0.73	0.83
DVT/thrombophlebitis (%)	0.66	4.00	0.004
Readmission within 30 days (%)	7.69	16.67	0.22
Acute renal failure (%)	0	0	1
Reoperation (%)	2.44	4.55	0.60
Unplanned return to the OR (%)	7.70	5.82	0.34

DVT Deep venous thromboembolism, *DLAP* diagnostic laparoscopy, *XLAP* exploratory laparotomy, *RSXN* pancreatic resection, *THBP* therapeutic gastric and/or biliary bypass

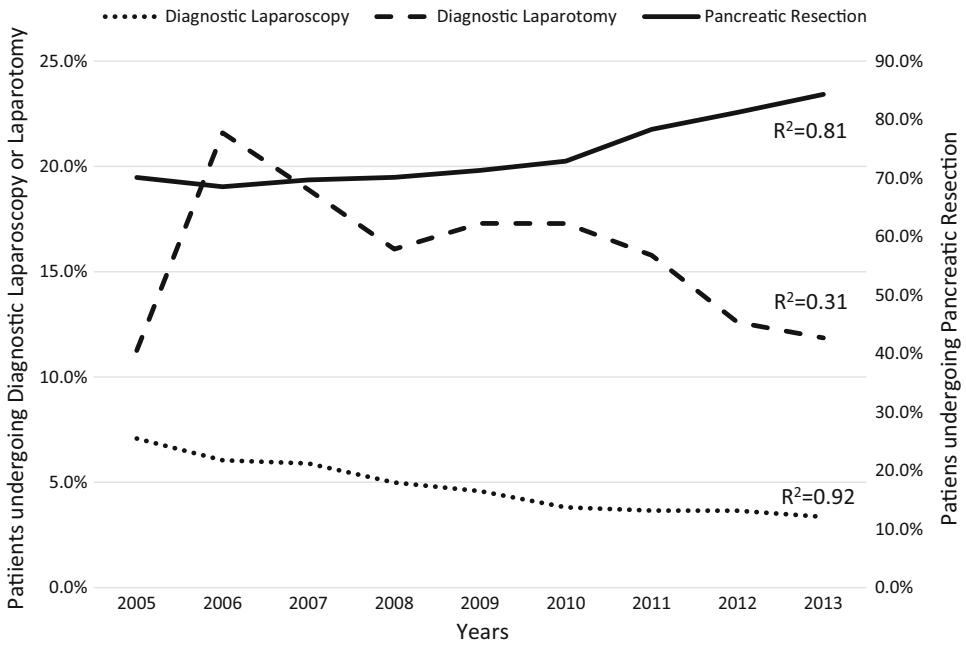

Fig. 1 Trends over time in the number of patients undergoing operations for pancreatic cancer in the National Surgical Quality Improvement Program (NSQIP) database (2005–2013)

laparoscopy in pancreatic cancer patients is declining. Our data also show an increase in the number of successful pancreatic resections. Still, our data suggest there is a subset to patients that would benefit from diagnostic laparoscopy, and are not receiving it.

White et al. [7] found that 14% of patients with radiographically resectable pancreas cancer were found to have unresectable disease at the time of operation. This group found that the strongest predictor of yield of diagnostic laparoscopy was tumor type, with yield being as high as 17% for pancreatic adenocarcinoma, with lesser yield for peripancreatic malignancy. In addition, numerous studies have found CA 19-9 and large primary tumor size to be potential predictors of unresectability despite radiographic evidence of resectability [2, 7, 12, 18–20]. Whether diagnostic laparoscopy is done as a separate operation or at the time of the planned resection is less well defined. However, for locoregionally advanced disease, or in those cases where

peritoneal dissemination may be suspected, performing diagnostic laparoscopy as a separate operation with peritoneal washings may be appropriate.

Our study also determined that while the utilization of exploratory laparotomy without other operations has decreased, there are still a number of patients who undergo exploratory laparotomy without subsequent resection or bypass, and who are therefore at a risk of higher morbidity and a delay in systemic therapeutic treatments.

There are a number of limitations to our analysis. Given the nature of large database analyses, there may be some in-hospital data and coding bias that may not account for out-of-hospital events, thus likely underestimating the true rates of complications and mortality. Additionally, NSQIP includes data on a select sampling of patients and does not include postoperative data after 30 days. Furthermore, data on stage of disease, neoadjuvant therapy and overall survival are not available in the NSQIP database.

Our data suggest that there are patients for whom diagnostic laparoscopy may prevent morbidity, decrease hospital stay, minimize pain and may improve time to systemic therapy. That these patients are not receiving care that is not only available, but is also economically effective, urges further study to better identify this subset. Additionally, an improved understanding of this subset of pancreatic cancer patients may aid in creating more universal parameters from which enhanced treatments may be planned, potentially avoiding unnecessary morbidity and mortality with better allocation of resources.

Conclusion

Diagnostic laparoscopy for pancreas malignancy is becoming less common. However, there remains a subset of patients with pancreas cancer who undergo laparotomy without subsequent resection or therapeutic bypass. In this subset of patients, diagnostic laparoscopy should be the initial operative intervention when possible. Further analysis to better delineate this subset of pancreas cancer patients is still required to determine who would benefit from diagnostic laparoscopy.

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