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Diagnostic Laparoscopy for Patients with Potentially Resectable Pancreatic Adenocarcinoma: Is It Cost-Effective in the Current Era?

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Abstract

Introduction For patients with potentially resectable pancreatic cancer, diagnostic laparoscopy may identify liver and peritoneal metastases that are difficult to detect with other staging modalities. The aim of this study was to utilize a population-based pancreatic cancer database to assess the cost effectiveness of preoperative laparoscopy.

Material and Methods Data from a state cancer registry were linked with primary medical record data for years 1996–2003. De-identified patient records were reviewed to determine the role and findings of laparoscopic exploration. Average hospital and physician charges for laparotomy, biliary bypass, pancreaticoduodenectomy, and laparoscopy were determined by review of billing data from our institution and Medicare data for fiscal years 2005–2006. Cost-effectiveness was determined by comparing three methods of utilization of laparoscopy: (1) routine (all patients), (2) case-specific, and (3) no utilization.

Results and Discussion Of 298 potentially resectable patients, 86 underwent laparoscopy. The prevalence of unresectable disease was 14.1% diagnosed at either laparotomy or laparoscopy. The mean charge per patient for routine, case-specific, and no utilization of laparoscopy was $91,805, $90,888, and $93,134, respectively.

Conclusion Cost analysis indicates that the case-specific or routine use of laparoscopy in pancreatic cancer does not add significantly to the overall expense of treatment and supports the use of laparoscopy in patients with known or suspected pancreatic adenocarcinoma.

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Introduction

Pancreatic cancer continues to be a major source of cancer mortality. There were 33,700 new cases diagnosed in 2006, with mortality nearly equaling incidence.[1] The economic impact of pancreatic cancer is substantial.[2] Cost estimates in 1999–2000 for treatment ranged from $7,279 to $15,143 monthly per patient depending on the extent of disease progression.[3] The majority of these costs are accrued by in-hospital treatments, including surgical procedures and chemotherapy.

For patients with pancreatic cancer, the only chance for cure is surgical resection, with best-reported 2- and 5-year actuarial survival 36% and 20%, respectively, after resection and adjuvant therapy.[4] Unfortunately, only 10–15% of patients present with resectable disease at the time of diagnosis.[5] The accurate and cost-effective identification of patients that are surgical candidates remains a significant clinical challenge.

Multi-detector helical computed tomography (CT) serves as the primary imaging study for most patients with potentially resectable pancreatic cancer. In recent years, the utilization of endoscopic ultrasound (EUS) with biopsy has increased, which may improve accuracy in assessing resectability.[6] Many surgeons also routinely employ diagnostic laparoscopy (DL) before proceeding to laparotomy. Laparoscopy is the only technique that allows direct visualization of peritoneal surfaces and the liver capsule and offers the possibility of minimally invasive diagnosis of small volume metastatic disease in these areas.[7–10] Patients diagnosed with metastatic disease at laparoscopy can be spared a non-resectional laparotomy. In recent years, however, developments in CT technology have led to a decreased yield from laparoscopy.[10] These advances have prompted some to assert that routine preoperative DL is not necessary and may not be cost-effective.[10,11] The benefits to those with metastatic disease diagnosed at laparoscopy who subsequently avoid a non-resectional laparotomy (NRL) include shorter hospital stay and lower morbidity. Most importantly, patients who are spared non-resectional laparotomy have a shorter interval to other, non-surgical treatments for pancreatic cancer including chemotherapy and radiation therapy. While multiple authors have examined the utility of incorporating DL in various staging methods, few have investigated the cost effectiveness of DL in pancreatic cancer.

The aim of this study was to utilize the clinical outcomes observed in a large population-based analysis of surgically treated pancreatic cancer patients to evaluate the cost effectiveness of diagnostic laparoscopy in patients with potentially resectable known or suspected pancreatic adenocarcinoma (PAC).

Material and Methods

Patients

Data from the Oregon State Cancer Registry (OSCaR) were linked with primary medical record data for years 1996–2003. According to Oregon statute, all cases of cancer must be reported to the registry. All patients with surgically treated PAC were identified using International Classification of Diseases, Version 9 (ICD-9) diagnosis codes and Current Procedure Terminology (CPT) codes.[12,13] Only patients with confirmed pathologic diagnosis of pancreatic ductal adenocarcinoma were included; excluded were proximal cholangiocarcinoma, any cancer of unknown primary, intraductal papillary mucinous neoplasms, mucinous cystadenocarcinoma, lymphomas, sarcomas, oncocytomas, giant papillary carcinomas, and neuroendocrine tumors of the pancreas. All patients with disease considered potentially resectable and who underwent procedures in any of the following categories were included in the analysis: DL, laparotomy, pancreaticduodenectomy, biliary and/or enteric bypass (a complete list of ICD-9 and CPT codes used is included in Appendix). The study period included the years 1996–2003. After study, candidates were identified in the registry, and their records were obtained from the treating institution. Records from 27 hospitals were submitted to OSCaR. The records were de-identified and then made available for review.

For each patient, we reviewed the admission history and physical, operative note, pathology report, imaging data, and discharge summary. Preoperative workup was determined and included multi-detector CT for the majority of patients (96%). CT findings were categorized as either predicting resectability or unresectability. A subset of scans demonstrated findings suspicious for metastases or locally advanced disease, but the findings were not definitive. These scans were described as "equivocal."

Operative notes and pathology reports were reviewed to determine the role and findings of laparoscopic exploration as well as the extent and type of resection performed. Demographic information, tumor characteristics, and presenting signs and symptoms were also recorded. Patients were excluded from the study if they had pancreatic neuroendocrine tumors, cystic neoplasms, or pathology other than pancreatic adenocarcinoma. This study was reviewed and approved by the institutional review board of the Oregon Health and Science University (OHSU) and the OHSU Cancer Institute.

Development of the Cost-Analytic Measure

Because cost accounting data were not available for all procedures or all study hospitals examined in this study, hospital charges from our institution (OHSU) were used to develop a uniform cost-analytic measure applied across all patients in the study. Because the measure is derived from charges rather than cost, the absolute monetary numbers are not broadly applicable and are not the primary outcome measure of the study. Instead, this methodology allowed us to formulate a single metric to compare the relative economic impact of different utilization strategies of laparoscopy across different hospital systems. Hospital length-of-stay, all pathology charges, and other hospital-based clinical service charges are included in the charge data. Not included in the analysis are charges for subsequent pancreatic cancer-related procedures including reoperation or endoscopic interventions such as stent placement for biliary or enteric obstruction.

To develop the cost-analytic tool, mean hospital charges for laparotomy, biliary bypass, enteric bypass, pancreatico-duodenectomy, and DL were determined by review of billing data from OHSU for fiscal years 2005–2006 using CPT codes and diagnosis-related group codes.[14] Physician charges were calculated from the Centers for Medicare and Medicaid Services regional physician fee schedule according to CPT code.[15] The charge for DL as an additional procedure (DL+) when combined with either pancreatico-duodenectomy or laparotomy was determined based on charge per minute of operative time, equipment, and OR processing charges. Upon review of the operative notes, we determined that the vast majority of surgeons, when they used DL, performed an examination of the peritoneum with little dissection in the lesser sac and no laparoscopic ultrasound. The time to perform this procedure is typically 30 min or less. Because a higher charge is ascribed to the first hour of operating room time, the contribution of OR time to the total cost of DL+ was determined from charges incurred for time beyond the first hour. This charge was added to the mean charge for each patient in each of the treatment arms employing DL.

Cost Analysis

Cost effectiveness was modeled for three different utilization strategies for diagnostic laparoscopy: (1) routine (all patients), (2) case-specific, and (3) no utilization. Case-specific utilization refers to the practice of using laparoscopy in some patients but not others. In this approach, the decision to perform laparoscopy was driven by clinical suspicion for metastatic disease from radiographic or clinical findings. We analyzed the outcomes from our clinical study to create an outcome model for each of the three utilization strategies for DL. We then applied the aggregate charge data to each arm of the model and determined an average charge per patient for each method of employing DL. For example, for the routine model in which laparoscopy would be utilized in all cases of known or suspected PAC, the charge for laparoscopy was added to each patient regardless of ultimate resectability. However, a subset of patients in this group avoided the expense associated with non-resectional laparotomy when metastatic disease was diagnosed at laparoscopy. To account for the false negatives inherent with laparoscopy, the same rate (26%) was applied to the NRL group so that ultimately, five patients that would undergo DL in this group were incorrectly deemed resectable. On laparotomy, these patients were unresectable but incurred the charge for both DL and laparotomy. We modeled the case-specific laparoscopy approach based on the observed practice in our clinical study. This included the charge of laparoscopy in a subset of patients, but also included the savings for the group of patients that were diagnosed with metastatic disease at laparoscopy where the expense of non-resectional laparotomy was avoided. To model the approach of non-utilization of laparoscopy, all patients avoided the additional charge of laparoscopy, but all patients with metastatic disease underwent laparotomy for diagnosis and incurred the charges associated with that procedure.

An additional subset analysis was performed based on lesion location. We focused this analysis on those tumors located only in the periampullary region of the gland (head and uncinate process). The one-way analysis of variance test was used to compare mean charges between the three approaches.

Results

A total of 298 patients with potentially resectable pancreatic adenocarcinoma were identified as surgical candidates during the study period (Table 1). Median age was 64.6 years (range 26–90). There was a nearly even distribution of the study population by gender (male, 52%). Most of the lesions were periampullary in location (79%), and the majority were clinical stage T3 based on preoperative imaging (59%). Presenting symptoms included but were not limited to jaundice, epigastric pain, and weight loss (63%, 62%, and 57%, respectively).

Preoperative imaging is depicted in Table 2 and included CT in 96% of patients and EUS in 34%. Of those who had EUS, the majority also had CT (96%). Four of the patients who had no record of CT had EUS as their primary preoperative imaging modality. In the 229 patients who had both a CT scan and a resection, CT scan accurately

Table 1 Patient Demographics and Clinical Outcome

	Number	Percentage
Median age, years (range)	64.6 (26–90)	NA
Gender		
Male	154	51.7
Female	144	48.3
Tumor location		
Periampullary	236	79.2
Distal	62	20.1
Tumor size (pre-op imaging)		
≤2 cm	31	10.4
>2 cm	124	41.6
Unknown	143	48.0
T stage[a]		
T1	16	5.4
T2	51	17.1
T3	175	58.7
T4	16	5.4
Unknown	40	13.4
Presenting symptoms/signs[b]		
Jaundice	187	62.8
Epigastric pain	184	61.7
Weight loss	170	57.1
Back pain	70	23.5
Pruritis	59	19.8
Anorexia	57	19.1

[a] AJCC Manual, 6th ed
[b] Patients may have more than one

predicted resection in 192 (84%). Another 32 patients with CT scan results deemed "equivocal" were also successfully resected despite apparent concerns for unresectability on CT. Of 231 patients deemed resectable after staging by CT scan, 39 (17%) were ultimately unresectable due to peritoneal or locally advanced disease. Endoscopic ultrasound correctly predicted resectability in 63 of 85 patients (74%), with 17 equivocal reports. Of the 74 patients who had EUS suggesting resectability, 11 (15%) had unresectable disease at either laparotomy or DL.

Patient characteristics and outcome were examined by the utilization of DL (Table 3). Laparoscopy was used in 86 patients (28.9%), of which, 73 had tumors located in the periampullary region and 13 had distal pancreatic tumors. In this group, laparotomy was avoided in 24 patients (28%) who had metastatic disease discovered at laparoscopy. Two of these patients underwent laparoscopic bypass procedures—one biliary and the other enteric bypass. Of the remaining 62 in whom laparotomy was performed, 46 (74%) were resected and 16 (26%) had a NRL. In the NRL group, nine were found to be unresectable due to vascular invasion, two had metastatic disease in lymph nodes that were in regions outside the planned resection, and five had distant disease precluding resection.

In the non-DL group, 212 patients were taken directly to laparotomy without laparoscopy. Of these, 194 (92%) were resected and 18 (8%) had a NRL due to either metastatic disease or local invasion precluding resection. Specifically, three patients had vascular involvement, 14 had metastatic disease in the liver or peritoneum, and one patient had positive regional lymph nodes that were considered to be outside the resection field.

Charge data are depicted in Table 4. Based on an operating room charge for 30 min of operative time and laparoscopic equipment charges, the additional charge for DL performed in the same operative session as pancreaticoduodenectomy or laparotomy was $3,529. Alternative procedures performed for unresectable disease in the NRL group included diagnostic laparotomy, biliary and/or enteric bypass.

When each of the treatment strategies is modeled using our analytic charge measure, the three strategies for DL are very similar in resource utilization (Table 5). Case-specific use of DL proves to be the least expensive at $90,888 per patient (Fig. 1). Next is routine use at $91,805 (Fig. 2). Non-utilization of laparoscopy is the most expensive at $93,134 per patient (Fig. 3). There was not a significant difference between these three values (p=0.9626).

In our study, it appears that 16 of 52 (26%) patients deemed resectable at laparoscopy had local or metastatic disease precluding resection. However, it should be noted that a number of these patients had M1 disease identified at DL, but went on to open palliative bypass.

When examining the subset of patients with only head and uncinate process lesions (n=236, 79.1%), we observed similar results. The mean charges for this group were $92,453, $93,889, and $93,928 in the case-specific, routine, and non-utilization arms, respectively. The difference between each group was not statistically significant (p=0.9882).

Table 2 Surgical Resectability by Preoperative Imaging Findings

Assessment of Resectability	Resection		Total
	Yes	No	
CT			285
Resectable	192 (84)	39 (17)	231
Equivocal	32 (65)	17 (35)	49
Unknown	5	0	5
No CT	11	2	13
EUS			100
Resectable	63 (85)	11 (15)	74
Equivocal	17 (85)	3 (15)	20
Unknown	5	1	6
No EUS	155	42	198

Numbers in parenthesis are percentages.

Table 3 Surgical Outcome for 298 Patients with Potentially Resectable Pancreatic Cancer

Course	Resected	NRL	M1 disease[a]	Total
Directly to laparotomy	194 (91.5%)	18 (8.5%)	NA	212 (71.1%)
Diagnostic laparoscopy	46 (74.2%)	16 (25.8%)	24 (27.9%)	86 (28.9%)
Total	240 (80.5%)	34 (11.4%)	24 (27.9%)	298

NRL non-resectional laparotomy, *M1* metastatic disease
[a] Identified at laparoscopy

Discussion

This study represents a statewide, population-based audit of the surgical practices utilized in the treatment of patients with potentially resectable pancreatic adenocarcinoma. We found that surgeons used diagnostic laparoscopy in 29% of the study patients. Laparoscopy contributed significantly to the staging in this subset of patients, with metastatic disease identified in 28% who were subsequently spared laparotomy. However, even the addition of laparoscopy did not allow completely accurate identification of resectable patients. Twenty-six percent of patients that underwent laparoscopy and had no laparoscopic indication of unresectability were eventually assessed as unresectable at laparotomy. The overall resectability rate (74%) was actually lower in the group of patients undergoing laparoscopy than the larger group of patients taken directly to laparotomy.

We suspect that the more favorable resectability rate for patients taken directly to laparotomy without laparoscopy relates to bias inherent in the selection of patients for staging laparoscopy that are high risk for metastatic disease. Unfortunately, the data available in this study do not allow us to determine with accuracy the criteria that surgeons used to select patients for laparoscopy. Such preoperative findings are likely to include suspicious, but not diagnostic, findings on CT scan and elevated preoperative CA 19-9. Some of these criteria may be difficult to measure even with the clinical data reviewed for this study.

Table 4 Estimated Charges for Pancreatic Cancer Procedures

Procedure	Charge ($)	SD ($)
DL[a]	3,529	NA
DL only	16,900	3,789
NRL	54,730	23,253
NRL + DL	58,575	21,710
PD	102,415	42,555
PD + DL	106,261	55,159

Charges for pancreatic cancer procedure include hospital charges, physician fees, equipment, and operating room costs
DL diagnostic laparoscopy, *NRL* non-resectional laparotomy (including biliary or enteric bypass), *NRL + DL* non-resectional laparotomy with diagnostic laparoscopy, *PD* pancreaticoduodenectomy, *PD +DL* pancreaticoduodenectomy with diagnostic laparoscopy, *SD* standard deviation
[a] Charge for DL as an additional procedure; does not include physician fees

Our data indicate that by using a uniform charge structure as a measurement of the relative differences between utilization strategies, laparoscopy may be performed routinely or on a case-specific basis without increasing the charges for care provided. We found that the average charge per patient was quite similar regardless of whether patients would have received laparoscopy routinely, on a case-specific basis, or not at all. In fact, the average per patient charge for groups in which DL was used either on a case-specific basis or routinely had a lower mean charge than those in whom DL was not used (Table 5).

The false negative rate for DL observed in this study (26%) was high compared to reported rates of 2–9%.[16–18] However, this group likely represents the appropriate use of DL—an additional staging method in patients who likely have occult metastatic disease. Thus, it is not surprising that many of these patients did in fact harbor locally advanced or distant disease undetectable by CT and DL despite a high index of suspicion on the part of the surgeon. It is notable that many of these procedures were performed in an era before durable endoscopic stents were widely available and surgical bypass was more commonly used for palliation. Thus, a portion of the patients with metastatic disease identified on DL ultimately underwent laparotomy with palliative bypass. More recent experience has demonstrated that patients diagnosed with metastatic disease at laparoscopy only rarely require operative intervention for palliation.[19] Even with the more liberal utilization of surgical bypass that was practiced in the early years of this series, the use of routine or case-specific DL was still economically neutral when compared to non-utilization of laparos-

Table 5 Projected Mean Charge Per Patient Based on Surgical Method of Employing DL

Approach to DL	Mean charge per patient—all lesions* ±SD	Mean charge per patient—Head and uncinate lesions** ±SD
Case-specific	$90,888±29,042	$92,453±29,360
Routine	$91,805±44,452	$93,889±45,381
No DL	$93,134±34,570	$93,928±35,226

SD standard deviation
*p=0.9626; **p=0.9882

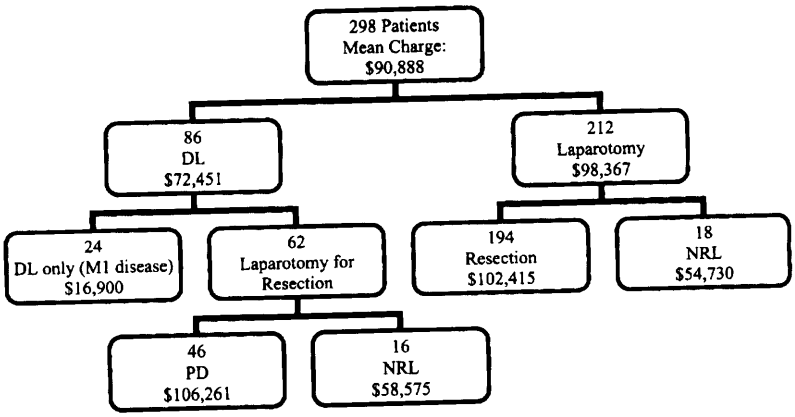

Figure 1 Mean charges in cost-analytic model for DL on a case-specific basis. All charges represent mean charge per patient in each associated subgroup. *DL* diagnostic laparotomy, *NRL* non-resectional laparotomy.

copy when modeled both for all lesions and those limited to the periampullary region.

The liberal utilization of laparoscopy has sound clinical rationale. Pancreatic cancer frequently spreads to the peritoneal surfaces and liver. CT alone rarely identifies small volume peritoneal and hepatic disease, with limited capability for detecting lesions <1 cm. In our study, 17% of patients with a CT scan predicting resectability were unresectable at laparotomy. In a study of patients with locally advanced disease, Liu and Traverso[20] demonstrated that as many as 34% of patients with no evidence of M1 disease on CT actually harbor occult disease. Among those who have examined the use of DL in patients with potentially resectable disease, the utility of DL varies widely for preventing unnecessary laparotomy 19–38%.[8,16–18,21] In our study, DL prevented an unnecessary laparotomy in a large percentage of patients (27.9%). Improvements in CT imaging have greatly enhanced the ability to determine resectability. However, CT alone is often unable to predict *unresectability* in a subset of patients. It is this group who benefit from the addition of staging laparoscopy. When used together, CT and DL have a reported sensitivity of 87% and a positive predictive value for unresectability as high as 100%.[22] The additive value of using these tools together enhances the diagnostic capability of either alone.

Few studies have directly assessed the role of staging laparoscopy in PAC, and there has been a diminishing yield of DL in those that have.[16–18,21,23] In publications that have addressed cost effectiveness, theoretical models have been created, and intervention/benefit ratios have been postulated, but neither cost nor charge data have been applied to actual clinical outcomes.[10,24] In a detailed cost analysis model, Tierney and colleagues[24] demonstrated that the combination of laparoscopy and EUS yielded the most cost-effective staging strategy and that laparoscopy alone led to the highest resection rate. Friess et al.[10] have suggested that laparoscopy must be seven times cheaper than laparotomy to offset the cost of "unnecessary" laparoscopy in patients who are ultimately resected. This group demonstrated relatively low rates of unresectability after CT (14%), but none of the patients actually underwent laparoscopy. Their analysis compared the cost of DL as a stand-alone procedure to diagnostic laparotomy, but did not include cost data, nor did they consider the cost of DL as a perioperative procedure. While our analysis demonstrates that the charge for DL as a stand-alone procedure was one third the cost of laparotomy, when the economic impact of laparoscopy is considered across a large cohort, the expense of DL is essentially neutral in resource utilization. Further, while the authors do continue to strongly recommend DL

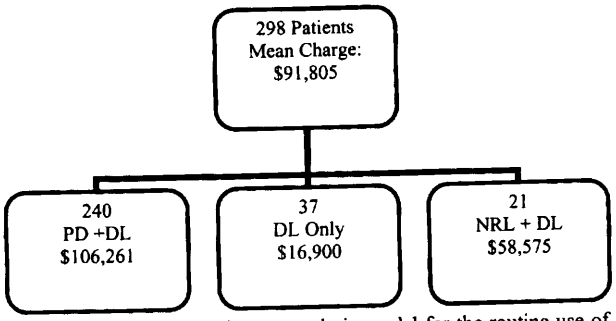

Figure 2 Mean charges in cost-analytic model for the routine use of DL. All charges represent mean charge per patient in each associated subgroup. *DL* diagnostic laparotomy, *PD* pancreaticoduodenectomy, *NRL* non-resectional laparotomy.

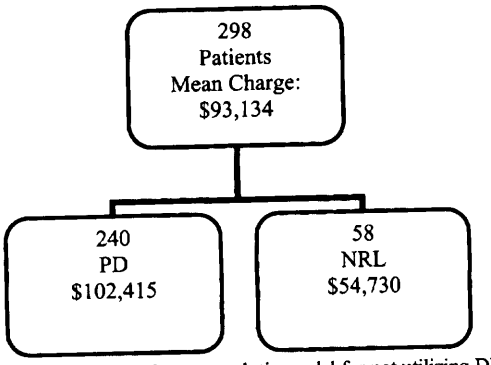

Figure 3 Mean charges in cost-analytic model for not utilizing DL. All charges represent mean charge per patient in each associated sub-group. *PD* pancreaticoduodenectomy, *NRL* non-resectional laparotomy.

for those patients in whom metastases cannot be excluded, they do not speculate on the cost benefit of this approach. We have shown that in these patients, a case-specific approach to DL is not cost-prohibitive.

Several limitations of our analysis must be acknowledged. This study extrapolates from hospital charges at a single institution to construct an analytic tool for the comparison of different strategies for the utilization of DL. Hospital charges represent neither incurred costs (direct or indirect) nor reimbursed costs, leading some to argue that hospital charge data are inadequate for cost analysis.[25] As the aim of this study was to survey practices and outcomes in a wide variety of facilities, it was necessary to construct a single analytic tool to apply to the entire study population. In this study, hospital charges are not designed to be an absolute measure of pancreatic cancer cost but rather serve as a tool to compare the relative costs of different utilization strategies for preoperative laparoscopy.

The most robust argument against the use of hospital charge analyses is that they tend to underestimate the financial impact of additional interventions or procedures. This has indeed been problematic in studies where laparoscopic procedures are shown to be more expensive than their open counterparts.[26,27] In those instances, however, laparoscopy led to a *higher* charge or a *higher* cost, or both. In fact, our study showed the opposite: that the addition of laparoscopy was cost neutral or possibly associated with a modest reduction in mean hospital charge per patient treated. Other authors have demonstrated similar cost effectiveness when analyzing cost and charge data for laparoscopy across numerous procedures in pediatric surgery.[28]

In this study, we have excluded patients with neuroendocrine tumors, duodenal cancer, and ampullary tumors—all disease sites in which preoperative laparoscopy may play a role. However, as the study uses the pathologic data from a variety of hospitals and there was not a central pathologic review, it is possible that there is some heterogeneity in the study group. In particular, it is possible that some of the patients had cancer arising in the distal bile duct rather than the pancreas. We do not believe, however, that this compromises the conclusions or clinical applicability of the study findings.

Conclusion

In summary, we found that DL may be performed either on a case-specific basis or routinely in all cases of suspected PAC. Neither of these approaches appears to significantly increase the economic burden of PAC care. When used as a preoperative technique, DL remains an important adjunct for identifying M1 disease that is missed on CT.

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Appendix

Table 6 A-CPT and ICD-9 Codes (Not Intended for Inclusion in Published Manuscript Unless Requested by Reviewers)

Diagnosis/Procedure	ICD-9	CPT
Pancreatic adenocarcinoma	157.0	
	157.1	
	157.2	
	157.3	
	157.4	
	157.8	
	157.9	
Pancreatic resections	52.51	48140
	52.52	48145
	52.53	48150
	52.59	48152
	52.6	48153
	52.7	48154
		48155
Laparoscopy–1999		56310
		56300
		56305
		56399
Laparoscopy–2004	54.51	44200
	52.21	49320
	54.21	49321
	54.23	49329
	54.24	
	65.11	
	65.13	
	68.15	
Other		
Extra-hepatic biliary cancer	156.1	
Ampulla of vater cancer	156.2	
Laparotomy		49000
Laparotomy/Exploration		47015
Hepatico-jejunostomy		47780
Gastro-jejunostomy		43820
Laparoscopic ultrasound		76986

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