

Safety of pancreatic resection in the elderly: a retrospective analysis of 556 patients

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Abstract

Background The safety of pancreatic resection for elderly patients is still controversial. We examined the postoperative morbidity and mortality in patients aged 75 years or more undergoing pancreatic resection.

Methods Patients undergoing pancreatic resection were studied retrospectively and the outcomes were compared between patients aged <75 and ≥75 years.

Results Of the 556 patients enrolled, 78 (14%) were ≥75 years old. Elderly patients had significantly more co-morbidities, especially cardiovascular pathology ($P=0.005$). Also, elderly patients had significantly lower body mass index prior to surgery ($P=0.005$). There were no significant differences in terms of surgical procedures and tumor types between age groups. The incidence of postoperative pancreatic fistula grade A was significantly lower in the elderly group ($P=0.022$), but no significant differences were noted in the overall morbidity or the incidence of postpancreatectomy hemorrhage, delayed gastric emptying, bile leakage, cardiac complications, pulmonary complications or septic complications. The 30-day mortality rate was similar between groups (0.8% vs. 1.3%; $P=0.532$).

Conclusion Pancreatic resection is a safe option for selected elderly patients. Our study confirms that age alone should not preclude potentially curative surgical therapy.

Keywords Pancreatic resection, elderly patients, outcome

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Introduction

The percentage of the world's population aged over 65 years is expected to almost double between 2008 and 2040, from 8% to 15% [1]. Due to this growing elderly population the absolute number of age-related diseases, such as cancer, are expected to increase [2], thus evoking a demand on a well-functioning and effective health care system to select the most suitable patients for a specific treatment and to avoid morbidity associated with ineffective treatment.

Pancreatic surgery offers the only hope for long-term survival for patients with an underlying pancreatic

malignancy [3]. Through advances in surgical technique, anesthesia and postoperative care, pancreatic surgery can nowadays be performed with increased safety and improved outcome. Despite these improvements, pancreatic surgery is still a complex procedure that requires a fit patient with enough physiological reserve to withstand an extended surgical procedure and a potentially prolonged and complicated postoperative course. Unfortunately, the compromised physiological reserve and co-morbidities of elderly patients may deny them potentially curative surgical treatment. This is illustrated by the observation that the likelihood of being evaluated by a surgeon decreases with age and older patients are less likely to undergo surgical resection [4].

Recent studies have been investigating the safety and benefit of pancreatic resection in the elderly. While some studies have indicated that age alone should not be a contraindication for pancreatic resection [5,6], other studies have reported that elderly patients have a higher incidence of postoperative complications, mortality and longer hospital stay [7-9].

The aim of the present study was to investigate the outcome of pancreatic resection in the elderly at a tertiary care center for pancreatic diseases, with special focus on postoperative morbidity and mortality.

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Conflict of Interest: None

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Patients and methods

Between January 2000 and August 2015, 556 patients underwent pancreatic resection at Skåne University Hospital, Lund and Malmö, Sweden. Patients selected for pancreatic resection were evaluated by both a surgeon and an anesthesiologist regarding co-morbidity and the benefits and risks of surgery. A retrospective review of the medical charts was performed. All pancreatic resections including pancreaticoduodenectomy, total pancreatectomy, distal pancreatectomy and enucleation were reviewed. Patients undergoing necrosectomy due to pancreatitis were excluded.

We divided patients into two age groups, <75 and ≥75 years of age [10]. The collected data included patient characteristics, intraoperative factors, postoperative complications, hospital mortality and length of stay. The Clavien-Dindo classification was utilized to categorize postoperative complications and a Clavien grade of III or higher was considered as major complications. Pancreatic surgery specific complications, including postoperative pancreatic fistula (POPF) [11], postpancreatectomy hemorrhage (PPH) [12] and delayed gastric emptying (DGE) [13], were graded according to the criteria from the International Study Group of Pancreatic Fistula (ISGPF) and International Study Group of Pancreatic Surgery (ISGPS). Mortality was defined as death occurring during the primary hospital stay or within 30 days of surgery.

Statistical analysis

Quantitative parameters are expressed as median (i.q.r.) unless indicated otherwise. The Mann-Whitney *U* test was used to compare quantitative parameters between groups. Categorical parameters are presented as frequencies and compared between groups using the χ^2 test, except when expected frequencies were less than 5, in which case Fisher's exact test was used. Two-sided *P* values were computed, and a difference was considered statistically significant at *P*<0.05. Data were analyzed in SPSS version 21.0 (IBM Corp, Armonk, NY, USA).

Results

The total cohort included 556 patients, with a median age of 66 (57-72) years and a male:female ratio of 291:265. There were 399 pancreaticoduodenectomies, 140 distal pancreatectomies, 7 total pancreatectomies, and 10 enucleations. The main histopathological diagnosis was pancreatic ductal adenocarcinoma (*n*=133; 24%). Postoperative complications (Clavien grade I-V) occurred in 355 patients (64%) and major complications (Clavien-Dindo grade ≥III) in 123 patients (22%). POPF occurred in 139 patients (25%), including grade A in 83 patients (15%), grade B in 40 patients (7.2%) and grade C in 16 patients (2.9%). PPH was registered in 74 patients (13%),

including grade A in 34 patients (6.1%), grade B in 16 patients (2.9%) and grade C in 24 patients (4.3%). DGE was registered in 216 patients (39%), including grade A in 108 patients (19%), grade B in 16 patients (10%) and grade C in 52 patients (9.3%). The 30-day mortality was 0.9%. Median hospital stay was 13 (10-20) days.

Patient characteristics

Of the 556 patients, 78 (14%) were aged ≥75 years (Table 1). The median age was 64 (55-69) years in the <75-year group and 77 (76-80) years in the ≥75-year group. Gender distribution was comparable. There was a significant difference in preoperative comorbidity between the two age groups with the elderly patients having higher American Society of Anesthesiologists (ASA) score (*P*=0.001) and higher incidence of hypertension (*P*=0.005) and cardiovascular disease (*P*=0.005). No significant differences were noted in terms of pulmonary disease or diabetes mellitus. Body mass index (BMI) was significantly lower in the elderly group (*P*=0.005). There were no significant differences between age groups regarding the rates of biliary decompression and neoadjuvant therapy.

Operative procedures

The most common type of resection was pancreaticoduodenectomy, followed by distal pancreatectomy and enucleation (Table 2). Total pancreatectomy was less frequently performed and all patients that underwent total pancreatectomy were <75 years. The distribution of surgical procedures, however, was not significantly different between groups. Operative duration, blood loss during surgery and consumption of blood products were comparable between groups. The rate of vascular resection was similar.

Table 1 Patient characteristics

	<75 years N=478	≥75 years N=78	<i>P</i> value
Age (years)*	64 (55-69)	77 (76-80)	<0.001
Female gender	223 (47)	42 (54)	0.238
ASA physical status ≥III	123 (26)	35 (45)	0.001
Hypertension	128 (27)	33 (42)	0.005
Cardiovascular disease	59 (12)	19 (24)	0.005
Pulmonary disease	28 (7.9)	6 (7.7)	0.608
Diabetes mellitus	90 (19)	18 (23)	0.409
Body mass index (kg/m ²)*	25 (22-28)	24 (21-27)	0.005
Preoperative biliary drainage	199 (43)	38 (49)	0.335
Neoadjuvant therapy	14 (3)	0 (0)	0.235

Values in parentheses are percentages unless otherwise indicated; *values are median (i.q.r.). The analysis is based on available patient data, ASA, American Society of Anesthesiologists

Histopathology

On histopathological evaluation, pancreatic ductal adenocarcinoma was the most frequent diagnosis in both groups, with no significant differences (Table 2). The rates of distal cholangiocarcinoma, ampullary carcinoma, duodenal carcinoma, cystic neoplasms and neuroendocrine tumors were also similar between groups.

Postoperative complications

Overall morbidity was 65% in the <75-year group and 59% in the ≥75-year group, which was not significantly different (Table 3). Also, major complications (Clavien-Dindo grade ≥III) did not differ and occurred in 23% and 21%, respectively. POPF grade A occurred in 16% in the <75-year group and 6.4% in the ≥75-year group (P=0.022), but there were no significant differences in the occurrences of POPF grades B and C. No significant differences were noted in PPH, DGE, bile leakage, cardiac complications, pulmonary complications or septic complications. Reoperation frequency was 4.8% in the <75-year group and 3.8% in the ≥75-year group. Hospital stay was slightly longer in the elderly group, but did not reach statistical significance (13 vs. 14 days; P=0.052).

Table 2 Surgical and pathological data

	<75 years N=478	≥75 years N=78	P value
Type of surgery			
Whipple	343 (72)	56 (72)	0.995
Distal pancreatectomy	120 (25)	20 (26)	0.919
Total pancreatectomy	7 (1.5)	0 (0)	0.601
Enucleation	8 (1.7)	2 (2.6)	0.638
Duration of surgery (min)*	447 (358-540)	440 (359-539)	0.683
Blood loss (mL)*	600 (350-1,100)	600 (400-1,175)	0.874
Intraoperative transfusion	115 (28)	29 (39)	0.075
Vascular resection	37 (7.8)	2 (3.8)	0.216
Tumor entity			
Pancreatic ductal adenocarcinoma	113 (24)	21 (27)	0.530
Distal cholangiocarcinoma	58 (12)	9 (12)	0.881
Ampullary carcinoma	56 (12)	8 (10)	0.708
Duodenal carcinoma	33 (6.9)	6 (7.7)	0.800
Cystic neoplasm	75 (16)	7 (9.0)	0.121
Neuroendocrine tumor	46 (9.6)	5 (6.4)	0.362
Others	97 (20)	22 (28)	0.114

Values in parentheses are percentages. The analysis is based on available patient data

Mortality

The 30-day mortality was 0.8% in the <75-year group and was not significantly different than the 30-day mortality rate of 1.3% seen in the ≥75-year group (Table 3).

Discussion

Elderly patients undergoing pancreatic surgery represent unique challenges mainly due to increased co-morbidity and diminished physiological reserve, which may negatively impact the postoperative course [4]. In this study, we analyzed the outcome of elderly patients undergoing pancreatic resection at our institution. Our data showed that the elderly patients had higher ASA scores, increased cardiovascular pathology and reduced BMI. Despite these observations, we found that pancreatic resection can be safely performed in the elderly patients with similar perioperative outcome as in younger patients.

Over the past years there have been many studies investigating the outcome of pancreatic surgery in elderly

Table 3 Postoperative course

	<75 years N=478	≥75 years N=78	P value
Overall morbidity	309 (65)	46 (59)	0.311
Clavien-dindo grade ≥III	107 (23)	16 (21)	0.692
POPF			
Grade A	78 (16)	5 (6.4)	0.022
Grade B	37 (7.8)	3 (3.8)	0.216
Grade C	11 (2.3)	5 (6.4)	0.060
PPH			
Grade A	29 (6.1)	5 (6.4)	0.803
Grade B	11 (2.3)	5 (6.4)	0.060
Grade C	23 (4.8)	1 (1.3)	0.230
DGE			
Grade A	88 (18)	20 (26)	0.137
Grade B	45 (9.4)	11 (14)	0.204
Grade C	44 (9.2)	8 (10)	0.772
Bile leakage	13 (2.7)	1 (1.3)	0.704
Cardiac complications	18 (3.8)	2 (2.6)	1.000
Pulmonary complications	43 (9.0)	3 (3.8)	0.124
Sepsis	18 (3.8)	1 (1.3)	0.261
30-day mortality	4 (0.8)	1 (1.3)	0.532
Reoperation	23 (4.8)	3 (3.8)	1.000
Hospital stay*	13 (9-19)	14 (11-22)	0.052

Values in parentheses are percentages unless otherwise indicated; *values are median (i.q.r.). The analysis is based on available patient data, DGE, delayed gastric emptying; POPF, postoperative pancreatic fistula; PPH, postpancreatectomy hemorrhage

Summary Box

What is already known:

- Cancer is a disease of the aging population
- As the elderly population increases, the number of new cancer cases, including pancreatic cancer, are expected to increase
- Pancreatic surgery in the elderly patients is controversial, with several previous studies reporting increased risk of postoperative morbidity and mortality

What the new findings are:

- Pancreatic resection is a safe option for selected elderly patients
- Age itself should not preclude potentially curative surgical therapy

patients. As there is no consensus definition of elderly, however, these studies differ in their definitions. Some studies have used 70 years of age as the cut-off for elderly patients [5,8,14], while others have used 75 years [10,15,16], 80 years [9,17] or even 90 years [18] as cut-offs. We adopted a cut-off of 75 years, based on a previous study, establishing standards of quality for elderly patients undergoing pancreatic resections [10].

Most studies demonstrate increased morbidity following surgical resection in patients ≥ 75 years. Bathe *et al* [16] reported an overall morbidity rate of 52% in patients < 75 years and 69% in patients ≥ 75 years, with major complications being significantly higher in elderly patients (31% vs. 63%; $P=0.045$). Lightner *et al* [19] reported a morbidity rate of 56% in patients < 75 years and 70% in patients ≥ 75 years, with major cardiac complications being more frequent among older patients ($P<0.005$). Pratt *et al* [10] reported a morbidity rate of 48% in patients < 75 years and 72% in patients ≥ 75 years, although this was mostly explained by differences in rates of minor complications, with moderate and major complications being equivalent. Scurtu *et al* [15] reported that, while overall morbidity rates between patients < 75 years and patients ≥ 75 years were similar, the incidence of DGE was significantly increased in the elderly. Our results suggest that age alone is not a risk factor for overall or major postoperative complications. Interestingly, we found that the elderly patients had a lower incidence of POPF grade A. According to the ISGPF criteria [11], POPF is defined as a drain output of any measurable volume of fluid on or after postoperative day 3 with an amylase content greater than 3 times the serum amylase level. Grade A represents a transient biochemical fistula bearing no clinical relevance, while POPF grades B and C require a change in the management of the patient. The significantly lower incidence of POPF grade A, but not grades B and C, in the elderly patients might represent an increase in

the percentage of pancreatic gland fibrosis which might occur with age [20].

Mortality rates are generally reported to be higher in patients ≥ 75 years. However, given the small number of patients and the low mortality rates, these differences do not often reach statistical significance [10,15,16]. In the study by Lightner *et al* [19], the outcomes of major pancreatic resections were examined using population-based data from the state of California and from the University of California, San Francisco Medical Center (UCSF), a high-volume tertiary care referral center. Although elderly patients had higher mortality rates than younger patients on a statewide basis, mortality at UCSF was the same for both groups (about 3%). This illustrates that the differences in mortality rates between age groups are more remarkable in the population-based studies than in series from high-volume centers specializing in pancreatic surgery. The perioperative mortality rate was $< 5\%$ in our study for both age groups, without significant differences, indicating that the mortality rates are acceptable in the elderly group, especially when performed in a tertiary care center.

The main limitation of the present study is due to its retrospective nature and the dependency on available patient data. The number of missing values was 14% for intraoperative transfusion and 12% for BMI but for all other variables the number of missing values were less than 5%. Regardless of these limitations, our analysis from a large patient cohort demonstrated that, while elderly patients have more comorbidities, especially cardiovascular pathology, they do not have increased postoperative morbidity or mortality after pancreatic resection. Therefore, pancreatic surgery should not be denied to elderly patients solely based on age. Careful patient selection, surgical planning and attentive postoperative management by an experienced multidisciplinary team are vital to reduce complications.

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