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Original Article

Outcome after spleen-preserving distal pancreatectomy by Warshaw technique for pancreatic body cancer

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Backgrounds/Aims: Distal pancreatectomy with splenectomy (DPS) is a common surgical procedure for pancreatic body cancer. However, spleen-preserving distal pancreatectomy (SPDP) utilizing the Warshaw technique (WT) in malignancies is generally not favored due to concerns about inadequate resection. This study aims to assess the feasibility and oncologic outcomes of employing SPDP with WT in pancreatic body cancer.

Methods: We conducted a retrospective analysis comparing 21 SPDP patients with 63 DPS patients matched by propensity score from January 2018 to November 2022. Clinical outcomes and follow-up data were analyzed using R.

Results: Both groups exhibited similar demographic, intraoperative, and pathological characteristics, with the exception of a reduced number of total lymph nodes ($p = 0.006$) in the SPDP group. There were no significant differences in the rates of postoperative complications, recurrence, or metastasis. Local recurrence predominantly occurred in the central region as opposed to the spleen region. There were no cases of isolated recurrences in the splenic region. Median overall survival and recurrence-free survival times were 51.5 months for SPDP vs 30.5 months for DPS and 18.7 months vs 16.8 months, respectively ($p > 0.05$). The incidence of partial splenic infarction and left-side portal hypertension in the SPDP group was 28.6% (6/21) and 9.5% (2/21), respectively, without necessitating splenic abscess puncture, splenectomy, or causing bleeding from perigastric varices.

Conclusions: SPDP did not negatively impact local recurrence or survival rates in selected pancreatic body cancer patients. Further studies are necessary for validation.

Key Words: Pancreatic body cancer; Distal pancreatectomy; Spleen preserving; Warshaw technique

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INTRODUCTION

According to 2024 statistics, among all malignant tumors in the United States, pancreatic cancer ranks 10th in men and 7th in women for new cases, while it ascends to 3rd place in related mortality rates [1]. The prevalent consensus regarding the treatment of pancreatic cancer suggests that if patients have the opportunity for tumor resection with curative intent, supplemented by optimal treatment, the median overall survival time (OS) can span from 35.5 to 53.5 months, which remains a poor prognosis [2,3]. Distal pancreatectomy with en-bloc splenectomy (DPS) is the standard surgical approach for treating cancer in the body and tail of the pancreas [3]. Retention of the spleen is generally contraindicated during malignant tumor surgery due to concerns over ensuring radical removal. Nevertheless,

retrospective studies have indicated that spleen-preserving distal pancreatectomy (SPDP) may be feasible in well-selected patients with a very low risk of involvement of the splenic hilar lymph nodes [4-6].

SPDP has become the standard treatment for benign and low-grade malignant lesions localized to the pancreatic body and tail, though it is performed with caution in malignancies. The Warshaw technique (WT) was introduced by Andrew L. Warshaw in 1988 for SPDP, sacrificing the splenic artery and vein unlike the posterior Kimura technique, which conserves these vessels [7,8]. While preserving the spleen, WT primarily affects the complete removal of splenic hilar vessels. The spleen is maintained by the short gastric vessels and left gastroepiploic vessels. The failure rate of spleen preservation during the perioperative period of WT surgery is 1.9%, with affected patients requiring subsequent splenectomy due to splenic infarction [9]. Splenomegaly may contraindicate this technique as the blood supply may be insufficient to support the increased tissue volume [7]. The potential drawback of WT is its contribution to splenic infarction or perigastric varices; although most instances remain asymptomatic, severe cases could present with high fever or hemorrhage [9].

The radical effect of surgery is crucial for prognosis, and lymph node metastasis is a significant independent factor in the prognosis of pancreatic cancer [10]. The number and ratio of lymph node metastases can be utilized to predict postoperative adverse survival in patients with pancreatic cancer, and serves as a staging strategy [11]. According to Malleo et al's study [12], the positive detection rate of harvested splenic hilar lymph nodes at station 10 in total patients with cancer of the pancreatic body and tail was 3.0%, and less than 5% even in N-positive patients. In pancreatic body cancer, the extent of lymph node dissection continues to be a topic of debate among experts, showing significant variability in dissection practices by individual surgeons. Recent studies, including that by Tanaka et al. [13], have suggested that dissection of splenic hilum lymph nodes may lack clinical significance in cases of body cancer.

Thus, the objective of this study is to assess the operation duration, safety, number of harvested lymph nodes, local recurrence rate, and survival time in selected patients diagnosed with cancer of the pancreatic body who underwent SPDP with WT as compared to those who underwent DPS, utilizing Propensity Score Matching analysis. It is hypothesized that local recurrence at the splenic hilum does not increase following SPDP with WT as compared to DPS.

MATERIALS AND METHODS

This is a single-center retrospective study involving a total of 27 patients with pancreatic body cancer who underwent SPDP in the First Affiliated Hospital of Nanjing Medical University from January 2018 to November 2022. Ethical approval for the study was obtained from the Institutional Review Board of the First Affiliated Hospital of Nanjing Medical University prior to the commencement of data collection (2024-SR-783). Data were collected prospectively via our Pancreas Center Database. The decision to employ an open or laparoscopic approach was contingent upon the surgeon's experience at our center. If the tumor was resectable without neoadjuvant therapy, located over 5 cm from the splenic hilum, not classified as T4, which indicates no invasion of the celiac axis, superior mesenteric artery, and/or the common hepatic artery, and did not invade adjacent organs (stomach, duodenojejunal junction, splenic colonic flexure, left kidney), the determination of whether patients underwent DPS or SPDP was based on the surgeon's choice. Six patients were deemed ineligible for the study, including two patients with other digestive tumors, two lost to early follow-up, one classified at T4 stage, and one with incomplete data. Twenty-one patients who underwent SPDP were included in the study. By utilizing tumor location, histologic grade and stage, along with preoperative cancer antigen (CA) 19-9 levels as matching variables, sixty-three patients with pancreatic body cancer at our center who underwent DPS were matched in a 1:3 ratio.

Abnormal tumor markers were evaluated based on serum levels exceeding the upper limits of normal (alpha-fetoprotein: 7.00 ng/mL, carcinoembryonic antigen: 4.70 ng/mL, CA19-9: 39.00 U/mL, CA125: 35.00 U/mL). Specimens were sectioned into 5 mm thickness and mounted on slides. The pathologic diagnosis was established by two expert pathologists through hematoxylin-eosin staining and immunohistochemistry, conforming to the WHO 2019 criteria [14]. The TNM stage and tumor grade were determined in accordance with the 8th edition of the American Joint Committee on Cancer (AJCC) [15]. An R0 resection was characterized by an absence of tumor cells within 1 mm of the resection margin. Postoperative morbidity was assessed using the International Study Group on Pancreatic Surgery (ISGPS) 2016 criteria [16-18]. The degree of postoperative complications was categorized into grades I–V according to the Clavien-Dindo system [19]. Patients with morbidity grades III–V were considered to have severe morbidity. Postoperative mortality was defined as death within 90 days following the surgical procedure.

The splenic hilum was defined as the termination of the splenic vein on contrast-enhanced computed tomography (CT). When preoperative CT or magnetic resonance imaging indicated that mid-body tumors had not invaded nearby large blood vessels (were not classified as T4 stage) and the spleen, and the spatial distance between the tumor's center and the splenic hilum exceeded 5 cm, an attempt to perform SPDP was made during surgery. The distance between the tumor and splenic hilum was calculated using a formula

$$\textit{Distance from tumor to splenic hilum} = \sqrt[2]{\textit{Horizontal distance between tumor and splenic hilum}^2 + (\textit{Number of spacer layers} \times \textit{Thickess of CT garphy})^2}$$

Table 1. Demographic and baseline characteristics

	SPDP group (n = 21)	DPS group (n = 63)	*p*-value
Sex (male)	13 (61.9)	36 (57.1)	0.801[a]
Age (yr)	63.8 ± 9.0	66.5 ± 9.5	0.258[b]
ASA score			0.826[a]
I	3 (14.3)	12 (19.0)	
II	14 (66.6)	37 (58.7)	
III	4 (19.0)	14 (22.2)	
ECOG-PS			0.256[a]
0	15 (71.4)	40 (63.5)	
1	4 (19.0)	21 (33.3)	
2	2 (9.5)	2 (3.17)	
Age-adjusted Charlson comorbidity index	3 (2–5)	4 (3–5)	0.131[c]
Comorbidities			
Hypertension	9 (42.9)	27 (42.9)	> 0.999[a]
Preoperative diabetes mellitus	6 (28.6)	23 (36.5)	0.602[a]
Preoperative weight loss	6 (28.6)	15 (23.8)	0.772[a]
Tumor marker			
AFP > 7.00ng/mL	2 (9.5)	4 (6.3)	0.637[a]
CEA > 4.70ng/mL	7 (33.3)	16 (25.4)	0.574[a]
CA125 > 25.00U/mL	3 (15.0%, n = 20)	10 (17.2%, n = 58)	> 0.999[a]
CA19-9 > 39.00U/mL	12 (57.1)	35 (55.6)	> 0.999[a]
CA19-9 (U/mL)	66.2 (9.10–223.7)	55.73 (12.3–192.6)	0.812[c]
Distance from tumor to splenic hilum (cm)	9.35 ± 1.93 (n = 17)	8.18 ± 2.57 (n = 49)	0.091[b]

Values are presented as number (%), mean ± standard deviation, or median (interquartile range).
ASA, American Society of Anesthesiology; ECOG-PS, Eastern Cooperative Oncology Group Performance Status; AFP, alpha-fetoprotein; CEA, carcinoembryonic antigen; CA, cancer antigen.
[a]Fisher's exact test; [b]t test; [c]Mann–Whitney U test.

All patients received pancreatic enzyme and insulin replacement therapy, as well as adjuvant chemotherapy, tailored to their specific needs. Follow-up data was sourced from the Pancreas Center database. Each follow-up interval was 3 months. The last follow-up was conducted until 30 June 2024. Recurrence-free survival (RFS) was defined as the period from the surgery date until local or regional disease recurrence or death. OS was defined as the period from the date of surgery to the date of death or the last follow-up date. Conditions such as splenic infarction and left-side portal hypertension were assessed through postoperative CT examinations. We categorized the sites of local recurrence into the spleen region and the central region, aligned vertically with the left kidney renal hilum. Some patients underwent postoperative CT/positron emission tomography (PET)-CT scans at local hospitals; recurrence data were documented in our hospital's outpatient clinic.

Statistics were expressed as frequency (percentage of the population), mean ± standard deviation, and median (interquartile range), based on the distribution and nature of the data. Categorical variables were analyzed using Fisher's exact test, while continuous variables were analyzed using the independent sample t-test or the Mann–Whitney U test. Kaplan-Meier curves were employed to demonstrate estimates of OS and RFS. All statistical analyses were conducted using R version 4.2.3. A *p*-value of less than 0.05 was considered statistically significant.

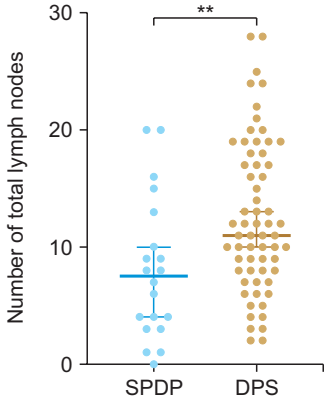

Fig. 1. The scatter plot illustrates the total number of lymph nodes harvested in two groups. (**$p < 0.01$). SPDP, spleen-preserving distal pancreatectomy; DPS, distal pancreatectomy with splenectomy.

RESULTS

A total of 84 patients who underwent distal pancreatectomy for pancreatic body cancer were included in this study. Of these, twenty-one patients underwent SPDP, and 63 patients underwent DPS. The sex distribution was 13 males (61.9%) and 36 males (57.1%), respectively. The mean ages were 63.8 years (± 9.0 years, range: 41–80 years) and 66.5 years (± 9.5 years, range: 36–84 years). No significant differences were observed in American Society of Anesthesiology (ASA) score, Eastern Cooperative Oncology Group Performance Status (ECOG-PS), age-adjusted Charlson comorbidity index (ACCI), preoperative comorbidities, tumor markers, and the distance from the tumor to the splenic hilum between the two groups ($p > 0.05$) (Table 1).

There were no differences in surgery time, intraoperative blood loss, or anesthesia duration between the two groups, thereby negating the impact of these factors on postoperative complications. A laparoscopic approach was employed in 37 patients (44.0%), with similar adoption rates between the SPDP and DPS groups (57.1% vs 39.7%; $p = 0.207$). The postoperative pathological types observed in patients within the SPDP

Table 2. Intraoperative and pathologic parameters

	SPDP group (n = 21)	DPS group (n = 63)	*p*-value
Surgery time (h)	2.92 ± 1.00	2.90 ± 1.00	0.935[b]
Blood loss (mL)	100 (75–200)	100 (100–300)	0.541[c]
Laparoscopic surgery	12 (57.1)	25 (39.7)	0.207[a]
Pathology			> 0.999[a]
PDAC	17 (81.0)	49 (77.8)	
Adenosquamous carcinoma	0 (0)	2 (3.2)	
IPMN-inv	3 (14.3)	8 (12.7)	
Undifferentiated carcinoma	1 (4.8)	4 (6.3)	
Tumor size (cm)	3.33 ± 1.33	3.36 ± 1.89	0.953[b]
T stage			0.584[a]
T1	4 (19.0)	16 (25.4)	
T2	11 (52.4)	36 (57.1)	
T3	6 (28.6)	11 (17.5)	
N stage,			0.923[a]
N0	14 (66.7)	38 (60.3)	
N1	6 (28.6)	20 (31.7)	
N2	1 (4.8)	5 (7.9)	
AJCC 8th stage			> 0.999[a]
IA–IIA	13 (61.9)	38 (60.3)	
IIB–III	8 (38.1)	25 (39.7)	
Grade			0.813[a]
Undifferentiated	0 (0)	3 (4.8)	
Low differentiated	1 (4.8)	3 (4.8)	
Middle and low differentiated	8 (38.1)	22 (34.9)	
Middle differentiated	8 (38.1)	28 (44.4)	
High and middle differentiated	4 (19.0)	7 (11.1)	
R0 resection			0.281[a]
R0	18 (85.7)	58 (92.1)	
R1 (< 1 mm)	3 (14.3)	3 (4.8)	
R1, direct	0 (0)	2 (3.2)	
Perineural invasion	12 (57.1)	43 (79.6) (n = 54)	0.079[a]
Number of total lymph nodes	8 [0-20]	11 [2–28]	0.006[c]
Number of metastatic lymph nodes	0 [0–3]	0 [0–8]	0.666[c]
Postoperative hospital stay (day)	11 (10–13)	12 (10–16)	0.107[c]

Values are presented as mean ± standard deviation, median (interquartile range), number (%), or median [min–max].
SPDP, spleen-preserving distal pancreatectomy; DPS, distal pancreatectomy with splenectomy; PDAC, pancreatic ductal adenocarcinoma; IPMN, intraductal papillary mucinous neoplasm; AJCC, American Joint Committee on Cancer.
[a]Fisher's exact test; [b]t test; [c]Mann–Whitney U test.

and DPS groups included pancreatic ductal adenocarcinoma (PDAC) (n = 17 vs 49), adenosquamous carcinoma (n = 0 vs 2), intraductal papillary mucinous neoplasm with invasive carcinoma (IPMN-inv) (n = 3 vs 8), and undifferentiated carcinoma (n = 1 vs 4). Both groups presented similar pathological types, tumor diameters, T stages, N stages, TNM stages, histological grades, and perineural invasion status ($p > 0.05$). The study also indicated no significant difference in the extent of radical resection between the groups. The total number of lymph nodes harvested in the SPDP group was smaller than in the DPS group, attributed to fewer dissected hilar and perisplenic lymph nodes ($p = 0.006$), as depicted in the scatter plot (Fig. 1). Nevertheless, there was no discrepancy in the number of positive lymph nodes retrieved (Table 2). The duration of postoperative hospital stays was comparable between the SPDP and DPS groups ($p > 0.05$).

Postoperatively, there was no significant difference in overall complications between the groups. The overall incidence of grade B pancreatic fistula was 34.5% (n = 29) while there were no instances of grade C pancreatic fistula. Splenic infarction and left portal hypertension commonly occurred following SPDP. The incidence of partial splenic infarction in the SPDP group was 28.6% (n = 6). Left portal hypertension primarily manifested as gastric varices and splenomegaly. All two patients with left portal hypertension in the SPDP group exhibited perigastric varices, and one displayed considerable splenomegaly (Table 3).

The rates of adjuvant chemotherapy and postoperative local recurrence or distant metastasis were comparable between the groups. Local recurrence predominantly occurred in the central region of the surgical site rather than the spleen region. No patient experienced an isolated recurrence in the splenic area. In the SPDP group, one recurrence was noted in the spleen region and three in the DPS group. Recurrent CT images of the patients were presented in Fig. 2, 3. Both groups exhibited higher rates of distant metastasis than local recurrence, principally occurring in the liver and lungs (Table 4). The median OS and RFS for the SPDP vs DPS groups were 51.5 vs 30.5 months ($p > 0.05$) and 18.7 vs 16.8 months ($p > 0.05$), respectively (Fig. 4).

DISCUSSION

This study is limited by its retrospective, non-randomized design, single-center focus, and small sample size, which diminish the statistical significance of most findings.

To assess the functional status of the patients, the ASA score, ECOG-PS, ACCI, and several representative comorbidities were evaluated (Table 1). The results demonstrate no significant difference in status between the two groups. Our data indicate that the SPDP group may have a lower incidence of severe morbidity (4.8% vs 14.3% in the DPS group). In cases of severe complications, only one patient in the SPDP group developed an abdominal infection with ascites and subsequently recovered following a CT-guided puncture and drainage. Conversely, eight patients in the DPS group underwent puncture and drainage, two of whom experienced complications due to a pancreatic fistula (Level B), and three were diagnosed

Table 3. Postoperative complications

	SPDP group (n = 21)	DPS group (n = 63)	*p*-value
Overall complications	12 (57.1)	32 (50.8)	0.801[a]
Clavien-Dindo classification			0.387[a]
I	4 (19.0)	5 (7.9)	
II	7 (33.3)	18 (28.6)	
IIIa	1 (4.8)	9 (14.3)	
Severe morbidity	1 (4.8)	9 (14.3)	0.439[a]
Pancreatic fistula, Grade B	8 (38.1)	21 (33.3)	0.792[a]
DGE, Grade B	0 (0)	8 (12.7)	0.192[a]
Postoperative hemorrhage	0 (0)	1 (1.6)	> 0.999[a]
Chyle leakage, Grade A	3 (14.3)	4 (6.3)	0.359[a]
Abdominal infection	1 (4.8)	3 (4.8)	> 0.999[a]
Ascites	1 (4.8)	3 (4.8)	> 0.999[a]
Pulmonary infection	2 (9.5)	1 (1.6)	0.153[a]
Incision complications	0 (0)	1 (1.6)	> 0.999[a]
Splenic infarction	6 (28.6)	-	
Left-side portal hypertension	2 (9.5)	-	

Values are presented as number (%).
SPDP, spleen-preserving distal pancreatectomy; DPS, distal pancreatectomy with splenectomy; DGE, delayed gastric emptying; NA, not available.
[a]Fisher's exact test.

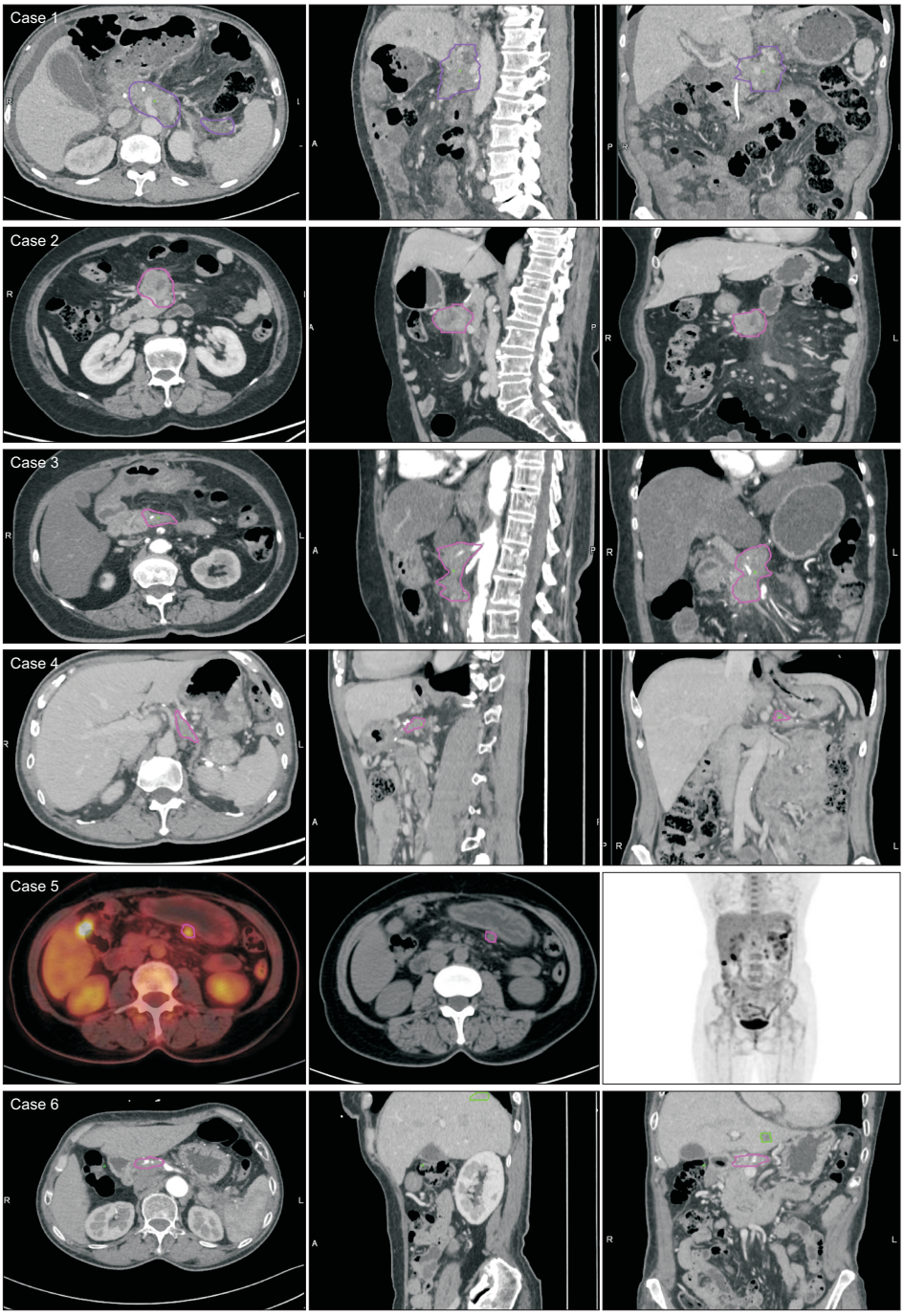

Fig. 2. Images depict the sites of local recurrence for six patients who underwent postoperative CT/PET-CT examinations in our hospital in the SPDP group (purple: recurrence, green: metastasis): All cases exhibited central region recurrence. Case 1 had a spleen region recurrence, and Case 6 experienced liver metastasis. Case 5 was documented from postoperative PET-CT. PET-CT, positron emission tomography–computed tomography; SPDP, spleen-preserving distal pancreatectomy.

with abdominal infections caused by gram-negative bacteria identified in the puncture fluid. Another patient with grade C delayed gastric emptying was managed with a nasal enteral nutrient solution administered via a nutrition tube placed under intervention. Given that this is a retrospective study, it is conceivable that more aggressive tumors were managed with DPS, potentially contributing to the observed higher rate of severe complications in this group.

In this study, we observed no difference in the incidence of overall complications and postoperative hospital days (Table 2). However, we believe that numerous benefits could be derived from performing SPDP. Spleen preservation is vital for perioperative recovery. The spleen, the largest secondary immune organ in the body, plays a crucial role in initiating the immune response to blood-derived antigens [20]. Spleen preservation contributes to maintaining immune function and the func-

tionality of the blood system during the treatment of low-grade malignant tumors [21,22]. Retrospective studies indicate that SPDP is associated with a shorter hospital stay, fewer postoperative days, and lower morbidity compared to DPS [23,24]. Preservation of the spleen also avoids complications associated with splenectomy. Infections, thromboembolism, and adhesive intestinal obstruction are common complications following splenectomy [25]. Moreover, compared to the general population, the risks of overall cancer and certain site-specific cancers significantly increase in patients with splenectomy [25,26].

In the present study, 29 cases (34.5%) developed clinically relevant pancreatic fistula. All grades were B level, and none died from this complication. The higher incidence of fistula may be attributable to our center's stricter criteria, which considers discharge with an abdominal drainage tube as a grade B fistula, more stringent than ISGPS criteria. The laparoscopic ap-

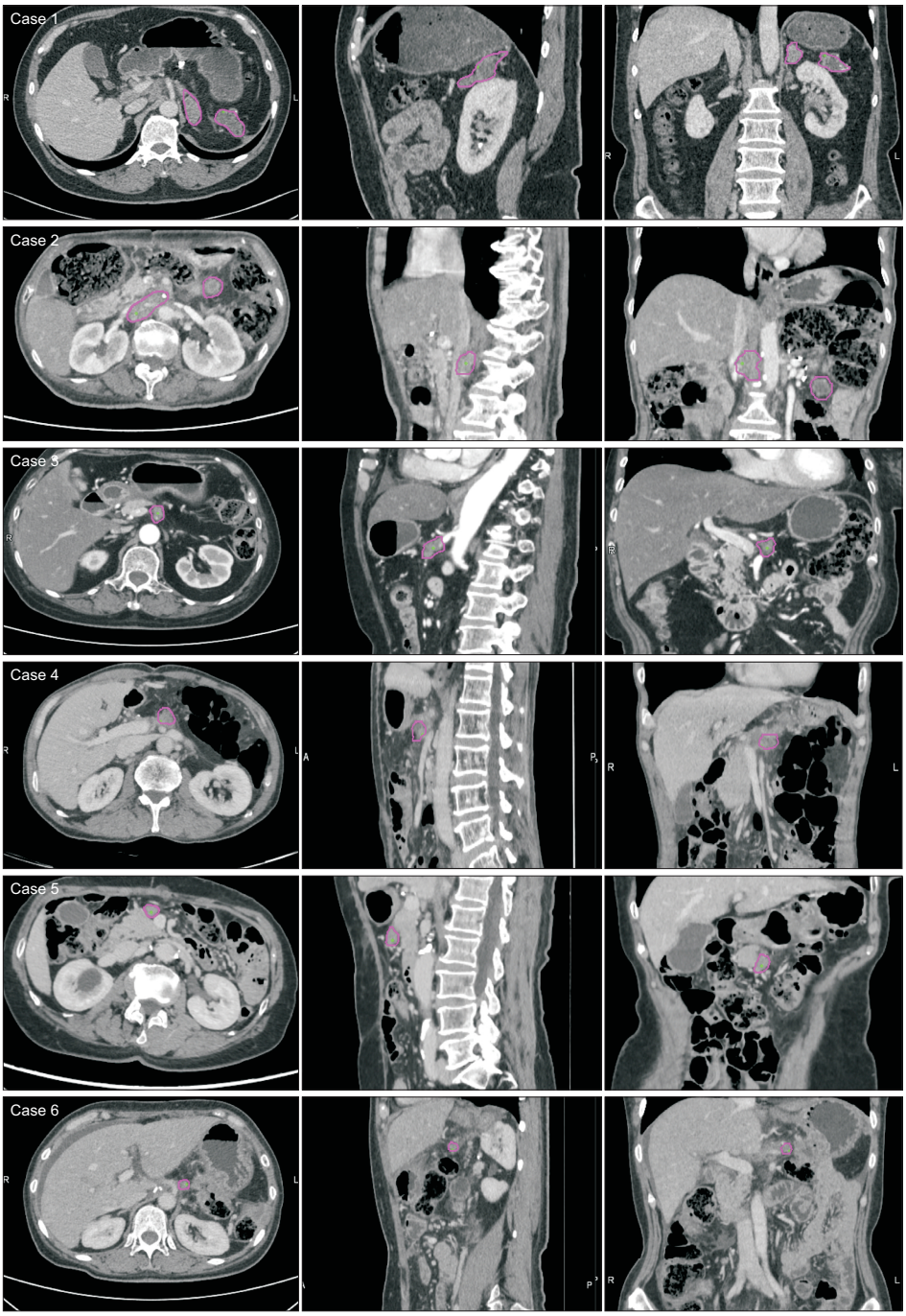

Fig. 3. Images show the sites of local recurrence for ten patients who underwent postoperative CT/PET-CT examinations in our hospital in the DPS group (purple: recurrence, green: metastasis): all cases exhibited central region recurrence. Cases 1 and 2 had spleen region recurrences. Case 9 experienced omental metastases, and Case 10 had liver metastases. Case 8 was documented from postoperative PET-CT. PET-CT, positron emission tomography–computed tomography; DPS, distal pancreatectomy with splenectomy.

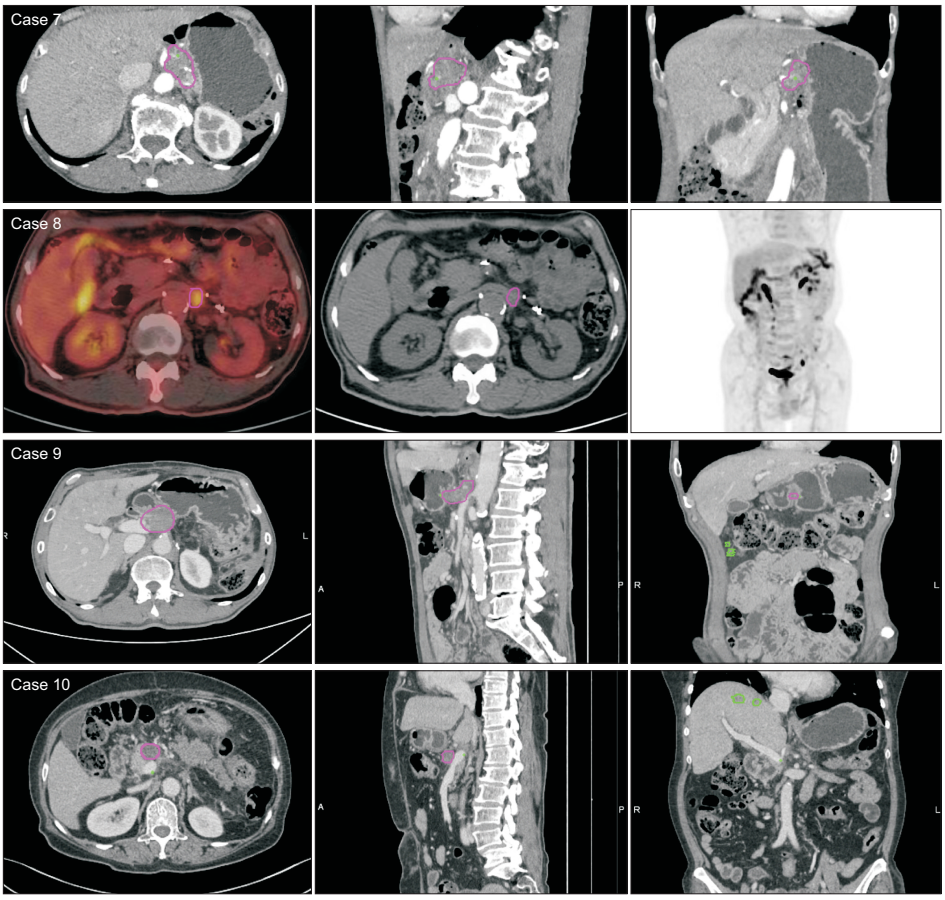

Fig. 3. Continued.

Table 4. Recurrence and metastasis

	SPDP group (n = 21)	DPS group (n = 63)	*p*-value
Adjuvant chemotherapy	17 (81.0)	53 (84.1)	0.742[a]
Recurrence/metastasis	11 (52.4)	34 (54.0)	> 0.999[a]
Type of recurrence and metastasis			-
Local recurrence	1	5	
Distant metastasis	3	17	
Local recurrence + distant metastasis	7	12	
Sites of recurrence and metastasis			-
Local recurrence	8 (38.1)	17 (27.0)	
Central region	7	14	
Central region + spleen region	1	3	
Distant metastasis	10 (47.6)	29 (46.0)	
Liver	4	19	
Lung	3	3	
Other	6	15	

Values are presented as number (%) or number only.
SPDP, spleen-preserving distal pancreatectomy; DPS, distal pancreatectomy with splenectomy; NA, not available.
[a]Fisher's exact test.

proach with high-definition magnification of the surgical field may further reduce operation time and enhance the minimally invasive [27] nature of the procedure. No patient in this study received a robotic approach, and the laparoscopic rates were

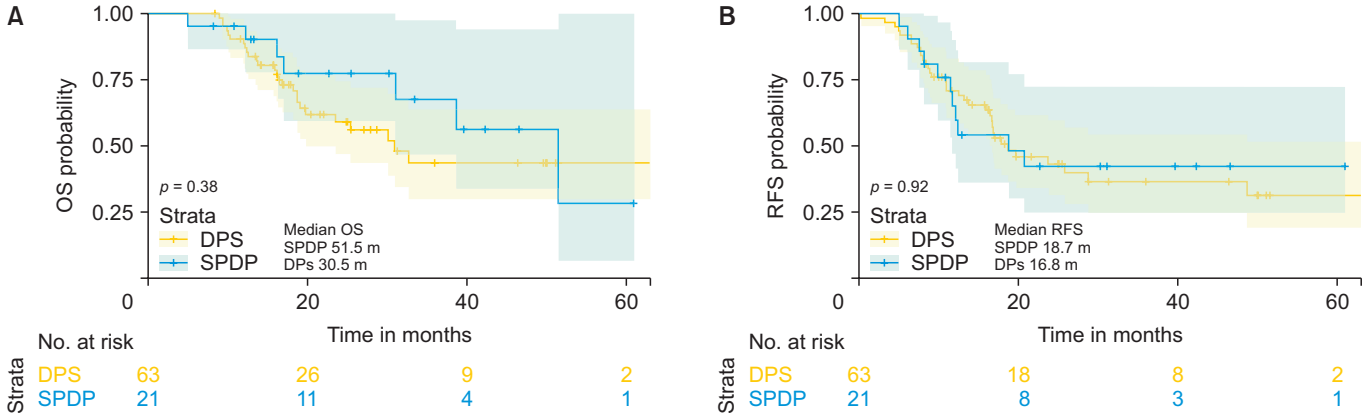

Fig. 4. Comparisons of overall survival and recurrence-free survival between patients in the SPDP group and the DPS group include: (A) Kaplan-Meier (K-M) curve and number at risk of OS in both groups. (B) K-M curve and number at risk of RFS in both groups. The median follow-up time was 30.2 vs 25.5 months. SPDP, spleen-preserving distal pancreatectomy; DPS, distal pancreatectomy with splenectomy; OS, overall survival; RFS, recurrence-free survival.

comparable between both groups. With comparable pathological grades and the efficacy of radical surgical treatments, the long-term postoperative survival, including OS and RFS for SPDP, was not inferior to that observed in the DPS group. The inclusion of multiple histological subtypes of pancreatic tumors, such as PDAC, adenosquamous carcinoma, and IPMN-inv, complicates the ability to draw definitive conclusions regarding long-term outcomes. These subtypes exhibit unique biological behaviors, treatment responses, and prognoses. We conducted separate comparisons of outcomes in patients with pathological PDAC (17 vs 49), yielding similar results (data not shown).

The postoperative recurrence was mainly concentrated in the central region of the pancreatic stump and head. Four patients (4.8%) experienced tumor recurrence in the splenic area, all with central area recurrence, and there were no instances of recurrence solely in the splenic area. Although the SPDP group had fewer harvested lymph nodes, there was no significant difference in recurrence rates in the splenic region between the groups. It must be acknowledged that inadequate lymphadenectomy may cause staging migration, potentially biasing survival outcomes in favor of SPDP.

Our study showed splenic infarction did not necessitate a splenic abscess puncture, and there were no clinical consequences of left-side portal hypertension in any patient during the follow-up period. However, the follow-up period is too brief to adequately evaluate the long-term risks associated with this complication, which often develops years after surgery and demands extended follow-up for a comprehensive understanding of its incidence and clinical impact. Other researchers have monitored patients after SPDP for up to 21 years, and left-side portal hypertension rarely resulted in clinically significant consequences [8].

The study involves a limited number of patients, and significant heterogeneity in the pathological outcomes. Therefore, the oncological outcomes presented in this article may not accurately represent the real-world outcomes.

In conclusion, our article preliminarily demonstrates that distal pancreatectomy with spleen preservation by WT does not adversely impact local recurrence and survival in selected cases of pancreatic body cancer. An analysis incorporating a larger cohort through a multicenter study is necessary. This research has the potential to serve as a crucial reference, aiding in the optimization of surgical strategies and the enhancement of patient outcomes.

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CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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