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Solid pseudopapillary tumor of the pancreas: A population-based comparison with pancreatic ductal adenocarcinoma

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ABSTRACT

Objective: Solid-pseudopapillary tumor of the pancreas (SPTP) is a rare neoplasm that has been investigated only in individual case series from individual institutions. Here, the goal was to perform a population-based analysis of these rare tumors.

Methods: A query of the Surveillance, Epidemiology, and End Results (SEER) database was made for patients with malignant SPTP and pancreatic ductal adenocarcinoma (PDAC) from 2001-2010. The primary outcome measure was five-year overall survival. Cox regression analyses were performed using age, race, gender, tumor location, stage of tumor, and histologic type.

Results: 107 patients with SPTP and 53,353 with PDAC were identified for study. Patients with SPTP were younger ($p<0.001$), more often female ($p<0.001$), and less commonly white ($p<0.001$) than those with PDAC. SPTPs were also more frequently located in the tail ($p<0.001$), of lesser stage ($p<0.001$), and more likely to undergo surgical treatment ($p<0.001$) than PDAC. The overall 5-year survival was 84.7% for SPTP and 2.8% for PDAC. For those patients who underwent surgical treatment, 5-year overall and cancer-specific survival was 92.7% and 95.9% for SPTP and 13.5% and 16.7% for PDAC, respectively.

Conclusion: SPTP is a rare pancreatic neoplasm found more commonly in young women in the tail of the pancreas and is associated with a significantly more favorable prognosis than PDAC.

Key words: *Pseudopapillary, pancreatic cancer, pancreatic mass, SPTP*

Introduction

Solid pseudopapillary tumor of the pancreas (SPTP) is a rare pancreatic neoplasm. It comprises less than 1% of all pancreatic tumors [1]. To date, these tumors have been studied in the form of individual case series at high-volume centers [2-4].

The rarity of these tumors can create a diagnostic challenge for the hepatobiliary surgeon. Preoperative diagnosis has been made in approximately 25% of patients undergoing surgical resection [2]. This pancreatic neoplasm occurs predominantly in young women with low-grade behavior [5]. Their malignant potential, however, is heterogenous and aggressive variants account for 15% of all cases [6].

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Obtaining an accurate diagnosis is of utmost importance as long-term survival has been reported with aggressive surgical resection even in patients with metastatic disease. These tumors differ significantly in behavior from the more common pancreatic ductal adenocarcinoma (PDAC). With this stark contrast in behavior, it is important to identify differences in presentation and survival between these two entities. Here, the aim was to investigate a nationwide database to describe the features and survival of SPTP in comparison with PDAC in a US population.

Methods

The study was designed as a retrospective review utilizing the Surveillance, Epidemiology, and End Results (SEER) database and thus was granted exemption from local Institutional Review Board review. The SEER database is a nationwide initiative coordinated by the National Cancer Institute and consists of data from 18 cancer registries. These data are representative of approximately 28% of the US population [7]. The data were obtained from the most recent iteration of the database, SEER Data 1973-2010, made available for use on April 24, 2013.

The time frame of the study was from 2001 to 2010. Adult patients with SPTP were identified by a query of the SEER database for ICD-0-3 code 8452.3. Data gathered on SPTP included demographics, year of diagnosis, tumor location within the pancreas, grade, staging information, surgical treatment, receipt of radiotherapy, and survival. Patients with PDAC during the same time period were identified by ICD-0-3 code 8140.3.

Univariate analyses were performed between patients with SPTP and PDAC using Chi-squared testing. Cox proportional hazards regression models were constructed to evaluate factors associated with survival amongst SPTP alone to include age group, race, gender, tumor location, and American Joint Commission on Cancer (AJCC) stage. The same model was then applied to all patients with SPTP and PDAC and adding pathologic diagnosis as a variable. Finally, patients who underwent surgical therapy exclusively were analyzed with the same model with the addition of surgical procedure as a variable. Kaplan-Meier survival analyses were performed to compare overall and cancer-specific 5-year survival between SPTP and PDAC. Significance was determined by $p < 0.05$. SEER*Stat 8.1.2 (National Cancer Institute, Bethesda, MD) was used to perform the case query and statistical analyses were performed using IBM SPSS 20.0 (IBM, Amherst, NY).

Results

A total of 107 patients with SPTP and 53,353 with PDAC were identified. Patients with SPTP were younger than those with PDAC as 80.4% were less than 55 years old (Table 1). There were a higher proportion of black and female patients with SPTP. PDAC occurred more commonly in the head of the pancreas while SPTP was most common in the pancreatic tail. SPTP tumors were smaller by the T stage and rarely

Table 1. Presentation characteristics.

Variable		SPTP	PDAC	p value
Age	18-34 years	46/107 (43.0%)	136/53353 (0.3%)	<0.001
	35-54 years	40/107 (37.4%)	6869/53353 (12.9%)	
	55-69 years	16/107 (15.0%)	19668/53353 (36.9%)	
	>70 years	5/107 (4.7%)	26680/53353 (50.0%)	
Ethnicity	Black	20/107 (18.7%)	6485/53214 (12.2%)	0.005
	White	74/107 (69.2%)	43205/53214 (81.2%)	
	Other	13 (12.1%)	3524/53214 (6.6%)	
Gender	Female	88/107 (82.2%)	25956/53353 (48.6%)	<0.001
	Male	19/107 (17.8%)	27397/53353 (51.4%)	
Tumor Location	Head	32/107 (29.9%)	27126/53353 (50.8%)	<0.001
	Body	9/107 (8.4%)	5975/53353 (11.2%)	
	Tail	50/107 (46.7%)	6300/53353 (11.8%)	
	Overlapping	8/107 (7.5%)	3821/53353 (7.2%)	
	Other	8/107 (7.5%)	10131/53353 (19.0%)	
T Stage	T1	7/94 (7.4%)	1490/38609 (3.9%)	<0.001
	T2	57/94 (60.6%)	10688/38609 (27.7%)	
	T3	26/94 (27.7%)	15874/38609 (41.1%)	
	T4	4/94 (4.3%)	10557/38609 (27.3%)	
N Stage	N0	91/100 (91.0%)	22852/37931 (60.2%)	<0.001
	N1	9/100 (9.0%)	15079/37931 (39.8%)	
AJCC Stage	IA	7/96 (7.3%)	557/47664 (1.2%)	<0.001
	IB	48/96 (50.0%)	2086/47664 (4.4%)	
	IIA	20/96 (20.8%)	4840/47664 (10.2%)	
	IIB	6/96 (6.3%)	5521/47664 (11.6%)	
	III	2/96 (2.1%)	6435/47664 (13.5%)	
	IV	13/96 (13.5%)	28225/47664 (59.2%)	
Surgical Treatment	PD[a]	24/105 (22.9%)	5240/52636 (10.0%)	<0.001
	DP[b]	40/105 (38.1%)	708 /52636 (1.3%)	
	TP[c]	13/105 (12.4%)	801/52636 (1.5%)	
	Local excision	6/105 (5.7%)	144/52636 (0.3%)	
	No surgery	22/105 (21.0%)	45743/52636 (86.9%)	
Radiation	Yes	4/105 (3.8%)	9526/52603 (18.1%)	<0.001
	No	101/105 (96.2%)	43077/52603 (81.9%)	

[a]PD=pancreaticoduodenectomy, [b]DP=distal pancreatectomy, [c]TP=total pancreatectomy

Table 2. Factors associated with mortality for SPTP.

Variables		HR (95% CI)[a]	p value
Age		——	0.063
Ethnicity		——	0.757
Gender	Female	1	——
	Male	4.5 (1.4-14.6)	0.012
Tumor Location		——	0.096
AJCC Stage		——	0.022
	I	1	——
	II	4.5 (0.8-24.7)	0.085
	III	16.7 (1.4-193.2)	0.025
	IV	10.6 (2.1-54.6)	0.005

SPTP=solid-pseudopapillary tumor of the pancreas, [a]Value = 1 indicates reference group

Table 3. Factors associated with mortality for all subjects.

Variable		HR (95% CI)[a]	p value
Age		——	<0.001
	18-34 years	1	——
	35-54 years	1.2 (1.0-1.5)	0.030
	55-69 years	1.4 (1.2-1.7)	<0.001
	>70 years	1.9 (1.6-2.3)	<0.001
Ethnicity		——	<0.001
	White	1	——
	Black	1.2 (1.1-1.2)	<0.001
	Other	0.96 (0.93-1.0)	0.048
Gender	Female	1	——
	Male	1.1 (1.0-1.1)	<0.001
Tumor Location		——	<0.001
	Head	1	——
	Body	1.0 (1.0 – 1.1)	0.127
	Tail	1.1 (1.09-1.16)	<0.001
	Overlapping	1.1 (1.06-1.14)	<0.001
	Other	1.2 (1.16-1.23)	<0.001
AJCC Stage		——	<0.001
	I	1	——
	II	1.1 (1.0-1.1)	0.006
	III	1.5 (1.4-1.6)	<0.001
	IV	2.7 (2.5-2.8)	<0.001
Pathology	SPTP[b]	1	——
	PDAC[c]	11.1 (6.4-19.1)	<0.001

[a]Value = 1 indicates reference group, [b]SPTP=solid-pseudopapillary tumor of the pancreas, [c]PDAC=pancreatic ductal adenocarcinoma

had any associated lymphadenopathy, with over half of patients presenting with AJCC stage I disease. In contrast, nearly 40% of PDAC cases had lymphadenopathy and 59.2% were AJCC stage IV at diagnosis. Most patients with SPTP underwent surgical treatment while only 13.1% of patients with PDAC were treated with surgery.

Table 4. Factors associated with mortality for subjects undergoing surgical treatment.

Variable		HR (95% CI)[a]	p value
Age		——	<0.001
	18-34 years	1	——
	35-54 years	1.0 (0.6-1.6)	0.875
	55-69 years	1.1 (0.6-1.8)	0.853
	>70 years	1.4 (0.8-2.3)	0.237
Ethnicity		——	0.002
	White	1	——
	Black	1.2 (1.1-1.3)	0.001
	Other	1.0 (0.9-1.1)	0.562
Gender	Female	1	——
	Male	1.1 (1.0-1.2)	0.001
Tumor Location		——	0.142
AJCC Stage		——	<0.001
	I	1	——
	II	1.8 (1.6-2.0)	<0.001
	III	2.7 (2.4-3.1)	<0.001
	IV	4.0 (3.5-4.6)	<0.001
Pathology	SPTP[b]	1	——
	PDAC[c]	21.3 (7.8-57.9)	<0.001
Surgical Treatment		——	<0.001
	PD[d]	1	——
	DP[e]	1.1 (1.0-1.2)	0.241
	TP[f]	1.2 (1.1-1.3)	<0.001
	Local Excision	1.6 (1.3-1.9)	<0.001
	Pancreatectomy, NOS	1.4 (1.2-1.6)	<0.001

[a]Value = 1 indicates reference group, [b]SPTP=solid-pseudopapillary tumor of the pancreas, [c]PDAC=pancreatic ductal adenocarcinoma, [d]PD=pancreaticoduodenectomy, [e]DP=distal pancreatectomy, [f]TP=total pancreatectomy

Among patients with SPTP, factors associated with poorer survival were male gender and higher AJCC stage (Table 2). For all patients, increasing age, black ethnicity, male gender, tumors in the tail or overlapping regions, and a more advanced AJCC stage were poor prognostic factors (Table 3). Patients with PDAC had an 11-fold increased risk of mortality. With subgroup analysis of only patients who underwent surgery, black ethnicity, male gender, and a more advanced AJCC stage remained factors associated with decreased survival (Table 4). Additionally, patients undergoing total pancreatectomy, local excision, or other pancreatectomy had decreased survival compared with pancreati-

Table 5. Survival of SPTP and PDAC.

Receptor Status	Histologic Subtype	5-Year Overall Survival	p value	5-Year Cancer-Specific Survival	p value
All	SPTP[a]	84.7% (76.7%-92.6%)	<0.001	88.9% (78.5%-94.4%)	<0.001
	PDAC[b]	2.8% (2.6%-3.0%)		3.8% (3.5%-4.0%)	
Surgical Patients	SPTP	92.7% (85.7%-99.9%)	<0.001	95.9% (90.0%-100%)	<0.001
	PDAC	13.5% (12.6%-14.5%)		16.7% (15.4%-17.9%)	

[a]SPTP=solid-pseudopapillary tumor of the pancreas, [b]PDAC=pancreatic ductal adenocarcinoma

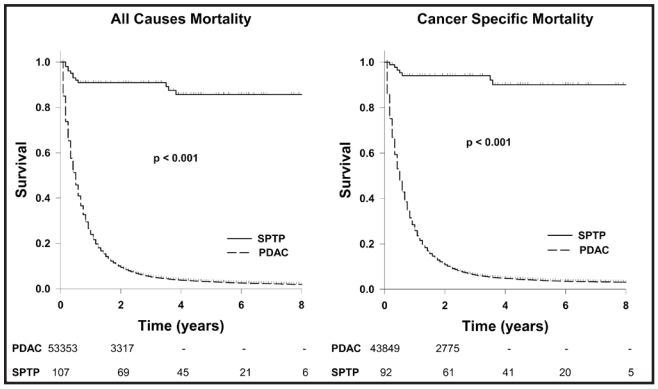

Figure 1. Survival for SPTP and PDAC – All patients.

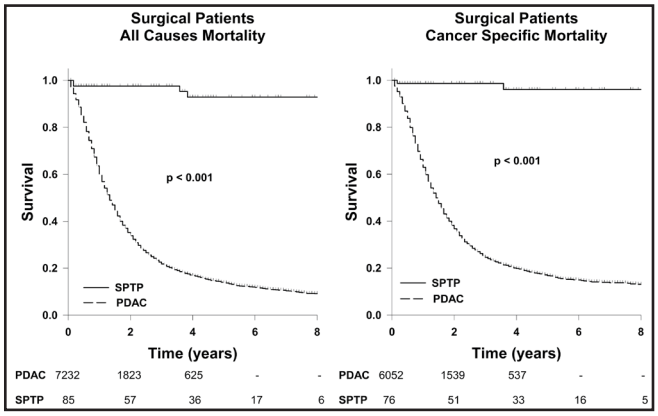

Figure 2. Survival for SPTP and PDAC – Surgical patients.

coduodenectomy. The survival risk conferred by PDAC compared with SPTP increased to 21-fold among surgical patients.

Five-year overall and cancer-specific survival for SPTP was 84.7% and 88.9%, respectively (Figure 1) (Table 5). In contrast, the same data for PDAC showed rates of 2.8% and 3.8%, respectively, over the same time period. For surgical patients, the 5-year overall and cancer-specific survivals improved to 92.7% and 95.9% for SPTP and 13.5% and 16.7% for PDAC, respectively.

Discussion

Tumors of the pancreas are often a diagnostic dilemma. Solid lesions are most commonly PDAC, portending a dismal prognosis. On the other hand, cystic lesions have a widely differential diagnosis, particularly when a solid component is present. SPTP is a rare histologic variant among these lesions. This neoplasm has been described in case series from select high-volume institutions.

The current study utilized the SEER database for a population-based analysis of patients with SPTP. The demographics of patients with SPTP varied greatly from PDAC. Patients with SPTP were much younger than those with PDAC. This is consistent with historical literature on the matter as SPTP has even been described in pediatric populations [8]. Conversely, PDAC was found to be exceedingly rare in patients younger than age 35.

There were a greater percentage of non-Caucasian patients with SPTP, though ethnicity did not impact survival. When analyzing all patients, black ethnicity was an independent predictor of diminished survival and "other" race designation was associated with improved survival when compared to white patients. The decreased survival in black patients remained when analyzing those who underwent surgery. This survival disparity has been investigated in previous studies and may be associated with reduced referral to high-volume centers [9,10]. It should continue to be a focus of quality improvement in pancreatic cancer.

SPTP occurs most commonly in female patients. Previous studies have described the proportion of female patients affected to be 90% [11]. There was a higher proportion of males in the current study cohort than previously described. A novel finding here was that male gender was associated with a greater than 4-fold risk of mortality. Through subgroup analysis, male patients were more likely to present with stage IV disease and less likely to undergo surgery than their female counterparts. It is unclear why males presented

with apparently more aggressive variants than females but this suggests there may be a hormonal impact. Future investigation of this phenomenon is warranted.

Another key feature of SPTP is the location within the pancreas. Nearly half of SPTPs were located in the tail. In contrast, PDAC was more likely to be found in the head of the pancreas. The differential diagnosis for a pancreatic tumor in the tail of the pancreas in a young female must include SPTP.

The most significant distinguishing feature of SPTP from PDAC is the stage at presentation. Early stage disease (stage I or II) was found in 84.4% of patients with SPTP compared with 27.4% with PDAC. Concordantly, 79.0% of patients with SPTP underwent surgery compared to only 13.1% with PDAC. It is unclear why less than half of patients with early stage PDAC underwent surgical treatment. A study by Bilimoria et al. found that only 28.6% of patients with clinical stage I PDAC receive surgical treatment, explained in part by a combination of patient and hospital factors [12]. What may be observed here is similar causative trends in these data. Overall, patients with SPTP were more likely to undergo more aggressive surgery (total pancreatectomy 12.4% vs. 1.5% in PDAC). However, these findings become similar in PDAC when investigating only patients who underwent surgery (total pancreatectomy in 11.6%). Additionally, adjuvant radiotherapy was rare in cases of SPTP versus PDAC.

PDAC is the fourth leading cause of cancer deaths in the US despite being only the eleventh most common in incidence [13]. This study reinforced the lethal nature of PDAC with 5-year overall and cancer-specific survival of 2.8% and 3.8%, respectively. This improved marginally among patients treated with surgery. On the contrary, SPTP was associated with excellent survival outcomes. This was particularly noteworthy in patients undergoing surgery, with 5-year cancer-specific survival of 95.9%. Aggressive surgical resection should continue to be the standard of care in SPTP in light of these findings.

The main limitations of this study are related to the SEER database. The number of patients available for study was less than desired. This underscores the rare nature of the disease. As well, other factors that could contribute to outcomes, such as co-morbid conditions, were not investigated. The impact of tumor markers, such as CA19-9 or carcinoembryonic antigens, was outside the scope of the database, as well. If there is reasonable uncertainty regarding the diagnosis of a pancreatic neoplasm, endoscopic ultrasound with fine needle aspiration may be useful in additional characterization of these lesions.

In conclusion, SPTP of the tumor is a rare pancreatic neoplasm found most commonly in the tail of the pancreas in young females. Once a diagnosis of SPTP has been made, aggressive surgical resection can lead to very favorable survival outcomes.

Conflict of interest statement

The authors have no conflicts of interest to declare.

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