The safety of a pancreaticoduodenectomy in patients older than 80 years: risk vs. benefits

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Abstract

Background: A pancreaticoduodenectomy (PD) offers the only chance of a cure for pancreatic cancer and can be performed with low mortality and morbidity. However, little is known about outcomes of a PD in octogenarians.

Methods: Differences in two groups of patients (Group Y, <80 and Group O, ≥80 year-old) who underwent a PD for pancreatic adenocarcinoma were analysed. Study end-points were length of post-operative stay, overall morbidity, 30-day mortality and overall survival.

Results: There were 175 patients in Group Y (mean age 64 years) and 25 patients in Group O (mean age 83 years). Octogenarians had worse Eastern Cooperative Oncology Group (ECOG) Performance Status (PS ≥1: 90% vs. 51%) and American Society of Anesthesiology (ASA) score (>2: 71% vs. 47%). The two groups were similar in underlying co-morbidities, operative time, rates of portal vein resection, intra-operative complications, blood loss, pathological stage and status of resection margins. Octogenarians had a longer post-operative stay (20 vs. 14 days) and higher overall morbidity (68% vs. 44%). There was a single death in each group. At a median follow-up of 13 months median survival appeared similar in the two groups (17 vs. 13 months).

Conclusions: As 30-day mortality and survival are similar to those observed in younger patients, a PD can be offered to carefully selected octogenarians.

Keywords
pancreatoduodenectomy, pancreatic cancer, age, post-operative morbidity, octogenarians, overall survival

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Introduction

Pancreatic cancer is the fourth leading cause of cancer deaths in the United States. The American Cancer Society reported that in 2010 more than 35 000 patients died of pancreatic cancer. Advanced age is a risk factor for pancreatic adenocarcinoma. The incidence of pancreatic cancer is 29 per 100 000 in patients younger than 65 years compared with 91 per 100 000 in patients 80 to 84 years old. Presented as a poster at the SSO 64th Annual Cancer Symposium (San Antonio, TX, March 2011).

The number of elderly in the US is rapidly growing. Americans older than 85 years are in fact the most rapidly growing segment of the elderly population, and will account for 5% of the overall population by 2050. Surgical resection remains the only treatment with curative potential for pancreatic adenocarcinoma. As the population ages, more octogenarians will be diagnosed with pancreatic cancer and referred to surgeons for curative resection.

Many reports have found acceptable morbidity and mortality after a pancreatoduodenectomy (PD) in patients over 70 years of age. However, only few authors have examined outcomes of a PD in patients aged 80 years and older.
In the present study, short-term outcomes and long-term survival after a PD for pancreatic adenocarcinoma in patients 80 years and older were analysed.

**Methods**

After Institutional Review Board (IRB) approval, we performed a retrospective review of patients operated on for pancreatic adenocarcinoma between 1990 and 2009 at NYU Medical Center. Patients referred to our Institution with pancreatic cancer are evaluated by a multidisciplinary team composed of surgical oncologists, gastroenterologists, medical oncologists, radiation oncologists and gastro-intestinal pathologists. Treatment is then customized according to stage and pathological features as well as to patient’s conditions. Typically, patients with resectable or borderline resectable patients are offered surgery if their Eastern Cooperative Oncology Group (ECOG) performance status is 2 or lower. Few exceptions have been made over the course of the study period, based on the subjective assessment of the operating surgeon.

In order to minimize confounding factors, we excluded from the current analysis peri-ampullary lesions other than pancreatic adenocarcinoma (bile duct cancers, duodenal cancers and ampullary tumours) as well as non-invasive intra-ductal papillary mucinous neoplasms and neuroendocrine tumours. Data collected included patient demographics, pre-operative co-morbidities, social history, tumour stage and pathological features, peri-operative events and complications, and status of disease at follow-up. Chart reviews were performed solely by experienced clinicians and recorded on standardized forms. Ambiguities in any data points were discussed by the study committee, researched, reviewed and corrected.

Data were entered into a secure web-based data entry system.

From our comprehensive pancreatic adenocarcinoma database consisting of 248 patients, we identified 200 patients who underwent a PD.

We then categorized study patients into two groups, according to age at the time of surgery: Group Y (<80 year-old) and Group O (≥80 year-old). Variables analysed in the two groups included demographic data, intra- and post-operative outcomes.

Differences between groups were evaluated by univariate analyses using the chi-square and independent samples t-test for categorical and continuous data, respectively. Survival analyses were performed using Kaplan–Meier curves with log rank tests for significance.

All statistics performed were two-sided and declared at the 5% significance level. Statistical analyses were performed with PASW Statistics v.17.0.2 (SPSS Inc., Chicago, IL, USA).

The study end-points were length of stay, overall morbidity and 30-day mortality.

**Results**

During the period of 1990 to 2009, 248 patients were operated on for pancreatic adenocarcinoma at the NYU Langone Medical Center. For the present study, our database for patients who underwent a PD was queried.

**Patient demographics and co-morbidities**

The present study population included 99 men and 101 women with a mean age of 66.7 ± 11.5 years (range 31–89) at the time of surgery. Table 1 describes the demographics and co-morbidities of the two study groups. Patients in Group Y had mean age of 64.4 years, as opposed to 83.1 years in Group O. There were no differences in term of gender composition (male 47.4% vs. 64.0%, P = 0.13).

**Table 1 Baseline characteristics of study patients**

<table>
<thead>
<tr>
<th></th>
<th>Group Y</th>
<th>Group O</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;80 years</td>
<td>≥80 years</td>
<td></td>
</tr>
<tr>
<td>Male gender</td>
<td>83 (47.4%)</td>
<td>16 (64.0%)</td>
<td>0.13</td>
</tr>
<tr>
<td>Age (mean ± SD)</td>
<td>64.4 ± 10.3</td>
<td>83.1 ± 2.4</td>
<td>-</td>
</tr>
<tr>
<td>Comorbidities and risk factors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ECOG Performance Status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>62 (49.2%)</td>
<td>2 (10.0%)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>1</td>
<td>44 (34.9%)</td>
<td>6 (30.0%)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>17 (13.5%)</td>
<td>10 (50.0%)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>2 (1.6%)</td>
<td>2 (10.0%)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>1 (0.8%)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>ASA score</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>7 (4.1%)</td>
<td>0</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>2</td>
<td>83 (48.5%)</td>
<td>7 (29.2%)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>73 (42.7%)</td>
<td>10 (41.7%)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>8 (4.7%)</td>
<td>7 (29.2%)</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>68 (38.9%)</td>
<td>15 (60%)</td>
<td>0.052</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>22 (12.6%)</td>
<td>5 (20.0%)</td>
<td>0.34</td>
</tr>
<tr>
<td>COPD</td>
<td>11 (6.3%)</td>
<td>1 (4.0%)</td>
<td>0.89</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>37 (21.1%)</td>
<td>3 (8.0%)</td>
<td>0.42</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>8 (4.6%)</td>
<td>3 (12.0%)</td>
<td>0.14</td>
</tr>
<tr>
<td>Any major comorbidity</td>
<td>88 (50.3%)</td>
<td>17 (68.0%)</td>
<td>0.13</td>
</tr>
<tr>
<td>Pre-operative lab</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Albumin (gm/dl)</td>
<td>3.8</td>
<td>3.6</td>
<td>0.14</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>0.9</td>
<td>1.0</td>
<td>0.01</td>
</tr>
<tr>
<td>Haemoglobin (g/dl)</td>
<td>13.0</td>
<td>13.3</td>
<td>0.76</td>
</tr>
<tr>
<td>Bilirubin (mg/dl)</td>
<td>6.5</td>
<td>7.4</td>
<td>0.60</td>
</tr>
<tr>
<td>Glucose (mg/dl)</td>
<td>137</td>
<td>128</td>
<td>0.60</td>
</tr>
</tbody>
</table>

SD, standard deviation; ECOG, Eastern Cooperative Oncology Group; ASA, American Society of Anesthesiology; COPD, chronic obstructive pulmonary disease.
ECOG Performance Status (PS) and American Society of Anesthesiology (ASA) scores were worse in the octogenarians group (ECOG 0: 49.2% vs. 10%, \( P < 0.01; \) ASA 3–4: 47.4% vs. 70.9%, \( P < 0.01 \)). However, there were no major differences in the incidence of specific comorbidities, and the rates of patients with at least one major comorbidity were similar between groups (50.3% vs. 68.0%, \( P = 0.13 \)). Levels of creatinine appeared slightly increased in Group O (0.9 vs. 1.0, \( P = 0.01 \)).

**Intra-operative outcomes (Table 2)**

Table 2 describes intra-operative and post-operative outcomes for the two study groups. No differences were noted in terms of length of surgery, rates of portal vein resection, intra-operative organ injury, blood losses and number of units of blood transfused.

**Pathology (Table 3)**

All patients included in this study were operated on for pancreatic adenocarcinoma. Overall resection margins were negative in 68% of the cases, without differences between groups. Pathological staging was performed according to the Seventh Edition of the Cancer Staging Manual edited by the American Joint Committee on Cancer (AJCC). The vast majority of cancers were in stage IIA and IIB, without significant differences within groups. Differentiation was well to moderate in 43.5% of our study population and poor in 52.5%.

**Post-operative outcomes (Table 4 and Fig. 1)**

There was a single death in each group (\( P = 0.23 \)). Overall morbidity was increased in Group O (44.0% vs. 68.0%, \( P = 0.03 \)). No differences were noted in terms of number of units of blood transfused post-operatively. Length of post-operative stay was longer in elderly patients (13.7 days vs. 20 days, \( P = 0.01 \)). Follow-up was available for 179 patients (89.5% of our population). At median follow-up of 13 months (35 months for survivors), 165 (92%) patients were deceased. The median overall survival, 1-year survival and 5-year survival were 17.3 months, 68.2%, 4.5% for older patients compared with 13.1 months, 51.3% and 5.8% in younger patients (\( P = 0.06 \)), respectively.

**Discussion**

A PD is a morbid procedure, but represents the only chance for cure in patients with adenocarcinoma localized in the pancreatic head. Advanced age is an aetiological risk factor for pancreas cancer. Previous population studies have shown that people are living longer, and the segment of the population over 80 years old is expected to significantly increase in the coming years. This in turn will lead to a greater number of octogenarians with
potentially resectable pancreas cancer being referred for surgery. It has been well established that a pancreatic resection can be performed safely in patients over the age of 70 years, but there are only five single-institution retrospective studies that analysed peri-operative outcomes of pancreatic resections in octogenarians. As summarized in Table 5, the patient population analysed in those reports was very heterogeneous, as indications for surgery included different types of pancreatic malignancies and peri-ampullary tumours as well as benign pancreatic diseases. Furthermore, some of those studies included both PD and distal pancreatectomy. Rates of perioperative mortality and overall morbidity for octogenarians appeared similar to younger patients. The only exception was represented by Makary et al., which reported on 197 octogenarians and 2491 younger controls, and did show a significantly higher morbidity and mortality in the older group (41.6% vs. 52.8% and 1.7% vs. 4.1%, respectively, both P < 0.05).

In our experience overall morbidity was also higher in octogenarians than in younger patients (44% vs. 68%, P = 0.03), whereas...
mortality although higher for octogenarians (0.6% vs. 4.0%) did not appear statistically different \((P = 0.23)\). A 1-year mortality similar between study groups (51.3% vs. 68.2%) would suggest equivalent short-term outcomes between groups. Unfortunately the performance status of survivors was not systemically recorded in the post-operative follow-ups, limiting our ability to comment on differences in post-operative recovery.

Similarly to the other reports listed in Table 5, the main limitation of our study is its retrospective nature. Two strategies to minimize the well-known difficulties in capturing accurately all the details of the retrospective morbidity data were employed. First, it was decided to exclude from the analysis the incidence of individual complications (e.g. pneumonia, bleeding and pancreatic leak) that could have been overlooked in a thorough yet retrospective review of medical records. On the other hand, identifying whether a patient had any sort of post-operative morbidity (i.e. overall morbidity) was accurate and reliable as a statement specifying whether the post-operative course had been uncomplicated or complicated is required in our discharge summary, and therefore prospectively recorded. Second, as the date of the operation and date of discharge from the hospital are always reported in administrative records, the objectively recorded length of stay as an additional surrogate for post-operative morbidity was used. The finding of a longer hospitals stay for octogenarians (13.7 vs. 20 days, \(P = 0.01\)) supports the validity of the present observed increased morbidity in octogenarians.

The present study, similar to the others mentioned above, only included patients who underwent a resection. This represents an element of selection bias, in so far as the selection of patients chosen to undergo a PD. In our experience patients in Group O had worse pre-operative ECOG performance status and ASA score compared with Group Y, and tumours with a similar AJCC stage. Nevertheless, it is certainly plausible that the surgeons selected the octogenarians most likely to do best after an operation (those with small volume disease and good overall health status) while referring unfit patients to best supportive care or systemic chemotherapy.

With a median follow-up of 35 months for pancreatic cancer survivors, our database has likely captured most of the cancer-related events. It was found that long-term survival was longer for Group O (median OS 13.1 vs. 17.3 months), although this felt short of statistical significance \((P = 0.06)\). Prior to the present study, only Lee et al. analysed survival of octogenians undergoing a PD for pancreatic adenocarcinoma and reported findings opposite to ours (shorter survival in the elder group: 18.1 vs. 11.6 months, \(P < 0.01\)). There is no clear explanation for these differences between the studies; given the retrospective nature of these reports, it is likely that selection bias may have played a role. As summarized in the last column of Table 5 other authors have also reported on long-term outcomes; however, interpretation of these data are difficult as patients with a different histology were included in the survival analyses.

Globally, these studies show that pancreatic resection for pancreatic adenocarcinoma or other malignancy can be performed safely and with acceptable complication rates in well-selected octogenarians. Extremely advanced age should not be considered an absolute contraindication to PD, especially in case of malignancy, as survivals may be comparable to those observed in younger patients.

Future research should focus on predicting what patients will do well after a PD. In 2009, the Veteran Administration Surgical Quality Improvement Program (VASQIP) released an online risk calculator that estimates 30-day mortality after specific general and subspecialty procedures of moderate or greater complexity.16 Use of the VASQIP Mortality Calculator (VMC) should facilitate pre-operative risk stratification and informed consent. However, the VMC does not provide prediction of morbidity, and its use has not been validated outside the VA.

Frailty is an entity that has recently been identified as a marker of physiological reserve in elderly patients and is unique from comorbidity and disability.17 Further prospective studies are necessary to determine whether a measurement of frailty may help clinicians in surgical decision-making for elderly patients.

**Conclusions**

The expected increase in the octogenarian population will result in a significant increase in the number of 80 year olds being diagnosed with pancreatic adenocarcinoma and referred to the surgeon for consideration of a PD. Multidisciplinary treatment planning, and careful selection for surgery is critical in managing these, and all pancreatic cancer patients. However, surgery, the only chance for cure, should not be denied to octogenarians with pancreatic adenocarcinoma, solely based on chronological age.

**Conflicts of interest**

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**References**


