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Primary sarcomas of the pancreas: A review of 253 patients from the National Cancer Data Base

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ABSTRACT

Introduction: Primary sarcomas of the pancreas are rare, and the limited data regarding their presentation, oncologic profile, and survival have been derived from small case series.

Methods: The National Cancer Data Base (1998–2012) was queried for patients with primary sarcomas of the pancreas. Demographic and clinical features at the time of diagnosis were evaluated for all patients. Subjects who underwent surgical resection were identified, and logistic regression was used to identify variables associated with resection. A Cox proportional hazards model was developed to identify factors associated with survival.

Results: In total, 253 patients were identified. The mean age at diagnosis was 63 years, with tumors occurring more frequently in women (57.3%) and those of white race (79.8%). Tumors in the head of the pancreas were most common (63.3%). The mean size was 7.5 cm. Only 100 patients (39.5%) underwent resection, with younger age (OR = 0.763, p = 0.04) and smaller tumor size (OR = 0.978, p < 0.01) associated with resection. Chemotherapy and radiation therapy use were similar in patients who underwent resection and those who did not. Patients who underwent resection had a median survival of 17 months, compared to 6 months for patients who were not resected (p < 0.01). Following adjustment, only older age (HR 1.257, p = 0.03) and higher tumor grade (HR 1.997, p = 0.01) were associated with an increased risk of death in resected patients.

Conclusions: Primary pancreatic sarcomas are rare and the majority of patients do not undergo resection; thus, little is known about their oncologic profile or outcomes following pancreatectomy. Patients who undergo resection have markedly improved survival; older age and higher tumor grade are associated with decreased survival.

1. Introduction

Primary sarcomas of the pancreas are exceedingly rare, with an incidence estimated to be 0.1% of all pancreatic malignancies [1]. With the current literature limited to small institutional studies and case reports, little is known about these tumors [2–5]. Thus, patient characteristics, rates of resection, and outcomes following diagnosis remain essentially unclear.

Leiomyosarcoma represents the most frequently occurring histology and most frequently described in the literature. In two of the largest studies to date, Xu et al. reviewed Chinese and English literature and identified 69 previously reported cases of primary leiomyosarcomas of the pancreas [6] and Zhang et al. identified 9 cases at the Mayo Clinic [7]. Given the rarity of these tumors and the paucity of literature on these sarcomas, a comprehensive national database is ideally suited to provide additional insight into these tumors.

The primary aim of this study was to determine patient characteristics, histological subtype, rates of surgical resection, and overall survival in patients with primary sarcomas of the pancreas utilizing a large, nationally representative database.

2. Methods

2.1. Data source

The National Cancer Data Base (NCDB) is a joint program of the Commission on Cancer of the American College of Surgeons and the American Cancer Society. The NCDB is a nationwide, facility-based,

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comprehensive clinical surveillance data set that currently captures 70% of all newly diagnosed malignancies in the United States. It was established in 1989 and currently contains more than 29 million cancer cases from more than 1500 Commission on Cancer-accredited cancer programs from all 50 states, Puerto Rico, and the District of Columbia [8].

Data were coded according to the Commission on Cancer Registry Operations and Data Standards Manual, and the International Classification of Disease for Oncology. To reduce data errors and maintain the integrity of the database, all data were extracted from medical records by trained and certified tumor registrars. Data were validated both locally and at the NCDB level. Data were de-identified and submitted to the NCDB in compliance with the Health Insurance Portability and Accountability Act (HIPAA). The Duke University institutional review board granted this study an exempt status.

2.2. Study design

The NCDB participant use data file for pancreatic cancer (1998–2012) was queried for all patients with a diagnosis of pancreatic sarcoma (ICD-O-3 histology codes: 8800 (sarcoma), 8801 (spindle cell sarcoma), 8802 (giant cell sarcoma), 8803 (small cell sarcoma), 8804 (epithelioid sarcoma), 8806 (desmoplastic small round cell tumor), 8890 (leiomyosarcoma), 8891 (Epithelioid leiomyosarcoma), 8980 (carcinosarcoma), and 8981(carcinosarcoma)). Inclusion was limited to adult patients ($\geq$18 years).

The study cohort was then categorized into two groups based on surgical resection. Patients who received any pancreatic resection were categorized into the resection group; all other patients were categorized into the no resection group.

Patient variables including age at diagnosis, race, gender, annual income, insurance status, year of diagnosis, distance travelled to treating institution, and comorbidity were extracted from the database. Comorbidity was represented by the modified Charlson/Deyo scoring system (1992). Annual income levels were assigned by the NCDB by linking a patient's zip code to the year 2000 US Census data.

2.3. Statistical analysis

Baseline characteristics were reported using frequencies and proportions for categorical variables and mean and standard deviation for continuous variables. Data were compared utilizing chi-square and Student's t-tests. Overall survival for both groups was defined from the time of diagnosis to the time of death or last follow-up. Survival time was censored for patients alive at the end of the study period. Patients with zero months of follow-up were excluded. Estimates and 95% confidence intervals (CIs) of overall survival proportions were computed using the Kaplan-Meier method, and survival distributions were compared across groups using the log-rank test.

A binary logistic regression model was developed to predict factors associated with surgical resection. The model included age, sex, race, facility type, income level, insurance status, tumor size, tumor location in the pancreas, and tumor grade.

A Cox proportional hazards model was developed for all patients who underwent surgical resection to predict factors associated with survival. The model included age, facility type, tumor size, tumor grade, surgical margin status, and lymph node status.

Two-sided statistical tests were specified in all analyses and p-values < 0.05 were considered statistically significant.

3. Results

In total, 253 patients met the inclusion criteria. The average age at diagnosis was 63 years and the majority of patients were female (57.3%) and of white race (79.8%). Tumors were most likely to be located in the head of the pancreas, averaged 7.5 cm in size, and were most likely to be poorly differentiated or undifferentiated (Table 1). Of the 253 patients, the most prevalent known histology type was leiomyosarcoma (n = 83, 32.81%) with carcinosarcoma (n = 71, 28.06%) as the second most prevalent (Fig. 1).

Table 1
Patient demographic, clinical, and pathologic characteristics.

	N = 253 (%)
Age (years)	63.1 ± 14.2
Gender (female)	145 (57.3)
Race	
Asian	[a]
Black	49 (20.2)
White	193 (79.8)
Grade	
Well differentiated	13 (10.2)
Moderately differentiated	18 (14.2)
Poorly differentiated	57 (44.9)
Undifferentiated	39 (30.7)
Location in pancreas	
Head	114 (63.3)
Body	22 (12.2)
Tail	44 (24.5)
Tumor size (cm)	7.5 ± 4.7
Positive lymph nodes	21 (24.7)
Distant metastases	14 (20.6)
Resected	100 (39.5)
Chemotherapy	97 (38.3)
Radiation Therapy	38 (15.0)

[a] Not reported in accordance with NCDB regulations.

Of the 253 total patients, 100 (39.5%) underwent surgical resection. Compared to patients who did not undergo surgical resection, patients who underwent surgical resection were more likely to have smaller tumors (7.2 cm vs. 7.7 cm, $p < 0.01$) and poorly or undifferentiated tumors (77.4% vs. 73.8%, $p = 0.02$). Patients who underwent resection were similar to patients who did not with regards to age, sex, race, insurance status, Charlson/Deyo score, and facility type (all $p > 0.05$, Table 2).

Unadjusted overall survival at 5 years was improved for patients who underwent resection when compared to those who did not undergo resection (33.3% vs 4.4%, $p < 0.01$). The median survival for patients who underwent resection was 16.6 months, while the median survival for patients who did not undergo resection was 5.9 months ($p < 0.01$, Fig. 2).

After adjustment for patient demographic, clinical, and pathologic factors, increasing patient age (Odds Ratio 0.76, 95% CI 0.59–0.98, $p = 0.04$) and increasing tumor size (OR 0.98, 95% CI 0.97–0.99, $p < 0.01$) were associated with patients not undergoing surgical resection (Table 3).

For patients undergoing surgical resection, after adjustment for patient demographic, clinical, and pathologic factors, increasing patient age (Hazard Ratio 1.26, 95% CI 1.03–1.54, $p = 0.03$) and poorly differentiated or undifferentiated tumor grade (HR 1.99, 95% CI 1.15–3.47, $p = 0.01$) was associated with compromised survival (Table 4). Lymph node status was not associated with survival (HR 0.61, 95% CI 0.39–1.74, $p = 0.60$).

4. Discussion

This study is the largest and only hospital-based analysis examining primary sarcomas of the pancreas. We examined patient characteristics, histological subtype breakdown, rates of surgical resection, and overall survival in these patients. Previous literature is limited to small institutional studies and cases reports. Due to the extraordinarily uncommon incidence of this tumor, this study provides important insights into these rare tumors that may guide clinical decision making.

Overall, primary sarcomas of the pancreas typically present as large, high-grade tumors, found in the head of the pancreas, and present in a