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Clinical Efficacy of Organ-Preserving Pancreatectomy for Benign or Low-Grade Malignant Potential Lesion

The clinical usefulness of organ-preserving pancreatectomy is not well established due to technical difficulty and ambiguity of functional merit. The purpose of this study is to evaluate the clinical efficacy of organ-preserving pancreatectomy such as duodenum-preserving resection of the head of the pancreas (DPRHP), pancreatic head resection with segmental duodenectomy (PHRSD), central pancreatectomy (CP) and spleen-preserving distal pancreatectomy (SPDP). Between 1995 and 2007, the DPRHP were performed in 14 patients, the PHRSD in 16 patients, the CP in 13 patients, and the SPDP in 45 patients for preoperatively diagnosed benign lesions or tumors with low-grade malignant potential. The clinical outcomes including surgical details, postoperative complications and long-term functional outcomes were compared between organ-preserving pancreatectomy and conventional pancreatectomy group. Major postoperative complications constituted the following: bile duct stricture (7.1% [1/14]) in DPRHP, delayed gastric emptying (31.2% [5/16]) in PHRSD, pancreatic fistula (21.4% [3/14]) in CP. There were no significant differences in postoperative complications and long-term functional outcomes between two groups. Organ-preserving pancreatectomy is associated with tolerable postoperative complications, and good long-term outcome comparing to conventional pancreatectomy. Organ-preserving pancreatectomy could be alternative treatment for benign or low-grade malignant potential lesion of the pancreas or ampullary/parapapillary duodenum.

Key Words : *Pancreatectomy; Organ-Preserving; Low-Grade Malignant*

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INTRODUCTION

Owing to being shared vascular supply and anatomical proximity and hold the pancreatic duct in common, spleen or duodenum is considered to be resected together with the pancreas in case of resection of tail of pancreas or head of pancreas. However, advance in surgical skill and surgical anatomy makes the organ-preserving pancreatectomy possible.

Until now, various types of organ-preserving pancreatectomy have been introduced such as duodenum-preserving pancreatic head resection (DPPHR), pancreatic head resection with segmental duodenectomy (PHRSD), central pancreatectomy (CP), ventral pancreatectomy (1), segmental resection of pancreas (2), ductal branch-oriented minimal pancreatectomy (3), and spleen-preserving distal pancreatectomy (SPDP). It has been suggested that a limited resection has the advantage of preserving function of the pancreas and the organs around pancreas (4-8). However, its clinical usefulness is not well established due to the technical difficulty, ambiguity of functional merit and limited number of cases.

In this study, to determine the clinical efficacy and feasibility of the organ-preserving pancreatectomy, we retrospectively analyzed the clinical outcomes of various type of organ-preserving pancreatectomy and compared with those of conventional pancreatectomy such as pylorus-preserving pancreaticoduodenectomy (PPPD) and distal pancreatectomy.

MATERIALS AND METHODS

Between 1995 and 2007, the duodenum-preserving resection of the head of the pancreas (DPRHP) was performed in 14 patients, the PHRSD in 16 patients, the CP in 14 patients, and the SPDP in 45 patients at the Department of Surgery, Seoul National University Hospital, Seoul, Korea. They were preoperatively diagnosed as benign lesions or tumors with

low-grade malignant potential at the pancreas or ampullary/parapapillary duodenum. During the same period, the PPPD and the distal pancreatectomy (DP), which are classified as kinds of the conventional pancreatectomy, were performed in 70 patients and in 143 patients, respectively for benign lesions or tumors with low-grade malignant potential at the pancreas or ampullary/parapapillary duodenum.

The DPRHP and PHRSD were performed in the same manner as described in our previous report (9) (Fig. 1, 2). For the CP, SPDP, and DP, proximal stump of the pancreas was reinforced with suture by 4-0 black silk and 5-0 polypropylene (prolene*, Ethicon, Somerville, NJ, USA). The main pan-

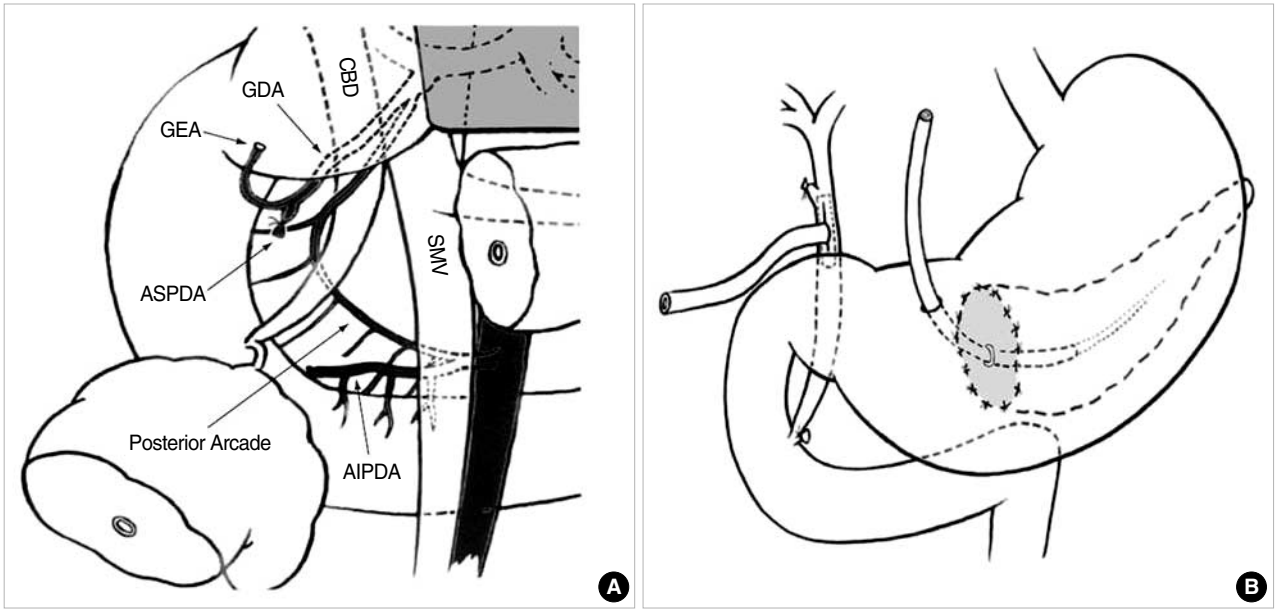

Fig. 1. Schematic diagram of the duodenal-preserving resection of the head of the pancreas (adopted from ref.9, Arch Surg 2003;138:162-8). (A) Operative procedure of DPRHP. ASPDA indicates anterior superior pancreaticoduodenal artery. (B) View after the total resection of the head of the pancreas, pancreatogastrostomy, T tube insertion, and pancreatic diversion were performed.
AIPDA, anterior inferior pancreaticoduodenal artery; CBD, common bile duct; GDA, gastroduodenal artery; GEA, gastroepiploic artery; SMV, superior mesenteric vein.

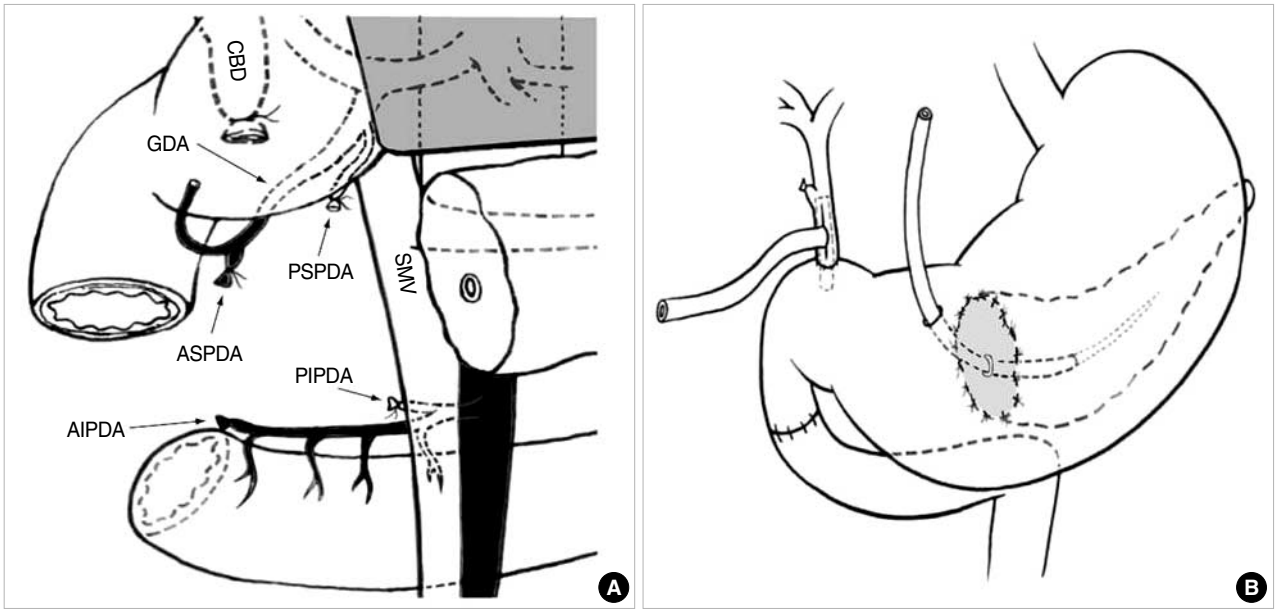

Fig. 2. Schematic diagram of the pancreas head resection with segmental duodenectomy (adopted from ref.9, Arch Surg 2003;138:162-8). (A) Operative procedure of PHRSD. (B) View after the resection, a pancreatogastrostomy, an end-to-side choledochoduodenostomy with a T-tube stent, and an end-to-end duodenoduodenostomy were performed.

creatic duct in proximal stump was ligated with non-absorbable suture directly. In the CP, pancreaticogastrostomy or pancreaticojejunostomy with two-layer duct-to-mucosa anastomosis technique were performed to the distal stump. In the SPDP, both splenic artery and vein were preserved.

Clinical data were obtained from the patient's medical records (surgical reports, pathologic reports, postoperative data, hospital course, and outpatient medical records). The surgical factors (including operation time, estimated blood loss, and transfusion) and postoperative complications were analyzed. The postoperative long-term outcomes (endocrine and exocrine function, recurrence, and weight change) were also evaluated. We divided the organ-preserving pancreatectomy into two types according to the location of lesion, i.e., pancreatic head or ampullary/parapapillary duodenum and pancreatic body/tail. We compared the DPRHP and the PHRSD with the PPPD for lesion of head of the pancreas or ampullary/parapapillary duodenum, and compared the CP and the SPDP with DP for the lesion of the body or tail of the pancreas.

Data from multiple determinations were expressed as mean ±standard deviation. We used a chi-square test and Fisher exact test for categorical comparison of data. Differences in the means of continuous measurements were tested with the Mann-Whitney U test. *P* values of less than 0.05 were considered significant.

RESULTS

Table 1 lists the patient's demographics and postoperative diagnosis. There were no significant differences in age, sex, and postoperative diagnosis between the DPRHP and the PPPD, between the PHRSD and the PPPD, between the CP and the DP, and between the SPDP and the DP. In the PHRSD, there were 5 patients diagnosed as malignant disease. The final diagnosis of 2 patients having villous adenoma on the preoperative endoscopic biopsy specimen was proved to be an early duodenal cancer. On the postoperative pathologic report, it was shown to be well differentiated adenocarcinoma confined to mucosa. A patient with a metastatic renal cell carcinoma had a history of a radical nephrectomy for renal cell carcinoma 8 yr prior to PHRSD. The preoperative radiologic diagnosis was a nonfunctioning islet cell tumor of the pancreas. The preoperative diagnosis of a patient having pancreatic cancer was intraductal papillary mucinous neoplasm. On the postoperative pathologic report, it was shown to be a moderately differentiated adenocarcinoma, extending beyond pancreas, bile duct and pancreatic soft tissue. And the last one whose preoperative diagnosis was intraductal papillary mucinous neoplasm was proven as invasive intraductal papillary mucinous carcinoma. In the SPDP, there was one patient diagnosed as malignant disease. The patient with a metastatic carcinoma in lymph node had a history of a left hemihepatectomy for combined hepatocellular and cholangiocarcinoma 2 yr before SPDP. Because the metastatic lymph node was so closely attached to pancreatic parenchyma and could not be dissected from parenchyma, SPDP was performed. On the postoperative pathologic report, there was no parenchymal invasion of carcinoma.

Surgical factors

Table 2 shows the perioperative factors and there were no

Table 1. Patient's demographics and postoperative diagnoses

Parameters	DPRHP (n=14)	PHRSD (n=16)	PPPD (n=70)	*P* value		CP (n=14)	SPDP (n=45)	DP (n=143)	*P* value	
				DPRHP vs. PPPD	PHRSD vs. PPPD				CP vs. DP	SPDP vs. DP
Age (yr)	47±14	56±10	56±14	0.065	0.952	46±7	50±14	52±15	0.046	0.101
Male:Female	1:1.8	1:1.3	1.5:1	0.143	0.254	1:3.5	1:1.6	1:1.7	0.126	0.235
Diagnosis				0.442	0.551				0.341	0.424
Benign										
Cystic neoplasm	6	3	8			8	16	44		
Intraductal papillary mucinous neoplasm	4	2	15			1	8	19		
Solid pseudopapillary neoplasm	1	0	2			2	8	16		
Islet cell tumor	2	2	6			2	5	9		
Tubovillous adenoma of ampulla of Vater	0	4	15			0	0	0		
Others*	1	0	11			1	7	34		
Malignant	0	5†	13‡			0	1§	22‡		

*Epidermal cyst, chronic pancreatitis, pseudocyst, etc.; †Duodenal cancer, pancreatic cancer, intraductal papillary mucious carcinoma, metastatic renal cell carcinoma; ‡intraductal papillary mucious carcinoma, malignant islet cell tumor; §Metastatic hepatocelluar carcinoma.
DPRHP, duodenum-preserving pancreatic head resection; PHRSD, pancreatic head resection with segmental duodenectomy; PPDD, pylorus-preserving pancreaticoduodenectomy; CP, central pancreatectomy; SPDP, spleen-preserving distal pancreatectomy; DP, distal pancreatectomy.

Table 2. Comparison of perioperative factors

Factors	DPRHP (n=14)	PHRSD (n=16)	PPPD (n=70)	*P* value		CP (n=14)	SPDP (n=45)	DP (n=143)	*P* value	
				DPRHP vs. PPPD	PHRSD vs. PPPD				CP vs. DP	SPDP vs. DP
Operation time (min)	380±98	369±53	337±62	0.202	0.072	228±67	223±130	211±94	0.668	0.514
Estimated blood loss (mL)	411±209	417±240	443±300	0.780	0.774	292±530	384±241	477±749	0.411	0.519
Intraoperative transfusion (yes)	0	0	5 (7.1%)	0.219	0.218	1 (7.1%)	2 (4.4%)	11 (7.7%)	0.932	0.628
Pancreatic leakage	1 (7.1%)	3 (18.8%)	10 (14.3%)	0.625	0.225	3 (21.4%)	6 (13.3%)	21 (14.7%)	0.590	0.875
Pseudoaneurysm	0	1 (6.3%)	2 (2.9%)	0.439	0.479	0	0	0		
Intra-abdominal abscess	1 (7.1%)	2 (12.5%)	7 (10.0%)	0.924	0.660	1 (7.1%)	3 (6.7%)	11 (7.7%)	0.968	0.977
DGE	0	5 (31.3%)	12 (17.1%)	0.283	0.149	0	0	0		
Bile duct stricture	1 (7.1%)	0	0	0.057		0	0	0		
Portal vein thrombosis	0	0	0			0	0	3 (2.1%)		0.239
OPSI	0	0	0			0	0	1 (0.7%)		0.498
Postoperative hospital stay (days)	22±15	30±11	23±10	0.873	0.034	17±7	16±9	15±9	0.842	0.758
Hospital mortality	0	0	0			0	0	0		

DPRHP, duodenum-preserving pancreatic head resection; PHRSD, pancreatic head resection with segmental duodenectomy; PPDD, pylorus-preserving pancreaticoduodenectomy; CP, central pancreatectomy; SPDP, spleen-preserving distal pancreatectomy; DP, distal pancreatectomy; DGE, Delayed gastric emptying; OPSI, Overwhelming postsplenectomy sepsis.

significant differences in operation time, estimated blood loss, and intraoperative transfusion between the DPRHP and the PPPD, between the PHRSD and the PPPD, between the CP and the DP, and between the SPDP and the DP.

Postoperative complications and hospital course

Table 2 shows the postoperative complications of the procedures and postoperative hospital stay. Pancreatic leakage was defined as drainage of more than 30 mL of fluid with an amylase level higher than 600 U/dL on or after postoperative week 1 (10). Pancreatic leakages were detected in 3 (18.8% [3/16]) patients who underwent PHRSD and in 3 patients (21.4% [3/14]) who underwent CP. All the patients in whom pancreatic leakages occurred recovered well with conservative management with percutaneous drainage and short-period fasting. There was no significant difference between the PHRSD and the PPPD group and between the CP and the DP group.

Major postoperative bleeding presenting as gastrointestinal tract bleeding occurred in one patient who underwent PHRSD, after hospital discharge. This patient required an additional operation to control the bleeding from the inferior pancreaticoduodenal vessels caused by a leakage from the pancreaticogastrostomy site. There was no significant difference in pseudoaneurysm between the PHRSD and the PPPD group.

There was no hospital mortality associated with surgical complication.

Delayed gastric emptying was defined as nasogastric drainage for more than 10 days, or a reinsertion of a nasogastric tube because of vomiting, or a failure to tolerate a semisolid diet 14 days after surgery (11). In 5 (5/16 [31.3%]) patients who underwent PHRSD, delayed gastric emptying developed, and was managed conservatively with a complete recovery. There was no significant difference in delayed gastric emptying development between PHRSD and PPPD group. Hospital stay was longer in PHRSD group than in PPPD group for management of delayed gastric emptying (P=0.034).

In one patient with intraductal papillary mucinous neoplasm who underwent DPRHP, obstructive jaundice due to a focal bile duct stricture developed a few days after hospital discharge. We routinely insert a T tube for all the patients who underwent the DPRHP and the patient's condition was managed successfully by an interventional balloon dilatation through the T tube tract. The patient has been healthy with normal liver function for 30 months.

There was one patient who had the potential for splenic infarct after SPDP. On the computed tomography (CT) scan 4 yr after surgery, the appearance of volume loss with multifocal low attenuated lesions at the spleen with intact splenic artery was seen without any overt symptom. The patient is still alive without problems 7 yr after the surgery.

Splenic vein thrombosis occurred in one patient who underwent DP due to hematologic disease. He received anticoagulation treatment. There was no more progression of the thrombosis. Portal vein thrombosis occurred in three patients after distal pancreatectomy. They received no specific treatment, and thrombosis was improved on radiologic image study.

There was one patient who was suspected as overwhelming postsplenectomy sepsis (OPSI) after distal pancreatectomy and he was only one patient who experienced septic shock in our study. Intravenous antibiotics treatment was performed

Table 3. Long-term outcome after surgery

Outcomes	DPRHP (n=14)	PHRSD (n=16)	PPPD (n=70)	*P* value		CP (n=14)	SPDP (n=45)	DP (n=143)	*P* value	
				DPRHP vs. PPPD	PHRSD vs. PPPD				CP vs. DP	SPDP vs. DP
Follow-up period (months)	32±20	31±18	42±38	0.095	0.087	30±21	33±29	36±33	0.494	0.624
Diabetes mellitus										
Newly developed	0	1 (6.3%)	7 (10.0%)	0.143	0.846	0	4 (8.9%)	16 (11.2%)	0.477	0.898
Unchanged	1 (7.1%)	1 (6.3%)	24 (34.3%)	0.022	0.036	0	4 (8.9%)	16 (11.2%)	0.477	0.898
Aggravated	0	0	0			0	0	0		
Steatorrhea	0	1 (6.3%)	6 (8.6%)	0.177	0.694	0	0	0		
Weight loss	0	2 (12.5%)	14 (20.0%)	0.240	0.846	0	0	0		
Recurrence	0	0	4 (5.7%)	0.235	0.218	0	0	2 (1.4%)	0.570	0.337

DPRHP, duodenum-preserving pancreatic head resection; PHRSD, pancreatic head resection with segmental duodenectomy; PPDD, pylorus-preserving pancreaticoduodenectomy; CP, central pancreatectomy; SPDP, spleen-preserving distal pancreatectomy; DP, distal pancreatectomy.

and his medical condition had been improved. There was no hospital mortality associated with this study.

Long-term outcomes of patients

Long-term outcomes were followed to keep track of pancreatic endocrine and exocrine function, weight change, gastrointestinal tract symptoms, and disease recurrence (Table 3). Regarding the endocrine function, 6 patients had diabetes mellitus and 2 patients had insulinoma with hypoglycemia preoperatively in organ-preserving pancreatectomy group. Normoglycemia was obtained after removing the insulinoma. Newly developed diabetes mellitus was noted in 1 patient after PHRSD and in 7 patients after PPPD, and there was no significant difference between two groups. Newly developed diabetes mellitus was noted in 4 patients after SPDP and in 16 patients after DP, there was no significant difference between two groups. Three patients complained of postoperative steatorrhea with intermittent abdominal cramping pain in the early posthospital days after PHRSD. One of the aforementioned patients is still suffering from postprandial diarrhea and severe steatorrhea. The others recovered within 3 months postoperatively. There were 6 patients who suffered from steatorrhea after PPPD and no significant difference between PHRSD and PPPD group. Weight loss was defined as loss of weight more than 10% of their preoperative body weight during the postoperative 3 months. Weight loss was detected in two patients who underwent the PHRSD and 14 patients after PPPD. There was no significant difference between the two groups. Symptoms of cholangitis, which might occur due to choledochoduodenostomy, were not observed in any patient after PHRSD. There was no evidence of recurrence in all the patients who underwent organ-preserving pancreatectomy including two patients with early duodenal cancer and pancreatic cancer at 31 and 28 months after the operation, respectively. There were four patients who experienced recurrence after PPPD. They underwent PPPD for intraductal papillary mucinous carcinoma or malignant islet cell tumor and liver metastasis occurred during follow-up period. There were two patients with recurrence who underwent distal pancreatectomy for intraductal papillary mucinous neoplasm, borderline and malignant islet cell tumor.

DISCUSSION

Pancreaticoduodenectomy and DP with splenectomy are standard operation for patients with pancreatic neoplasm with the introduction of the concept of less invasive surgery and in consideration of postoperative quality of life, for patients with benign lesions or low-grade malignant potential tumor, other parenchymal sparing or spleen-preserving techniques are attempted.

Despite the improvement of operative technique, materials and instruments, pancreatic fistula after pancreaticoduodenctomy is the most common and serious complication. Recent large series have reported that the failure rate of the pancreaticoenteric anastomosis is 9-18% (12-16). In our study, the rate of pancreatic leakage was 7.1% in DPRHP group and 18.8% in PHRSD group. In PHRSD group, the rate is slightly higher than in PPPD group (14%), but the difference was not significant. The cause of high incidence of pancreatic leakage after PHRSD was uncertain. In all cases with pancreatic leakage, there was no history of pancreatitis. Their pancreatic parenchyma, however, were soft and it was thought to be the main reason of the leakage. The results of this study suggest that the weak point of CP was a high risk of pancreatic leakage. The leakage rate after CP was 21.3%, which was slightly higher than PPPD or DP group. However, the differences were not significant between CP and PPPD group (data was not shown), and between CP and DP group. The rate of pancreatic leakage after CP is reported up to 60% (17, 18). The high incidence may be a result of the creation of two pancreatic remnants with CP, each of which is a potential source of pancreatic leakage.

Delayed gastric emptying, which is non-life-threatening

complication, has been described as one of the leading causes of postoperative morbidity after PPPD, occurring up to 50% of patients (19-21) and after PHRSD occurring up to 38% (22). In our study, delayed gastric emptying occurred in no patient after DPRHP and in 5 patients (31% [5/16]) after PHRSD. And there was significant difference between the DPRHP and the PHRSD group (P=0.051). The reason of these results is not clear, however, it was surmised that duodenectomy might disrupt the coordination of gastric and intestinal motility. And preservation of the duodenum in DPRHP seem to be more physiologic and showed better results over PHRSD or PPPD.

Only one biliary complication from DPRHP was experienced. This patient had a stricture of the distal common bile duct, which was successfully managed by dilatation and temporary stenting. A focal ischemia or a sealed-off microperforation might be the cause of the stricture, which appears to be a procedure (DPRHP)-related complication.

Splenectomy in conjunction with DP is clearly indicated in most patients with adenocarcinoma of the pancreas, as splenic preservation may compromise the oncologic resection. However, for benign and low-grade malignant disease, the issue of splenic preservation may have a role. Splenic-preservation has been performed because of consideration of overwhelming postsplenetomy sepsis (23, 24) and immunologic function of the spleen (25, 26). In our study, there were no significant differences in postoperative complication rate, operative time, or length of postoperative hospitalization between SPDP and DP group. However we experienced one case with overwhelming postsplenectomy sepsis in distal pancreatectomy group. Although technically demanding, SPDP can be performed safely and has the advantage of reducing the risk of overwhelming postsplenectomy infection.

The percentage of patients who become diabetic after Whipple's operation amounts to 20% to 40% (27). A prospective study performed by Bittner et al. (28) to evaluate the endocrine pancreatic function following DPRHP showed in most patients, DPRHP did not lead to an impairment of glucose tolerance. In our study, one patient (7%) became diabetic after PHRSD and 4 patients (11%) became diabetic after SPDP. Their diabetes mellitus were under control with taking oral hypoglycemic drugs.

Organ-preserving pancreatectomy is associated with tolerable perioperative risk, postoperative complications, and good long-term outcome in the aspects of preservation of function and curability in tumors with low-grade malignant potential when compared to conventional pancreatectomy. Organ-preserving pancreatectomy could be alternative treatment for benign or low-grade malignant potential lesions of pancreas or ampullary/parapapillary duodenum. Even then, organ-preserving pancreatectomy will be suitable for only a small group of patients and should only be performed by experienced surgeons.

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