

A Central Pancreatectomy for Benign or Low-Grade Malignant Neoplasms

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Abstract

Introduction A central pancreatectomy is a parenchyma-sparing procedure that is performed to reduce long-term endocrine and exocrine insufficiency.

Method In this study, we analyzed the perioperative course, the frequency of postoperative onset of diabetes mellitus, and long-term change of body weight in patients undergoing a central pancreatectomy, in comparison to the patients undergoing a distal pancreatectomy for low-grade neoplasms including cystic neoplasms and neuroendocrine tumors.

Results and Discussion The rate of postoperative complications including grade B/C pancreatic fistula was no different between both groups. Only one patient undergoing a central pancreatectomy (4.7%) developed new onset of mild diabetes, whereas 35% in the distal pancreatectomy group developed new onset or worsening diabetes ($p=0.0129$). The body weight in the distal pancreatectomy group was significant lower than that in the central pancreatectomy group at 1 and 2 years after surgery (1 year; $P<0.0001$, 2 years; $P=0.0055$), and the body weight in the patients undergoing a central pancreatectomy improved to preoperative values within 2 years after surgery.

Conclusion A central pancreatectomy is a safe procedure for the treatment of low-grade malignant neoplasms in the pancreatic body; the rate of onset of diabetes is minimal, and the body weight improves early in the postoperative course.

Keywords Central pancreatectomy · Postoperative complication · Diabetes mellitus · Body weight change

Introduction

In recent years, the incidental discovery rate of benign or low-grade malignant neoplasms of the pancreas has increased with the advance of diagnostic imaging system.^{1,2} The resection of neoplasms located in the pancreatic body traditionally has been accomplished by a distal pancreatectomy (DP) as a standard operation.^{3–5} However, the use of a DP for isolated, small, and low-grade malignant neoplasms in the pancreatic body, such as noninvasive intraductal papillary mucinous

neoplasm (IPMN), mucinous cystic neoplasm (MCN), benign neuroendocrine tumor (NET), and pancreatic metastases from other tumors, results in the removal of unaffected normal pancreatic tissue, increasing the risk of endocrine and exocrine malfunction. Whereas tumor enucleation, which is considered an indication for benign neoplasm such as an insulinoma, should be avoided when the main pancreatic duct may be injured or the margins are not defined.⁶ Under these circumstances, a central pancreatectomy (CP) has been proposed as an alternative technique in the patients with isolated and small neoplasms in the pancreatic body, not required with lymph node dissection, for preserving the pancreatic parenchyma and reducing the risk of exocrine and endocrine insufficiency.^{7–9}

In 1957, Guillemin and Bessot¹⁰ first performed a central segmental pancreatic resection for a patient with pancreatitis, and 2 years later, Letton and Wilson¹¹ performed in two cases of severe traumatic injury of the pancreatic body. The first CP for a neoplasm was done by Dagradi and Serio¹² in 1984 for benign insulinoma. Since then, several institutions have reported perioperative

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course and postoperative complications of this technique using the following terminology: CP,^{7–9} middle pancreatectomy,¹³ or middle segmental pancreatectomy.¹⁴

Most reports revealed higher pancreatic fistula rates of CP, as opposed to standard pancreatic resection.^{9,15,16} These reports are convinced because a CP requires handling two divided edges of the pancreas, creating two opportunities for pancreatic fistula. Regarding pancreatic function, a few reports revealed preservation of endocrine and exocrine functions in the patients undergoing a CP, in comparison to those undergoing a DP.^{6,13,14} However, the DP group in the previous studies enrolled the patients with pancreatic ductal carcinoma, requiring lymph node dissection and adjuvant therapy, and chronic pancreatitis.^{3,17} Indeed, these patients may have impaired pancreatic function after surgery; therefore, the comparison of both surgical techniques may not be suitable for patients with high-grade malignancies or chronic pancreatitis.

In the present study, evaluating the benefit of a CP more accurately, we analyzed the patients with benign or low-grade malignant neoplasms in terms of postoperative complications, onset of diabetes mellitus, and body weight change.

Material and Methods

Patients

Data were prospectively collected in a database from October 1999 through September 2008 for the patients undergoing a CP at Wakayama Medical University Hospital (WMUH). The indication for surgery was a symptomatic or an asymptomatic localized neoplasm in the pancreatic body of unknown histology. The potential suitability for a CP was determined by preoperative imaging in all cases, such as ultrasonography (US) and computed tomography (CT), with most patients undergoing magnetic resonance imaging, or endoscopic US, or endoscopic retrograde pancreatography.

To evaluate perioperative and long-term functional outcomes for a CP, we compared a CP and a DP for only patients with benign or low-grade malignant neoplasms during the same time. Informed consent was obtained from all patients, and this clinical study was conducted according to the guidelines of the Ethical Committee of WMUH.

Surgical Procedure for a CP

After a midline upper abdominal laparotomy, the lesser sac was opened by division of the gastrocolic ligament preserving the gastroepiploic vessels. The anterior aspect of the pancreas was exposed by dividing the adhesions between the posterior surface of the stomach and the pancreas. Intraoperative US of the pancreas was used to

detect the tumor and determine the relationship of the tumor to the vascular structure and the main pancreatic duct. The superior mesenteric, portal, and splenic veins were dissected free from the posterior aspect of the pancreas, with care taken to ligate multiple small side branches to the pancreas. The lesion, localized in the body of the pancreas, was resected with a margin of at least 1 cm to both cut pancreatic ends. Both cut ends were submitted for an intraoperative frozen section analysis in all patients. No anastomoses were performed in the proximal pancreatic remnant. Reconstruction of the distal pancreatic remnant was performed by a duct-to-mucosal, an endo-to-side pancreaticojejunostomy in 21 patients, and a pancreaticogastrostomy in three patients. External suture rows were performed as a single suture between the remnant pancreatic capsule, parenchyma, and jejunal or gastric seromuscular. Internal suture rows, duct-to-mucosa, were performed between the pancreatic ductal and jejunal or gastric mucosa.¹⁸ A 5-French polyethylene

Table 1 Characteristics of 52 Patients with Benign or Low-Malignant Neoplasms of the Pancreatic Body

Characteristics	Central pancreatectomy (n=24)	Distal pancreatectomy (n=28)	P value
Median age [year (range)]	69.0 (26–81)	68.5 (20–78)	0.7550
Gender ratio, (male/female)	10/14	9/19	0.4771
Pathology			
IPMN (%)	16 (66)	13 (46)	0.1430
Minimally invasive carcinoma	1	1	
Carcinoma in situ	2	2	
Adenoma	13	10	
Mucinous cystic neoplasm (%)	2 (8)	3 (10)	0.7716
Carcinoma in situ	0	1	
Adenoma	2	2	
Serous cystic adenoma	2 (8)	4 (14)	0.5030
Solid pseudopapillary tumor	1 (4)	1 (3)	0.9114
Benign neuroendocrine tumor	2 (8)	5 (17)	0.3150
RCC metastasis	1 (4)	0 (0)	0.2754
Lymphoepithelial cyst	0 (0)	1 (3)	0.3499
Accessory spleen	0 (0)	1 (3)	0.3499
Mean size of tumor (cm)	3.0±1.0	3.5±2.0	0.0191

IPMN intraductal papillary mucinous neoplasm, RCC renal cell carcinoma

pancreatic duct drainage tube (Sumitomo Bakelite Co., Japan) was used in 12 patients and no stent in 12 patients. One 10-mm Penrose drain was routinely placed near the pancreatic anastomosis.¹⁹

Perioperative Course and Postoperative Complications

Perioperative mortality, defined as in-hospital death after surgery, and postoperative complications were evaluated. The pancreatic fistula definition was retrospectively assessed according to the International Study Group on Pancreatic Fistula (ISGPF) recommendations.²⁰ Intra-abdominal abscess was defined as intra-abdominal fluid collection with positive cultures identified by US or CT associated with persistent fever and elevations of white blood cells.^{18,19} Delayed gastric emptying was defined as prolonged aspiration of 500 ml/day from a nasogastric tube left in place for ≥ 10 days after surgery, the need for reinsertion of a nasogastric tube, or the failure to maintain oral intake by postoperative 14th postoperative day.^{18,19}

Onset of Diabetes Mellitus and Change of Body Weight

The follow-up was based on clinical, radiologic, and laboratory assessments every 6 to 12 months, to evaluate tumor recurrence as well as the endocrine and exocrine function.

The onset of diabetes was evaluated by monitoring the fasting glucose blood level and HbA1c levels. Patients suspected of having diabetes were diagnosed using an oral glucose tolerance test and thereafter were treated by diabetes specialists. New-onset diabetes was defined as diabetes with requirement of diet and/or medical treatment. Worsening diabetes was defined as deterioration in the metabolic control of previously diagnosed diabetes, thus requiring a modification of the medical treatment.

Percent change in body weight (%BW) and the presence of severe diarrhea (loose bowel movements more than ten times per day) were assessed as the exocrine function in both groups (CP and DP).

Table 2 Perioperative Course and Postoperative Complications

Variable	Central pancreatectomy (n=24)	Distal pancreatectomy (n=28)	P value
Operative median time [min (range)]	279 (205–399)	155 (100–401)	<0.0001
Blood loss median volume [ml (range)]	355 (20–4070)	425 (20–1630)	0.5882
Blood transfusion (%)	3 (13)	2 (7)	0.5136
Median size of remnant pancreatic tail [cm (range)]	5.6 (1.5–9.8)	–	
Comorbid pancreatitis	0 (0)	0 (0)	–
Reconstruction			
Pancreaticogastrostomy (%)	3 (12)	–	
Pancreaticojejunostomy (%)	21 (88)	–	
Overall morbidity (%) ^a	7 (29)	5 (18)	0.3346
Surgical complication (%)			
Pancreatic fistula ^b			
Grade A	12 (50)	6 (21)	0.0309
Grade B	3 (13)	4 (14)	0.8505
Grade C	0 (0)	0 (0)	–
Intra-abdominal abscess	1 (4)	2 (7)	0.6463
Delayed gastric emptying	1 (4)	0 (0)	0.2754
Wound infection	1 (4)	1 (3)	0.9114
Hemorrhage	0 (0)	0 (0)	–
Need of reoperation (%)	0 (0)	0 (0)	–
Need of interventional procedure (%)	3 (13)	5 (18)	0.5935
Nonsurgical complication (%)			
Pneumonia (%)	1 (4)	0 (0)	0.2754
Hepatic failure (%)	1 (4)	0 (0)	0.2754
Postoperative hospital stay [day (range)]	21.5 (11–58)	14.5 (8–57)	0.0362
Mortality			
During 30 postoperative days	0 (0)	0 (0)	–
During hospital stay	1 (4)	0 (0)	0.2754

^a Overall morbidity is represented as morbidity other than grade A pancreatic fistula

^b The pancreatic is defined according to the International Study Group on Pancreatic Fistula recommendation.

Statistical Analysis

Continuous variables were expressed as the mean±standard deviation. Comparison between two groups was performed with the Mann–Whitney *U* test, while categorical variables were compared by the χ^2 test and Fisher exact test when cell counts were less than five. A *P* value of <0.05 was considered to be statistically significant.

Results

Clinical Characteristics

Table 1 shows the clinical characteristics of the two groups (CP and DP). Twenty-four patients (ten men and 14 women) underwent a CP and 28 (nine men and 19 women) underwent a DP. The median age was 69.0 (range, 26–81 years) in the CP group and 68.5 years (range, 20–78 years) in the DP group. The definitive histology of the resected neoplasms in the CP group

were 16 IPMN (13 branch type and three mixed type), two MCN, two serous cystadenoma, one solid pseudopapillary tumor, two benign NET, and one pancreatic metastasis from renal cell carcinoma, whereas that in the DP group included 13 IPMN (four branch type, three mixed type, and six main-duct type), three MCN, four serous cystadenoma, one solid pseudopapillary tumor, and five benign NET. Regarding IPMN, the incidence of main-duct type in the DP group was higher than that in the CP group (46% vs. 0%, *P*=0.0138). No differences were found between the two groups regarding age, gender, and incidence of each disease; however, the patients undergoing a DP had a larger neoplasm than the patients undergoing a CP (3.0±1.0 vs. 3.5±2.0 cm, *P*=0.0191; Table 1).

Surgical Resections and Perioperative Data

In addition to a pancreatic resection, one patient underwent cholecystectomy due to cholelithiasis in the CP group and 26 (93%) splenectomy, four cholecystectomy due to

Table 3 Onset of Diabetes Mellitus and Body Weight Change During More than 6 Months Follow-up After Surgery in Patients Undergoing Central Pancreatectomy and Distal Pancreatectomy

	Central pancreatectomy	Distal pancreatectomy	<i>P</i> value
Median follow-up [month (range)]	33.5 (3–111)	26.5 (3–110)	
Endocrine function			
New onset or worsening diabetes (%)	1/21 (5)	9/26 (35)	0.0129
New diabetes	1	6	
Diet treatment	1	2	
Oral drug	0	2	
Insulin	0	2	
Worsening diabetes ^a	0	3	
Diet treatment→oral drug	0	1	
Oral drug→insulin	0	2	
Body weight change			
Body weight change at 6 months after surgery			
Available for follow-up	21	26	
Median %BW	97.2 (91.8–110.3)	93.0 (80.0–103.1)	0.0003
Decreasing %BW <95%, <i>n</i> (%)	4 (19)	18 (69)	0.0006
Decreasing %BW <90%, <i>n</i> (%)	0 (0)	6 (23)	0.0184
Body weight change at 1 year after surgery			
Available for follow-up	20	26	
Median %BW	99.5 (92.1–113.2)	92.5 (76.9–102.1)	<0.0001
Decreasing %BW <95%, <i>n</i> (%)	2 (10)	19 (73)	<0.0001
Decreasing %BW <90%, <i>n</i> (%)	0 (0)	8 (31)	0.0063
Body weight change at 2 years after surgery			
Available for follow-up	17	19	
Median %BW	100.0 (92.1–117.6)	92.9 (76.9–108.9)	0.0055
Decreasing %BW <95%, <i>n</i> (%)	2 (12)	12 (63)	0.0016
Decreasing %BW <90%, <i>n</i> (%)	0 (0)	5 (26)	0.0164
Postoperative severe diarrhea (%)	0 (0)	0 (0)	–

^a Worsening diabetes is defined as a deterioration in the metabolic control of previously diagnosed diabetes, requiring a modification of the medical treatment

%BW percent change of body weight compared to the preoperative body weight

cholecystolithiasis, and one left nephrectomy due to renal cell carcinoma in the DP group. In the CP group, the median size of distant remnant was 5.6 cm (range, 1.5–9.8 cm). The pathological findings of stump in all resected specimens revealed no evidence of chronic pancreatitis, such as stromal fibrosis or lymphoplasmacytic infiltration, associated with primary disease including IPMN. Although the CP group required a longer operative time than the DP group (median; 279 vs. 155 min, $P<0.0001$), the operative blood loss volume (median, 355 vs. 425 ml, $P=0.5880$) and the percentage of patients needing blood transfusions (13% vs. 7%, $P=0.5136$) were not significantly different between both groups (Table 2).

Perioperative Course and Complications

The mortality during the first 30 postoperative days was zero in both groups, and one patient of IPMN with severe liver cirrhosis undergoing a CP died 55 days after surgery due to hepatic failure, uncontrollable ascites, icterus, and gastrointestinal bleeding. Although the incidence of grade A pancreatic fistula (transient fistula without any clinical impact) in the CP group was 50%, the rate of clinically significant fistula (grade B and C by the ISGPF)²⁰ was only 13%, which was not a significantly different incidence in the DP group (14%, $P=0.8505$). The rate of overall morbidity excluding grade A pancreatic fistula was not significantly different between the two groups (CP vs. DP; 29% vs. 18%, $P=0.3346$), and no differences were found between the two groups regarding the need for interventional procedures (CP vs. DP; 13% vs. 18%, $P=0.5935$). The postoperative hospital stay in the DP group was shorter than that in the CP group (median; 21.5 days vs. 14.5 days, $P=0.0362$).

Postoperative Onset of Diabetes Mellitus and Change of Body Weight

The pancreatic function was analyzed in the 21 patients undergoing a CP and 26 undergoing a DP with more than 6 months follow-up after surgery. The median follow-up was 33.5 months (range, 3–111 months) for the CP group and 26.5 months (range, 3–110 months) for the DP group.

No patient had preoperative diabetes in the CP group, whereas three patients had preoperative diabetes in the DP group. Only one patient (4.7%) developed new onset of mild diabetes treated with diet alone in the CP group, in comparison to nine (35%) patients in the DP group ($P=0.0129$) who developed new onset diabetes or worsening diabetes (Table 3).

The ratios of patients with decreasing %BW at 6 months, 1 year, and 2 years after surgery in the DP group were higher than that in the CP group (Table 3). However, the

rate of patients taking pancreatic enzyme supplementation was not significantly different (CP vs. DP; 43% vs. 42%, $P=0.9698$). Furthermore, the body weight in the patients undergoing a CP had recovered to preoperative body weight within 2 year after surgery, whereas patients undergoing a DP remained at %BW of 93% at 2 years after surgery (Fig. 1).

No patient in the both groups had continued postoperative severe diarrhea (Table 3).

No patient in either group showed any evidence of either local recurrence or distant metastases during the follow-up.

Discussion

A CP is a procedure for localized tumor in the pancreatic body to avoid the extended loss of functional unaffected pancreatic parenchyma and is accepted as a method of choice for benign and low-grade malignant neoplasms or pancreatic metastases from other carcinomas, not requiring lymph node clearance.^{7,8,13,14} In the present study, the final pathologic examination after a CP showed that 16 patients had IPMN, including one minimally invasive carcinoma, two carcinoma in situ, and 13 adenoma, two MCN, two

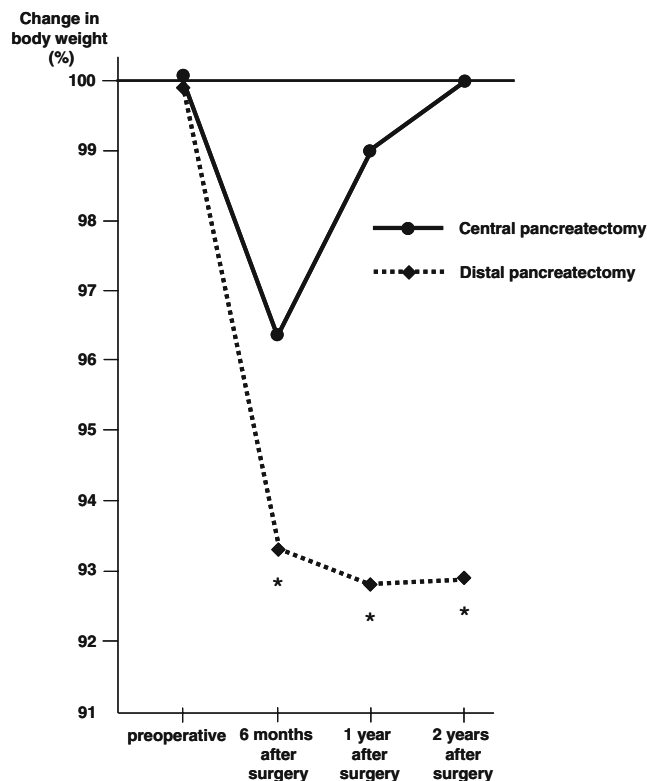


Figure 1 Percent change of body weight in patients with a central pancreatectomy and distal pancreatectomy. The preoperative body weight is defined as 100%. A significant difference is found between the patients with a central pancreatectomy and a distal pancreatectomy at 6 months, 1 year, and 2 years after surgery ($*P<0.05$).

serous cystadenoma, one solid pseudopapillary tumor, two benign NET, and one metastasis from renal cell carcinoma. Regarding IPMN, a few reports revealed the recurrence of remnant parenchyma after a CP.^{13,14,16,21} Our data showed that three patients had malignant IPMN with negative resection margins, and these patients have to be followed up strictly, although no patients have recurrence including local recurrence or distant metastasis.^{1,22} Intraoperative frozen section analysis of the two resection margins (pathological findings of cut ends of duodenal site and splenic site) is essential for avoiding recurrence of remnant pancreas in patients undergoing a CP. In addition, preoperative and intraoperative diagnosis of define negative margins is difficult in main-duct type IPMN; therefore, main-duct type IPMN may not be indicated for a CP.

The aim of this study is to assess the advantage and disadvantage of CP, concerning perioperative course, postoperative complication, and long-term pancreatic function, in comparison to the patients undergoing a DP as a control group. To compare both surgical procedures, only patients with benign or low-grade malignant neoplasms were selected as a DP group, excluding patients with high malignancies requiring extended surgery and adjuvant therapy and chronic pancreatitis because postoperative pancreatic function of these patients are often getting poor.^{3,17}

Our data showed that surgery-related mortality was zero in both groups, and the incidence of overall morbidity was no different between the two groups (CP vs. DP; 29% vs. 18%, $P=0.3346$). The rate of clinically significant pancreatic fistula (grade B and C) was no different between the CP and DP groups (13% vs. 14%, $P=0.8505$), and these results are consistent with other reports following a CP.^{13,14,21} The data of our present study indicate that a CP is a safe procedure with acceptable morbidity and mortality rates.

In the literature, most reports have stressed the good endocrine function after a CP.^{6,13,14,21} In this study, only one patient undergoing a CP developed new onset of mild diabetes, receiving diet counseling and requiring no medical therapy. However, six patients (23%) developed new onset of diabetes (two diet therapy, two taking oral drug, and two insulin treatment), and three (12%) developed worsening diabetes in the DP group. The most important reason for high endocrine insufficiency in patients undergoing a DP may be extended resected volume of normal parenchyma.^{23–25}

The assessment of exocrine function is difficult because of nonexistence of objective and easy examination for exocrine function.^{13,14,16} In this study, we follow up the postoperative body weight and evaluate the %BW compared to the preoperative values as an exocrine function. The median %BW in the DP group was significantly lower than that in the CP group at 6 months, 1 year, and 2 year

after surgery, and the median %BW in patients undergoing a CP improved at 2 years after surgery, whereas that of the DP group remained low at 2 years. The differences in body weight between after a CP and a DP are significant, suggesting that CP preserves and improves the pancreatic exocrine function within at least 2 years after surgery.

Conclusion

Our data show that CP is a safe technique for the treatment of benign or low-grade malignant neoplasms. Furthermore, the rate of new onset of diabetes mellitus was minimal after a CP, and the body weight improved within 2 years after a CP, suggesting that CP is an effective procedure for selected patients.

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