Evolving Preoperative Evaluation of Patients with Pancreatic Cancer: Does Laparoscopy Have a Role in the Current Era?

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BACKGROUND: Recent years have brought important developments in preoperative imaging and use of laparoscopic staging of patients with pancreatic adenocarcinoma (PAC). There are few data about the optimal combination of preoperative studies to accurately identify resectable patients.

STUDY DESIGN: We conducted a statewide review of all patients with surgically managed PAC from 1996 to 2003 using data from the Oregon State Cancer Registry, augmented with clinical information from primary medical record review. We documented the use of all staging modalities, including CT, endoscopic ultrasonography, and laparoscopy. Primary outcomes included resection with curative intent. The association between staging modalities, clinical features, and resection was measured using a multivariate logistic regression model.

RESULTS: There were 298 patients from 24 hospitals who met the eligibility criteria. Patients were staged using a combination of CT (98%), laparoscopy (29%), and endoscopic ultrasonography (32%). The overall proportion of patients who went to surgical exploration and were resected was 87%. Of patients undergoing diagnostic laparoscopy, metastatic disease that precluded resection was discovered in 24 (27.6%). For patients who underwent diagnostic laparoscopy and were not resected, vascular invasion was the most common determinant of unresectability (56.6%). In multivariate analysis, preoperative weight loss and surgeon decision to use laparoscopy predicted unresectability at laparotomy.

CONCLUSIONS: This population-based study demonstrates that surgeons appear to use laparoscopy in a subset of patients at high risk for metastatic disease. The combination of current staging techniques is associated with a high proportion of resectability for patients taken to surgical exploration. With current imaging modalities, selective application of laparoscopy with a dual-phase CT scan as the cornerstone of staging is a sound clinical approach to evaluate pancreatic cancer patients for potential resectability. (J Am Coll Surg 2009;208:87–95. © 2008 by the American College of Surgeons)

Despite advances in perioperative management and the evolving techniques of pancreatic surgery, pancreatic adenocarcinoma (PAC) remains extremely difficult to cure.[1] Complete resection remains the only possibility for long-term survival; but only 10% to 20% of patients with PAC are eligible for resection at the time of presentation.[2] Accurate selection of patients for laparotomy and pancreaticoduodenectomy remains a challenge for surgeons, radiologists, and gastroenterologists. In the past, the proportion of patients resected at surgical exploration has been as low as 50%.[3,4]

The optimal sequence of staging studies should identify patients with resectable disease while enabling surgeons to avoid a nonresectional laparotomy in patients with metastatic disease or unresectable, locally advanced disease. This has become more important as increasingly durable biliary and duodenal stents have facilitated delivery of palliative chemotherapy and radiation without the risks and delays associated with surgical bypass.[5]

Recent years have been associated with marked developments in pancreatic imaging. Modern pancreatic CT scans

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Abbreviations and Acronyms

DL = diagnostic laparoscopy
EUS = endoscopic ultrasonography
M1 = metastatic disease
OSCaR = Oregon State Cancer Registry
PAC = pancreatic adenocarcinoma

involve images obtained through multidetector scanners during both arterial and portal venous contrast phases.[6] These techniques provide high-resolution images that offer detail about local vascular involvement and distant metastatic disease. In addition, gastroenterologists increasingly use endoscopic ultrasonography (EUS) to obtain accurate images of the tumor and adjacent structures and to biopsy lesions and regional lymph nodes. Surgeons have also incorporated laparoscopy with or without laparoscopic ultrasonography into the preoperative staging program. Laparoscopy serves to allow identification and biopsy of small-volume liver and peritoneal disease, allowing patients to avoid unnecessary exploration and pursue other palliative therapies without the recovery period associated with a laparotomy.

The aim of this study is to provide a population-based audit of the current staging methods used in management of patients with known or suspected pancreatic cancer. In addition, this study aims to measure the ability of current preoperative staging strategies to select patients accurately for operative exploration.

METHODS

Data sources

We queried the database of the Oregon State Cancer Registry (OSCaR) for all cases of PAC diagnosed between January 1, 1996, and December 31, 2003. This time period reflects the inception of the cancer registry through the most recent update to the registry at the time our study was undertaken. Data from this project are the results of a combination of information abstracted from deidentified patient medical records and data collected by OSCaR, resulting in a retrospective cohort study design.

To identify patients with PAC who underwent preoperative staging and surgical exploration, OSCaR requested cancer registrars from 27 hospitals in Oregon to query their medical records for patients with PAC and several procedural codes, including diagnostic laparoscopy (DL). This query was based on the ICD-9 (157.0 to 157.4, 157.8, and 157.9) and the Common Procedural Terminology codes specific to laparoscopy. The information was then forwarded to OSCaR and the registry. This generated three distinct groups of patients with PAC: patients who had a DL and no laparotomy; patients who had a DL and a laparotomy (with or without a resection); and, finally, patients who had a laparotomy (with or without a resection). Data about use of CT scan and ultrasonography were derived from patient records, including admission history and physical and the indications section of the operative reports.

The state registry then requested all hospitals in Oregon with cases of pancreatic cancer during the study period that had an operative intervention to provide the operative note, pathology report, discharge summary, and the admission history and physical pertaining to the PAC operation for each patient. These records were then returned to OSCaR, sorted by the registry staff, and deidentified. The registry then released the records to the research team. We constructed a comprehensive database that merged clinical data with registry data using Statistical Package for Social Sciences (version 13.0; SPSS, Inc). The study was reviewed and approved by the Oregon Health and Science University Cancer Institute Clinical Research Review Committee and the Oregon Health and Science University Institutional Review Board.

Study population

For study eligibility, we required that patients were diagnosed between 1996 and 2003 and had a confirmed pathologic diagnosis of PAC. All study patients were considered potentially resectable by a surgeon after preoperative imaging evaluation and either a laparoscopy or laparotomy was performed.

Patients were excluded from the analysis if they were taken to the operating room for a procedure with palliative intent (eg, choledochojejunostomy) or if pancreatic cancer was not suspected at the time of operation (eg, trauma laparotomy). We also excluded atypical histologies, including intraductal papillary mucinous neoplasms, lymphoma, sarcoma, and cystadenocarcinoma. In addition, we excluded patients with duodenal adenocarcinomas and ampullary cancers from analysis.

Clinical variables

We developed the clinicopathologic predictor variables in this analysis from a combination of medical record review and from the OSCaR database. Clinical signs at presentation, including weight loss, were captured from the patients' history and physical. Radiographic reports and clinic notes were reviewed to determine the use of EUS or if the CT scan was felt to be equivocal (ie, CT findings suggested potential unresectability). Operative notes were used for specific determinants of unresectability in patients who did not undergo resection and for other details of the operation. The pathology report provided details on the

size of the neoplasm, extent of the lymphadenectomy, and margin status.

Statistical analysis

The main outcomes of interest included resection with curative intent. Several clinicopathologic variables were analyzed to adjust for potential confounding and effect modification. A two-sample *t*-test was used to assess the association between the main outcomes and the continuous independent covariates, and a chi-square test was used to assess the association with categorical covariates. We used a multivariable logistic regression analysis as the principal analytic tool. The logistic regression variable selection procedure was based on recommendations from Hosmer and Lemeshow[7] and Greenland.[8] We developed a univariate logistic regression model for each of the covariates of interest and evaluated the models using the Likelihood Ratio Test. Next, to account for the possible confounding attributable to DL, we developed bivariate models in which DL was always present and to which select covariates of interest were added individually to assess the impact on the log odds (probability) of each variable. We considered variables with > 10% change in the odds ratio as confounders of the relationship between DL and resection with curative intent. This method is described by Greenland.[8] To identify variables for inclusion in the multivariate model, we selected variables using the Hosmer and Lemeshow criteria of $p < 0.25$ in combination with important clinical variables and confounders. We then applied the backward selection method and retained the variables with $p < 0.05$ or variables that were considered clinically important. We evaluated potential effect modification of DL by testing selected pairwise interactions among the remaining significant variables. Assumptions of linearity of the continuous variables were evaluated using orthogonal polynomial contrasts (eg, quadratic or cubic). We used the Hosmer and Lemeshow goodness-of-fit test and receiver operating characteristic curve to evaluate the model's performance and discriminative ability. Significance levels were set at $p < 0.05$. All tests were two-sided.

RESULTS

Statewide query

Two hundred ninety-eight (72.9%) of the 378 cases we received satisfied the study inclusion criteria. The majority (62.5%) of patients who were excluded had histopathology other than adenocarcinomas (eg, neuroendocrine malignancies). Records were received for 27 hospitals throughout the state; but patients satisfying the eligibility criteria were from only 24 hospitals throughout the state and from 30 of Oregon's 36 counties.

Table 1. Demographic and Clinical Characteristics of Patients with Potentially Resectable Pancreatic Adenocarcinoma

Characteristic	Total (n = 298)
Demographics	
Age (y), mean ± SD	64.6 ± 11.2
Male, n (%)	154 (51.7)
Tumor size (cm), mean ± SD	3.3 ± 1.4
Presenting symptoms, n (%)	
Weight loss	171 (57.3)
Jaundice	187 (62.8)
Back pain	70 (23.5)
Epigastric pain	184 (61.7)
Anorexia	57 (19.1)
Pruritus	59 (19.8)
Preoperative imaging/staging, n (%)	
Preoperative stent	128 (43.0)
Preoperative CT	285 (95.6)
Preoperative EUS	100 (33.6)
Diagnostic laparoscopy	86 (28.9)
Location, n (%)	
Head, neck, uncinate process	238 (79.9)
Distal	60 (21.1)
Year of operation, n (%)	
1996 to 1999	134 (45.0)
1999 to 2003	164 (55.0)

EUS, endoscopic ultrasonography.

Based on observed pancreatic cancer incident rates, we estimated that there would be 320 potentially resectable pancreatic cancer patients during the study period. The observed number of 298 patients suggests that this study population represents a high rate of capture, and the study cohort is not selected to favor resectable patients.

Demographic and clinicopathologic characteristics

The mean age of the study population was 64.6 years old (SD 11.2 years), ranging from 26 to 90 years old. Men constituted 51.7% of the study population (Table 1). Jaundice (62.8%), epigastric pain (61.7%), and weight loss (57.3%) were the most common presenting clinical symptoms. The majority of cases (79.9%) were malignancies of the periampullary region (defined as head of pancreas, neck, or uncinate process; nonpancreatic tumors involving the duodenum and ampulla of Vater were excluded). Approximately one-third of patients had EUS before their operation. Overall, 28.9% of patients in the cohort underwent laparoscopic exploration before their planned resection. There was no statistically significant difference in the clinicopathologic characteristics of patients who were laparoscopically explored compared with patients who were not.

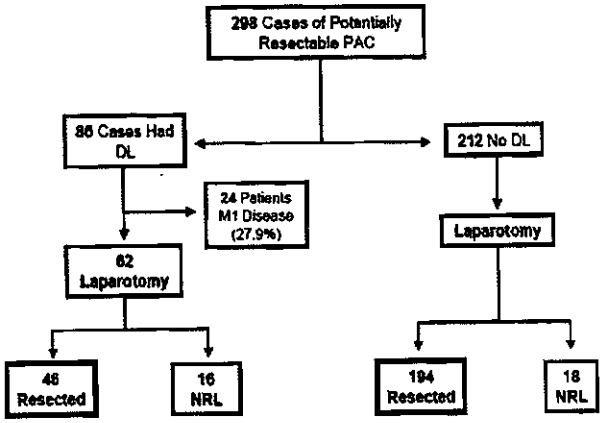

Figure 1. Case-flow diagram of the 298 patients undergoing planned resection for pancreatic adenocarcinoma from 1996 to 2003 in Oregon. DL, diagnostic laparoscopy; M1, metastatic disease; NRL, nonresectional laparotomy; PAC, pancreatic adenocarcinoma.

Operative characteristics and outcomes

Two hundred ninety-eight patients went to the operating room for planned resection of their pancreatic lesion. Overall, the proportion of patients resected was 87.6%. Figure 1 depicts the outcomes of patients who were laparoscopically explored compared with those who were not. Of 86 patients undergoing DL, 62 (72.1%) underwent resection with curative intent after laparoscopic exploration, and 194 of 212 (91.5%) patients proceeding directly to open exploration were resected. Metastatic disease (M1) was identified in 27.9% (24 of 86) of patients who underwent laparoscopic exploration. There were 32 biopsies sent for frozen section in the DL group. Twenty-two of 32 (68.8%) biopsies were identified as malignant (M1). Two patients had biopsies that were not submitted for pathologic examination by frozen section intraoperatively. Final pathology confirmed M1 disease in all patients.

Of the 298 patients who underwent resection for PAC, 6 did not have complete preoperative staging information (ie, no CT or EUS reports available). In this group, 87.7% of patients were resected. Of the 292 patients with complete information, 141 patients (47.3%) underwent CT imaging only, 48 (16.1%) underwent both CT and DL, and 32 (10.7%) had all 3 preoperative staging modalities (Table 2). For patients who were staged with CT scan only, the proportion resected at laparotomy was 92%. The addition of EUS to CT was associated with a similarly high proportion resected (90%). Although application of DL in the preoperative setting identified a subset of patients with metastatic disease, it was associated with a decreased proportion of patients resected after proceeding to laparotomy. The addition of DL to the staging evaluation was associated with a resected proportion of 77% if EUS was also used and 67% if DL was added to CT alone.

Table 2. Preoperative Evaluation and Operative Outcomes

Preoperative evaluation	n	%	Patients proceeding to laparotomy n	%	Resected n	%
All patients*	292		268†		235	87.7
CT only	141	47.3	141	100	130	92.2
CT + EUS	64	21.5	64	100	58	90.6
CT + DL†	48	16.1	27	56.3	18	66.6
CT + EUS + DL†	32	10.7	30	93.8	23	76.7

*Six patients were excluded from analysis in this table because complete preoperative imaging reports were not available.
†Includes the 82 patients who were diagnosed laparoscopically before the decision for laparotomy.
DL, diagnostic laparoscopy; EUS, endoscopic ultrasonography.

Thirty-four patients of the 298 were not resected after exploration (Table 3). Sixteen (47.1%) of 34 patients underwent DL. The most common reasons for a nonresectional procedure in the group after laparoscopy was arterial vascular invasion (T4 lesion), found in 56.3% of patients not resected; this difference corresponded to an odds ratio of 7.03 (95% CI, 2.26 to 21.85), with $p < 0.0001$ compared with the group that was not laparoscopically explored. In contrast, occult M1 disease was the primary cause for unresectability in 66.7% of patients not resected after laparotomy without laparoscopic exploration; but the difference in detection of M1 disease with and without laparoscopic exploration was not significant ($p = 0.70$).

Measures of association

To assess potential predictors of unresectability, 11 variables were considered for analysis by multivariate logistic

Table 3. Summary of the Reasons for Nonresectional Laparotomy in 34 Patients

Reasons for nonresectional laparotomy	Diagnostic laparoscopy n	%	Laparotomy only n	%	Total n	%
Arterial invasion (T4)	9	56.3	5	27.8	14	41.2
Distant disease (M1)	5	31.2	12	66.7	17	50.0
Positive regional lymph nodes	2	12.5	1	5.5	3	8.8
Total	16	47.1	18	52.9	34*	100

*There were 34 patients with information regarding whether they were laparoscopically explored or not.

Table 4. Summary of the Significance of the Covariate by Univariate and Multivariate Regression Models to Determine Association with Resection with Curative Intent of the Pancreatic Adenocarcinoma

Variable	Univariate p value	Multivariate p value	Odds ratio*
Age	0.39	0.34	1.017 (0.983, 1.057)
Gender	0.17	—	—
Weight loss	0.01	0.02	0.346 (0.143, 0.838)
Back pain	0.05	—	—
Tumor size	0.09	0.103	0.459 (0.073, 2.892)
CT equivocal	0.51	—	—
EUS	0.75	—	—
Tumor location	0.80	—	—
Diagnostic laparoscopy	0.001	< 0.001	0.212 (0.090, 0.499)
Year of operation	0.34	—	—
Mean hospital volume per year of pancreatic resections	0.20	0.126	0.430 (0.146, 1.269)

*Odds ratio with 95% confidence interval is in relation to the final multivariate model.
EUS, endoscopic ultrasonography.

regression modeling. Primary outcomes included resection of the pancreatic tumor with curative intent. These variables included age, gender, weight loss, back pain, preoperative tumor size, equivocality of the preoperative CT findings, use of preoperative EUS, location of the cancer (head/neck/uncinate versus distal), use of DL, year of operation, and the hospital volume of pancreatic cancer operations per year (Table 4). Of note, the 24 patients who had metastatic disease diagnosed by laparoscopy did not undergo operative exploration; 274 patients were considered for this portion of the analysis (Fig. 1).

In univariate analyses, weight loss ($p = 0.018$) and use of DL ($p = 0.001$) were the only covariates that were significantly associated with resection (Table 4).

After stepwise regression modeling, five variables were chosen for the final multivariate model: age, use of DL, weight loss, preoperative tumor size, and institutional volume. No pairwise interactions were statistically significant. The Hosmer and Lemeshow test for goodness of fit for the final model was 0.86. A receiver operating characteristic curve had an area under the curve of 0.80. The covariate age was left in the final model to maximize the number of covariate patterns. The covariates tumor size and hospital volume were included in the model, even though they were not significant, because they improved the fit and discriminative ability of the model. The preoperative reporting of weight loss was significantly associated with a decreased probability of undergoing a resectional procedure after laparotomy. After adjustment for confounders, a patient reporting preoperative weight loss had significantly less chance of resection with curative intent (odds ratio = 0.35; 95% CI, 0.14 to 0.84; $p = 0.02$). Patients who underwent laparoscopic exploration and then proceeded to laparotomy also had a significantly decreased chance of undergoing resection (odds ratio = 0.21; 95% CI, 0.09 to 0.50; $p < 0.001$) compared with patients who were not laparoscopically explored (Table 5).

DISCUSSION

The aims of our study were to assess the current modalities used for preoperative evaluation of pancreatic cancer patients and measure the success of use of these methods in identifying a group of patients who have resectable disease at laparotomy. We observed that CT scan was the principal preoperative staging modality, and this examination was used in virtually all patients taken to the operating room for planned resection. A relatively small subset of patients (30%) was chosen for DL, and 28% had EUS. We found that in this population-based audit, surgeons using CT imaging predominantly for patient selection achieved resection in 87% of patients taken to the operating room for attempted resection, and, remarkably, the group of patients who had CT only for preoperative evaluation were resected in > 90% of the patients. This proportion of resectability is higher than many previous series, most of which were single-institution reports. This finding underscores the improving diagnostic accuracy of CT in recent years, and it reaffirms use of CT as the primary preoperative staging modality for patients with known or suspected pancreatic cancer.

We found that DL was not used routinely in management of this group of patients. In this population-based review, surgeons appeared to select patients for preoperative laparoscopy when clinical factors increased their suspicion for unresectable disease. In this group of patients, we found that DL did demonstrate disease that precluded resection in a substantial subset (27.9%) of patients. Laparotomy was avoided in all of these patients. Even with the additional disease detection afforded by DL, the overall proportion

Table 5. Summary of the Univariate Regression Analysis of the Clinicopathologic Factors Associated with Resection

Variable	Total (n = 274)		Resected (n = 240)		Not resected (n = 34)		p Value*
Demographics							
Age (y), mean ± SD	65.1 ± 11.9		65.3 ± 11.8		63.6 ± 11.9		0.390
	n	%	n	%	n	%	
Male	139	50.7	118	49.1	21	61.7	0.244
Presenting symptoms							
Weight loss	154	56.2	128	53.3	26	74.5	0.018†
Back pain	59	21.5	47	19.6	12	35.3	0.062
Preoperative tumor size category (cm)							0.133
0–2.5	50	18.2	48	20.0	2	5.9	—
2.6–3.5	45	16.4	41	17.1	4	11.8	—
3.6–10	47	17.2	39	16.3	8	23.5	—
Tumor size unknown	132	48.2	112	46.7	20	58.8	—
CT equivocal	38	13.9	32	13.3	6	17.5	0.677
Preoperative EUS	98	35.8	85	35.4	13	38.2	0.897
Location of cancer							0.982
Head, neck, and uncinate	222	81.0	195	81.3	27	81.0	—
Distal	52	19.0	45	18.8	7	20.6	—
Diagnostic laparoscopy	62	22.6	46	19.2	16	47.1	0.001†
Year of operation category							0.437
1996–1999	124	45.3	106	44.2	18	52.9	—
2000–2003	150	54.7	134	55.8	16	47.1	—
Volume per year category							0.202
Very low	70	25.5	65	27.1	5	14.7	—
Low	60	21.9	49	20.4	11	32.4	—
Moderate	73	26.6	62	25.8	11	32.4	—
High	71	25.9	64	26.7	7	20.6	—

Percentages reflect the proportion of each group with respect to column total.
*Chi-square test of homogeneity used to evaluate significance of categorical covariates, and *t*-test of independent sample means used to evaluate significance for continuous covariates.
†Significant at the p = 0.05 level.
EUS, endoscopic ultrasonography.

of patients resected in this subset of patients (74%) was considerably less than that observed in patients taken directly to laparotomy after CT alone. For patients who underwent DL and appeared to be resectable, if they were found to be unresectable at laparotomy, the major determinant of unresectability was local vascular invasion (56%). In contrast, for patients taken directly to laparotomy, distant metastases were the most common determinant of unresectability (67%). This finding confirms the strength of laparoscopy in evaluating peritoneal disease and its weakness in assessing locally advanced disease. The overall low use rate with a relatively high yield from laparoscopy reflects a process of patient selection in which surgeons use laparoscopy more liberally in patients with clinical features that raise concern for unresectability. Although the data used for this study did not allow us to determine specifically which clinical features prompted surgeons to choose laparoscopy, we suspect that it might have been a constellation of clinical findings. Some of these can be subtle imaging findings or a combination of clinical features, such as back pain, weight loss, and elevated carbohydrate antigen 19-9. Location of the pancreatic tumor in the body or tail of the gland is generally considered to be associated with increased risk of metastasis and is believed to be an indication for laparoscopy.[9-12] We found that the location of the tumor within the gland had no association with resectability or use of laparoscopy. The relatively small number of patients with body or tail lesions in this series prompts us to interpret these negative findings with caution, and we do not believe that these results necessarily contradict the findings of other investigators. Taken together, our results suggest that a variety of clinical features are used by surgeons to select high-risk patients for laparoscopic evaluation before proceeding to open laparotomy.

The process of preoperative evaluation, including the role of laparoscopy, for pancreatic cancer has clearly evolved during the past 10 years. In the early reports of

laparoscopic evaluation, the overall proportion of patients resected was approximately 60% of patients taken to operative exploration. During this era, use of laparoscopy identified metastatic disease and prevented nonresectional laparotomy in 20% to 25% of patients.[3] Our population-based data suggest that the role of laparoscopy has diminished since the time of its introduction. Our data indicate that CT alone can serve as a very accurate predictor of resectability. EUS is likely to add to this accuracy, although during the time course of our study, EUS was not widely used.

The role of EUS in the preoperative staging of pancreatic cancer patients remains a topic of debate. In some institutions it is an essential component of preoperative evaluation, and in others it is used in selected patients only. Recently, four studies have evaluated the test characteristics of EUS in determining resectability as compared with CT.[13-16] Two of the five studies found EUS to be superior to CT in determining resectability[13,14] and two found the two modalities to be equivalent.[15,16] There are several sources of bias that make these studies difficult to interpret. Selection bias likely plays a large role, because many EUS patients had CT previously, as part of their management, and the clinicians interpreting the studies were not blinded to earlier radiographic information; only patients deemed resectable by CT were considered for EUS. This results in a biased sample of patients undergoing EUS. In addition, the ability of EUS to determine resectability is highly operator dependent. In a review of this subject by Hunt and Faigel,[17] the authors conclude that EUS is a useful adjunct to a dual-phase helical CT and might be more accurate in smaller (or nonvisualized) tumors and in determining vascular invasion. EUS appears equivalent to CT in determining overall resectability, but it is less accurate at predicting involvement of the superior mesenteric artery and distant metastatic disease. It has the added benefit of making a tissue diagnosis, which is necessary before patients can be considered for neoadjuvant, adjuvant, or palliative chemoradiotherapy; this might be important in the future, as treatment protocols could shift toward neoadjuvant treatment requiring pathologic confirmation offered by fine-needle aspiration with EUS.

In our analysis, EUS was used in 33.6% of the 298 patients. As shown in Tables 2, 4, and 5, EUS did not statistically impact the odds of a successful resection. In our analysis of 34 patients who underwent laparotomy but were not resected with curative intent, EUS was used in 38.2%. We assessed the use of laparoscopy and EUS to see if there was a confounding relationship; but there was no overall difference in the use of EUS between the DL groups (40.7% versus 30.7%; $p = 0.127$). It is important to remember that during the time frame of this study, many endosonographers were early in their experience, and the yield of these examinations has likely improved with time.

Several other authors have demonstrated the declining role of diagnostic laparoscopy in the setting of continued improvements in pancreatic and abdominal imaging. Pisters and colleagues[18] have demonstrated that laparoscopy is likely to change management in only 10% to 14% of pancreatic cancer patients; they advise against its routine use. White and colleagues[19] recently reported on the evolving yield of preoperative laparoscopy for pancreatic cancer at the Memorial Sloan-Kettering Cancer Center. These authors report that the yield of laparoscopy has diminished on an annual basis since introduction of the procedure in 1995. Since 1999, the yield of laparoscopy has dropped to 14% overall and it exceeds 10% only for patients with pancreatic adenocarcinoma. The authors also note the association between the quality of preoperative imaging and the yield of laparoscopy. Unlike our data, this is a report from a single, high-volume center. Similar to our report, the overall proportion of pancreatic cancer patients undergoing resection has improved and the Memorial Sloan-Kettering Cancer Center group reported 86% resectability after laparoscopy.

Given the declining yield of laparoscopy, a selective approach to laparoscopy has theoretical appeal. Several centers selectively use DL in patients with clinical factors suggestive of M1 disease. These factors include substantial weight loss, back pain, large tumor size, tumors located in the body or tail, hypoalbuminemia, low-volume ascites on CT, and elevated carbohydrate antigen 19-9.[18,20-23] The selective application of laparoscopy in patients with PAC might alleviate some surgeons' concerns with scheduling conflicts and the additional cost of the procedure.[24] Thomson and colleagues[25] scored preoperative CT images in patients subsequently undergoing laparoscopy and laparoscopic ultrasonography and demonstrated a correlation between preoperative CT grades and resectability; the authors advocate for selective use of laparoscopic staging modalities.

Laparoscopy also appears to have a potentially important role in the evaluation of locally advanced, unresectable patients. Liu and Traverso[26] analyzed the added benefit of DL and peritoneal lavage cytology in patients with locally advanced disease by CT and found that laparoscopy identified occult M1 disease in 34% of patients. These patients were referred for systemic chemotherapy alone rather than chemoradiotherapy. The authors conclude that even the best CT scanning protocol cannot completely capture all patients with occult M1 disease, which could be detected at DL.

Our study is one of the few population-based studies of surgically treated pancreatic cancer in which the clinical detail of the study is enhanced by the access provided to individual patient records. Many studies examining the impact of laparoscopy come from single institutions[9-12] or are retrospective reviews[18,27,28] that hypothetically assess use of diagnostic laparoscopy. This distinction is presented in recent review by Stefanidis and colleagues.[29]

Despite the strengths of a population-based analysis, our study has several limitations that must be acknowledged. Because of the retrospective design of the study, there might be unmeasured clinical factors we could not capture that influence decision making about the use of diagnostic laparoscopy. In addition, we have adjusted for hospital surgical volume, but there might be practice and referral patterns within the state that influence the types of patients seen by various surgeons at various facilities. Use and accuracy of laparoscopy of staging is likely to be related to surgeon training and experience. It is possible that certain surgeons perform laparoscopy routinely, and it might be that these surgeons are preferentially referred complex patients with more advanced disease, thereby confounding apparent outcomes of laparoscopy. The deidentification process that was inherent in this study did not allow us to analyze outcomes at the level of individual surgeons. We were able to study the effect of volume at the hospital level and assess the indirect impact it can have as a surrogate for level of surgeon specialty training. As shown in Tables 4 and 5, there were no statistical differences between the 4 designated levels of mean hospital volume. Despite these limitations, a population-based analysis is the most likely approach to providing a balanced representation of the use and outcomes of surgical techniques across the spectrum of patients.

An additional potential confounder relates to the changing use of surgical palliation for pancreatic cancer. During the past 10 to 15 years, endoscopic palliation for pancreatic cancer has improved. Current endoscopically placed stents offer durable palliation of jaundice.[5] Given this development, the clinical benefit from surgical biliary bypass has diminished. In the past, surgeons might have been more likely to explore patients who were at high risk for unresectability, because they believed that the benefit of surgical bypass justified the procedure. This has not been the case more recently.[30] As such, surgeons in our study might have selected patients more meticulously for laparotomy. Nevertheless, such a change in practice does not diminish the fundamental observations of this report. Specifically, current staging offers a very high success of determining resectable patients.

In conclusion, our population-based study suggests that surgeons use a combination of CT scan and, increasingly, EUS to stage pancreatic cancer patients for resectability. Laparoscopy is used selectively in a group of patients who present with clinical suspicion for metastatic disease and unresectability. This approach yields a high rate of resectability, and relatively few patients undergo laparotomy without resection. Our findings suggest that spiral CT alone is an appropriate preoperative staging evaluation for most patients with known or suspected pancreatic adenocarcinoma. Although the yield of laparoscopy has diminished in recent years, it remains useful in patients with suspicious or equivocal imaging findings or other clinical signs that raise concern for metastatic disease.

Author Contributions

Study conception and design: Mayo, Austin, Billingsley
Acquisition of data: Mayo, Shipley, Billingsley
Analysis and interpretation of data: Mayo, Austin, Sheppard, Mori, Billingsley
Drafting of manuscript: Mayo, Billingsley
Critical revision: Mayo, Billingsley

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