
Radical Pancreatectomy for Pancreatic Cancer in the Elderly

Is it Safe and Justified?

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Surgical resection provides the only potential cure for pancreatic cancer, yet resection in patients 70 years of age and older remains controversial because of presumed increased morbidity and mortality. Our aim was to determine the operative results in patients 70 years of age or older undergoing potentially curative radical pancreatic resection for pancreatic cancer from 1982 through 1987. Of 206 consecutive patients explored for potential resection, 42 patients (mean age, 75 years) had potentially curative procedures, including radical pancreaticoduodenectomy in 23 patients, total pancreatectomy in 8 patients, and distal pancreatectomy in 11 patients. Ductal adenocarcinoma was the most frequently encountered neoplasm (69%), but cystadenocarcinoma and islet cell carcinoma accounted for 12% and 7%, respectively. The overall operative mortality rate was 9%, while surgical morbidity was 28%, and medical morbidity was 12%. Overall median survival was 19 months, and 5-year survival was 4%. Despite the low overall incidence of resectability and postoperative cure rate for pancreatic carcinoma, exploration for potential curative resection should not necessarily be withheld for healthy, selected patients who are older than 70 years. Morbidity and mortality rates, although slightly greater than for patients who are older than 70 years, are acceptable.

SURGICAL EXCISION OFFERS the only potential cure for pancreatic malignancy. However the efficacy and rationale for radical pancreatic resection in the treatment of pancreatic neoplasia has been questioned by some investigators given the high operative mortality rates and dismal long-term survival rates reported in the past.^{1,2} The magnitude of this controversy is even greater for patients 70 years of age and older^{3,4} for several reasons. First the peak incidence of pancreatic neoplasia occurs in the sixth and seventh decades of life, and second, as the average duration of life expectancy continues to increase,

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an increasingly older population is at greater risk for developing pancreatic cancer. These factors may magnify the already-increasing incidence of pancreatic cancer.

Recommendations regarding the appropriate treatment of pancreatic cancer in the elderly remain based on surgical experience reported in the distant past and may not be unjustified. More recently surgeons from many centers worldwide with an interest in and experience with surgery for pancreatic cancer have reported markedly decreased morbidity (less than 30%) and mortality rates (less than 5%) after radical pancreatic resections for pancreatic cancer. Furthermore there has been a suggestion that long-term survival may be increased as well for reasons that are unknown.⁵⁻⁸ Currently most pancreatic surgeons believe that major pancreatic resection should be performed with an overall mortality of less than 5%. Indeed, if documentation of reduced perioperative morbidity and mortality can be confirmed in the elderly, such treatment should not be withheld solely on the basis of age. With these concepts in mind, we have reviewed our experience with major pancreatic resection for all types for pancreatic neoplasia during a recent 5-year interval. Our intent was to determine the perioperative morbidity and mortality rates of radical pancreatic resection in patients who are 70 years of age or older.

Clinical Material

The medical records of all consecutive patients aged 70 years or older undergoing exploration for all biopsy-proved primary pancreatic malignancy between 1982 and 1987 were reviewed. This time period was selected as recent reports⁵⁻⁸ have suggested improved trends in perioperative morbidity and long-term (5-year) survival in

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current surgical practice. These patients were considered to have resectable lesions based on physical examination and radiologic investigation; all were deemed fit to tolerate a major surgical procedure based on performance status. Performance status was estimated by impairment of physical activity as noted by the American Cancer Society, Eastern Cooperative Oncology Group (ECOG). Scores of 0 to 4 are assigned as to the degree of impairment, with 0 = unrestricted, 1 = restriction from strenuous physical activity, 2 = capable of self care, 3 = confined patients, and 4 = invalid patients. Of the patients undergoing curative resection, all but one patient were ECOG class 0 and 1; one patient who had undergone abdominal exploration without resection elsewhere was ECOG class 3. Curative resection was defined as resection of all known tumor with pathologically confirmed free margins. Multiple clinical variables were abstracted from each record to define the clinical presentation and to concentrate on the perioperative morbidity and mortality. Follow-up data concerning survival was obtained in all patients who had undergone curative resections, either by telephone contact with the patient or with next of kin if the patient had died. Death certificates were reviewed if available. Because of the retrospective nature of this study, meaningful data on the important topic of quality of life, such as long-term morbidity related to pancreatectomy, maintenance of pain relief, and so on, could not be determined. Of the 164 patients that had palliative procedures or exploration only, follow-up was available in 66% of patients through our cancer registry.

Results

Patient Characteristics

During this 6-year period (January 1982 through December 1987), 206 patients aged 70 years or older underwent exploration for potential resection of biopsy-proved primary pancreatic tumors. Palliative biliary and/or gastric bypass was performed in 118 patients, while 46 patients with unresectable disease were explored with biopsy only; the 42 remaining patients were found to have resectable lesions and underwent a pancreatic resection

TABLE 1. Presenting Symptoms in Patients ≥ 70 Years Old Undergoing Radical Pancreatic Resection for Malignancy

Symptom	Percentage
Weight loss	31
Jaundice	20
Abdominal pain	18
Steatorrhea	10
Anorexia/nausea	9
Generalized fatigue	7
Pruritis	4
Asymptomatic	1

TABLE 2. Histopathology of Pancreatic Resections in Patients ≥ 70 Years Old

Histopathology	Number (%)
Ductal adenocarcinoma	28 (68)
Cystadenocarcinoma	6 (13)
Islet cell carcinoma	3 (7)
Ampullary carcinoma	2 (5)
Squamous cell carcinoma	2 (5)
Carcinosarcoma	1 (2)
Total	42

with curative intent (overall resectability rate in patients aged 70 years or older, 21%). These latter 42 patients constituted the study group in this report.

The mean age of the patients undergoing curative resection was 75 years; seven patients were older than 80 years, and the oldest patient was 85 years of age. There were 22 men and 20 women. The most common presenting symptoms were weight loss, jaundice, and pain (Table 1). Patient presentation was similar to that in younger patients, with weight loss of more than 5 pounds the most frequent symptom (30%). The mean duration of symptoms was 6 weeks. Laboratory evaluation revealed hyperbilirubinemia (more than 2.0 mg/dL) in 55% of patients, while alkaline phosphatase and serum glutamylxyl transferase were each elevated in approximately one third of the patients before operation.

Pathologic Characteristics

The most frequently encountered neoplasm was ductal adenocarcinoma (69%); islet cell carcinoma, ampullary cancer, cystadenocarcinoma, adenoacanthoma, and carcinosarcoma comprised the remaining malignancies (Table 2). Neoplasms involved the periampullary region or head of the pancreas in 31 patients. Radical pancreaticoduodenectomy was performed in 23 patients, four of whom had a pyloric-preserving modification of that procedure. The mean operative time was 5.5 hours. Eight patients underwent total pancreatectomy because the resection margins were positive after radical pancreaticoduodenectomy or both pancreatic endocrine and exocrine insufficiency were present before operation. The mean operative time for total pancreatectomy was 6 hours. The remaining 11 patients had tumors confined to the body of the gland and underwent radical distal pancreatectomy with a mean operative time of 4.75 hours.

Mortality and Morbidity

Operative mortality. The operative mortality, defined as death before discharge or within 30 days of operation, was 9% (four patients). Their ages were 72, 75, 76, and 77 years. One patient died suddenly of a pulmonary em-

bolus just before discharge after an otherwise uncomplicated postoperative course. The other three patients had complicated postoperative courses. One patient developed a leak at the choledochojejunostomy and another had a leak from a gastrostomy tube; both developed sepsis and required reoperation for drainage of intra-abdominal abscesses; they eventually died of multiple-organ failure on the 41st and 11th postoperative days, respectively. The third patient had undergone choledochoduodenostomy and distal pancreatectomy elsewhere for complications believed to be secondary to pancreatitis. Review of the surgical specimen revealed ductal adenocarcinoma, and he was re-explored and underwent a completion total pancreatectomy. After operation he developed portal vein thrombosis and eventually died of liver failure. Thus three deaths occurred after pancreatoduodenectomy, and one followed a completion total pancreatectomy. Overall operative mortality rate for resection of lesions in the pancreatic head was 12% (4 of 31 patients) and for distal lesions was 0% (0 of 11 patients).

Operative morbidity. Overall morbidity rate was 31%. Significant surgical morbidity related to the technical aspects of the procedure, including hemorrhage, sepsis presumed related to the pancreaticojejunostomy or the pancreatic closure, gastric or biliary leakage, or postoperative small bowel obstruction occurred in 28% of patients overall. Medical morbidity, including respiratory failure requiring ventilatory support, renal failure requiring temporary dialysis, pulmonary embolus, myocardial infarction, and hepatic failure occurred in 12% of patients (Table 3). The median duration of hospitalization was 16 days, with a median stay in the intensive care unit of 2 days.

Survival

Median overall survival time was 19 months, and 1-year and 5-year survival rates were 66% and 4%, respectively. Median survival time in the patients with ductal adenocarcinoma, the most commonly encountered neoplasm, was 18 months, although two patients have survived for more than 5 years. In addition eight patients are alive at a mean of 33 months, six of whom had ductal adenocarcinoma. In contrast with the above, survival time

in the patients who underwent a nonresective procedure was only 5.5 months; meaningful comparison between these groups, however, cannot be made.

Discussion

Our study demonstrated that major curative pancreatic resection in selected healthy patients who are 70 years old or older with pancreatic cancer can be carried out with satisfactory results. The operative morbidity (31%) and mortality (9%) rates are somewhat greater than our previously reported results with resection in patients of all ages.⁹⁻¹¹ These factors must be considered when contemplating resection in the elderly; nevertheless surgical resection offers the only potential procedure for long-term survival.

Reluctance to undertake radical pancreatectomy stems from past reports of prohibitive operative morbidity and mortality, each exceeding 40%,^{12,13} and from opinions of physicians and surgeons alike that geriatric patients tolerate resection less well than do younger patients.¹⁴ Recently many institutions have reported markedly decreased operative morbidity (less than 40%) and mortality (less than 5%) rates after major pancreatic resection for primary pancreatic malignancy.^{5,6,8,12} Furthermore several recent reports have suggested an increase in long-term survival (5-year survivals approaching 15%) after curative pancreaticoduodenal resection for ductal adenocarcinoma^{5,6,8} and especially with adjuvant radiotherapy.⁷ However these reports did not specifically attempt to address or define operative risk factors for radical pancreatectomy in the elderly (patients older than 70 years) as a subgroup. With the continued increase in our geriatric population and increased incidence of pancreatic cancer in the elderly, and with the increasing overall incidence of pancreatic cancer over the last several decades,¹⁵ appropriate treatment of elderly patients with a pancreatic neoplasm becomes an important consideration. Our results, and those of Kairaluema and colleagues,¹⁶ support the contention that age alone should not necessarily be a limiting factor for a potentially curative pancreatic resection. Although our study was not designed to investigate the quality of life after resection or to compare survival

TABLE 3. Postoperative Morbidity in Patients ≥ 70 Years Old Undergoing Radical Pancreatic Resection for Malignancy

Surgical	Number (%)	Medical	Number (%)
Hemorrhage	9 (19)	Respiratory failure	2 (5)
Sepsis	7 (16)	Renal failure	2 (5)*
Biliary leak	4 (9)	Pulmonary embolus	2 (5)
Gastrostomy leak	1 (2)	Myocardial infarction	1 (2)
Small bowel obstruction	1 (2)	Hepatic failure	1 (2)
Total	12 (28)	Total	5 (12)

* Requiring temporary hemodialysis.

in patients resected *versus* comparable patients who underwent only a palliative procedure,¹ we believe that attempts at curative resection are justified. Others have reported that resection improves palliation and prolongs survival.⁸ The median survival time in our elderly population after resection was 19 months, and 66% of patients survived for 3 years. Furthermore two patients with ductal adenocarcinoma survived for more than 5 years without evidence of disease, which implies a cure of their malignancy. Nonresective surgical palliation in these patients would have prevented this possibility for prolonged survival.

Obviously we have not excluded elderly patients from curative resection on the basis of age alone in the past. Indeed a previous study from our institution in patients undergoing all forms of operative therapy showed that age alone was not necessarily a major predictive factor in operative mortality.¹⁷ Today we continue to advocate an aggressive approach toward resection in selected patients aged 70 years or older who have pancreatic cancer. The characteristics of the patient population who underwent resection in our study make this a select group. All were medically fit and all but one were of a satisfactory performance status (ECOG class 0 or 1). Despite preoperative findings that suggest less advanced, localized disease at the time of exploration, only 21% proved resectable. This was not unexpected given the many ductal adenocarcinomas. Of the four patients who died after operation, pre-existing medical conditions were not apparent deciding factors in their deaths. The predominant complication was sepsis related to biliary or enteric leaks after pancreatoduodenectomy and total pancreatectomy (three patients). One additional patient had an uncomplicated postoperative course but died of a fatal pulmonary embolus just before discharge. Whether these complications or the host's ability to deal effectively with the sequelae can be attributed to advanced age is unknown.

Operative morbidity and mortality rates in patients older than 70 years are somewhat greater than in younger patients undergoing major pancreatic resection.⁹⁻¹¹ However results are acceptable and survival time appears to be increased. Despite the low incidence of resectability

and the dismal long-term prognosis without resection, major pancreatic resection should not necessarily be withheld for medically healthy patients who are older than 70 years.

References

1. Crile G Jr. The advantages of bypass operation over radical pancreatoduodenectomy in the treatment of pancreatic carcinoma. *Surg Gynecol Obstet* 1970; 130:1049-1053.
2. Shapiro TM. Adenocarcinoma of the pancreas: a statistical analysis of bypass vs Whipple resection in good risk patients. *Ann Surg* 1975; 182:715-721.
3. Forrest JF, Longmire WP. Carcinoma of the pancreas and periampullary region. A study of 279 patients. *Ann Surg* 1979; 189:129-138.
4. Herter FP, Cooperman AM, Ahlborn TN, Antincic C. Surgical experience with pancreatic and periampullary cancer. *Ann Surg* 1982; 195:274-281.
5. Trede M. The surgical treatment of pancreatic carcinoma. *Surgery* 1985; 97:28-35.
6. Grace PA, Pitt HA, Tompkins RK, et al. Decrease morbidity and mortality after pancreatoduodenectomy. *Am J Surg* 1986; 151:141-149.
7. Kalser MH, Ellenberg SS. Pancreatic cancer: adjuvant combined radiation and chemotherapy following curative resection. *Arch Surg* 1985; 120:899-903.
8. Crist DW, Sitzmann JV, Cameron JL. Improved hospital morbidity, mortality and survival after the Whipple procedure. *Ann Surg* 1987; 206:358-365.
9. VanHeerden JA, McIlrath DC, Ilstrup DM, Weiland LH. Total pancreatectomy for ductal adenocarcinoma of the pancreas: an update. *World J Surg* 1988; 12:658-662.
10. VanHeerden JA. Pancreatic resection for carcinoma of the pancreas: Whipple versus total pancreatectomy—an institutional perspective. *World J Surg* 1984; 8:880-888.
11. Obertep H, Bruining HA, Ectinck Schattenkerk M, et al. Operative approach to cancer of the head of the pancreas and periampullary region. *Br J Surg* 1982; 69:573-576.
12. Edis AJ, Kiernan PD, Taylor WF. Attempted curative resection of ductal carcinoma of the pancreas: review of Mayo Clinic experience 1951-1975. *Mayo Clin Proc* 1980; 55:531-536.
13. Gilsdorf RB, Spanes P. Factors influencing morbidity and mortality in pancreaticoduodenectomy. *Ann Surg* 1973; 177:332-337.
14. Lansing PB, Blalock JB, Oschner JL. Pancreaticoduodenectomy: a retrospective review, 1949-1969. *Ann Surg* 1972; 38:79-86.
15. American Cancer Society. *Cancer Facts and Figures*, 1988.
16. Kairaluoma MI, Kiuinicari H, Stahlberg M. Pancreatic resection for carcinoma of the pancreas and the periampullary region in patients over 70 years of age. *Br J Surg* 1987; 74:116-118.
17. Hosking MP, Warner MA, Lobdell CM, et al. Outcomes of surgery in patients 90 years of age and older. *J Am Med Assoc* 1989; 261:1909-1915.