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## Resected pancreatic cancer outcomes in the elderly



Jessica M. Frakes<sup>a</sup>, Tobin Strom<sup>a</sup>, Gregory M. Springett<sup>b</sup>, Sarah E. Hoffe<sup>a</sup>, Lodovico Balducci<sup>c</sup>, Pamela Hodul<sup>b</sup>, Mokenge P. Malafa<sup>b</sup>, Ravi Shridhar<sup>a,\*</sup>

<sup>a</sup>Department of Radiation Oncology, Moffitt Cancer Center, Tampa, FL, USA

<sup>b</sup>Gastrointestinal Tumor Program, Moffitt Cancer Center, Tampa, FL, USA

<sup>c</sup>Senior Adult Oncology, Moffitt Cancer Center, Tampa, FL, USA

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### ABSTRACT

**Objective:** To determine if age affects outcome in patients with resected pancreatic head cancer.

**Materials and Methods:** An IRB-approved pancreatic cancer database was queried for patients with upfront resected pancreatic head cancer treated at our institution between 2000 and 2012. Overall survival (OS) curves were calculated according to the Kaplan–Meier method and log-rank analysis. Multivariate analysis was performed using the Cox proportional hazard model.

**Results:** We identified 193 patients. Patients  $\geq 70$  years were less likely to receive adjuvant treatment ( $p = 0.002$ ); however there were no other significant differences between age groups. There was a trend towards increased pancreatic leaks in the elderly group ( $p = 0.06$ ), but no difference in post-operative complications or mortality. There was no difference in overall survival based on age. Median and 5-year OS were 23 months and 26.7% in patients  $< 70$  years, 23.4 months and 23% in those 70–75, 16.1 months and 0% in those 76–80, and 18.7 months and 15.4% in those  $> 80$  years ( $p = 0.62$ ). On univariate analysis, there was increased OS in patients with lower T stage, N0 status, post-operative CA19-9 level  $< 90$ , and use of chemoradiotherapy ( $p < 0.05$ ). Multivariate analysis revealed that lower tumor stage, N0, post-operative CA19-9 level  $< 90$ , and use of any adjuvant therapy predicted decreased mortality ( $p < 0.05$ ). Age, gender, tumor site, tumor grade, and positive margins were not prognostic on multivariate analysis.

**Conclusions:** There is no difference in outcomes when comparing elderly patients with resected pancreatic cancer to those patients  $< 70$  years of age.

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\* Corresponding author at: Department of Radiation Oncology, Gastrointestinal Tumor Program, Moffitt Cancer Center, 12902 Magnolia Dr, Tampa, FL 33612, USA. Tel.: +1 813 745 1824; fax: +1 813 745 7231.

E-mail address: [ravi0421@yahoo.com](mailto:ravi0421@yahoo.com) (R. Shridhar).

## 1. Introduction

The estimated number of new cases of pancreatic cancer in the United States in 2014 is approximately 46,420 people diagnosed with an estimated 39,590 that will die from their disease.<sup>1</sup> The median age at diagnosis of pancreatic cancer is 72, with approximately 43% of all patients aged  $\geq 75$  in the United States.<sup>2</sup> Outcomes continue to remain dismal with the only chance of cure being margin negative (R0) resection.

Age is not a contraindication to surgical resection and has been extensively researched.<sup>3–6</sup> Some studies show increased operative time and post-operative complication in the elderly population, however no differences in post-operative mortality validate its use.

Chemotherapy remains a mainstay of treatment in the adjuvant setting, however the addition of post-operative radiation therapy (PORT) continues to be a topic of controversy. Several studies have shown an overall survival (OS) benefit<sup>7–9</sup> compared to surgery alone where others have shown no benefit and possible detriment.<sup>10–12</sup> Some institutions recommend chemotherapy alone and others recommend the addition of PORT.

Very few studies have looked at PORT and chemotherapy in the elderly population.<sup>13,14</sup> We have retrospectively reviewed our institutions data to hopefully better understand the role of PORT and chemotherapy in the elderly population.

## 2. Material and Methods

### 2.1. Patients

An analysis of patients with upfront surgically resected pancreatic head cancer treated at our institution between 2000 and 2012 was performed to compare outcomes of patients  $>80$ , 76–80, 70–75, and  $<70$  years. Included patients underwent upfront surgical resection for AJCC (6th ed) stage I–III cancer without the use of neoadjuvant therapy. Patients with unusual histologies including lymphoma, cystadenoma, intraductal papillary mucinous neoplasm, signet ring cell carcinoma, neuroendocrine tumors, islet cell tumors such as gastrinoma, insulinoma, glucagonoma, and VIPoma were excluded. This study was approved by the Institutional Review Board.

### 2.2. Treatment

#### 2.2.1. Surgery

Patients with pancreatic head tumors underwent pancreaticoduodenectomy with or without a pylorus-sparing procedure.

#### 2.2.2. Adjuvant Therapy

Following surgery, patients received chemoradiation with or without neoadjuvant or adjuvant chemotherapy, chemotherapy alone, or no adjuvant therapy. Adjuvant therapy was initiated within 4 months from the time of surgery in all cases. There was equal proportion of patients treated with adjuvant therapy based on stage.

Patients treated with chemotherapy alone received single-agent gemcitabine. Patients treated with chemotherapy followed by radiation were treated in a similar fashion to the Radiation Therapy Oncology Group (RTOG) 9704 protocol with 1 month of gemcitabine followed by concurrent chemoradiation with continuous infusion 5-fluorouracil (5-FU) or gemcitabine, followed by adjuvant gemcitabine. Patients treated with chemoradiation alone received concurrent radiation with 5-FU or gemcitabine. The median radiation dose was 50 Gy (range 43.2–63 Gy) in 180 to 200 cGy daily fractions for a median of 28 fractions (range 24–35) to the pancreatic tumor bed and regional lymphatics; a minority of patients received a boost to the tumor bed (median 0 Gy, range 0–14.4 Gy).

### 2.3. Statistical Analysis

The primary endpoint was overall survival (OS), defined as the interval from surgery to date of death. Statistical analysis was performed using SPSS® version 21.0 (IBM®, Chicago, IL). Continuous variables were compared using both Wilcoxon rank sum test and the Kruskal–Wallis test as appropriate. Pearson's Chi-square test was used to compare categorical variables. Actuarial rates of overall survival were calculated using the Kaplan–Meier method and the log-rank test. A Cox multivariate model was performed for overall survival, including all clinical, histopathologic, and treatment variables. Continuous variables for inclusion in the multivariate model were split at clinically meaningful cut-points; post-operative CA19-9 level was split at  $<90$  and  $\geq 90$ . All statistical tests were two-sided and an  $\alpha$  (type I) error  $<0.05$  was considered statistically significant.

## 3. Results

We evaluated a total of 193 patients who underwent pancreatic resection. Patient characteristics are presented in Table 1. Patients  $\geq 70$  years of age received adjuvant treatment less frequently ( $p < 0.001$ ); however there were no differences based on tumor size, tumor stage, nodal status or nodes removed, margin status, grade, and tumor stage. There were differences based on median days to surgery and post op CA19-9.

Post-operative complications are presented in Table 2. There was no difference in post-operative complications between the groups with respect to gastric/jejunum tube leaks, atrial fibrillation, pulmonary embolism, infections, wound complications, or fistulas. There were differences observed between the groups in regards to post-operative mortality, however there was not an increase based on increasing age.

Fig. 1 illustrates the OS and progression-free survival (PFS) curves for all patients according to age. There was no difference in OS or PFS based on age. Median and 5-year OS were 23 months and 26.7% in patients  $<70$  years, 23.4 months and 23% in those 70–75, 16.1 months and 0% in those 76–80, and 18.7 months and 15.4% in those  $>80$  years

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