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Minimally Invasive Surgery

Impact of minimally invasive vs. open distal pancreatectomy on use of adjuvant chemoradiation for pancreatic adenocarcinoma

Kevin L. Anderson Jr. [a], Mohamed A. Adam [b], Samantha Thomas [c, d], Sanziana A. Roman [b, d], Julie A. Sosa [b, d, e, f, *]

[a] Duke University School of Medicine, Durham, NC 27710, USA
[b] Department of Surgery, Duke University Medical Center, Durham, NC 27710, USA
[c] Department of Biostatistics and Bioinformatics, Duke University Medical Center, Durham, NC 27710, USA
[d] Duke Cancer Institute, 20 Duke Medicine Circle, Durham, NC 27710, USA
[e] Department of Medicine, Duke University Medical Center, Durham, NC 27710, USA
[f] Duke Clinical Research Institute, Durham, NC 27710, USA

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ABSTRACT

Background: Published data examining the impact of minimally invasive distal pancreatectomy (MIDP) on survival are generally limited to experiences from high-volume institutions. Our aim was to compare utilization of adjuvant chemoradiation and time from surgery until its initiation following MIDP vs. open surgery (ODP) at a national level.

Methods: Adult patients undergoing distal pancreatectomy for Stage I and II pancreatic adenocarcinoma were identified from the National Cancer Data Base, 2010–2012.

Results: A total of 1807 patients underwent distal pancreatectomy for adenocarcinoma at 506 institutions (27.9% MIDP). After adjustment, those who underwent MIDP were more likely to have complete tumor resections and a shorter hospital length of stay. Patients undergoing MIDP vs. ODP were more likely to receive adjuvant chemotherapy; time to initiation of adjuvant chemotherapy or radiation was not different between groups. After adjustment, overall survival for MIDP vs. ODP remained similar (HR 0.85, CI 0.67–1.10, p = 0.21).

Conclusion: MIDP is associated with increased use of adjuvant chemotherapy; further study is needed to understand the etiology and impact of this association.

Synopsis

Potential benefits of minimally invasive distal pancreatectomy include faster recovery and increased utilization of adjuvant treatment, which has demonstrated a survival benefit when delivered after resection for curative intent. This analysis demonstrates that on a national level, there is an association between minimally invasive surgical approaches and increased use of adjuvant chemotherapy for pancreatic adenocarcinoma.

1. Introduction

Pancreatic cancer is currently the fourth leading cause of cancer death in the United States, with 40,560 Americans anticipated to succumb to the disease this year.[1] With the number of incident cases of pancreatic cancer continuing to increase, it is estimated that by 2020, it will become the second most common cause of cancer death behind lung cancer.[2] Surgical resection represents the only chance for cure for patients with early stage pancreatic adenocarcinoma. National Comprehensive Cancer Network (NCCN) guidelines recommend that adjuvant chemotherapy should accompany any curative intent surgical resection for pancreatic cancer.[3] Randomized clinical trials have demonstrated an association between adjuvant therapy and long-term survival when combined with surgical resection.[4,5] Despite this, evidence suggests that more than 30% of eligible patients never receive chemotherapy in the postoperative setting.[6]

* Corresponding author. Duke University Medical Center, Box 2945, Durham, NC 27710, USA.
E-mail addresses: kla24@duke.edu (K.L. Anderson), mohamed.adam@dm.duke.edu (M.A. Adam), samantha.thomas@dm.duke.edu (S. Thomas), sanziana.roman@dm.duke.edu (S.A. Roman), julie.sosa@dm.duke.edu (J.A. Sosa).

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Since the first laparoscopic pancreatic resection procedure was performed in 1994 by Gagner and Pomp, the role of laparoscopy in pancreatic surgery has continued to evolve.[7–9] As surgical technology and imaging have continued to improve, more surgeons are performing laparoscopic distal pancreatectomies because the surgery does not require anastomosis or other reconstruction, and it presents fewer technical challenges than other major laparoscopic procedures.[10] A number of studies have demonstrated advantages to minimally invasive distal pancreatectomy, such as reduced postoperative pain, faster recovery, decreased number of surgical site complications, and decreased morbidity.[11,12]

Adam et al. illustrated enhanced short-term perioperative outcomes in a nationally representative study comparing minimally invasive vs. open distal pancreatectomy.[13] Given that adjuvant chemotherapy has consistently been shown to improve survival, there has been substantial interest in understanding whether MIDP may lead to increased utilization and earlier initiation of postoperative chemotherapy, theoretically secondary to faster postoperative recovery.[14,15] However, this association remains unproven. We sought to examine the potential association between minimally invasive vs. open distal pancreatectomy and utilization and time to initiation of adjuvant chemotherapy and radiation for patients with Stage I and II pancreatic adenocarcinoma. To our knowledge, this study is the first to evaluate the potential impact of surgical approach on time to initiation of therapy at a national level.

2. Methods

The Duke University Institutional Review Board granted exempt status for this retrospective analysis of the National Cancer Data Base (NCDB). The NCDB is administered jointly by the American College of Surgeons and the American Cancer Society, and at present, contains data from over 1500 Commission on Cancer-accredited institutions, and includes records from more than 30 million patients. It is estimated that approximately 70% of all new cancer diagnoses in the United States are captured in the NCDB.

The 2010–2012 NCDB Participant User File was queried for all adult patients undergoing distal pancreatectomy for Stage I and II pancreatic adenocarcinoma. Patients with pancreatic adenocarcinoma were identified using International Classification of Diseases for Oncology, 3rd Edition (ICD-O-3) topography and histology codes. Of these patients, only those with Stages I and II (localized) disease who underwent distal pancreatectomy were included. Patients who had undergone distal pancreatectomy were then classified by surgical approach: minimally invasive (MIDP) vs. open distal pancreatectomy (ODP). Patients were excluded if data were missing regarding use of chemotherapy and radiation.

Baseline characteristics and outcomes were compared between groups using the Rank Sum test for continuous variables and Chi-square/Fisher's exact tests for categorical variables. Primary outcomes were utilization and time to initiation of chemotherapy in patients with Stages I and II pancreatic adenocarcinoma. Secondary endpoints included use and time to initiation of adjuvant radiation therapy, conversion rate of MIDP to ODP with intent to treat, short-term perioperative outcomes, and overall survival following surgery. For analyses regarding time to initiation of adjuvant therapy, patients who received neoadjuvant chemotherapy had to be excluded, as only the earliest date for initiation of chemotherapy is provided by the NCDB, and thus the starting date for postoperative chemotherapy for these patients was unknown, and duration could not be calculated. Regardless of their neoadjuvant treatment status, all patients were included in analyses of overall use of adjuvant chemotherapy and radiation.

In order to best estimate the independent effect of minimally invasive vs. open techniques on use of adjuvant chemotherapy and time to initiation of therapy, multivariable logistic models were developed. They included the following variables, chosen *a priori*: surgical technique (laparoscopic vs. open procedure); patient age, gender, race, Charlson-Deyo comorbidity index, and insurance status; cancer stage and lymph node status; and hospital type. The variables included in the final model for use of adjuvant chemotherapy were chosen by backward selection at a significance level of 0.20. These variables were patient age, Charlson-Deyo comorbidity index, insurance status, cancer stage, and lymph node status. Analysis of time to initiation of chemotherapy and radiation was conducted after log-transformation due to the non-normal distribution of this variable.

Estimates of overall survival proportions were computed using the Kaplan-Meier method, and survival distributions were compared across groups using the log-rank test. Cox proportional hazards modeling was used to evaluate independent predictors of overall survival. A two-sided p-value of <0.05 indicated statistical significance. All statistical analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, NC).

3. Results

A total of 1807 patients met study criteria and were included; 505 (27.9%) underwent MIDP and 1302 (72.1%) underwent ODP. The minimally invasive group included 51 (10.1%) laparoscopic cases and 454 (89.9%) robotic cases. Patients who underwent MIDP were more likely to be male (52.1 vs. 46.2%, $p = 0.02$), have more comorbidities (31 vs. 28%, $p = 0.03$), and be treated at an academic medical center (67.9 vs. 58.4%, $p < 0.01$) compared to those who underwent ODP. Use of MIDP increased from 2010 to 2012 (25.9 vs. 41.4% of all cases, $p < 0.01$) (Table 1).

In unadjusted analysis of perioperative outcomes between treatment groups (Table 2), patients who underwent MIDP had a lower rate of positive surgical margins (14.1 vs. 21.0%, $p < 0.001$) and a shorter hospital length of stay (median 6 vs. 7 days, $p < 0.0001$). The number of lymph nodes harvested surgically was similar between patients who underwent ODP vs. MIDP (median 12 vs. 12, $p = 0.35$); 90-day postoperative mortality was similar (2.2 vs. 3.3%, $p = 0.43$).

3.1. Impact of surgical approach on use and time to initiation of adjuvant therapy

Of those patients who received adjuvant chemotherapy, 292 (57.8%) underwent MIDP and 701 (53.8%) ODP. ($p = 0.11$) Adjuvant radiation was utilized in 112 (22.2%) MIDP patients and 323 (24.8%) ODP patients. ($p = 0.30$) In unadjusted analysis, use of adjuvant chemotherapy and radiation were not statistically different between the MIDP vs. ODP groups ($p = 0.11$ and $p = 0.30$ respectively). After adjustment for patient demographic and clinical variables including age, Charlson-Deyo comorbidity score, insurance status, clinical stage, and presence of lymph node metastases, MIDP was associated with increased use of adjuvant chemotherapy compared to ODP (Odds Ratio [OR] 1.29, 95% Confidence Interval [CI] 1.03–1.62, $p = 0.03$). Other factors associated with increased use of postoperative chemotherapy included younger patient age, insured status, a more advanced cancer stage, and the presence of lymph node metastases (Table 3). Utilization of adjuvant radiation (OR 0.92, 95% CI 0.71–1.19, $p = 0.51$) was similar between MIDP and ODP.

While more MIDP patients received adjuvant chemotherapy, patients who underwent MIDP had similar median time to initiation of adjuvant chemotherapy (51 vs. 51 days, $p = 0.90$) and