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Laparoscopic pancreaticoduodenectomy for adenocarcinoma provides short-term oncologic outcomes and long-term overall survival rates similar to those for open pancreaticoduodenectomy

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ABSTRACT

Background: The long-term efficacy of laparoscopic pancreaticoduodenectomy (LPD) relative to open pancreaticoduodenectomy (OPD) for pancreatic adenocarcinoma has not been well studied.
Methods: The National Cancer Data Base was used to compare patients undergoing LPD and OPD for stage I-II pancreatic adenocarcinoma between 2010 and 2013.
Results: 828 (10%) patients underwent LPD and 7385 (90%) OPD. There were no differences in tumor or demographic characteristics between groups. On multivariable analysis adjusted for hospital volume, LPD was associated with a lower rate of readmission ($p < 0.01$) and trends toward shorter initial length of stay ($p = 0.14$) and time to adjuvant chemotherapy ($p = 0.11$). There were no differences between patients undergoing LPD and those undergoing OP in rates of margin negative resection, number of lymph nodes examined, perioperative mortality and median overall survival (20.7 vs 20.9 months, $p = 0.68$).
Conclusions: For patients with localized pancreatic adenocarcinoma, LPD provides short-term oncologic and long-term overall survival outcomes identical to OPD and is associated with decreased rates of readmission and a trend towards accelerated recovery.

1. Introduction

The laparoscopic approach to pancreaticoduodenectomy (LPD) is a technically demanding procedure that has been slow to gain widespread acceptance in application to patients with pancreatic cancer. There have been national and international concerns regarding the safety and oncologic efficacy of LPD when done in patients with cancer. In spite of these concerns several centers have continued to pioneer the procedure and there is a growing body of literature suggesting that the technical challenges of LPD can be surmounted.[1,2] Multiple retrospective series from high volume centers have demonstrated that LPD is a safe option for pancreaticoduodenectomy (PD) and has short-term oncologic outcomes equivalent to open PD (OPD).[1–5] Meta-analyses comparing minimally invasive PD to OPD have suggested similar or improved rates of margin negative resection, increased lymph node yields, decreased intraoperative blood loss, decreased length of stay, and similar complication and perioperative mortality rates with the minimally invasive approach.[6,7] In a previous study from our group examining the early national experience with LPD using the National Cancer Data Base (NCDB), we found short term oncologic outcomes for LPD and OPD to be statistically identical, although the risk of 30-day perioperative mortality was higher for LPD in a center's early experience with LPD but that this difference in perioperative mortality disappeared as the number of LPDs performed in a center exceeded 10 in a two year time period.[8]

Taken together, these studies demonstrate short-term outcomes

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for LPD to be comparable to OPD. There are, however, very little data comparing long-term outcomes for the two approaches in pancreatic cancer. Three retrospective series have reported overall survival rates for patients undergoing LPD to be similar to those undergoing OPD at the same institutions.[3–5] These have been single institutional reports with relatively short follow up. There have been no larger, multi-institutional evaluations of the long-term outcomes of LPD and OPD to date. In our current study we compare safety, oncologic efficacy and the long-term overall survival (OS) of LPD and OPD using data from the NCDB from 2010 to 2013.

2. Methods

2.1. Data set and study population

The NCDB a nationwide, facility-based oncology dataset that collects data from Commission on Cancer accredited centers and captures approximately 70% of all newly diagnosed cancers in the US.[9] Institutional review board approval was waived for this study as the collected information was de-identified, no protected health information was reviewed, and the analysis was retrospective. The American College of Surgeons and the Commission on Cancer have not verified and are not responsible for the analytic or statistical methodology employed, or the conclusions drawn from these data by the investigators.

The 2013 participant user file of the National Cancer Data Base (NCDB) was used to analyze data from 2010 to 2013. Analysis started in 2010 as this was the first year the NCDB captured data on the surgical approach as laparoscopic, robotic, or open. Patients that underwent PD for PDAC with pathologic stage I-II disease were included for analysis. Patients with more than one lifetime cancer, those with metastatic or locally advanced disease, and who had incomplete information on pathologic staging were excluded. Patients who had robotic PD were also excluded. Cases documented as laparoscopic converted to open (n = 326) were excluded because there was no distinction made in the NCDB between cases converted to open as a result of a technical problem and those converted to open as part of a plan to perform diagnostic laparoscopy prior to open PD. The primary endpoint was median overall survival. Secondary endpoints included margin status, number of lymph nodes examined, surgical length of stay (LOS), unplanned readmission, 30 and 90-day mortality, and time to adjuvant chemotherapy. Overall survival, 30-day mortality, and 90-day mortality data were available for years 2010–2012.

Age, surgical LOS, number of lymph nodes examined, time to adjuvant chemotherapy, and PD volume were analyzed as continuous variables. Other demographics, facility variables, tumor, and treatment characteristics were analyzed as categorical variables. Staging information (stage IA, IB, IIA, IIB) was in accordance with the American Joint Committee on Cancer 7th edition.[10] Survival information was available for 2010–2012 and was reported as all-cause alive or dead.

A threshold of 20 LPD over the 4-year study period was considered high volume as an extrapolation of the threshold of 10 LPDs over a 2-year study period described in our group's previous NCDB paper examining short-term outcomes for LPD.[8]

2.2. Statistics

All analyses were performed using SPSS statistical software version 19.0 (IBM Corp, Armonk, NY). All statistical tests were two-sided and a p-value of <0.05 was considered statistically significant. Chi-square tests and t-tests were used to compare secondary outcomes. Six separate multivariable logistic regressions were done to examine predictors of margin negativity (negative compared to positive), adequate lymph nodes examined (≥12 nodes compared to <12 nodes), prolonged surgical LOS (greater than one standard deviation from the mean, or 21 days compared to <21 days), 30-day mortality, 90-day mortality, and delay to adjuvant chemotherapy (>90 days). Odds ratio (OR) > 1 signified higher odds of the aforementioned events. All confidence intervals (CI) are reported at the 95% significance level. A Cox proportional hazards model was used for survival analysis and to estimate median overall survival (OS). Hazard ratio (HR) > 1 signified a higher hazard of mortality.

3. Results

8213 patients underwent PD for PDAC from 2010 to 2013, 828 (10%) underwent LPD and 7385 (90%) OPD. Approximately one third of 607 hospitals reporting to the NCDB in our dataset reported performing at least one LPD during the study period. 25% of LPD were done at what we would consider higher volume centers (≥20 LPD over the study period). Patients undergoing LPD were less likely to be of a minority race (17.2% vs 19.0%, p = 0.03). The frequency of all other demographic and tumor characteristics, as well as rates of neoadjuvant therapy, were statistically identical in the cohorts of patients undergoing LPD and OPD (p > 0.05) [Table 1].

Table 1
Comparisons between laparoscopic and open pancreaticoduodenectomy, n = 8213.

Characteristic	LPD (n = 828)	OPD (n = 7385)	P-value
Demographics			
Mean age	65.9 ± 10.7	65.7 ± 10.4	0.49
Caucasian	688 (82.8%)	6006 (81.0%)	***0.03***
African American	74 (8.9%)	754 (10.2%)	
Hispanic	36 (4.3%)	432 (5.8%)	
Asian	23 (2.8%)	185 (2.5%)	
Charlson index 0	542 (65.2%)	4832 (65.2%)	0.82
Charlson index 1	232 (27.9%)	2032 (27.4%)	
Charlson index 2	57 (6.9%)	551 (7.4%)	
Community	1 (0.1%)	136 (1.8%)	***<0.01***
Comprehensive	190 (23.1%)	1866 (25.4%)	
Academic	587 (71.5%)	4798 (65.2%)	
Integrated network	43 (5.2%)	541 (7.4%)	
Tumor characteristics			
Stage IA	40 (4.8%)	313 (4.2%)	0.52
Stage IB	49 (5.9%)	364 (4.9%)	
Stage IIA	178 (21.5%)	1612 (21.8%)	
Stage IIB	561 (67.8%)	5096 (59.0%)	
Tumor <2 cm	149 (18.0%)	1248 (16.9%)	0.62
Tumor 2–4 cm	500 (60.2%)	4618 (62.3%)	
Tumor >4 cm	168 (20.2%)	1431 (19.3%)	
Node negative	263 (31.6%)	2225 (30.0%)	0.12
Node positive	566 (68.1%)	5127 (69.1%)	
Neoadjuvant chemo	105 (12.6%)	941 (12.7%)	0.97
Neoadjuvant RT	56 (6.7%)	535 (7.2%)	0.89
Perioperative outcomes			
Negative margins	651 (79.1%)	5623 (76.8%)	0.13
Mean nodes examined	18.1 ± 9.5	17.1 ± 9.6	***0.01***
Surgical LOS	10.2 ± 8.5	11.8 ± 9.3	***<0.01***
Unplanned readmission	56 (6.8%)	674 (9.2%)	***0.02***
30-day mortality[a]	24 (4.1%)	203 (3.8%)	0.71
90-day mortality[a]	41 (6.9%)	391 (7.3%)	0.23
Adjuvant chemotherapy[b]	444 (61.4%)	3844 (60.4%)	0.87
Adjuvant radiation[b]	198 (25.6%)	1870 (27.3%)	0.35
Time to adjuvant chemo[b]	58.9 ± 28.0	61.1 ± 29.7	0.15

LPD *laparoscopic pancreaticoduodenectomy*; OPD *open pancreaticoduodenectomy*; RT *radiation therapy*; chemo *chemotherapy*. The bold italics represent significant p-values (p < 0.05).
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[a] Only available years 2010–2012, n = 6060.
[b] For patients that did not receive neoadjuvant therapy, n = 7623.