

# A Single Institution Experience with Solid Pseudopapillary Neoplasm of the Pancreas: Clinicopathological Correlation and Review of the Literature

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**Introduction:** SPN is a rare, low-grade malignancy that accounts for 1-3% of all pancreatic neoplasms and tends to affect young females. It can be asymptomatic or present with abdominal pain, and surgical resection is the only curative treatment.

**Methods:** A retrospective study was conducted on patients with biopsy proven Solid Pseudopapillary Neoplasm (SPN) of the pancreas between January 2016 and June 2021. The study included 14 cases, including 7 resection specimens and 7 biopsies, and was conducted at a tertiary referral center in Pakistan

**Results:** All 14 patients were female and ranged in age from 15 to 48 years old, with a mean age of 24. The most common symptom was abdominal pain, and the head of the pancreas was the most common location of the tumor. Tumor size ranged from 5 cm to 18 cm, and one patient had lymph node involvement and two patients had hepatic metastasis. Most patients received surgical treatment, and follow-up information was available for 8 out of the 14 patients, who were all alive with no recurrence or metastasis.

**Conclusion:** Due to its rarity, non-specific clinical presentation, and imaging findings, it can be challenging to diagnose. There is a lack of data on SPN from South Asia, so this study provides valuable insights into the occurrence and treatment of SPN in this region.

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## Introduction

Solid Pseudopapillary Neoplasm (SPN) is a rare low-grade neoplasm of the pancreas. World Health Organization (WHO) Classification of Digestive System Tumors describes this neoplasm as having poorly cohesive epithelial cells that form solid and pseudopapillary structures and lack a specific pancreatic epithelial differentiation [1]. SPN accounts for 1-3% of all pancreatic neoplasms but the incidence is rising due to increased use of cross-sectional imaging and better understanding of the tumor [2]. It was first described by Franz in 1959 as pancreatic papillary cystic tumors and since then has been known by many pseudonyms but was classified as solid pseudopapillary neoplasm by the World Health Organization in 2010 [3]. These tumors have a predilection for young females [4-6] and can have a wide age range from 2 to 85 years [5] but primarily affects them in their second and third decades of life with a mean age of 22 years [7]. However, there is literature reporting its occurrence in men at 3.9% and 6.6% [5, 8].

SPN follows an indolent course and can either be asymptomatic or present with abdominal pain, and less commonly as nausea, vomiting and weight loss. Just as its clinical presentation is variable, the imaging features of SPNs are also nonspecific. It is oftentimes seen as a large, solitary, mostly well-circumscribed and well demarcated lesion with either cystic, solid, or mixed component. Histopathology, immunohistochemistry (IHC) and cytological evaluation are the mainstay of diagnosis; and for differentiating it from other tumors of the pancreas [9]. The common features on IHC include positivity for progesterone receptor, vimentin,  $\alpha$ -1-antitrypsin, CD10, and  $\beta$ -catenin while having rare or no atypia, mitosis, and Ki.67 [10, 11]. Histologically, these tumors show solid areas alternating with a pseudopapillary pattern with cystic spaces which are the results of degenerative changes occurring in the solid neoplasm [12]. According to some studies, SPN has a predilection for head and tail of the pancreas but can occur anywhere in the pancreas [13, 14]. The mean tumor size ranged from 4.7 to 9.5 cm based on a number of studies [15, 16]. Surgical resection is the only curative treatment and has a very good prognosis with a five-year survival rate of 94-97% [17]. Pancreaticoduodenectomy, distal pancreatectomy and enucleation are the commonly performed surgical procedures [11, 18]. Recurrence and metastasis have been reported in small percentage of cases (5-15%), especially in young patients with larger tumors and the most common region being peritoneum and the liver [19-22]. It has been reported that even with local invasion and unresectable metastasis, prognosis is favorable and long-term survival is achievable [11, 23].

Due to its rarity, nonspecific clinical presentation, and inconsistent imaging findings, SPN can be difficult to diagnose. There is a lack of data on SPN from South Asia, so our research aims to present cases from a developing country in this region. This is important for physicians and patients in Pakistan, as it provides insight into the behavior of this tumor in this population and adds to the two previous reports that have described cases from this region.

## Materials and Methods

A retrospective study was performed on all patients with biopsy proven solid pseudopapillary neoplasm of the pancreas (SPN) at Shifa International Hospital, Islamabad, Pakistan between January 2016 to June 2021. All patients were identified using a prospectively maintained institutional registry. These included 7 resection specimens and 7 biopsies. A database of the characteristics of these patients was developed and included patient demographics (age, gender, symptoms), tumor characteristics (size, location, stage, nodal involvement, metastasis), treatment (surgery, chemotherapy, radiotherapy, surveillance), follow-up status, histopathological findings, immunohistochemical findings and imaging findings. Data was derived from medical and surgical records, radiological investigations, and surgical pathology. Preoperative ultrasound (US) was performed in four patients, computed tomography (CT) in nine patients, magnetic resonance imaging (MRI) in one patient, ultrasound guided fine needle aspiration cytology (EUS-FNAC) in four patients and fine needle biopsy (EUS-FNB) in three patients. For patients who underwent resection, the date of their last follow up and latest living status was noted. The study was approved by the Institutional Review Board for Human Research and Ethics Committee.

## Results

Over a period of five years from January 2016 to June 2021, 14 cases of biopsy-proven SPN were identified at Shifa International Hospital. Of these, 5 cases were referred from outside hospitals for a second opinion. All the patients were females (100%). Mean age was 24 years (15-48).

The most common presenting symptom was abdominal pain. Other symptoms included nausea, vomiting and weight loss. 10 patients (71%) presented with abdominal pain mostly centered at epigastrium, 3 (21%) patients had additional symptoms of nausea and vomiting, 2 (12%) patients reported weight loss and 2 (12%) patients had incidental diagnosis upon imaging. The head of the pancreas was the most common location of the tumor in our patients. In 8 patients (57%), the

tumor was in the head, in 3 patients (21%) the tumor was in the tail and in 2 patients (21%) the tumor involved both the body and tail of the pancreas. Mean tumor size was 7 cm (5-18). 1 patient had lymph node involvement and 2 patients had hepatic metastasis. In two patients who had hepatic metastasis, location of primary tumor was tail in the first and tail and body in the second patient (Table 1).

Patient No.	Age/Gender	Presentation	Tumor location	Size (cm)	NodalInvasion	DistantMetastasis	Surgery
Patient 1	21/F	Epigastric Pain, vomiting	Tail	8.5 x 7.0 x 6.0	No	No	Pancreaticoduodenectomy + extended lymphadenectomy
Patient 2	15/F	Abdominal pain	Head	7.0 x 7.0 x 4.0	No	No	Pancreaticoduodenectomy
Patient 3	16/F	Epigastric pain, weight loss	Head	6.0 x 3.5 x 3.5	No	No	Pancreaticoduodenectomy
Patient 4	25/F	Right side abdominal pain, nausea, vomiting	Head	10 x 9.0 x 7.0	No	No	Pancreaticoduodenectomy
Patient 5	15/F	Epigastric pain, weightloss, nausea, vomiting	Head	5.0 x 3.5 x 3.0	No	No	Pancreaticoduodenectomy
Patient 6	48/F	Incidental	Head	6.5 x 6.1 x 5.4	No	No	Information not available
Patient 7	32/F	Abdominal pain	Body + Tail	8.5 x 7.0 x 6.5	Yes (2/7) Nodes involved	Hepatic Metastasis	Distal Pancreatectomy + Splenectomy + Liverwedge resection
Patient 8	26/F	Abdominal pain	Surgery	6.0 x 6.0	No	No	Distal pancreatectomy + Splenectomy
Patient 9	15/F	Abdominal pain	Head	6.0 x 4.5 x 4.5	No	No	Pancreaticoduodenectomy
Patient 10	21/F	Right side abdominal pain	Tail + Body	18.0 x 15.0 x 8.2	No	No	Distal pancreatectomy + Splenectomy
Patient 11	25/F	Epigastric pain	Head	5.0 x 5.0	No	No	Information not available
Patient 12	26/F	Incidental	-	-	-	-	Information not available
Patient 13	35/F	Abdominal pain	Tail	-	-	Hepatic Metastasis	Information not available
Patient 14	22/F	Epigastric pain	Head	-	-	-	Information not available

**Table 1. Patient and Tumor Characteristics.**

On CT, the tumor appeared well circumscribed, well defined, and heterogenous encasing and displacing the nearby vasculature. The mass appeared solid as well as cystic and oftentimes had clustered internal calcifications (Figure 1).

**Figure 1. Findings on a CT Scan. Picture “A” shows multiple liver lesions enhancing on arterial phase consistent with metastasis. A large metastatic liver mass is shown by a red arrow. Picture “B” shows a large lobulated heterogeneously enhancing mass in body and tail of pancreas with calcifications, it is encasing and obstructing**

the splenic vein and compressing the adjacent proximal small bowel as indicated by a red arrow.

4 patients underwent EUS-FNAC and 3 underwent EUS-FNB. 19G and 22G needles were used to perform FNAC and FNB. EUS guided FNAC or FNB diagnosed all 7 patients who underwent an EUS.

Histologically, most of the tumor mass had a pseudopapillary architecture (71%) with areas of solid as well as cystic degeneration (Table 2).

Histological Features	No of cases present	Percentage (%)
Pseudopapillary architecture	10	71
Solid areas	10	71
Fibrosis	1	7
Hemorrhage	7	50
Necrosis	2	14
Cystic degeneration	4	29
Hyalinization	6	43
Cholesterol clefts	1	7
Mitotic activity	2	14
Eosinophilic cytoplasm	6	43
Calcification	1	7
Nuclear grooves	5	36
Infarction	2	14
Hemosiderin laden macrophages	3	21
Atypical cells	1	7

**Table 2. Histological Features (n=14).**

In two cases, rare mitotic activity was noted and in one case atypical cells were found with high nuclear to cytoplasmic ratio. Changes of hyalinization were noted in 6 cases, fibrosis in one, hemosiderin laden macrophages in 3, cholesterol clefts and calcifications were seen in one case. The immunohistochemical findings are summarized in (Table 3).

Immunohistochemical Features	No of cases who were positive (%)	No of cases who were negative (%)
Beta-Catenin	13 (93)	-
Progesterone Receptor (PR)	6 (43)	-
CD56	5 (36)	-
CD10	2 (14)	-
Synaptophysin	5 (36)	3 (21)
Chromogranin	-	9 (64)
SOX-11	5 (36)	-
Cyclin D1	1 (7)	-
P16	1 (7)	-
CAM 5.1	1 (7)	-

**Table 3. Immunohistochemical Features (n=14).**

9 (64%) out of the 14 patients had undergone surgery. Six patients had pancreaticoduodenectomy (Whipple procedure), three patients had distal pancreatectomy with additional splenectomy, and one patient with liver metastasis also had liver wedge resection in addition to distal pancreatectomy and splenectomy. Of the nine patients who had surgery, eight were alive with no reported recurrence during the follow-up period, which ranged from 4 weeks to 117 weeks. One patient who had surgery was lost to follow-up. In addition, five patients referred from outside hospitals had not undergone surgery at the time of their biopsy and were also lost to follow-up

(Table 4).

Follow-up Status in Patients who underwent Resection (n=9)					
Sr No	Age at Resection	Surgery(Yes/No)	Year of Surgery	Tumor Stage	Follow-up Status (weeks)
1	21	Yes	2018	pT4N0	Alive and well 21 weeks after resection
2	15	Yes	2021	pT3N0	Alive and well 4 weeks after resection
3	16	Yes	2018	pT4N0	Alive and well 117 weeks after resection
4	25	Yes	2019	pT3N0	Alive and well 26 weeks after resection
5	15	Yes	2020	pT3N0	Alive and well 34 weeks after resection
6	32	Yes	2020	pT3N1M1	Alive and well 52 weeks after resection
7	26	Yes	2019	-	Alive and well 82 weeks after resection
8	15	Yes	2019	-	Alive and well 4 weeks after resection
9	21	Yes	2021	pT3N0	No follow-up information available
Patients in whom information regarding Resection and Follow-up was not available (n=5)					
	Age at Diagnosis	Surgery	Year of Diagnosis	Tumor Stage	Follow-up information
10	48	Not known	2018	-	No further information available
11	25	Not known	2021	-	No further information available
12	22	Not known	2020	-	No further information available
13	35	Not known	2020	-	No further information available
14	26	Not known	2019	-	No further information available

**Table 4. Follow-up Status in Patients.**

None of the patients in our cohort received chemotherapy or radiotherapy.

## Discussion

SPN is a low-grade pancreatic neoplasm that accounts for 1-2% of all exocrine pancreatic tumors and less than 10% of the cystic tumors of the pancreas [24]. It predominantly affects young females in their second and third decades of life with male to female ratio of 1:5.3- 9.78 [5]. There is now literature reporting its occurrence in men and in children [8]. Another study found similar clinicopathological correlation upon comparing men and the pediatric population, however better survival outcomes were reported in children [25]. Wu (2020) reported a peak incidence at approximately 64 years old with a poorer prognosis in men. Our study consisted of a female population with an age range of 15 to 48 years and a mean age of 24 years [26].

SPN has a nonspecific presentation with the most common symptom being abdominal pain, in our study the pain was mostly centered at the epigastrium. Less frequently SPN can also present with weight loss, nausea, vomiting, an enlarging mass, or compression symptoms caused by the growing tumor. SPN can also be completely asymptomatic and oftentimes discovered incidentally on the abdominal imaging. Similarly, the preoperative tumor markers (AFP, CEA, CA 19-9 and CA 125) are also normal [27]. Although SPN has been reported from all parts of the pancreas, in our study head was the most common location. On a cut surface SPN may show areas of cystic changes, extensive necrosis and hemorrhage with tumor being large and well demarcated [28]. Invasion of locoregional lymph nodes and adjacent structures is rare. In our study 2 patients had duodenal wall invasion and 2 patients had adjacent lymphovascular invasion.

CT is the most frequently performed imaging modality [5, 29]. In our study CT findings showed large lobulated, well-defined lesions displacing and compressing the adjacent structures as shown in (Figure 1). It has been reported in the literature that capsule and intramural hemorrhage are more specific characteristics of SPN; and hence, CT and MRI are superior to US in diagnosing SPNs [30]. On US, the tumor typically appears as a homogeneous hypoechoic mass which is either solid, cystic, or mixed and sometimes can only be solid looking with calcifications and internal septations [31, 32]. SPN has uncertain cellular differentiation. Mehta (2010) [33] studied cytomorphological features of SPN on FNAC and found that the smears demonstrated hypercellularity along with abundant papillary fragments, discohesive and monomorphic tumor cells with foamy macrophages in the background. FNAC performed in our patients' demonstrated smears which were moderately cellular with nests of tumor cells arranged in pseudopapillary pattern.

Histologic patterns on large biopsy resected specimens demonstrated features of a pseudopapillary architecture with areas of solid as well as cystic degeneration and tumor cells having eosinophilic cytoplasm with moderate cellularity, nuclear grooves, and areas of hemorrhage (Figure 2, Figure 3).

**Figure 2. Features on Histopathology and Immunohistochemistry; A, Liver tissue showing infiltration by SPN (H/E, original magnification 10x); B, Synaptophysin immunostaining in the metastatic tumor (IHC, original magnification 10x); C, Section from the primary tumor showing pseudopapillary structures (H/E, original magnification 10x); D, Strong nuclear B-catenin immunostaining in the tumor cell (IHC, original magnification 10x).**

**Figure 3. Features on Histopathology. A, Classic morphology of SPN with pseudo papillae showing fibrovascular cores (H/E, original magnification 10x); B & C, SPN showing perineural (PNI) and lymphovascular invasion (LVI) respectively (H/e, original magnification 20x); D, Section from the EUS biopsy showing solid nests of tumor cells (H/E, original magnification 20x).**

IHC is key in confirming the diagnosis of SPN. IHC markers used to make a diagnosis of SPN

include  $\beta$ -catenin, Progesterone receptor (PR), CD56, vimentin, CD10, CD99, alpha-1 antitrypsin and synaptophysin [15, 34]. Progesterone receptor is positive in most cases as was reported too, in which it was performed and positive in all 6 cases, however its negative staining is negatively associated which indicates worse prognosis, poor disease-free survival (DFS), poor disease specific survival (DSS) and is predictive of poor prognosis [34, 35].

SPN of the pancreas is treated with surgery, the only curative option and mainstay of the treatment with excellent prognosis and a 5-year survival rate of up to 97% [36-38]. Resection with microscopic clear margins is desired [39, 40]. The type of surgical procedure depends on tumor size and location. Tumors of the head of the pancreas are usually resected through Pancreaticoduodenectomy (Whipple) [41]. 5 patients in our series who had SPN of the head of the pancreas were treated with Whipple procedure. Tumors of the tail and body are treated with distal pancreatectomy with or without splenectomy depending on the involvement of the splenic vasculature and hilum. For the tumors located in the neck of the pancreas, it is recommended to perform central pancreatectomy with distal pancreaticojejunostomy or pancreaticogastrostomy [42, 43]. For small tumors located distant from the pancreatic duct, enucleation can be done, however, it is associated with an elevated risk of pancreatic fistula [42]. Although SPN is generally a low-grade malignant tumor with a low risk of becoming more aggressive, approximately 10-15% of cases have the potential to metastasize. The role of lymphadenectomy is still unclear, however, if locoregional or distant nodes are involved intraoperatively, these should be removed. Metastasectomy of the liver can be performed at the time of primary resection or at the time of recurrence [39]. The prognosis of SPN is generally good following resection and aggressive therapy [44]. It has been reported that even with metastasis and recurrence after surgical resection, the prognosis is good as was in our patient who had hepatic metastasis. Following treatment; annual surveillance has been suggested for at least 5 years [45]. SPN can mimic any solid or cystic neoplasms of the pancreas in young females. Differentials include pseudocyst, serous cystadenoma, mucinous cystic neoplasm, pancreatic neuroendocrine tumor [46].

WHO-defined criteria for classification of solid pseudopapillary carcinoma includes angioinvasion, perineural invasion, deep infiltration into the surrounding tissue and metastasis. Wang (2021) [47] evaluated the predictive value of the WHO criteria for malignant potential of SPNs from the perspective of surgical prognosis and found out that "microscopic infiltrative growth" correlated significantly with the WHO criteria for malignancy. Another study found the adverse prognostic factors to be male gender, positive lymph nodes, R1 margins and lymphovascular invasion [29]. The role of Ki-67 has been uncertain and controversial in predicting the malignant potential of SPN [48]. Some studies correlate a Ki-67 of more than 5% to be associated with tumor recurrence while other studies report expression of Ki-67 along with histological features, such as extensive necrosis, nuclear atypia, and high mitotic rate to be associated with aggressive behavior [49]. In our study only one patient had a Ki-67 of 5-10% with locoregional lymph node involvement and liver metastasis who underwent distal pancreatectomy with splenectomy and liver wedge resection, he reported no recurrence on follow up 1 year later.

Surgical resection is the only curative option for SPN of the pancreas, however in the cases involving distant spread of the tumor, resection is not performed, and other options are considered including therapeutic interventions. However, the role of radiotherapy and chemotherapy is not well defined in the literature. Some studies have reported adjuvant chemotherapy in unresectable cases with superior results and others have reported SPN to be responsive to radiotherapy in unresectable tumors [50, 51]. None of the patients in our cohort received adjuvant or neoadjuvant chemotherapy or radiotherapy. Neoadjuvant chemoradiation with 5- fluorouracil and gemcitabine have been reported for preoperative downstaging [52]. Similarly, Hah (2007) [53] reported a preoperative chemotherapeutic treatment with cisplatin, ifosfamide, etoposide, and vincristine followed by intraoperative radiofrequency ablation of metastatic liver lesion and complete surgical resection of the primary tumor, to be effective. Multiple and extensive liver metastasis can also be attempted to be treated by trans arterial chemoembolization (TACE) with gemcitabine and lipoidal followed by gelfoam embolization as reported in a study by Prasad et al., (2015) [54].

There are several limitations to our study that should be acknowledged. Firstly, we were unable to follow up on the unresected cases due to the retrospective nature of our study. Another limitation is the small sample size of our study, and finally, we had a shorter follow-up period for resected cases, particularly those diagnosed in 2020 and later.

SPN of the pancreas is a rare tumor entity with low malignant potential that typically affects young women and has favorable prognosis even in the presence of distant metastasis. It can pose a significant diagnostic dilemma and pre-operative EUS FNA/B can help in confirming pre-operative diagnosis.

#### *Author's Contribution*

AZK was involved in conception and design of the study, drafting the manuscript, data collection, interpretation and revising the manuscript. HMK was involved in conception and design of the study and revising the manuscript. ZA was involved in revising the manuscript. HSS was involved in data collection and revising the manuscript. ASK, was involved in revising and critically reviewing the manuscript. MA was involved in conception and design of the study and revising the manuscript.

## References

## References

1. Nagtegaal ID, Odze RD, Klimstra D, Paradis V, Rugge M, Schirmacher P, Washington KM, Carneiro F, Cree IA. The 2019 WHO classification of tumours of the digestive system. *Histopathology*. 2020; 76(2)[DOI](#)
2. Law JK, Ahmed A, Singh VK, Akshintala VS, Olson MT, Raman SP, Ali SZ, et al. A systematic review of solid-pseudopapillary neoplasms: are these rare lesions?. *Pancreas*. 2014; 43(3)[DOI](#)
3. Bosman FT, Carneiro F, Hruban RH, Theise ND. Bosman FT. WHO classification of tumours of the digestive system: WHO Classification of Tumours, volume 3. IARC Press, Lyon, France. 2010.
4. Estrella JS, Li L, Rashid A, Wang H, Katz MH, Fleming JB, Abbruzzese JL, Wang. Solid pseudopapillary neoplasm of the pancreas: clinicopathologic and survival analyses of 64 cases from a single institution. *The American Journal of Surgical Pathology*. 2014; 38(2)[DOI](#)
5. Papavramidis T, Papavramidis S. Solid pseudopapillary tumors of the pancreas: review of 718 patients reported in English literature. *Journal of the American College of Surgeons*. 2005; 200(6)[DOI](#)
6. Hruban RH, Pitman MS, Klimstra DS. Armed Forces Institute of Pathology. In Tumors of the Pancreas, AFIP Atlas of Tumor Pathology Fourth Series Fascicle 6. 2007.
7. Yan SX, Adair CF, Balani J, Mansour JC, Gokaslan ST. Solid pseudopapillary neoplasm collides with a well-differentiated pancreatic endocrine neoplasm in an adult man: case report and review of histogenesis. *American journal of clinical pathology*. 2015; 143(2)[DOI](#)
8. Lam KY, Lo CY, Fan ST. Pancreatic solid-cystic-papillary tumor: clinicopathologic features in eight patients from Hong Kong and review of the literature. *World Journal of Surgery*. 1999; 23(10)[DOI](#)
9. Chowdhury MM, Ullah AA, Karim R, Farmidi AA, Mohammed S, Sobhan SA, Ahmed A, Mahmud R, Pradhan R, Chowdhury P. Solid Pseudopapillary Tumor of the Pancreas: A Case Report. *Mymensingh medical journal: MMJ*. 2019; 28(2)
10. Ohara Y, Oda T, Hashimoto S, Akashi Y, Miyamoto R, Enomoto T, Satomi K, Morishita Y, Ohkohchi N. Pancreatic neuroendocrine tumor and solid-pseudopapillary neoplasm: Key immunohistochemical profiles for differential diagnosis. *World journal of gastroenterology*. 2016; 22(38)[DOI](#)
11. Ud Din N, Arshad H, Ahmad Z. Solid pseudopapillary neoplasm of the pancreas. A



- clinicopathologic study of 25 cases from Pakistan and review of Literature. *Annals of Diagnostic Pathology*. 2014; 18(6)[DOI](#)
12. Santini D, Poli F, Lega S. Solid-papillary tumors of the pancreas: histopathology. *JOP: Journal of the pancreas*. 2006; 7(1)
  13. Wang P, Wei J, Wu J, Xu W, Chen Q, Gao W, Jiang K, Miao Y. Diagnosis and treatment of solid-pseudopapillary tumors of the pancreas: A single institution experience with 97 cases. *Pancreatology: official journal of the International Association of Pancreatology (IAP) ... [et al.]*. 2018; 18(4)[DOI](#)
  14. Dai G, Huang L, Du Y, Yang L, Yu P. Solid pseudopapillary neoplasms of the pancreas: clinical analysis of 45 cases. *International Journal of Clinical and Experimental Pathology*. 2015; 8(9)
  15. Zaladni A, Kis-Orha V. Solid-pseudopapillary Neoplasms of the Pancreas is still an Enigma: a Clinicopathological Review. *Pathology oncology research : POR*. 2020; 26(2)[DOI](#)
  16. Dubova EA, Podgornova MN, Schegolev AI. Expression of adhesion molecules and cyclin d1 in cells of solid-pseudopapillary tumors of the pancreas. *Bulletin of Experimental Biology and Medicine*. 2009; 148(6)[DOI](#)
  17. Reddy S, Cameron JL, Scudiere J, Hruban RH, Fishman EK, Ahuja N, Pawlik TM, Edil BH, Schulick RD, Wolfgang CL. Surgical management of solid-pseudopapillary neoplasms of the pancreas (Franz or Hamoudi tumors): a large single-institutional series. *Journal of the American College of Surgeons*. 2009; 208(5)[DOI](#)
  18. Jutric Z, Rozenfeld Y, Grendar J, Hammill CW, Cassera MA, Newell PH, Hansen PD, Wolf RF. Analysis of 340 Patients with Solid Pseudopapillary Tumors of the Pancreas: A Closer Look at Patients with Metastatic Disease. *Annals of Surgical Oncology*. 2017; 24(7)[DOI](#)
  19. Butte JM, Brennan MF, Gönen M, Tang LH, D'Angelica MI, Fong Y, Dematteo RP, Jarnagin WR, Allen PJ. Solid pseudopapillary tumors of the pancreas. Clinical features, surgical outcomes, and long-term survival in 45 consecutive patients from a single center. *Journal of Gastrointestinal Surgery: Official Journal of the Society for Surgery of the Alimentary Tract*. 2011; 15(2)[DOI](#)
  20. Lee SE, Jang J, Hwang DW, Park K, Kim S. Clinical features and outcome of solid pseudopapillary neoplasm: differences between adults and children. *Archives of Surgery (Chicago, Ill.: 1960)*. 2008; 143(12)[DOI](#)
  21. Nishihara K, Nagoshi M, Tsuneyoshi M, Yamaguchi K, Hayashi I. Papillary cystic tumors of the pancreas. Assessment of their malignant potential. *Cancer*. 1993; 71(1)[DOI](#)
  22. Zinner MJ, Shurbaji MS, Cameron JL. Solid and papillary epithelial neoplasms of the pancreas. *Surgery*. 1990; 108(3)
  23. Yu P, Hu Z, Wang X, Guo J, Cheng X, Zhang Y, Xu QI. Solid pseudopapillary tumor of the pancreas: A review of 553 cases in Chinese literature. *World Journal of Gastroenterology : WJG*. 2010; 16(10)[DOI](#)
  24. Yao J, Song H. A Review of Clinicopathological Characteristics and Treatment of Solid Pseudopapillary Tumor of the Pancreas with 2450 Cases in Chinese Population. *BioMed research international*. 2020; 2020[DOI](#)
  25. Waters AM, Russell RT, Maizlin II, Beierle EA. Comparison of Pediatric and Adult Solid Pseudopapillary Neoplasms of the Pancreas. *The Journal of Surgical Research*. 2019; 242[DOI](#)
  26. Wu J, Mao Y, Jiang Y, Song Y, Yu P, Sun S, Li S. Sex differences in solid pseudopapillary neoplasm of the pancreas: A population-based study. *Cancer Medicine*. 2020; 9(16)[DOI](#)
  27. Yagci A, Yakan S, Coskun A, Erkan N, Yıldırım M, Yalcın E, Postacı H. Diagnosis and treatment of solid pseudopapillary tumor of the pancreas: experience of one single institution from Turkey. *World journal of surgical oncology*. 2013; 11[DOI](#)
  28. Din NU, Rahim S, Abdul-Ghaffar J, Ahmed A, Ahmad Z. Clinicopathological and immunohistochemical study of 29 cases of solid-pseudopapillary neoplasms of the pancreas in patients under 20 years of age along with detailed review of literature. *Diagnostic Pathology*. 2020; 15(1)[DOI](#)
  29. Cruz MAA, Moutinho-Ribeiro P, Costa-Moreira P, Macedo G. Solid Pseudopapillary Neoplasm of the Pancreas: Unfolding an Intriguing Condition. *GE Portuguese Journal of*

- Gastroenterology*. 2021; 29(3)[DOI](#)
30. Choi J, Kim M, Kim JH, Kim SH, Lim JS, Oh YT, Chung J, Yoo HS, Lee JT, Kim KW. Solid pseudopapillary tumor of the pancreas: typical and atypical manifestations. *AJR. American journal of roentgenology*. 2006; 187(2)[DOI](#)
  31. Coleman KM, Doherty MC, Bigler SA. Solid-pseudopapillary tumor of the pancreas. *Radiographics: A Review Publication of the Radiological Society of North America, Inc*. 2003; 23(6)[DOI](#)
  32. Lee Dh, Yi Bh, Lim Jw, Ko Yt. Sonographic findings of solid and papillary epithelial neoplasm of the pancreas. *Journal of ultrasound in medicine : official journal of the American Institute of Ultrasound in Medicine*. 2001; 20(11)[DOI](#)
  33. Mehta N, Modi L, Patel T, Shah M. Study of cytomorphology of solid pseudopapillary tumor of pancreas and its differential diagnosis. *Journal of cytology / Indian Academy of Cytologists*. 2010; 27[DOI](#)
  34. Ersen A, Agalar AA, Ozer E, Agalar C, Unek T, Egeli T, Ozbilgin M, Astarcioglu I, Olguner M, Obuz F, Sagol O. Solid-Pseudopapillary neoplasm of the pancreas: A clinicopathological review of 20 cases including rare examples. *Pathology, Research and Practice*. 2016; 212(11)[DOI](#)
  35. Jiang Y, Xie J, Wang B, Mu Y, Liu P. TFE3 is a diagnostic marker for solid pseudopapillary neoplasms of the pancreas. *Human Pathology*. 2018; 81[DOI](#)
  36. Xu Y, Zhao G, Pu N, Nuerxiati A, Ji Y, Zhang L, Rong Y, Lou W, Wang D, Kuang T, Xu X, Wu W. One Hundred Twenty-One Resected Solid Pseudopapillary Tumors of the Pancreas: An 8-Year Single-Institution Experience at Zhongshan Hospital, Shanghai, China. *Pancreas*. 2017; 46(8)[DOI](#)
  37. Yu P, Cheng X, Du Y, Yang L, Xu Z, Yin W, Zhong Z, Wang X, Xu H, Hu C. Solid Pseudopapillary Neoplasms of the Pancreas: a 19-Year Multicenter Experience in China. *Journal of Gastrointestinal Surgery: Official Journal of the Society for Surgery of the Alimentary Tract*. 2015; 19(8)[DOI](#)
  38. Hanada K, Kurihara K, Itoi T, Katanuma A, Sasaki T, Hara K, Nakamura M, et al. Clinical and Pathological Features of Solid Pseudopapillary Neoplasms of the Pancreas: A Nationwide Multicenter Study in Japan. *Pancreas*. 2018; 47(8)[DOI](#)
  39. Lanke G, Ali FS, Lee JH. Clinical update on the management of pseudopapillary tumor of pancreas. *World Journal of Gastrointestinal Endoscopy*. 2018; 10(9)[DOI](#)
  40. Romics L, Oláh A, Belágyi T, Hajdú N, Gyurus P, Ruzinkó V. Solid pseudopapillary neoplasm of the pancreas--proposed algorithms for diagnosis and surgical treatment. *Langenbeck's Archives of Surgery*. 2010; 395(6)[DOI](#)
  41. Grace PA, Pitt HA, Longmire WP. Pylorus preserving pancreatoduodenectomy: an overview. *The British Journal of Surgery*. 1990; 77(9)[DOI](#)
  42. Machado MCC, Machado MAC, Bacchella T, Jukemura J, Almeida JL, Cunha JEM. Solid pseudopapillary neoplasm of the pancreas: distinct patterns of onset, diagnosis, and prognosis for male versus female patients. *Surgery*. 2008; 143(1)[DOI](#)
  43. Panieri E, Krige JE, Bornman PC, Graham SM, Terblanche J, Cruse JP. Operative management of papillary cystic neoplasms of the pancreas. *Journal of the American College of Surgeons*. 1998; 186(3)[DOI](#)
  44. Marchegiani G, Andrianello S, Massignani M, Malleo G, Maggino L, Paiella S, Ferrone CR, et al. Solid pseudopapillary tumors of the pancreas: Specific pathological features predict the likelihood of postoperative recurrence. *Journal of Surgical Oncology*. 2016; 114(5)[DOI](#)
  45. Gerry JM, Poultsides GA. Surgical Management of Pancreatic Cysts: A Shifting Paradigm Toward Selective Resection. *Digestive diseases and sciences*. 2017; 62(7)[DOI](#)
  46. Huang Y, Feng JF. Clinicopathologic characteristics and surgical treatment of solid pseudopapillary tumor of the pancreas. *Hippokratia*. 2013; 17(1)
  47. Wang X, Zhu D, Bao W, Li M, Wang S, Shen R. Case Report: Targeted Therapy for Metastatic Solid Pseudopapillary Neoplasm of the Pancreas With CTNNB1 and PTEN Mutations. *Frontiers in Oncology*. 2021; 11[DOI](#)
  48. Yang F, Wu W, Wang X, Zhang Q, Bao Y, Zhou Z, Jin C, Ji Y, Windsor JA, Lou W, Fu D. Grading Solid Pseudopapillary Tumors of the Pancreas: the Fudan Prognostic Index. *Annals*

- of Surgical Oncology*. 2021; 28(1)[DOI](#)
49. Tang LH, Aydin H, Brennan MF, Klimstra DS. Clinically aggressive solid pseudopapillary tumors of the pancreas: a report of two cases with components of undifferentiated carcinoma and a comparative clinicopathologic analysis of 34 conventional cases. *The American Journal of Surgical Pathology*. 2005; 29(4)[DOI](#)
  50. Fried P., Cooper J., Balthazar E., Fazzini E., Newall J.. A role for radiotherapy in the treatment of solid and papillary neoplasms of the pancreas. *Cancer*. 1985; 56(12)[DOI](#)
  51. Matsuda Y., Imai Y., Kawata S., Nishikawa M., Miyoshi S., Saito R., Minami Y., Tarui S.. Papillary-cystic neoplasm of the pancreas with multiple hepatic metastases: a case report. *Gastroenterologia Japonica*. 1987; 22(3)[DOI](#)
  52. Maffuz A, Bustamante FDH, Silva JA, Torres-Vargas S. Preoperative gemcitabine for unresectable, solid pseudopapillary tumour of the pancreas. *The Lancet. Oncology*. 2005; 6(3)[DOI](#)
  53. Hah JO, Park WK, Lee NH, Choi JH. Preoperative chemotherapy and intraoperative radiofrequency ablation for unresectable solid pseudopapillary tumor of the pancreas. *Journal of pediatric hematology/oncology*. 2007; 29(12)[DOI](#)
  54. Prasad TV, Madhusudhan KS, Srivastava DN, Dash NR, Gupta AK. Transarterial chemoembolization for liver metastases from solid pseudopapillary epithelial neoplasm of pancreas: A case report. *World Journal of Radiology*. 2015; 7(3)[DOI](#)