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Pancreatic Resection in the Octogenarian: A Safe Option for Pancreatic Malignancy

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Abstract

BACKGROUND—The incidence of pancreatic cancer is age related; patients older than the age of 65 represent 60% of all cases. We assessed our institution's experience and outcomes with pancreatic resection for malignancy in patients in their ninth decade.

STUDY DESIGN—We reviewed records of patients undergoing pancreatic resection for malignancy at our institution between 1990 and 2007. Demographics, laboratory, treatment, and outcomes data were gathered. Comparisons were made between patients older and younger than the age of 80. Survival was analyzed using the Kaplan-Meier method and comparisons between groups were performed using the log-rank test. Regression methods were used to evaluate predictors of outcomes.

RESULTS—There were 517 pancreatic resections for cancer reviewed. Of these, 27 patients were 80 years or older (age range 80 to 91 years), compared with 490 patients less than 80 (range 20 to 79 years). The distribution of clinical characteristics was similar between the 2 groups. The majority of patients undergoing pancreatic resection harbored a mass in the head of the pancreas, so the most common procedure was pancreaticoduodenectomy (n = 398, 78%). There were no significant differences in complication rates for younger and older groups (59% vs 52%, respectively, p = 0.4), median length of stay (11 vs 12 days, p = 0.33), or perioperative mortality rates (3.7% vs 3.7%, p = 1.0). Overall survival between the 2 groups was similar (21.9 vs 33.3 months, p = 0.18).

CONCLUSIONS—Pancreatectomy for malignancy is a safe option for the elderly. Patients older than age 80 achieved similar results, with similar rates of perioperative complications and mortality. Pancreatectomy for cancer offers a similar survival benefit in both groups.

Pancreatic cancer is the fourth leading cause of cancer deaths in the United States. In 2009, the American Cancer Society estimated that more than 42,470 patients were diagnosed with pancreatic cancer, and more than 35,240 died of disease.¹ The incidence of pancreatic cancer is strongly age related, with patients over the age of 65 representing 60% of all cases diagnosed.² In particular, patients 20 to 29 years old have an annual incidence of 0.1 cases

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Author Contributions

Study conception and design: Hatzaras, Schmidt, Bloomston Acquisition of data: Hatzaras, Schmidt, Klemanski, Bloomston Analysis and interpretation of data: Hatzaras, Schmidt, Bloomston Drafting of manuscript: Hatzaras, Schmidt, Bloomston Critical revision: Schmidt, Klemanski, Muscarella, Melvin, Ellison, Bloomston

of pancreatic cancer per 100,000 population; patients 80 and older have an annual incidence of 87.2 cases per 100,000 population.^{2,3} Patients with pancreatic cancer have a particularly dismal prognosis due to multiple factors including late presentation, aggressive tumor biology, complex surgical management, and the lack of effective systemic therapies.⁴

Surgical resection remains the only potentially curative treatment for pancreatic malignancies. Over the past 20 years, advances in preoperative evaluation, surgical techniques, and postoperative care have reduced the perioperative morbidity and mortality associated with pancreatic surgery, particularly in the elderly.²⁻¹³ With people aged 65 and older representing the fastest growing subset of the population in the United States, management of complex surgical issues promises to become even more challenging. In 2008, the elderly numbered 38.9 million people or 12.8% of the US population; with a rising standard of living, they are projected to account for nearly 20% of the population by the year 2030.¹⁴ In addition, by 2050, people over age 85 are projected to account for 24% of the elderly population and 5% of the overall population.^{14,15} This growing elderly population is expected to have a significant effect on health care, with increasing demand for complex surgical operations. In particular, considering the general increase in average life expectancy, the prevalence of pancreatic cancer is likely to increase.^{2,15}

The purpose of this study was to analyze our experience and outcomes after pancreatic resection for cancer in patients 80 years and older and compare it with the younger population. A secondary aim of this study was to assess whether advanced age is implicated in the long-term survival of patients undergoing pancreatectomy for cancer.

METHODS

The study protocol was approved by the Institutional Review Board at the Ohio State University. We retrospectively reviewed the records of all patients who underwent pancreatic resection for all pancreatic malignancies in our institution from January 1990 through December 2007. Data was obtained from hospital and clinic charts and included demographics, clinical presentation, operative findings, tumor pathologic characteristics, perioperative outcomes, and long-term survival. Perioperative mortality was defined as death within 30 days from operation, or during index admission. Overall survival was determined from date of operation until date of death from any cause, as determined by hospital records and/or the Social Security death index as of September 30, 2009 (ssdi.rootsweb.ancestry.com).

Data comparisons of the primary groups were made by Student's *t*-test and Wilcoxon rank sum test, where appropriate, for continuous variables. We used contingency tables analysis (chi-square test or Fisher's exact test, where appropriate) for discrete variables. Overall survival curves were created using the Kaplan Meier method and compared by the log rank test. Multivariate analysis was undertaken using variables from univariate analysis most likely to affect survival (ie, $p < 0.2$) by binary logistic regression and Cox proportional hazards regression. For the multivariate Cox proportional hazards analysis, perioperative deaths were excluded. All statistical tests were 2-tailed. Statistical analyses were performed using STATA 10.1 for Macintosh (StataCorp LP). Survival analysis-related graphics were performed with SPSS Statistics 18.0 for Macintosh (SPSS Inc).

RESULTS

There were 517 pancreatic resections for cancer in our institution from January 1990 through December 2007. Of these, 27 were patients 80 years or older. Sex distribution was similar between groups, as was the incidence of comorbidities (Table 1). Specifically, major

comorbidities such as cardiovascular (43.7% vs 59.3%), pulmonary (13.5% vs 14.8%), and diabetes (22% vs 18.5%) occurred at similar frequencies in those under 80 or 80 and older, respectively ($p > 0.05$). When the number of comorbidities per patient was considered, patients 80 or older were more likely to have 3 concomitant comorbidities (18.5% vs 5.5%, $p = 0.006$); more patients under the age of 80 had no comorbidities (36.4% vs 14.8%, $p = 0.023$). In total, the mean number of comorbidities per patient was different between those younger or older than 80, respectively (0.95 vs 1.44, $p = 0.008$). The majority of patients undergoing pancreatic resection harbored an adenocarcinoma, with the remainder being neuroendocrine carcinomas. The distribution of tumor types was similar between age groups, as was the location. Most tumors were in the head of the pancreas, so the most common procedure in both groups was pancreaticoduodenectomy. Also, preoperative jaundice was present in the majority of patients, although in similar distribution and with similar incidence of preoperative biliary stenting between groups.

Total complications after pancreatectomy were not significantly different in those older and younger than 80 (Table 2). The rates of infectious (19% vs 15%, $p = 0.8$) and pulmonary (8% vs 4%, $p = 0.7$) complications were similar between the 2 groups, as was the rate of pancreatic leak (11% for both groups). The rate of cardiovascular complications was higher for the older group (4% vs 15%, $p = 0.03$). The older group had no incidence of delayed gastric emptying. Postoperative hemorrhage was also similar between the 2 groups; however, the rate of perioperative transfusion was higher for the younger group (20% vs 4%, $p = 0.04$). Complications that occurred too seldom to tabulate in separate categories were all grouped under "other." These included small bowel obstruction, thromboembolic events, and ischemic bowel at similar rates between groups (10% vs 15%, $p = 0.5$). Perioperative mortality was also similar between the 2 groups (3.7%).

Median overall survival for all patients after pancreatectomy was 22.2 months. As expected, survival for ductal adenocarcinoma was significantly shorter than that for neuroendocrine carcinoma (21.4% vs 78.7%, $p = 0.04$). The group-specific survival was higher for the older group, but this did not meet statistical significance (21.9 months vs 33.3 months, $p = 0.18$; Table 3, Fig. 1). When the 2 age groups were stratified for neuroendocrine tumors and adenocarcinoma, age was not predictive of survival ($p = 0.91$). Patients with neuroendocrine tumors nevertheless had better survival than patients with adenocarcinoma, regardless of their age group. By univariate analysis, female sex, older age, positive resection margins, lymphovascular invasion, complications, reoperation, and overall length of stay in the hospital met the p value threshold ($p \leq 0.2$) as potential predictors of overall survival. We next constructed a multivariate Cox proportional hazards regression model. In this model, the only predictor of survival by multivariate analysis was lymphovascular invasion; age 80 or more was not a significant predictor of long-term survival (Table 4).

DISCUSSION

Over the last 20 years it has been well established that pancreatectomy is safe in patients over the age of 70.^{2,3,5-8,11,15-23} Other studies have shown that advanced age may be a predictor of morbidity and mortality in patients undergoing resection, but this finding is based on multi-institutional studies, pooling data from several small and large volume hospitals.²⁴ As such, in our institution, we have selectively offered resection to these patients. When the age is over 80, however, particularly when considering malignancy, the specter of pancreatectomy inevitably becomes more daunting. Outcomes in octogenarians undergoing pancreatectomy are sparsely reported.¹⁵⁻²³ Focusing on this perceived higher risk group, we show that not only is pancreatectomy safe, long-term outcomes are also acceptable.

Our study population consists of patients who underwent pancreatectomy for ductal adenocarcinoma and neuroendocrine carcinomas. Commensurate with their overall advanced age, comorbidities were common, but not statistically more so in the group over 80. In those over 80 with comorbidities, they were more likely to have multiple comorbidities than their younger counterparts. Still, not only were complication rates similar, the patterns of complications were largely similar. Simply stated, elderly patients were, as expected, more susceptible to cardiovascular complications. Somewhat surprising was the nearly 1-year increased overall survival in the elderly group. This trend likely reflects the careful patient selection process applied to patients of very advanced age.

This study has several potential limitations. It is a retrospective cohort review of patients undergoing pancreatic resection. By design, this study spans 18 years of experience. With changing approaches to pancreatic resection and with evolving chemotherapy and best supportive care, there may be an element of lead time bias; patients treated more recently may be doing better subsequent to lessons learned from previous experiences, better approaches to chemotherapy with newer agents, and overall better supportive care. Furthermore, this cohort includes only patients who underwent a resection; this represents an element of selection bias, in so far as the selection of patients chosen to undergo pancreatectomy, particularly for the older than 80 group. It is plausible that the surgeons selected the patients most likely to do best after an operation; in particular, patients with small volume disease and good overall health status. It is also possible that during the study, we undertook a more aggressive approach to these patients, learning from past experiences. Finally, this study, although one of the larger reports in the literature, may still be underpowered to identify smaller, subtle differences between the groups compared.

Although we are careful not to overstate our findings, this study suggests that extremely advanced age should not be a factor in avoiding pancreatectomy, even in the face of malignancy. Instead, they should be considered based on their physiologic age rather than their chronologic age. In summary, the limitations of this study notwithstanding, the data presented here can be used to lift potential inhibitions of physicians related to resection in the face of locally confined pancreatic cancer at all ages. Elderly patients should not be denied a priori the opportunity for surgery, their only chance of cure, particularly if the patient represents an ideal candidate.

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Figure 1. Overall survival in patients with malignancy after pancreatectomy. Green line, age ≥ 80 ; blue line, age < 80 .

Table 1

Clinicopathologic Characteristics of Patients Undergoing Pancreatic Resection in the Setting of Malignancy

Characteristic	Total (n = 517)	Age < 80 y (n = 490)	Age ≥ 80 y (n = 27)	p Value
Mean age, y (range)	62.9 (20–91)	61.8 (20–79)	83.4 (80–91)	<0.01
Female sex, n (%)	230 (44.5)	217 (44.3)	13 (48.1)	0.69
Comorbidities, n (%)	325 (62.9)	306 (62.4)	19 (70.4)	0.40
Mean preoperative CA19-9, units/mL (range)	1,056 (0–43,316)	1,057 (0–43,316)	1,032 (0–5,500)	0.49
Tumor location, n (%)				
Heads	398 (77)	378 (77)	20 (74)	0.4
Body/tail	119 (23)	114 (30)	5 (25)	
Preoperative bilirubin, mg/dL (range)	2 (0.2–33.8)	4.7 (0.2–33.8)	4.7 (1.0–13.8)	0.4
Preoperative jaundice, n (%)	308 (59.5)	292 (59.6)	16 (59.2)	0.9
Preoperative stent, n (%)	210 (41)	199 (44)	11 (44)	0.9
Operation, n (%)				
PD	398 (77)	378 (77)	20 (74)	0.4
Distal/subtotal	119 (23)	114 (30)	5 (25)	
Histology, n (%)				
PCA	423 (82)	399 (81)	24(89)	0.4
NEC	94 (18)	91(19)	3 (11)	
Mean tumor size, cm (range)	3.6 (1–17.5)	3.6 (1–17.5)	3.6 (1–8.5)	0.98
Nodal metastases, n (%)	277 (54)	263 (59)	14 (56)	0.7
Lymphovascular invasion, n (%)	198 (38)	189 (40)	9 (33)	0.5
Neural invasion, n (%)	282 (54)	267 (56)	15 (55)	0.9
Positive margins, n (%)	79 (15.9)	76 (16.2)	3 (11.1)	0.59
Mean hospital stay, d (range)	13.4 (3–87)	13.3 (3–87)	15.0 (6–60)	0.33
Mean ICU stay, d (range)	1.8 (0–15)	1.8 (0–15)	1.9 (0–6)	0.88

NEC, neuroendocrine carcinoma; PCA, pancreatic adenocarcinoma; PD, pancreaticoduodenectomy.

Table 2

Complications after Pancreatectomy for Malignancy

Complication	Age < 80 y (n = 490)		Age ≥ 80 y (n = 27)		p Value
	n	%	n	%	
Overall	289	59	14	52	0.4
Infectious	92	19	4	15	0.8
Pulmonary	39	8	1	4	0.7
Cardiovascular	20	4	4	15	0.03
Pancreatic leak*	53	11	3	11	1.0
DGE	34	7	0	0	0.2
Perioperative transfusion	97	20	1	4	0.04
Other	51	10	4	15	0.5
Reoperation	31	6	1	4	1.0
Perioperative mortality	18	3.7	1	3.7	0.9

* Pancreatic leak defined according to international pancreatic fistula group definition.²⁵

DGE, delayed gastric emptying defined as inability to tolerate oral diet by postoperative day 7, or the need for reinstitution of gastric drainage.

Table 3

Overall Survival after Pancreatectomy for Pancreatic Malignancy

Survival	Age < 80 y	Age ≥ 80 y
Median, mo (95% CI)	21.9 (17, 26)	33.3 (13, 54)
2-y, %	45.5	56.6
5-y, %	34.8	33.1

Table 4

Cox Proportional Hazards Regression Analysis for Overall Survival

Variable	Univariate	Multivariate
Age $\geq$ 80 y	0.18	NS
Female sex	0.11	NS
Positive margins	0.09	NS
LVI	0.005	0.005 (HR 1.37; 95% CI 1.1, 1.7)
Complications	0.073	NS
Length of stay	0.15	NS

HR, hazard ratio; LVI, lymphovascular invasion; NS, not significant ($p > 0.05$).