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*Original Article*

# Solid pseudopapillary neoplasms of the pancreas: clinical analysis of 45 cases

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**Abstract:** Aims: This study investigated the clinicopathological features and surgical management of solid pseudopapillary neoplasms (SPNs) at a single institution in China. Methods: We investigated 45 patients who underwent surgery for pathologically confirmed SPNs between 1996 and 2014. Results: The 45 cases included 44 female and 1 male patients, and the average age was 32.2 years. The tumor was located in the body and/or tail in 33 patients, the head in 9 patients and the neck in 3 patients. The median tumor size was 6.3 cm (range 1.5 to 16). All 45 patients had curative resections including 29 distal pancreatectomies, 9 pancreaticoduodenectomy, 5 central pancreatectomy and 2 enucleation. 2 patients required superior mesenteric vein resection due to local tumor invasion. Eight patients had malignant tumors. Ki-67 was detected positive in 5 patients with malignant potential. After a median follow-up of 51.7 months, one patient with malignant SPN had evidence of tumor recurrence. Conclusion: SPN is an infrequent tumor, typically affect young women with low malignant potential. Surgical resection is warranted even in the presence of local invasion or metastases as patients demonstrate excellent long-term survival. Positive immunoreactivity for Ki-67 may predict the malignant potential and poor outcome of SPNs.

**Keywords:** Solid-pseudopapillary neoplasms, diagnosis, treatment, prognosis

## Introduction

Solid pseudopapillary neoplasm (SPN) of the pancreas is a rare tumor, representing 1~3% of all pancreatic tumors [1]. SPN predominantly affects females during their reproductive phase and exhibits relatively indolent biological behavior with a favorable prognosis [2]. A description of SPN was first published by Frantz in 1959 [3]. The World Health Organization (WHO) classified these tumors as solid pseudopapillary tumors (SPTs) in 1996 and reclassified them as solid pseudopapillary neoplasms (SPNs) in 2010 [4]. Owing to their rarity, studies regarding SPNs thus far have been small series or case reports. Limited data are available on the diagnosis, malignant potential and optimal surgical strategy for SPN. In this study, we report our clinical experience with 45 cases of SPNs.

## Materials and methods

Between January 1999 to December 2014, 45 consecutive patients who underwent surgery for a pathologically confirmed SPN at the department of abdominal surgery, Zhejiang cancer hospital were retrospectively reviewed. Patients' clinical presentation, radiological details, surgical data, pathological features, postoperative course, and long-term survival were collected and analyzed. Outpatient records combined with telephone interviews were used for follow-up. Written informed consent was obtained from all the study participants. The study was approved by the Ethics Committee of the five hospitals.

Pathologically, SPN was defined as malignant if it demonstrated extrapancreatic invasion, distant metastases, lymph node involvement, pancreatic parenchymal invasion, perineural or vascular invasion. Surgical morbidity was defined as any complication at any time and was classified according to a previous report [5]. Pancreatic fistula was defined in accordance with the recommendations of the International Study Group on Pancreatic Fistula [6].

Continuous data are presented as median (i.q.r.) unless indicated otherwise, with analysis

**Table 1.** Clinical features of 45 patients with SPNs

| Clinical characteristics | No. of patients (n=45) |
|---|---|
| Age (years) | |
| Mean (range) | 32.2 (15-57) |
| Gender | |
| Female/Male | 44/1 |
| Symptoms | |
| Abdominal pain | 17 (37.8%) |
| Abdominal distension | 14 (31.1%) |
| Back pain | 6 (13.3%) |
| Vomiting | 4 (8.9%) |
| Asymptomatic | 4 (8.9%) |
| Location | |
| Body and/or tail | 33 (73.3%) |
| Head | 9 (20.0%) |
| Neck | 3 (6.7%) |
| Size (cm) | |
| Mean (range) | 6.3 (1.5-16) |

by the independent t test or Mann-Whitney U test, as appropriate. Comparisons of categorical data were performed using $\chi^2$ and Fisher's exact tests. All statistical analyses were performed with the SPSS 16.0 statistics software package (SPSS Inc., Chicago, IL, USA). A *P* value <0.05 was considered to indicate statistical significance.

## Results

*Patient characteristics*

The 45 patients included 44 females and one male, with a median age of 32.2 years (range 15~57). The clinical presentation is unspecific, including abdominal pain (37.8%), abdominal distension (31.1%), back pain (13.3%) and vomiting (8.9%). 4 patients (8.9%) whose SPNs were found during routine physical examinations were asymptomatic. The patients had a median symptom duration of 1.7 month (range 5 days to 13 months). The tumors were 6.3 cm in diameter on average (range 1.5 to 16 cm), and were located in the body and/or tail in 33 patients, the head in 9 patients and the neck in three patients. The clinical features of the 45 patients are listed in **Table 1**.

*Preoperative examinations and diagnoses*

Radiological investigations were performed before operation, including computed tomography (CT) in 37 patients, ultrasonography (US) in 23 patients, magnetic resonance imaging (MRI) in 13 patients and 18F-fluorodeoxyglucose (FDG) positron emission tomography (PET) in two patients. **Figure 1** shows the radiological images of SPN.

The mass was described on cross-sectional imaging as heterogenous (solid and cystic) in 38 patients, solid in 5 patients and cystic in 2 patients. Calcifications were present in 11 of the 45 patients, while hemorrhage and/or necrosis were detected in 12 patients. Concomitant tumors were found in two patients (4.4%), including ovarian teratoma (n=1) and breast cancer (n=1).

Inaccurate preoperative diagnoses were made for 15 of 45 patients, including pancreatic adenocarcinoma (n=7), neuroendocrine tumor (n=4), cystadenoma (n=2), islet cell tumor (n=1), and pancreatic cyst (n=1).

*Surgical data*

All 45 patients underwent surgical exploration. 29 patients with lesions in the body and/or tail underwent a distal pancreatectomy including three spleen-preserving resections. 9 patients underwent pancreaticoduodenectomy, and two of them had partial superior mesenteric vein resection and artificial vascular graft reconstruction. 5 patients underwent central pancreatectomy and two patients underwent enucleation of SPN. The total surgery time was 223±97 min, and intra operative blood loss was 261±115 ml. Blood transfusion was needed in 6 patients during surgery, each patient received 2 U blood.

All 45 patients had R0 resections and there were no surgical mortalities. Postsurgical complications occurred in 9 (20.0%) patients. Including pancreatic fistula (5, 11.1%), infection (3, 6.7%), delayed gastric emptying (1, 2.2%), bleeding (1, 2.2%). Pancreatic fistulas were classified as Grade A in 2 patients, Grade B in 2 patients, and Grade C in one patient. Three infection cases included two pneumonia, and one wound infection. Most of these patients were conservatively managed with a successful outcome, but reoperation was necessary in one patient due to the intraabdominal bleeding. The median postsurgical stay was 13.3 days (range 7 to 31 days) (**Table 2**).

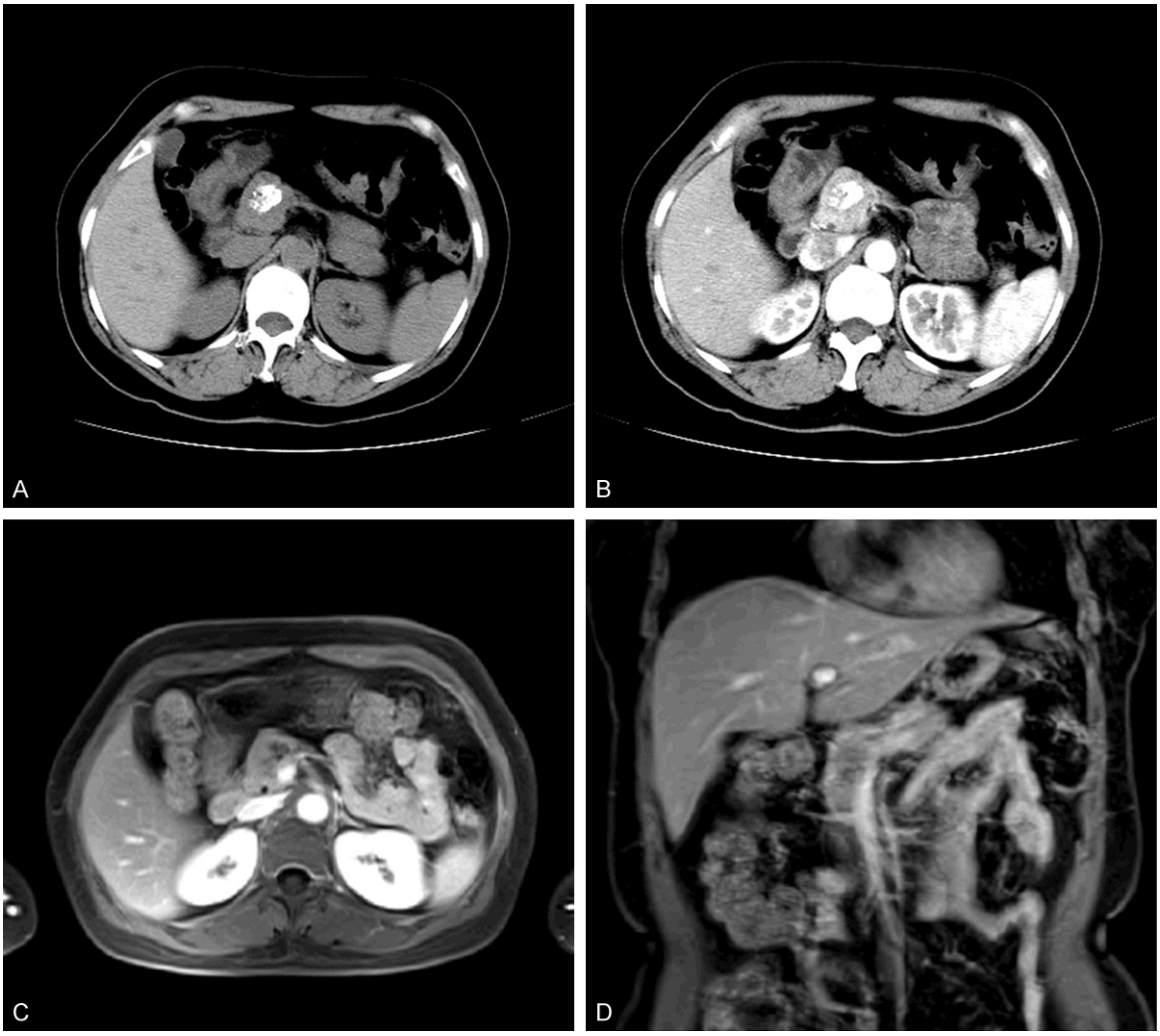


**Figure 1.** A: A CT scan showed a low density mass of the pancreas head with calcification; B: Enhanced CT scan showed a slightly enhanced solid areas. C and D: MRI showed a well-demarcated mass in the pancreas head, and was close to the superior mesenteric vein.

*Pathological features*

Grossly, the tumor is well-encapsulated and is usually well demarcated from the pancreas. The cut surface shows large spongy areas of hemorrhage alternating with both solid and cystic degeneration. 8 patients were diagnosed with malignant SPN due to vascular invasion in 4 patients (superior mesenteric vein in 2 patients, and splenic vein in 2 patients), pancreatic parenchyma infiltration in 3 patients, and lymph node involvement in one patient.

Immunohistochemical studies were performed in all 45 cases. Vimentin (Vim) was positive in 37 of 41 patients, α1-antitrypsin (AAT) was positive in 33 of 38 patients, neuron-specific enolase (NSE) was positive in 29 of 35 patients, progesterone receptors (PR) was positive in 26 of 33 patient. Estrogen receptors (ER), synaptophysin (Syn), cytokeratin (CK) and chromogranin A (CgA) were expressed only focally in a few tumors. Ki-67 was detected positive in 5 patients with malignant neoplasms. **Figure 2** shows the histopathologic image results.

Follow-up included clinical examination, routine laboratory tests, abdominal US and CT/MRI every 3 months. Only one patient had recurrence at a median follow-up of 51.7 months (range 10-179 months).

*Predictive factors of malignancy*

The positive rate of Ki-67 was 62.5% (5/8) in patients diagnosed with a malignant neoplasm,

**Table 2.** Surgical procedures and postoperative outcomes of 45 SPN patients

| | No. of patients (n=45) |
|---|---|
| Operative procedure | |
| Distal pancreatectomy | 29 (64.4%) |
| Pancreaticoduodenectomy | 9 (20.0%) |
| Central pancreatectomy | 5 (11.1%) |
| Enucleation | 2 (4.4%) |
| SMV resection | 2 (4.4%) |
| Operative time (min) | 223±97 |
| Blood loss (ml) | 261±115 |
| Postoperative complications | 9 (20.0%) |
| Pancratic fistula | 5 (11.1%) |
| Grade A | 2 (4.4%) |
| Grade B | 2 (4.4%) |
| Grade C | 1 (2.2%) |
| Infection | 3 (6.7%) |
| Pneumonia | 2 (4.4%) |
| Wound infection | 1 (2.2%) |
| Delayed gastric emptying | 1 (2.2%) |
| Bleeding | 1 (2.2%) |
| Postoperative stay (days) | 13.3 (7-31) |

SMV: Superior mesenteric vein.

and was comparable to 11.1% (3/27) of the patients diagnosed to have a benign neoplasm ($P<0.001$). On univariate analysis, none of the features including age, tumor size, tumor location, increased tumor markers, and tumor characteristics were predictive of malignant SPNs (**Table 3**).

## Discussion

SPN is an uncommon neoplasm of the pancreas, which is predominantly observed in female patients in their second or third decade [7]. The pathogenesis of the tumor is unknown, although its tendency to affect young women has suggested that sex hormones may involve in the origin of SPN [8]. However, no differences in immunohistochemical stains for sex hormone-receptor proteins or in clinicopathologic characteristics had been found attributable to gender alone [9]. SUN reported that 62.5% of SPN patients had been infected by Hepatitis B virus (HBV) [10], and in our previous study, 76.3% of female patients had taken contraceptive drugs for a long time. This suggests that an investigation is needed to determine whether hepatitis B virus infection or contraceptive drugs may be involved in the pathogenesis of SPNs, since these factors are still unclear.

CT is the most frequently used method for diagnosing SPN, and shows the presence of a heterogeneously enhanced solid and cystic mass [11]. However, the imaging may vary greatly depending on the distribution of solid and cystic components and the hemorrhagic changes [12]. MRI is better than CT in differentiating the cystic or solid component inside the tumor and providing information about respectability [13]. A fine-needle aspiration cytology (FNAC) could be used to increase the accuracy of the preoperative diagnosis. However, seeding of the needle tract by neoplastic cells and complications, such as bleeding, pancreatic fistula and biliary fistula during the procedure also had been reported [14]. According to our experience, data from CT/MRI scans combined with age and gender are sufficient for making a clinical diagnosis of SPN, and FNAC should be performed when the radiological diagnosis was not clear enough.

Complete aggressive surgical resection is the treatment of choice for SPNs even with metastasis or local recurrence [15]. Surgical approach depends on the location, size, and nature of the neoplasms. Routine lymphadenectomy is not recommended, due to the rare incidence of lymph node metastasis [16]. For the local invasion or metastases, there is also general consensus that surgical therapy should be performed [17]. Cheng and colleagues reported that en bloc synchronous portal vein-superior mesenteric vein or adjacent organ resection should be carried out to achieve a complete resection [18]. The two patients in the present study who underwent synchronous superior mesenteric vein resection and artificial vascular graft reconstruction remain alive without recurrence.

Some studies have shown a correlation between tumor size >5 cm, tumor necrosis, male sex, and SPN with malignant potential [19, 20]. However, several univariate analyses indicated that the clinical factors, including sex, age, tumor size, tumor location, increased tumor markers, and tumor characteristics were not intensively related to the malignant poten-

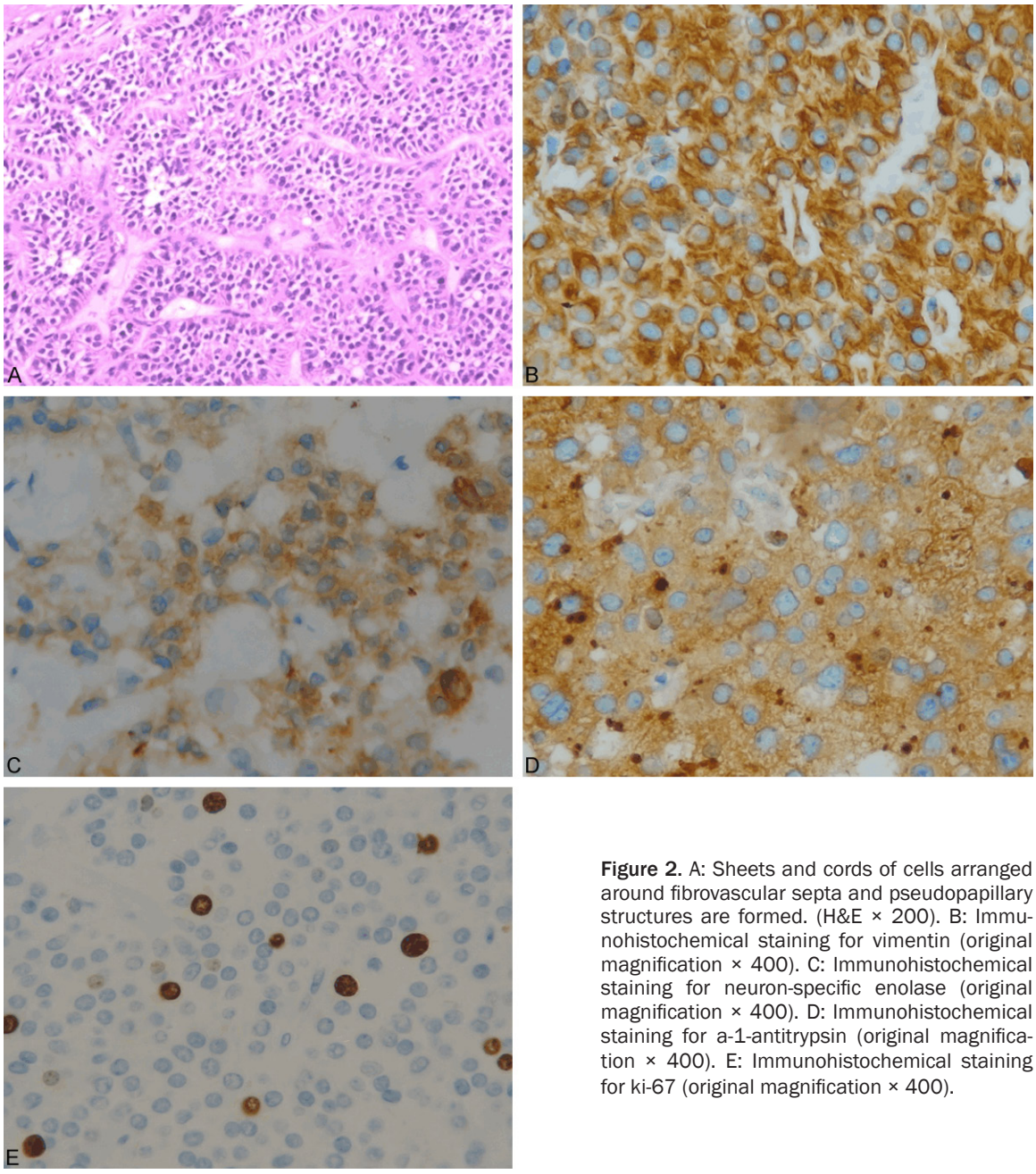


**Figure 2.** A: Sheets and cords of cells arranged around fibrovascular septa and pseudopapillary structures are formed. (H&E × 200). B: Immunohistochemical staining for vimentin (original magnification × 400). C: Immunohistochemical staining for neuron-specific enolase (original magnification × 400). D: Immunohistochemical staining for a-1-antitrypsin (original magnification × 400). E: Immunohistochemical staining for ki-67 (original magnification × 400).

tial of SPNs [21, 22]. These results were consistent with that in our study. Besides, we found that the positive rate of Ki-67 was 62.5% in patients diagnosed with a malignant neoplasm, and was comparable to 11.1% of the patients diagnosed to have a benign neoplasm ($P<0.001$). Our findings indicate that positive status for Ki-67 may correlate with the malignancy and poor outcome of SPNs. However, the accumulation of large-scale clinical data is still necessary to support this view.

An SPN is composed of small, uniform tumor cells with round nuclei and eosinophilic cytoplasm [23]. The tumor is characterized by a combination of solid components consisting of pseudopapillae with fibrovascular stalks and cystic components with variable degeneration and hemorrhage [24]. Immunohistochemically, SPNs are typically positive for Vim (vimentin), AAT (a-1-antitrypsin), AACT (a-1-antichymotrypsin), and NSE (neuron-specific enolase) [25], but the unique immunohistochemical features

**Table 3.** Predictive factors of malignant SPNs

| Clinicopathologic factors | Malignant (n=8) | Benign (n=37) | *P*-value |
|---|---|---|---|
| Mean age (years) | 34.6 (18-57) | 30.7 (15-53) | 0.42[a] |
| Sex ratio (F:M) | 8:0 | 36:1 | 0.64[b] |
| Symptoms | | | |
| Present | 7 | 34 | |
| Absent | 1 | 3 | 0.69[b] |
| Tumor location | | | |
| Body and/or tail | 7 | 26 | |
| Head | 1 | 8 | 0.55[b] |
| Neck | 0 | 3 | |
| Tumor size (cm) | | | |
| <5 | 2 | 16 | |
| >5 | 6 | 21 | 0.34[b] |
| Calcification | | | |
| Present | 3 | 8 | |
| Absent | 5 | 29 | 0.34[b] |
| Hemorrhage/Necrosis | | | |
| Present | 2 | 10 | |
| Absent | 6 | 27 | 0.91[b] |
| Tumor feature | | | |
| Solid and Cystic | 7 | 31 | |
| Solid | 1 | 4 | 0.79[b] |
| Cystic | 0 | 2 | |
| Ki-67 (positive rate) | 62.5% (5/8) | 11.1% (3/27) | <0.001[b] |

a: Mann-Whitney U test; b: Fisher's exact test.

with expression of PR and CD10 were not consistent in recent study.

The prognosis of SPN is good, even with local recurrence as well as metastases or invasions. More than 95% of patients with SPN limited to the pancreas are cured by complete surgical excision [26]. Recurrence, local invasion, or limited metastases are not contraindications for resection, and long-term survival was also observed in patients with malignant SPNs [27]. The role of chemotherapy or chemoradiotherapy for the treatment of SPN is unclear, but some small series or case reports have documented successful chemotherapy regimens [28, 29].

In conclusion, SPNs are rare neoplasms that most commonly occur in young females with a malignant potential. Surgical resection is warranted even in the presence of local invasion or metastases as patients demonstrate excellent long-term survival. Further studies should aim at acquiring more understanding of SPNs and establishing guidelines for diagnosis and treatment.

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## Disclosure of conflict of interest

None.

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