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High volume pancreaticoduodenectomy performed at an academic community cancer center

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ABSTRACT

Background: We sought to evaluate the post-operative outcomes of patients undergoing pancreaticoduodenectomy at a high volume academic community cancer center.
Methods: A retrospective review was performed of patients undergoing pancreaticoduodenectomy over a 10-year period.
Results: Over 10 years, 213 patients underwent pancreaticoduodenectomy. Median age was 66y. Most patients had significant comorbidities (median ASA = 3) and were overweight (median BMI = 27). Median operative time and blood loss were 253 min and 500 ml, respectively. 160 (75%) out of 213 patients had a malignant lesion on final pathology. 121 (76%) out of 160 had R0 resection. Median lymph nodes harvested was 13. Overall incidence of DGE was 31% (67/213), with clinically significant DGE in 15% (32/213). Pancreatic leak rate was 18% (37/213), with clinically significant leaks in 10% (21/213). Median length of stay was 8 days. Grade 3/4 morbidity rate was 21% (44/206), and 30-day mortality was 2% (5/213).
Conclusions: At a high volume academic community cancer center, pancreaticoduodenectomy can be performed with excellent outcomes on par with any academic center or university hospital.

Introduction

Pancreaticoduodenectomy is one of the most complex abdominal operations and can be fraught with significant morbidity and mortality.[1–7] Over time, the number of pancreatic resections performed has increased and it has been shown that complex resections can be safely performed.[8] Most of the published series on pancreatic resections come from academic medical centers, which perform a large number of cases per year, and the relationship between case volume and outcome has been established in pancreatic surgery as well as other complex operations.[4,9–13] This has led to the concept that pancreatic surgery should be regionalized and performed in large high-volume academic centers in order to reduce potential complications and even death.[3,9–11,14]

As a result of improved outcomes in high volume centers, there has been extensive regionalization of complex cancer surgery.[15–18] However, regionalization can be a significant burden to cancer patients and hinder treatment. The majority of cancer care actually takes place in the community, and many patients from rural areas do not have the financial means to seek care at a regional referral center. Barriers to care such as distance, travel, and lack of social support affect the delivery of optimal cancer treatment.[19]

It is possible that community cancer centers with adequate resources can provide effective cancer care and perform complex operations such as pancreaticoduodenectomy with minimal morbidity and mortality.[20–23] Many series of pancreatic resections performed in low volume centers and community hospitals have been published, however these reports contain small patient numbers and outcomes such a morbidity and mortality vary widely.[24–26]

In our study, we sought to evaluate the post-operative outcomes of patients undergoing pancreaticoduodenectomy at a high-volume community cancer center after the implementation of a multidisciplinary pancreatic cancer team composed of dedicated

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surgical oncologists and support staff.

Materials and methods

This study setting was in a previously funded community-based, 1100-bed hospital with a general surgery residency training program, and a National Cancer Institute selected Community Cancer Center (NCI Community Cancer Center Program). The hospital is a Level 1 Trauma Center with greater than 39,000 surgical procedures performed annually, along with a 22-bed surgical intensive care unit. The division of surgical oncology is composed of fellowship trained surgical oncologists who performed 100% of the surgical procedures. Post operatively, the patients were cared for continuously by a combination of the operative surgical attending, in house surgical staff, dedicated surgical nurses, and anesthesia, surgical intensivist and interventional radiology support as needed.

A retrospective review of a prospectively maintained database of pancreatic resections was performed to capture all patients who underwent pancreaticoduodenectomy from 2007 to 2017. The medical record was queried to collect patient demographics, operative variables and the post-operative hospital course in order to evaluate the clinical outcomes of these patients. Patients who presented with metastatic disease, patients who did not have surgery, or patients who had palliative procedures were excluded. A board-certified pathologist evaluated all specimens. The study was approved by the Institutional Review Board.

Results

Demographics

From February 2007 to March 2017, 213 patients were brought to the operating room after multidisciplinary evaluation and successfully had a pancreaticoduodenectomy. The characteristics and thirty-day outcomes of the patient population are shown in Table 1. There was generally an even distribution between males and females and most patients presented in the later stages of life with a median age of 66 years (Range 21–89). As expected, the patient population requiring surgery tended to present with multiple medical comorbidities such as obesity, hypertension, diabetes and cardiac disease and the median ASA was 3.[27] These patients all underwent preoperative risk stratification and optimization of comorbidities before surgery.

Table 1
Patient characteristics and thirty day outcomes.

Patient Demographics	No.	%
Total Resections	213	
Female	110	52%
Male	103	48%
Median Age (y)	66 (21–89)	
Median BMI	27 (17–46)	
Median ASA	3	
1	0	
2	31	
3	157	
4	25	
Comorbidities		
Hypertension	141	66%
Diabetes	71	33%
CHF/CAD	67	31%
COPD	27	13%
Renal Insufficiency	10	5%
Operative Data		
Median Operative Time (min)	253 (178–631)	
Median EBL (mL)	500 (100–2800)	
Tumor Characteristics		
Resections for Benign Disease	53	25%
Resections for Malignancy	160	75%
Median Tumor Size (cm)	3	
Median Lymph Nodes Harvested	13 (1–60)	
R0 Resections	121	76%
R1 Resections	39	24%
Portal Vein Reconstruction	21	13%
Outcomes		
Median LOS (Days)	8 (4–57)	
30 Day Readmission (patients)	36	17%
Median Readmission LOS (Days)	3 (1–36)	
30 Day Morbidity (Grade 3–4)	44	21%
DGE (All Grades)		
DGE Grade A	35	16%
DGE Grade B	15	7%
DGE Grade C	17	8%
Pancreatic Leak (All Grades)		
Biochemical Leak	16	8%
Grade B	16	8%
Grade C	5	2%
Hospital Mortality	6	3%
30 Day Mortality	5	2%

Operative course

All resections were performed by at least one of two surgeons (JJB, RZA) who were fellowship trained in surgical oncology. The technical complexity of the operations varied by patient disease and tumor size. Some patients even required concomitant major liver resection for advanced cholangiocarcinoma or vena cava resections for large pancreatic adenocarcinomas (data not shown). Reconstruction of the portal vein either by primary repair or interposition vein graft were required in 13% of patients. Blood loss and operative time varied based on the complexity of the resection with a median estimated blood loss of 500 ml (Range 100–2800) and median operative time of 253 min (Range 171–631). For resections performed for malignancy the average tumor size was 3.1 cm. The majority (76%) of resections were R0 with a median lymph node harvest of 13 (Range 1–60) nodes.

Hospital course

All patients were admitted post-operatively to the surgical intensive care unit or step-down unit for the first 24–48 h after which they were transitioned to a surgical floor bed. Patients underwent a standardized post-operative protocol which was shared with the nursing staff and surgical residents. The median length of stay in the hospital was 8 days (Range 4–57). Thirty-six patients (17%) were readmitted to the hospital within 30 days of surgery. However, the majority of readmission issues were resolved within a short period of time and the readmission length of stay was a median of 3 days (Range 1–36).

Pathology

The final pathology of the resected specimens is shown in Table 2. Of the 213 patients who underwent resection, the majority (75%) were for malignant neoplasms. The remainder of the resections for benign disease (25%) were patients with a myriad of indications such as intraductal papillary mucinous neoplasms, chronic pancreatitis, adenomas, and pancreatic epithelia neoplasms.

Morbidity

The thirty-day morbidity and mortality rates are shown in Table 1, and clinically significant post-operative complications (Grade 3/4) are listed in Table 3. The majority of post-operative

Table 2
Final pathology after surgical resection.

Pathology	No.	%
Pancreatic Adenocarcinoma	81	38%
Ampullary Adenocarcinoma	29	14%
Neuroendocrine tumor	21	10%
IPMN	16	8%
Chronic Pancreatitis	15	7%
Cholangiocarcinoma	14	7%
Cystic Neoplasms	10	5%
Duodenal Adenocarcinoma	9	4%
PANIN	7	3%
Ampullary Adenoma	2	1%
Duodenal GIST	2	1%
Renal Cell Cancer	2	1%
Gastric Adenocarcinoma	2	1%
Duodenal Adenoma	1	<1%
Hematoma	1	<1%
Other (No tumor identified)	1	<1%
Total	213	

complications were minor and did not affect patient overall clinical course.

The incidence of delayed gastric emptying (DGE) and pancreatic leak are listed in Table 1. The overall rate of DGE was 31% with 8% of patients developing clinically significant (Grade C) gastric dysmotility with prolonged inability to tolerate oral intake. Only 4% of patients required placement of a feeding tube due to severe DGE.

The overall rate of combined pancreatic fistula and leak was 18% (Grade A-C), with 10% (Grade B/C) being considered a true leak based on the current ISGPS definition.[28] The majority of leaks required no intervention and were managed with the use of drains that had been placed intraoperatively. Six patients (3%) required radiologically guided drains to manage the pancreatic leak and only 2% of patients developed leaks (grade C) that had profound clinical sequela.

The overall rate of post-operative complications that were clinically significant (Grade 3/4) and required intervention was 21% and is listed in Table 3. Fifteen patients (7%) developed intra-abdominal abscesses that required placement of radiologically guided drains. Six patients (3%) developed post-operative respiratory complications requiring ventilator support. The incidence of post-operative bleeding, biliary leak, failure to thrive and stroke were all less than 1%.

A total of 6 (3%) patients required reoperation. Two patients were taken back to the operating room to control intraabdominal bleeding from the superior mesenteric artery and small bowel mesentery. Two patients required re-exploration for leakage from the hepaticojejunostomy and required revision of the biliary anastomosis. One patient developed severe systemic sepsis from an infected pancreatic leak requiring laparotomy and drainage and another patient developed a fascial dehiscence requiring reoperation.

Table 3
Post-operative complications.

Grade 3 & 4 Morbidity	No.	%
Total	*43*	*20%*
Intra-Abdominal Abscess	15	7%
DGE Requiring Feeding Tube	8	4%
Pancreatic Leak Requiring IR Drain	6	3%
Ventilator Dependent Respiratory Failure	6	3%
Bleeding	3	1%
Biliary Leak	2	1%
Cholangitis	1	<1%
Failure to Thrive	1	<1%
Stroke	1	<1%
Reoperation Indications		
Total	*6*	*3%*
Biliary Leak	2	1%
Bleeding	2	1%
Wound Dehiscence	1	<1%
Bacteremia	1	<1%

Mortality

The 30-day operative mortality in our series was 5 of 213 patients (2%), and total in hospital mortality was 6 patients (3%). The detail of each mortality is listed in Table 4. Two patients had post-operative myocardial infarctions resulting in death. One patient developed bleeding from a hepatic artery pseudoaneurysm requiring angiographic and surgical control, however he died of multisystem organ failure. Two patients developed systemic sepsis from biliary and pancreatic leaks and subsequently expired. One patient developed a massive pulmonary embolism on post-operative day seven and expired.

Discussion

In a previous publication, we demonstrated excellent long-term outcomes and survival after establishing a multispecialty gastric cancer team. Our data were equivalent to that published from other regional academic centers and NCDB and AJCC reported survival.[29] That study and our favorable results encouraged us to look at our experience with performing pancreaticoduodenectomy since this operation is much more complex and has potential for increased morbidity and mortality.

The current study investigates our hospital experience with pancreaticoduodenectomy in a community cancer center. The goal of the study was to show that complex pancreatic surgery could be safely performed in a community cancer center with adequate resources and support staff. We do not believe that pancreaticoduodenectomy can be safely performed at any community cancer center. This study is the largest reported series of patients undergoing pancreaticoduodenectomy from a community cancer center. Over a 10-year period 213 patients underwent resection with an average of 21 resections per year, which is consistent with a high-volume center.

Before the establishment of the cancer center, patient care was fragmented amongst many surgeons and not standardized. In fact, we previously reported our outcomes for pancreaticoduodenectomy in which 63 resections were performed by 15 different surgeons over a 9-year time frame.[26] After this previous study was published, a multidisciplinary pancreatic cancer team was instituted which consisted of dedicated surgical, medical and radiation oncologists as well as collaboration with gastroenterology and interventional radiology. In addition, the preoperative workup, intra-operative technique and post-operative care were all standardized by our two dedicated surgical oncologists (JJB and RZA). All patients were ultimately referred to the surgical oncology team which performed all pancreaticoduodenectomies reported in this study. We then sought to evaluate our operative outcomes over the next 10 years in comparison to large series from major academic centers.

Comparison of outcomes against academic centers can be challenging because patient demographics and health status can differ. In addition, uniform definitions of complications are often not used. The patient population in our series was elderly patients with multiple medical comorbidities like those seen in a tertiary referral center. This reflects the aging population that now requires

Table 4
Post-operative deaths.

Age	Gender	Diagnosis	Complication	Description	Death
49	F	Pancreatic Adenocarcinoma	Cardiac Arrest	Pulseless electrical activity	POD 1
66	F	Ampullary Cancer	Pulmonary Embolism	Massive pulmonary embolism	POD 7
80	F	Pancreatic Adenocarcinoma	Biliary Leak	Persistent biliary leak leading to respiratory decompensation and cardiac arrest	POD 12
72	M	Pancreatic Adenocarcinoma	Pancreatic Leak	Severe sepsis from infected pancreatic leak with subsequent cardiac arrest	POD 28
58	M	Pancreatic Adenocarcinoma	Bleeding	Hepatic artery pseudoaneursym requiring angiography and laparotomy with subsequent multisystem organ failure	POD 30
73	F	Pancreatic Adenocarcinoma	Cardiac Arrest	Myocardial infarction	POD 35

complex surgery.[30] In addition, the complexity of cases in our series was similar to what is seen in large academic centers. In order to effectively treat this population, all patients were seen preoperatively by specialists to optimize and manage their existing medical comorbidities. Patients were taken to the operating room after multidisciplinary evaluation.

The majority of resections performed in our series were for malignant lesions. In many instances concomitant liver resection, caval resection or portal vein resection was required due to complex and locally advanced tumors. Despite this, the median operative time and blood loss were similar to many large series from academic centers.[31–35] The majority of patients underwent margin negative resections with adequate lymphadenectomy, and the rate of R1 resections was low in concordance to published standards.[36] The ability to successfully complete complex multi-visceral resection was likely due to the presence of trained surgical oncologists who were able to handle larger and advanced tumors.

Post-operatively, patients were initially managed in the surgical intensive care unit by experienced nursing and surgical resident staff and standardized protocols designed by the surgical oncologists. Patients' post-operative regimen was available to all members of the surgical team. The combination of short operative times and minimal blood loss along with a standardized post-operative pathway likely resulted in a low median length of stay (8 days) which is shorter than many large series.

Many high volume academic institutions have published their experience with pancreaticoduodenectomy which show a large number of cases per year, low morbidity and mortality and short length of stay. Table 5 is a comparative analysis of our data against a few of these institutions.[31–35] Although the number of resections performed per year is lower than other centers, our institution is still considered a high-volume center in accordance with published standards.[1–4,13,37] In our series, median blood loss and operative time are lower than other published series indicating that these resections can be safely and efficiently performed. In addition, morbidity and mortality was low. Grade 3/4 morbidity was 21% which is expected considering the complexity of the operations and comorbidities of the patient population. The incidence of delayed gastric emptying and pancreatic leak were on par with data published from other large series as shown in Table 5. Our 30-day and in-hospital mortality rate was 2% and 3% respectively, which is low and once again consistent with published data from large series. The mortalities were composed of two patients who died from cardiac arrest and one patient who died from massive pulmonary embolism likely reflecting exacerbations of preexisting medical comorbidities. Only 2 patients over a 10-year period expired due to systemic sepsis resulting from biliary and pancreatic leaks.

Over the years, there have been numerous reports published which demonstrate reduced morbidity and mortality and improved survival when complex cases are performed in high volume centers.[9,38,39] This is the reasoning for advocating tertiary referral centers to perform advanced operations. Despite the benefits of surgery in major academic centers, with regionalization of cancer care, patients face other difficulties such as increased travel burden, financial strain, and potential loss of local support structures. However, it may be possible for a community cancer center to handle complex cases with minimal morbidity and mortality while preserving the benefits of local treatment. In our series, we demonstrate that high volume pancreaticoduodenectomy can be performed safely, with excellent surgical and oncologic outcomes. This is likely related to the influence of multiple factors such as hospital infrastructure, ancillary staff and surgeon experience.

One of the main factors which influenced the outcomes in our study was the hospital infrastructure. Due to the large volume of surgical procedures performed at our institution, the hospital was staffed with an experienced team of providers who were available to provide 24-h intervention if necessary. Post operatively the patients were cared for in a dedicated surgical intensive care unit and the presence of in house surgical residents allowed patients who developed complications to be triaged and managed expeditiously. The availability of anesthesia, gastroenterology and interventional radiology physicians, allowed patients who developed complications to be treated rapidly and avoid further clinical decline. As shown in the literature, the ability to rescue and manage patient complications is a significant factor in the low morbidity and mortality rate seen in our series.[4]

Another factor which likely influenced outcomes in our study was the presence of formally trained surgical oncologists. Before the study period there was no mandatory referral or evaluation of patients who required pancreatic surgery to the surgical oncology service. With infrastructure changes, patients who needed pancreatic surgery were seen and evaluated by the surgical oncologist as well as a multidisciplinary hepatobiliary pancreatic cancer team. Patients were then offered the most appropriate therapy such as surgical resection, neoadjuvant therapy, or palliative therapy. Due to advanced surgical and oncology training and expertise, complex resections were able to be completed successfully and safely with minimal complications.

After the development of our cancer center and the hepatobiliary pancreatic cancer team, the number of complex pancreatic operations has increased over time. The high volume of pancreatic resections performed in our institution despite close proximity to multiple NCI designated cancer centers, reflects the preference of patients to be treated locally and not have to travel for cancer care.

Table 5
Post-operative outcomes after pancreaticoduodenectomy at major high volume academic centers.

Author/Year	Number of Resections	Resections/ Year	Median Age (y)	EBL (ml)	Operative Time (min)	Delayed Gastric Emptying	Pancreatic Leak	Length of Stay (days)	30-Day Mortality Rate
Bennett 2018	213	27	66	500	253	15%	18%	8	2.0%
Schmidt 2004	516	24	58	1300	300	7%	9%	13	3.9%
House 2008	356	60	69	612	295	4%	15%	13	1.7%
Cameron 2015	1000	112	66	x	355	24%	18%	10	1.4%

Conclusions

We are able to show that at a high-volume community cancer center with a dedicated surgical oncology team, pancreaticoduodenectomy can be performed with excellent post-operative outcomes on par with any major academic center.

Conflicts of interest

All of the authors for this manuscript do not report any conflict of interests.

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