

# Surgical Management of Solid Pseudopapillary Neoplasms of Pancreas: A Single-Center Experience of 60 Patients

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## Keywords

Solid pseudopapillary neoplasm · Pancreas · Surgical resection · Parenchyma-preserving surgery

## Abstract

**Background:** Solid pseudopapillary neoplasms (SPNs) of the pancreas are rare neoplasms, and the selection of surgical approaches is still under debate. The aim of this study was to analyze the clinicopathological characteristics and surgical outcomes of SPN patients and to compare the short-term and long-term outcomes between conventional operations and parenchyma-preserving operations. **Methods:** Patients who underwent pancreatic resection for SPNs between February 2010 and May 2019 in Fujian Medical University Union Hospital were identified. Clinicopathological details, perioperative data, and long-term follow-up results were retrospectively analyzed. **Results:** Sixty patients underwent surgical resection for SPNs during the study period: 48 females and 12 males. The mean age was 32.2 years. All patients underwent margin-negative surgical resection. The median follow-up period was 47 months (range: 3–118 months). One patient developed liver metastases 14 months after the operation and received local ablation therapy. All patients were alive during the follow-up. The incidence of postoperative

pancreatic fistula was higher in the parenchyma-preserving surgery group than in the conventional surgery group (40.0 vs. 11.1%,  $p = 0.034$ ). There was no significant difference in the tumor recurrence rate between the 2 groups. Eight (17.7%) and 6 patients (13.3%) in the conventional surgery group demonstrated endocrine and exocrine pancreatic insufficiency, respectively; furthermore, no patients in the parenchyma-preserving surgery group had endocrine or exocrine pancreatic insufficiency, but the incidences were not significantly different between the 2 groups. **Conclusions:** Margin-negative surgical resection of SPNs yields a very low rate of tumor recurrence and excellent long-term survival.

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## Introduction

Solid pseudopapillary neoplasm (SPN) of the pancreas is rare, accounting for 0.9–2.7% of exocrine pancreatic tumors [1, 2]. Over the past decades, the incidence of this tumor has been increasing [3]. The World Health Organization (WHO) classified these tumors as solid pseudopapillary tumors in 1996 and reclassified them as SPNs in 2010.

SPNs tend to occur in young women, with a mean age of 31–37 years [4–7]. SPNs have malignant potential, and approximately 9–28% of cases have malignant biological behavior [6, 8] or malignant pathological features [5, 9, 10]. Patients with SPNs have a favorable prognosis, and the 5-year survival rate after surgical resection is more than 95% [5, 11]. Long-term survival can be achieved after surgical resection even in patients with metastasis [12, 13].

Due to the rarity of SPNs, most of the current data are from case reports and retrospective case series. The biological behavior and prognosis of SPNs are still difficult to predict, and pancreatic SPN is still an enigma [14, 15]. Surgery remains the mainstay of therapy [6, 7, 16], but selection of surgical approaches is still under debate. Some authors have advocated function-preserving surgical approaches [7, 10], while others favor aggressive surgical resection [17] or have considered parenchyma-preserving resection as a significant risk factor for tumor recurrence [8]. In this study, we present the clinicopathological characteristics and surgical outcomes of 60 SPN patients from our center over a 10-year period and compare the short-term and long-term outcomes between conventional operations and parenchyma-preserving operations.

## Methods

From February 2010 to May 2019, a total of 60 patients with pathologically confirmed SPNs underwent surgical resection at our institution (Fujian Medical University Union Hospital, Fuzhou, China). The study protocol was approved by the institutional review board at Union Hospital in accordance with the Declaration of Helsinki. The medical records were retrospectively reviewed, and perioperative clinicopathological variables were collected and analyzed, such as sex, age, body mass index (BMI), symptoms, pathological diagnosis, tumor size, surgical records, postoperative morbidity, and follow-up information.

Severity of complications was evaluated according to the Clavien–Dindo [18] classification system. According to the newly updated International Study Group on Pancreatic Surgery (ISGPS) classification, grade B and C pancreatic fistulas were considered clinically relevant [19]. The long-term changes in endocrine and exocrine functions and tumor recurrence were evaluated based on radiological, clinical, and laboratory assessments. Endocrine pancreatic insufficiency was diagnosed as new-onset diabetes [20–22]. Exocrine pancreatic insufficiency

**Table 1.** Demographic and clinical characteristics of patients with SPNs ( $n = 60$ )

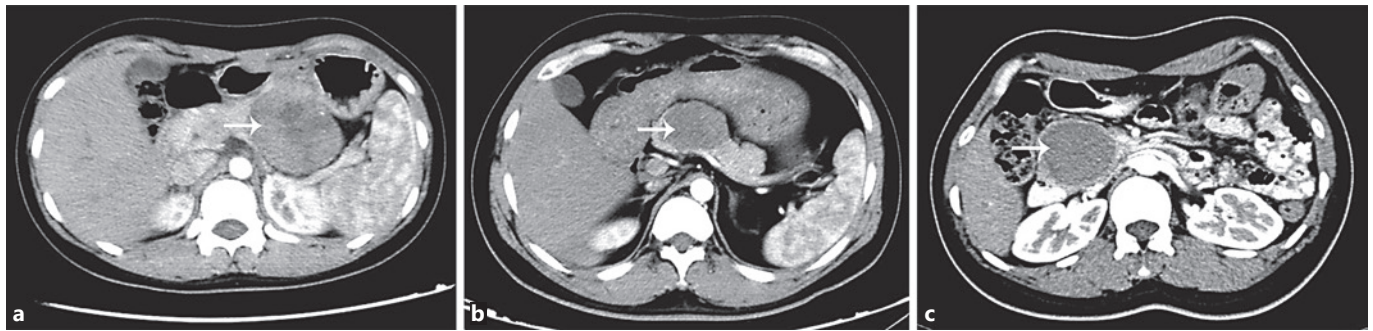
| Clinical features                |                 |
|----------------------------------|-----------------|
| Sex, $n$ (%)                     |                 |
| Male                             | 12 (20.0)       |
| Female                           | 48 (80.0)       |
| Age (mean $\pm$ SD), years       | 32.2 $\pm$ 13.0 |
| Symptoms, $n$ (%)                |                 |
| Asymptomatic                     | 39 (65.0)       |
| Abdominal pain                   | 19 (31.7%)      |
| Abdominal distension             | 2 (3.3%)        |
| Tumor size (mean $\pm$ SD), cm   | 5.8 $\pm$ 3.4   |
| Tumor location, $n$ (%)          |                 |
| Head + neck                      | 16 (26.7)       |
| Neck                             | 10 (16.7)       |
| Body + tail                      | 34 (56.7)       |
| CT examination, $n$              | 57              |
| SPN diagnosed by CT, $n$ (%)     | 32 (56.1)       |
| MRI examination, $n$             | 46              |
| SPN diagnosed by MRI, $n$ (%)    | 27 (58.7)       |
| Radiographic appearance, $n$ (%) |                 |
| Heterogeneous                    | 33 (55.0)       |
| Solid                            | 21 (35.0)       |
| Cystic                           | 6 (10.0)        |

was defined as diarrhea and steatorrhea, which improved with pancreatic enzyme supplementation [21–23].

Quantitative variables were expressed as median and range or mean  $\pm$  SD, and qualitative variables were reported as numbers and percentages. Student's  $t$  test or the Mann-Whitney  $U$  test was used for comparisons of quantitative variables, and categorical data were compared using a  $\chi^2$  test or Fisher's exact test. Data were considered significant at  $p < 0.05$ . All statistical analyses were performed by using SPSS version 19.0 (IBM, Armonk, NY, USA).

## Results

Demographic and clinical characteristics of the 60 patients with SPNs are listed in Table 1. Of the 60 patients, 48 were female and 12 were male, with a ratio of 4:1. The mean age was 32.2  $\pm$  13.0 years. Most patients were asymptomatic (40, 66.7%), and the most common symptom was abdominal pain (20, 33.3%). The mean tumor size was 5.8  $\pm$  3.4 cm in diameter. Most tumors were located in the body and tail of the pancreas (34, 56.7%), 16 (26.7%) were located in the head of the pancreas, and 10



**Fig. 1.** CT images of different SPN patients. A 12-year-old female patient with a solid-cystic neoplasm in the body and tail of the pancreas (a), a 29-year-old male patient with a solid neoplasm in the body of the pancreas (b), and a 31-year-old female patient with a cystic neoplasm in the head of the pancreas (c).

patients (16.1%) had tumors located in the neck of the pancreas.

In the preoperative imaging (CT and/or MRI scan), diagnosis of an SPN was correctly made in 44/60 patients. CT was performed in 57 patients, and an SPN was diagnosed in 32 patients. Forty-six patients underwent MRI examination, and 27 were diagnosed with SPNs. Tumors had radiologically heterogeneous (solid and cystic) features (Fig. 1a) in 33 patients (55.0%). Solid features (Fig. 1b) were found in 21 patients (35.0%), and cystic features (Fig. 1c) were found in 6 patients (10.0%).

The type of operation and outcomes of surgical management are summarized in Table 2. All patients underwent complete surgical resection. Conventional surgical procedures included pancreaticoduodenectomy (13, 21.7%), distal pancreatectomy with splenectomy (11, 18.3%), and spleen-preserving distal pancreatectomy (21, 35.0%). Parenchyma-preserving procedures included central pancreatectomy (9, 15.0%) and tumor enucleation (6, 10.0%). Thirty-four patients (56.7%) underwent laparoscopic pancreatectomy, 11 patients (18.3%) underwent robotic pancreatectomy, and open pancreatectomy was applied in 15 patients (25.0%).

A total of 22 (36.7%) patients experienced postoperative complications. Postoperative pancreatic fistula (11, 18.3%) was the most common morbidity following pancreatectomy for pancreatic SPNs, followed by intra-abdominal infection (6, 10.0%). There were no reoperations or mortalities.

Twenty patients (33.3%) had tumors with histologically malignant features, with peripancreatic tissue infiltration (14 patients, 23.3%) as the most frequent feature. Four patients (6.7%) had perineural invasion, and 2 (3.3%) had vascular invasion. No lymph nodes were

**Table 2.** Surgical outcomes and clinicopathological characteristics of patients with SPNs ( $n = 60$ )

| Clinical features                       |           |
|---|-----------|
| Surgery mode I, $n$ (%)                 |           |
| PD                                      | 13 (21.7) |
| DPS                                     | 11 (18.3) |
| SPDP                                    | 21 (35.0) |
| CP                                      | 9 (15.0)  |
| Enucleation                             | 6 (10.0)  |
| Surgery mode II, $n$ (%)                |           |
| Open surgery                            | 15 (25.0) |
| Laparoscopic surgery                    | 34 (56.7) |
| Robotic surgery                         | 11 (18.3) |
| Postoperative complications, $n$ (%)    |           |
| Postoperative pancreatic fistula        | 11 (18.3) |
| Intra-abdominal infection               | 6 (10.0)  |
| Respiratory complications               | 3 (5.0)   |
| Delayed gastric emptying                | 2 (3.3)   |
| Microscopic malignant features, $n$ (%) |           |
| Peripancreatic tissue invasion          | 10 (16.7) |
| Perineural invasion                     | 4 (6.7)   |
| Vascular invasion                       | 2 (3.3)   |
| LN metastasis, $n$ (%)                  | 0         |

PD, pancreaticoduodenectomy; DPS, distal pancreatectomy with splenectomy; SPDP, spleen-preserving distal pancreatectomy; CP, central pancreatectomy; LN, lymph node.

pathologically confirmed to be metastatic. A negative margin was obtained in all patients.

The median follow-up period was 47 months (range: 3~118 months). Abdominal CT/MRI was performed every year. All patients were alive during the follow-up. One patient developed liver metastases 14 months after the

**Table 3.** Comparison between the conventional surgery group and the parenchyma-preserving surgery group

| Clinical features                                | Conventional surgery<br>( <i>n</i> = 45) | Parenchyma-preserving surgery<br>( <i>n</i> = 15) | <i>p</i> value |
|--|--|---|----------------|
| Sex ratio (F:M)                                  | 37:8                                     | 11:4  | 0.709          |
| Age (mean ± SD), years                           | 32.4±14.0                                | 31.7±9.7  | 0.865          |
| Tumor size (mean ± SD), cm                       | 5.9±3.0                                  | 3.8±1.5   | 0.014          |
| Tumor location, <i>n</i> (%)                     |  |   |                |
| Head   | 13 (28.9)                                | 4 (26.7)  | 1.000          |
| Neck   | 0  | 9 (60.0)  | 0.000          |
| Body + tail                                      | 32 (71.1)                                | 2 (13.3)  | 0.000          |
| Surgery mode, <i>n</i> (%)                       |  |   |                |
| Open surgery                                     | 9 (20.0)                                 | 6 (40.0)  | 0.228          |
| Laparoscopic surgery                             | 27 (60.0)                                | 7 (46.7)  | 0.367          |
| Robotic surgery                                  | 9 (20.0)                                 | 2 (13.3)  | 0.847          |
| Postoperative complications, <i>n</i> (%)        | 14 (31.1)                                | 8 (53.3)  | 0.122          |
| Postoperative pancreatic fistula                 | 5 (11.1)                                 | 6 (40.0)  | 0.034          |
| Intra-abdominal infection                        | 5 (11.1)                                 | 1 (6.7)   | 1.000          |
| Respiratory complications                        | 2 (4.4)                                  | 1 (6.7)   | 1.000          |
| Delayed gastric emptying                         | 2 (4.4)                                  | 0   | 1.000          |
| Microscopic malignant features, <i>n</i> (%)     | 16 (30.4)                                | 4 (13.3)  | 0.527          |
| Follow-up, months, median (IQR)                  | 44 (18–76)                               | 65 (43–89)  | 0.086          |
| Recurrence, <i>n</i> (%)                         | 1 (2.2)                                  | 0   | 1.000          |
| Endocrine pancreatic insufficiency, <i>n</i> (%) | 8 (17.7)                                 | 0   | 0.188          |
| Exocrine pancreatic insufficiency, <i>n</i> (%)  | 6 (13.3)                                 | 0   | 0.320          |

operation. He received local ablation therapy and remained alive with liver metastasis for 48 months.

Forty-five patients underwent conventional surgery, and 15 patients underwent parenchyma-preserving surgery. Comparisons between the conventional surgery group and the parenchyma-preserving surgery group are listed in Table 3. The tumor size in the parenchyma-preserving surgery group was smaller than that in the conventional surgery group ( $3.8 \pm 1.5$  vs.  $5.9 \pm 3.0$  cm,  $p = 0.014$ ). Compared with the conventional surgery group, in the parenchyma-preserving surgery group, more tumors were located in the neck of the pancreas (60.0% vs. 0,  $p = 0.000$ ) and fewer tumors were located in the body and tail of the pancreas (13.3 vs. 71.1%,  $p = 0.000$ ). The incidence of postoperative pancreatic fistula was higher in the parenchyma-preserving surgery group than in the conventional surgery group (40.0% vs. 11.1%,  $p = 0.034$ ). There was no significant difference in the tumor recurrence rate between the 2 groups. Eight (17.7%) and 6 patients (13.3%) in the conventional surgery group showed endocrine and exocrine pancreatic insufficiency, respectively; additionally, no patients in the parenchyma-preserving surgery group had endocrine or exocrine pan-

creatic insufficiency, but the incidences were not significantly different in the 2 groups.

## Discussion

Most SPNs are found in young female patients. The largest single-institution case series from Europe ( $n = 52$ ) reported that the female-to-male ratio was 5.5:1 [8], and the ratio was 6.1:1 in the largest single-institution case series from the US ( $n = 78$ ) [4]. A multicenter analysis in Korea reported that the female-to-male ratio was 9.3:1 [5], while a nationwide multicenter study in Japan and the largest single-institution case series from China ( $n = 243$ ) found that the ratio was 3:1 [7, 24]. The female-to-male ratio was 4:1 in our study, indicating a difference in incidence between different countries and races and that the number of male patients is increasing.

At least one-third of patients with SPNs were asymptomatic in previous studies [4, 5, 10], and 66.7% of the tumors from patients in our study were incidentally discovered during regular abdominal examination. Notably, jaundice is a rare symptom of SPNs. Liu [7] reported that

among 64 patients with SPNs in the pancreatic head, only 1 presented with jaundice. These results were similar in some other studies [4, 16]. In our study, 16 patients (26.7%) had tumors in the head of the pancreas, but none had jaundice. Obstructive jaundice is a common symptom of pancreatic head cancer. Therefore, the absence of jaundice can be an important feature for distinguishing SPNs in the pancreatic head from pancreatic cancer.

Abdominal CT and MRI are widely used to diagnose SPNs. The typical features are well-circumscribed, heterogeneously enhancing solid and cystic mass lesions [25], but approximately half of SPNs are atypical [26]. Typical CT characteristics were found in 56.1% (32/57) of the patients, and 58.7% (27/46) of the patients had typical MRI imaging features in this study. Small ( $\leq 3$  cm in diameter) SPNs were atypical, and they frequently appeared as a purely solid pancreatic mass with a sharp border [26]. For atypical cases, SPNs are hard to differentiate from pancreatic ductal adenocarcinoma and pancreatic neuroendocrine tumors with CT or MRI [27]. Therefore, fine-needle aspiration cytology may be useful in the diagnosis of SPNs. Law et al. [28] reported that addition of endoscopic ultrasound fine needle aspiration (EUS-FNA) significantly increased the preoperative diagnostic yield of SPNs to 82.4%. Lubezky et al. [29] reported that the sensitivity and specificity of this technique were 90.9 and 100%, respectively. EUS-FNA is a safe diagnostic tool for SPNs [28, 30], and complications related to EUS-FNA are rare [31]. This study lacked the experience of EUS-FNA. In our opinion, typical radiological findings are an indication for surgery, and preoperative pathological results are not necessary for patients with SPNs. We agree that EUS-FNA should be recommended for unresectable cases [7].

Surgical resection of pancreatic SPNs is effective. In our study, all the patients were alive after resection during a median follow-up period of 47 months. Data from the National Cancer Database demonstrate that the 5-year survival rate is 98% in patients who undergo primary surgical resection and 40% in patients who do not undergo surgical resection [32]. Lubezky et al. [29] reported that the 5-year and 10-year disease-free survival rates were 96.5 and 89.6%, respectively, after surgical resection. Estrella et al. [33] reported that the 10-year disease-specific survival rate was 96%. Therefore, surgical resection is recommended for patients with pancreatic SPNs [6, 7, 32].

However, the choice of procedure for pancreatic SPNs is controversial. As pancreatic SPNs are usually diagnosed in young adults, patients can have long survival times after resection. Function-preserving surgery can be

performed to maintain the function of the pancreas and the adjacent organs; therefore, function-preserving surgery is suggested [7, 10]. However, another study found that parenchyma-preserving resections harbored a significant risk for tumor recurrence [8]. There are few studies comparing different procedures for SPNs. Wang et al. [34] reported that compared with conventional pancreatic resection (including pancreaticoduodenectomy and distal pancreatectomy), enucleation for SPNs had a shorter duration of surgery, less blood loss, a lower rate of exocrine insufficiency, and comparable morbidity, with no increased risk of tumor recurrence. However, enucleation of SPNs in children has the disadvantages of prolonged fasting times and hospital stays to recover from moderate pancreatic fistulas [35]. In the present study, the conventional surgery group (including pancreaticoduodenectomy and distal pancreatectomy) was compared with the parenchyma-preserving surgery group (including central pancreatectomy and enucleation). The tumor size in the parenchyma-preserving surgery group was smaller than that in the conventional surgery group. More tumors were located in the neck of the pancreas, and fewer tumors were located in the body and tail of the pancreas in the parenchyma-preserving group than in the conventional surgery group. These characteristics indicated that parenchyma-preserving surgery was more frequently applied than conventional surgery for small SPNs located in the neck of the pancreas in our center. The rate of pancreatic fistula formation was higher in the parenchyma-preserving surgery group than in the conventional surgery group, which is similar to the results of previous studies [22, 36]. The tumor recurrence rate was very low and similar in both groups. The rate of endocrine and exocrine insufficiency in the parenchyma-preserving surgery group seemed to be lower than that in the conventional surgery group, although the differences were not significant. Margin-negative parenchyma-preserving surgery for pancreatic SPNs can result in similar oncological outcomes to conventional surgery and can result in potentially better long-term functional outcomes.

There were some limitations in this study. First, due to the rarity of SPNs, the present study was a single institutional retrospective analysis with a relatively small sample size. Second, due to the limited sample size of this study, the number of pancreatic SPN patients with synchronous metastases was zero, which could be a limitation to our study. Finally, there were only 15 SPN patients in the parenchyma-preserving surgery group, and the baseline characteristics of both groups were different (smaller tumors in the parenchyma-preserving surgery group than

in the conventional surgery group), which may result in a bias in the comparison between the 2 groups.

In conclusion, margin-negative surgical resection of SPNs yields a very low rate of tumor recurrence and excellent long-term survival. Parenchyma-preserving surgical approaches may be more suitable than conventional surgical approaches for small SPNs located in the neck of the pancreas. Parenchyma-preserving procedures result in similar oncological outcomes to conventional surgery and potentially better long-term functional outcomes than conventional procedures.

### Statement of Ethics

The Medical Ethical Committee of Fujian Medical University Union Hospital reviewed and approved the study design, and all study participants, or their legal guardians, provided informed written consent prior to study enrollment.

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### Disclosure Statement

The authors of this manuscript declare that they have no conflicts of interest to disclose.

### Funding Sources

This study was funded by the Joint Funds of Scientific and Technological Innovation Program of Fujian Province, No. 2017Y9059, and the National Key Clinical Specialty Construction Programs of China, No. [2012]649.

### Author Contributions

Xianchao Lin contributed to the design, interpretation of data, and drafting of the manuscript. Ronggui Lin contributed to the data analysis and interpretation. Fengchun Lu and Yanchang Chen contributed to the interpretation and critical review. He-guang Huang contributed to the design, interpretation, and critical review. All authors read and approved the final manuscript.

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