Can pancreaticoduodenectomy performed at a comprehensive community cancer center have comparable results as major tertiary center?

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ABSTRACT

Background: Pancreatic resection is a definitive treatment modality for pancreatic neoplasm. Pancreaticoduodenectomy (PD) is the primary procedure for tumor arising from head of pancreas. Prognosis is overwhelmingly poor despite adequate resection. We maintained a prospective database covering years 2001 to 2010. Outcome data is analyzed and compared with those from tertiary centers.

Methods: Sixty-two patients with various histology were included. Pylorus preserving pancreatico-duodenectomy (PPPD), classic pancreaticoduodenectomy, and subtotal pancreatectomy were procedures performed. Three patients had portal venorrhaphy performed to obtain clinically negative margin. Forty six patients had malignancy on final pathologic analysis.

Results: The average age of patients was 63. Mean preoperative CA19-9 for exocrine pancreatic malignancies was higher than for more benign lesions. There was a decrease in operative time during this period. Blood transfusion was uncommon. There was very few pancreatic leak among the patients. Two bile leaks were identified, one controlled with the drainage tube and the other one required repeat surgery. The primary reason for the prolonged hospitalization was gastric ileus. For patients without a gastrostomy tube, nasogastric tube was kept in until gastric ileus resolved. 30 days mortality rate was calculated at 4.8. Mean survival time during our follow up was 30.6 months. Comparing to published literature, present series' mortality, morbidity, and survival are similar. Five year survival was 39%.

Conclusion: Despite overall poor outcome for patients with pancreatic and biliary malignancies, we conclude that surgery can be performed in community hospitals with special interest in treating pancreatic disorder, offering patients equivalent survival and quality of life as those operated in tertiary centers.

KEY WORDS pancreaticoduodenectomy for pancreatic cancer; surgical outcome; community hospital

J Gastrointest Oncol 2011; 2: 143-150. DOI: 10.3978/j.issn.2078-6891.2011.035

Introduction

With about 44000 new cases and about 37600 cancer deaths in 2011, pancreatic cancer ranks fourth among cancer-related deaths in the United States. It is the second leading cause of death due to gastrointestinal tract neoplasm. It is one of the few cancers whose survival has not improved over the past 40 years (1).

Pancreatic cancer affects more commonly elderly, and less than 20% of patients present with localized, potentially curable tumors (2). The average life expectancy after diagnosis with metastatic disease is three to six months. Average five year survival is 6%. Seventy-five percent of patients die within first year of diagnosis. Pancreatic cancer has the highest death rate of all major cancers (3).

Symptoms of pancreatic cancer depend on the location, as well as on the stage of the disease. Significant number of tumors develops in the head of the pancreas and usually led to cholestasis, abdominal discomfort and nausea. Obstruction of the pancreatic duct may lead to pancreatitis. Most patients have systemic manifestations of the disease such as asthenia, anorexia, and weight loss. Less common manifestations include venous thrombosis, liver-dysfunction, gastric obstruction, and depression (4-6).

No potential conflict of interest.

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Submitted Jun 30, 2011. Accepted for publication Aug 02, 2011.
Available at www.thejgo.org

ISSN: 2078-6891

Pancreaticoduodectomy (PD) is the most commonly performed surgery in patients with pancreatic cancer as 75% of tumors are located at head of pancreas. First successful pancreatic head resection was described by Walter Kausch in 1912, and later modified by Allen O Whipple in 1935 as two stage procedure whereby diversion was followed by definitive resection (7,8).

Method

In Appleton, Wisconsin, a community hospital cancer center was established in 2001. Patients underwent PD were followed from 2001 to 2010, 62 PD's were performed during this time interval by a surgical team with interest in gastrointestinal oncology. The results were compared with a large series of similar surgery performed elsewhere in the United States (9). The retrospective analysis of the database was approved by the local Institutional Review Board of ThedaCare Hospitals.

SAS 9.2 statistical software was used to perform statistical analysis. Student t-test was used to test the mean difference between two groups of patients. Fisher's exact test was used to examine the association between two factors in a table. Kaplan Meier survival curves were used to estimate survival.

A total of 62 patients (female 35, male 27) with histology-proven pancreatic cancer, ampullary carcinoma and other histological types, including benign histological entities, were included in the study (Tables 1 & 2). To query on the difference in outcome between the early and later time interval, we arbitrarily analyzed patients operated before and after year 2005.

Pylorus preserving pancreaticoduodenectomy (PPPD) was performed in forty one patients; twenty patients had traditional PD and one patient with subtotal pancreatectomy. Clinical pathway was adapted and utilized uniformly in the later period. Three patients had portal venorrhaphy due to tumor adherence to the portal vein. Forty six patients had malignant diagnoses, whereas sixteen patients had benign histology. One case had dual histology (ductal carcinoma and neuroendocrine tumor).

Final pathology showed pancreatic adenocarcinoma, cholangiocarcinoma, adenoma, lymphoma, ampullary carcinoma, duodenum carcinoma, leiomyosarcom, isolated metastatic carcinoma to pancreas, and neuroendocrine tumor. Benign histological diagnoses included, pancreatitis, IPMN, pseudotumor, and adenomatous hyperplasia (Table 3).

Majority of patients presented with jaundice, weight loss and abdominal pain. All of the patients had computed tomography scan done as part of their evaluation. Endoscopic retrograde cholangiopancreatography (ERCP) was performed for patients with symptoms related to bile duct obstruction. Preoperative biliary stents were placed at the discretion of the endoscopist, with relief of jaundice being the primary intent.

Mean age of patients was 63 years, with ages ranging from 39 to 78 years. Ethnicity among the patients included 34 Caucasians, 3 Asians, 5 Hispanics, and 13 patients of unknown origin.

Clinical data

Average operative time was 385 minutes for surgeries performed before 2005 and 348 minutes for surgeries performed after 2005. Comparing procedures performed pre-and post-2005, length of hospital stay was shorter (nearly reaching statistical significance) adjusted for gender, age, and ASA (p=0.06). Average length of stay for all patients was 16.1 days (range 0-87 days), mean ICU stay was 3 days (range 1-63 days). Among the covariates examined, only erythromycin use (as motility agent) changed significantly: there was a substantial increase in its usage (p=0.009). Erythromycin was ordered for 17 (73.91%) patients out of 23 surgeries performed before 2005 and 97.4% of patients received Erythromycin after the surgery (Table 4).

Blood transfusion was given to 15 patients requiring blood product. Mean preoperative CA19-9 for exocrine pancreatic malignancies was 638, whereas for benign lesions and endocrine tumors it was 122 (Table 5).

There were three perioperative deaths due to ischemic bowel and severe acidosis, equivalent to thirty day mortality rate of 4.8%. Major causes of 30 day postoperative death in our study were small bowel necrosis (ii) and disseminated intravascular coagulopathy (i). There was one pancreatic leak in our patient population. Two bile leaks were identified, one controlled with the drainage tube and one required laparotomy to repair the leak. Average length of stay was 15 days. The primary reason for prolonged hospitalization was gastric ileus. For patients without a gastrostomy tube, nasogastric tube was kept in until gastric ileus resolved.

Respiratory failure and renal failure occurred in 4.8% of patients. Wound infection, DVT, and incisional hernia each comprises 3.2% of our patient population (Table 6).

To date, 45% of our patients (N=28) have died, with two patients from causes unrelated to carcinoma. Mean survival during our study period was 30.6 months for all 62 individuals (Tables 7 & 8). Three year survival for patients with pancreatic cancer and carcinoma of non pancreas origin were 39% and 66%, respectively.

Table 1 Patient sex characteristic

Year	Sex		
Frequency Row Pct	F	M	Total
≤2004	13 56.52%	10 43.48%	23
≥2005	22 56.41%	17 43.59%	39
Total	35	27	62

p=1.0; Fisher's exact test was used to exam the association between two factors.

Table 2 ASA characteristic

Year	ASA		
Frequency Row Pct	2	3	Total
≤2004	9 39.13%	14 60.87%	23
≥2005	9 24.32%	28 75.68%	37
Total	18	42	60
Frequency Missing = 2			

p=0.25; Fisher's exact test was used to exam the association between two factors

Table 3 Histology of pancreatic mass

Benign neoplasm (16)	Carcinoma (46)
Pseudotumor (3)	Pancreatic ductal carcinoma (26)
IPMN (2)	Cholangiocarcinoma (5)
Mucinous cystadenoma (1)	Neuroendocrine carcinoma (2)
Chronic pancreatitis (6)	Ampullary carcinoma (4)
Benign adenomatosous hyperplasia (1)	Lymphoma (2)
Duodenal bleeding (2)	Renal cell carcinoma (1)
Adenoma (1)	Duodenal carcinoma (4)
	Leiomyosarcoma (1)
	Multiple histologies - ductal and neuroendocrine carcinoma (1)

Table 4 Erythromycin use by year

Year	Erythromycin		
Frequency Row Pct	n	y	Total
≤2004	6 26.09%	17 73.91%	23
≥2005	1 2.63%	37 97.37%	38
Total	7	54	61
Missing Data = 1			

p=0.0094.

Table 5 Descriptive statistics for continuous variables by year of surgery

Year	N	Variable	N	Mean	Std Dev	Median	Minimum	Maximum	p* vs ≤2004
≤2004	23	Age	23	64.33	10.01	67.48	43.03	77.96	
		LOS	22	19.05	16.04	15.00	8.00	87.00	
		OR_time	23	6.39	1.11	6.12	4.75	8.75	
		ICU_LOS	23	1.00	0.00	1.00	1.00	1.00	
		Crystalloids	23	4995.65	2010.54	5000.00	2000.00	9700.00	
		Colloids	23	413.04	333.45	500.00	0.00	1100.00	
		Blood	23	732.61	464.56	700.00	0.00	2400.00	
≥2005	39	Age	39	62.43	10.61	65.32	36.00	77.06	0.49
		LOS	39	13.18	7.86	12.00	0.00	40.00	0.06
		OR_time	37	5.81	1.68	5.35	2.02	11.50	0.15
		ICU_LOS	37	1.00	0.00	1.00	1.00	1.00	--
		Crystalloid	37	4918.92	2980.20	4600.00	0.00	16000.00	0.91
		Colloid	37	337.84	387.37	250.00	0.00	1500.00	0.44
		Blood	37	784.46	1303.09	500.00	0.00	8000.00	0.86

*Student T-test has been used to test the mean difference between two groups of patients. LOS=length of stay, OR_time=operating time from making incision to closure of skin, ICU_LOS=intensive care unit length of stay, Blood=blood transfusion given in ml.

Table 6 Post surgical complications

prolonged gastric ileus	18
respiratory failure	3
renal failure	3
wound infection/dehiscence	2
DVT	2
incisonal hernia	2
bowel leak	2
severe anemia	1
liver abscess	1
UGI bleeding	1
atrial fibrillation	1
coagulopathy	1
C-difficile collitis	1
acidosis	1
tension pneumothorax	1
re-operation	1

In our series of patients, 47.9% had metastatic disease in regional lymph nodes. 14.2% had positive margins. For patients without lymph node metastasis and negative margin, survival was 75%, 47%, and 47% at 12, 36 and 60 months post surgery, respectively. Patients with lymph node metastasis had 5 years survival rate of 39% whereas those without lymph node involvement had 5 year survival of 48%. Majority of the patients were offered adjuvant chemoradiation therapy based on tumor size greater than 2 cm or if lymph node metastasis was present. Overall five year survival in this patient population was 39% (Fig 1). Stage of cancer does not appear to have an impact on survival. Stages I/II had 5 year survival of 36%, and stages III/IV patients had survival of 34% (Fig 2).

Discussion

Our results were produced in a comprehensive community

Table 7 Overall survival in 30 days, 1,3, and 5years

Time (month)	Survival	Survival Standard Error	95%CI Lower	95%CI Upper
1	0.9032	0.0375	0.79721	0.95532
12	0.7308	0.0578	0.59788	0.82590
36	0.5681	0.0713	0.41737	0.69352
60	0.4519	0.0831	0.28647	0.60367

Table 8 Comparison with the Cameron et al (9) study

Time (month)	Preset Series		Cameron et al.	p
	Survival	SE	Survival	
1	90%	4%	99%	0.021
12	73%	6%	64%	0.116
36	57%	7%	27%	<0.0001
60	45%	8%	18%	0.001

Table 9 ASA classification of present study population

ASA	Frequency	Percent	Cumulative Frequency	Cumulative Percent
missing	13	20.97	13	20.97
non cancer	16	25.81	29	46.77
1/2	22	35.48	51	82.26
3/4	11	17.74	62	100.00

cancer center accredited by the American College of Surgeons Commission on Cancer. Multidisciplinary discussions were held during regularly scheduled tumor conferences. Many of the services providing diagnostic and therapeutic work up are readily available within the medical complex. Specialists with interest in gastrointestinal oncology participate in discussion forums to formulate treatment plans for each patient. Treatment progress notes are made available shortly after each encounter with the patient with an electronic medical record system.

There are numerous publications demonstrating an improvement of outcome after PD in high volume medical centers (10-13). Surgeon volume alone also significantly decreases mortality for complex procedures (14). An analysis of high volume centers has shown that there is a significant variability in mortality (0.7% to 7.7%) and, with other variables analyzed, demonstrates that the variability cannot be explained by hospital volume alone (15). Surgeon experience is an important determinant of overall morbidity. In the same study, it was concluded that experienced surgeons (those who have performed more than fifty PD) have equivalent results whether they are high volume surgeons (some performing more than 20 PD per year) or low volume surgeons (16).

In the literature, five year survival for pancreatic cancer patients treated with PD ranged from 3% in the early series to 20% in more recent publications (16-18). In our series, five year overall survival for patients treated for carcinoma was 39% .

We have chosen a single institution series from Johns Hopkins with one thousand consecutive PD to compare the results between the two institutions. Mortality, morbidity, and survivals are similar (19,20).

The learning curve in pancreatic surgery suggested that after 60 PD's, there are improved outcomes of estimated blood loss, operative time, length of stay, and margin status — factors which have been associated with overall outcome (21). The results presented in this study are consistent with the conclusions presented by published literature.

The benefits of regionalization of complex surgery were demonstrated in a number of studies. Benefits of a high volume center include a decrease in mortality and cost and the ability to perform prospective randomized trials and to provide surgical training (22,23).

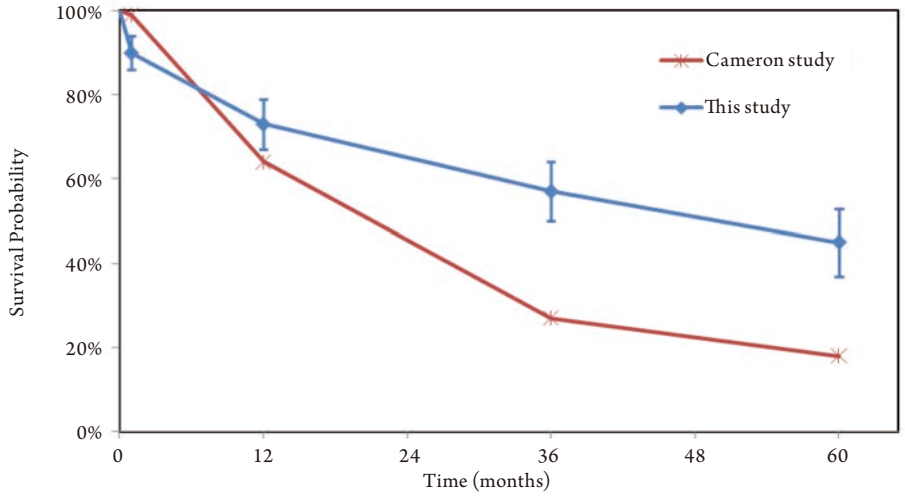

Figure 1 Comparison of survival data

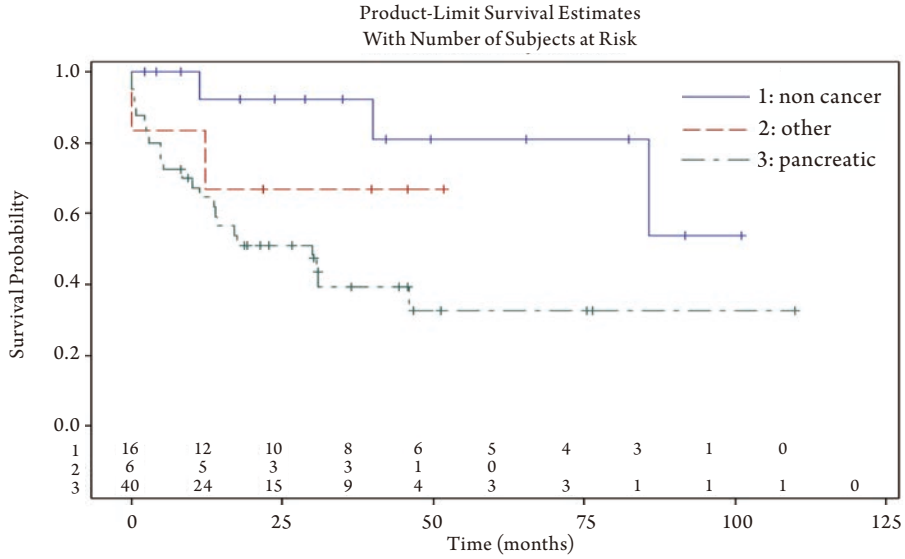

Figure 2 Survival of patients stratified by diagnosis

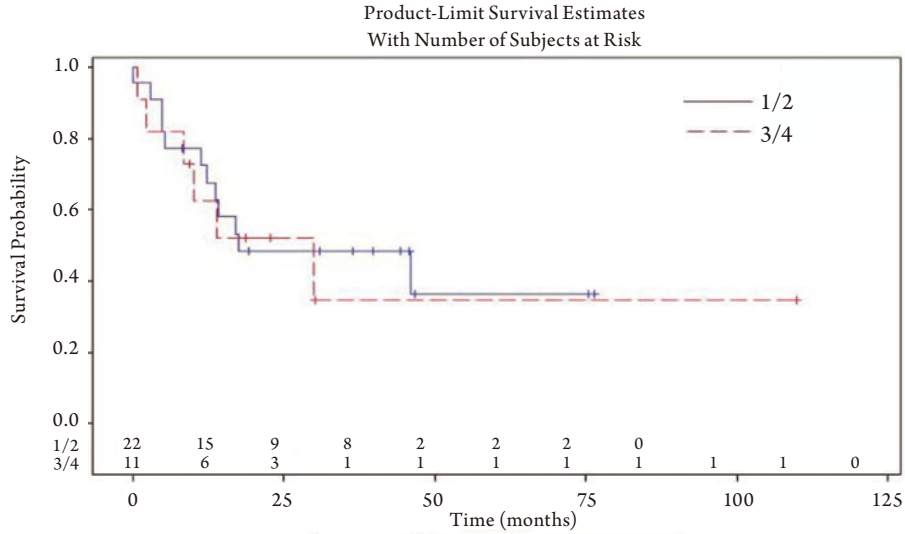

Figure 3 Survival analyzed with respect to ASA score

One of the goals of this study is to determine if we can provide excellent care to patients diagnosed with periampullary tumors. The closest medical center with pancreaticobiliary service to our center is approximately 90 miles. Given the choice for location of service, an overwhelming majority of patients preferred not to travel long distances. Having a pancreaticobiliary service in our encatchment area serves to facilitate treatment as well as to allow patient's family members easier access to the treating medical center.

There has been a dramatic improvement of surgical care in treating periampullary tumors over the last two decades. Anesthetic and perioperative care during the duration of our study have made the greatest contribution to decreasing perioperative mortality. The development of clinical pathways also has contributed to optimizing the outcome (24).

There are limitations to a single institutional series such as ours. Patient population is not large. Because of the small number of patients, meaningful statistical analysis is difficult to derive. Morbidity, mortality, and long term outcomes (cancer specific survival, overall survival) nevertheless have utility in assessing a cancer program. The data presented here gives support to continuing the pancreaticobiliary program at our institution.

Our results reflect the dedication of specialists with interest in treating pancreaticobiliary disorders. We assert that hospital volume alone cannot be the sole determinant of outcome. It is our belief that surgeon volume combined with a multidisciplinary approach and excellent ancillary support provide an excellent prediction of survival as demonstrated in this study of patients with pancreatic and biliary malignancies.

The factors contributing to improved survival for patients diagnosed with periampullary tumors are numerous. Improved perioperative critical care and improved surgical care decrease operating time. Advances in adjunctive therapies contribute to improved survival. It is through these novel therapies that we will see further improvement in survival rates (25).

References

1. American Cancer Society. Cancer Facts & Figures 2011. Atlanta: American Cancer Society;2011.
2. Ghaneh P, Costello E, Neoptolemos JP. Biology and management of pancreatic cancer. Gut 2007;56:1134-52.
3. Conlon KC, Klimstra DS, Brennan MF. Long-term survival after curative resection for pancreatic ductal adenocarcinoma. Clinicopathologic analysis of 5-year survivors. Ann Surg 1996;223:273-9.
4. Brand R. Pancreatic cancer. Dis Mon 2004;50:545-55.
5. Holly EA, Chaliha I, Bracci PM, Gautam M. Signs and symptoms of pancreatic cancer: a population-based case-control study in the San Francisco Bay area. Clin Gastroenterol Hepatol 2004;2:510-7.
6. Thomas RM, Ahmad SA. Current concepts in the surgical management of pancreatic cancer. Surg Oncol Clin N Am 2010;19:335-58.
7. Whipple AO, Parsons WB, Mullins CR. TREATMENT OF CARCINOMA OF THE AMPULLA OF VATER. Ann Surg 1935;102:763-79.
8. Hunt VC. SURGICAL MANAGEMENT OF CARCINOMA OF THE AMPULLA OF VATER AND OF THE PERIAMPULLARY PORTION OF THE DUODENUM. Ann Surg 1941;114:570-602.
9. Cameron JL, Riall TS, Coleman J, Belcher KA. One thousand consecutive pancreaticoduodenectomies. Ann Surg 2006;244:10-5.
10. Fong Y, Gonen M, Rubin D, Radzyner M, Brennan MF. Long-term survival is superior after resection for cancer in high-volume centers. Ann Surg 2005;242:540-4;discussion 544-7.
11. Lieberman MD, Kilburn H, Lindsey M, Brennan MF. Relation of perioperative deaths to hospital volume among patients undergoing pancreatic resection for malignancy. Ann Surg 1995;222:638-45.
12. Schmidt CM, Turrini O, Parikh P, House MG, Zyromski NJ, Nakeeb A, et al. Effect of hospital volume, surgeon experience, and surgeon volume on patient outcomes after pancreaticoduodenectomy: a single-institution experience. Arch Surg 2010;145:634-40.
13. Kotwall CA, Maxwell JG, Brinker CC, Koch GG, Covington DL. National estimates of mortality rates for radical pancreaticoduodenectomy in 25,000 patients. Ann Surg Oncol 2001;9:847-54.
14. Hannan EL, Radzyner M, Rubin D, Dougherty J, Brennan MF. The influence of hospital and surgeon volume on in-hospital mortality for colectomy, gastrectomy, and lung lobectomy in patients with cancer. Surgery 2002;131:6-15.
15. Riall TS, Nealon WH, Goodwin JS, Townsend CM Jr, Freeman JL. Outcomes following pancreatic resection: variability among high-volume providers. Surgery 2008;144:133-40.
16. Nitecki SS, Sarr MG, Colby TV, van Heerden JA. Long-term survival after resection for ductal adenocarcinoma of the pancreas. Is it really improving? Ann Surg 1995;221:59-66.
17. Conlon KC, Klimstra DS, Brennan MF. Long-term survival after curative resection for pancreatic ductal adenocarcinoma. Clinicopathologic analysis of 5-year survivors. Ann Surg 1996;223:273-9.
18. Connolly MM, Dawson PJ, Michelassi F, Moossa AR, Lowenstein F. Survival in 1001 patients with carcinoma of the pancreas. Ann Surg 1987;206:366-73.
19. Ferrone CR, Brennan MF, Gonen M, Coit DG, Fong Y, Chung S, et al. Pancreatic adenocarcinoma: the actual 5-year survivors. J Gastrointest Surg 2008;12:701-6.
20. Bilimoria KY, Talamonti MS, Sener SF, Bilimoria MM, Stewart AK, Winchester DP, et al. Effect of hospital volume on margin status after pancreaticoduodenectomy for cancer. J Am Coll Surg 2008;207:510-9.
21. Tseng JF, Pisters PW, Lee JE, Wang H, Gomez HF, Sun CC, et al. The learning curve in pancreatic surgery. Surgery 2007;141:456-63.
22. Gordon TA, Burleyson GP, Tielsch JM, Cameron JL. The effects of

regionalization on cost and outcome for one general high-risk surgical procedure. Ann Surg 1995;221:43-9.

23. Sosa JA, Bowman HM, Gordon TA, Bass EB, Yeo CJ, Lillemoe KD, et al. Importance of hospital volume in the overall management of pancreatic cancer. Ann Surg 1998;228:429-38.
24. Kennedy EP, Grenda TR, Sauter PK, Rosato EL, Chojnacki KA, Rosato FE Jr, et al. Implementation of a critical pathway for distal pancreatectomy at an academic institution. J Gastrointest Surg 2009;13:938-44.
25. O'Reilly EM. Refinement of adjuvant therapy for pancreatic cancer. JAMA 2010;304:1124-5.