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ORIGINAL ARTICLE

Longitudinal Pancreaticojejunostomy for Pancreaticodigestive Tract Anastomotic Stricture After Pancreaticoduodenectomy

Ippei Matsumoto | Keiko Kamei | Kohei Kawaguchi | Yuta Yoshida | Masataka Matsumoto | Dongha Lee | Takaaki Murase | Shumpei Satoi | Atsushi Takebe | Yoshifumi Takeyama

Department of Surgery, Kindai University Faculty of Medicine, Osaka, Japan

Correspondence
Ippei Matsumoto, Department of Surgery, Kindai University Faculty of Medicine, 377-2 Ohno-higashi, Osakasayama, Osaka, 589-8511, Japan.
Email: ippeimm@gmail.com

Abstract

Aim: Pancreaticodigestive tract anastomotic stricture is a long-term complication of pancreticoduodenectomy (PD). However, optimal treatment has not yet been defined. We conducted longitudinal pancreaticojejunostomy (LPJ) in symptomatic patients with anastomotic stricture after PD. This study aimed to evaluate the efficacy of this procedure.

Methods: Pancreticoduodenectomy was performed in 605 patients at our institution between January 2005 and April 2020. Of these, 15 patients (2.5%) developed symptomatic pancreaticodigestive tract anastomotic stricture after PD. Three patients were referred to our institution owing to recurrent pancreatitis with anastomotic stricture after PD. LPJ was indicated for these 18 patients, and they were enrolled in this study.

Results: The median time from the initial operation to LPJ was 2.0 y. Preoperative clinical presentations included obstructive pancreatitis in 10 patients, a rapid deterioration of glucose tolerance in nine, and severe steatorrhea in two. Surgical morbidity ≥grade III defined by the Clavien–Dindo classification was not observed. After LPJ, preoperative symptoms improved in 16 patients (89%) during a median follow-up of 39 mo. Nine of the 10 patients with obstructive pancreatitis achieved complete pain relief. All nine patients with a rapid deterioration of glucose tolerance showed improved endocrine function. Daily insulin requirement was significantly decreased after LPJ (11.6 ± 3.3 vs 3.4 ± 4.3 units, $P = .0239$). Four of the seven patients who required insulin injections were free of insulin after LPJ.

Conclusion: LPJ is a safe and effective surgical procedure for symptomatic patients with stricture of the pancreaticodigestive tract anastomosis after PD.

KEYWORDS

anastomotic stricture, longitudinal pancreaticojejunostomy, pancreaticoduodenectomy, pancreaticogastrostomy, pancreaticojejunostomy

1 | INTRODUCTION

Pancreaticoduodenectomy (PD) has been established as a standard procedure for the treatment of pancreatic and periampullary lesions. Many studies have described the short-term complications of PD (pancreatic fistula, delayed gastric emptying, post-pancreatectomy hemorrhage). However, little has been published regarding long-term complications, particularly pancreaticodigestive tract anastomotic stricture. Although stricture of the anastomosis is often asymptomatic, pancreatic exocrine and endocrine function after PD is affected by the patency of pancreaticodigestive tract anastomosis.[1-4] Some patients present with symptoms such as abdominal and/or back pain due to elevation of pancreatic pressure, which can impair pancreatic function. Symptomatic and painful presentations are difficult to treat solely with medication, and the optimal surgical treatment has not yet been defined.

In chronic pancreatitis, longitudinal pancreaticojejunostomy (LPJ) is the treatment of choice for patients with a dilated main pancreatic duct (MPD) without an inflammatory mass in the pancreatic head. This procedure is associated with low morbidity and mortality rates. Immediate and lasting pain relief is reported in 80% (range, 42%–100%) of patients with a follow-up of 62 mo (range, 15–110 mo).[5-7] It is a relatively simple, safe, and effective surgical procedure for patients with dilated MPD.

We conducted LPJ for symptomatic patients with anastomotic stricture after PD according to the surgical indication. This study aimed to describe the surgical technique and evaluate the efficacy of the procedure.

2 | METHODS

2.1 | Patients

Pancreticoduodenectomy was performed on 605 patients at Kindai University Hospital between January 2005 and April 2020. Of these, 15 patients (2.5%) developed symptomatic pancreaticodigestive tract anastomotic stricture after PD. The other three patients, who originally underwent PD at different hospitals, were referred to our institution owing to recurrent obstructed pancreatitis with pancreaticodigestive tract anastomotic stricture. LPJ was indicated for these 18 patients after PD, and they were enrolled in this study. After an explanation of the clinical condition, treatment option, and benefit and risk of LPJ, informed consent was obtained from all patients before LPJ. Clinicopathological and surgical outcomes were retrospectively analyzed. The maximum diameter of the MPD was measured using preoperative multidetector-row computed tomography (MDCT; Figure 1).

2.2 | Surgical procedure of PD

Pancreticoduodenectomy for initial surgery was performed with subtotal stomach-preserving pancreaticoduodenectomy as a standard procedure at our institute in which the distal stomach was divided 3 cm proximal to the pylorus ring. Regional lymphadenectomy was performed according to the malignancy grade. The pancreaticodigestive tract anastomosis was reconstructed using pancreaticogastrostomy (PG, n = 468) or pancreaticojejunostomy (PJ, n = 137). PG and PJ were performed using a one-layer invagination technique and end-to-side two-layer duct-to-mucosa anastomosis, respectively. An end-to-side hepaticojejunostomy and ante-colic, end-to-side gastrojejunostomy were performed.

FIGURE 1 Representative image of multidetector-row computed tomography. CT scan showing an anastomotic stricture of pancreaticogastrostomy and dilation of the main pancreatic duct with pancreatic stone (white arrow)

2.3 | Surgical indication and procedure of LPJ

The surgical indication of LPJ after PD was dilation of the main pancreatic duct (MPD ≥ 5 mm) due to anastomotic stricture in patients with recurrent obstructive pancreatitis or rapid deterioration of glucose tolerance. Obstructive pancreatitis was defined as acute onset of severe epigastric and/or back pain with serum pancreatic amylase activity at least three times greater than the upper limit of normal and characteristic findings of acute pancreatitis on imaging studies. Rapid deterioration of glucose tolerance was defined as a rapid increase in serum hemoglobin (Hb) A1c levels (≥2.0%) over a few mo (2–6 mo).

For the second operation, the PG was carefully identified and dissected (Figure 2A). After the gastric wall was closed, MPD of the remnant pancreas was identified using intraoperative ultrasonography. Ductotomy was performed using an electrocautery device. The MPD was opened longitudinally and leftward toward the tail. The opening of the MPD should be extended to the tail side to facilitate complete drainage of the duct system (Figure 2B). A Roux-en-Y limb was then constructed. The Roux limb was opened longitudinally at the anti-mesenteric side, matching the length of the opened MPD. LPJ was performed in a two-layer fashion. The anastomosis was started at the tail of the pancreas, first applied to the caudal side from the tail to the head (Figure 2C), and then repeated on the cranial side using 4-0 polydioxanone (PDS, Ethicon, Raritan, NJ) running

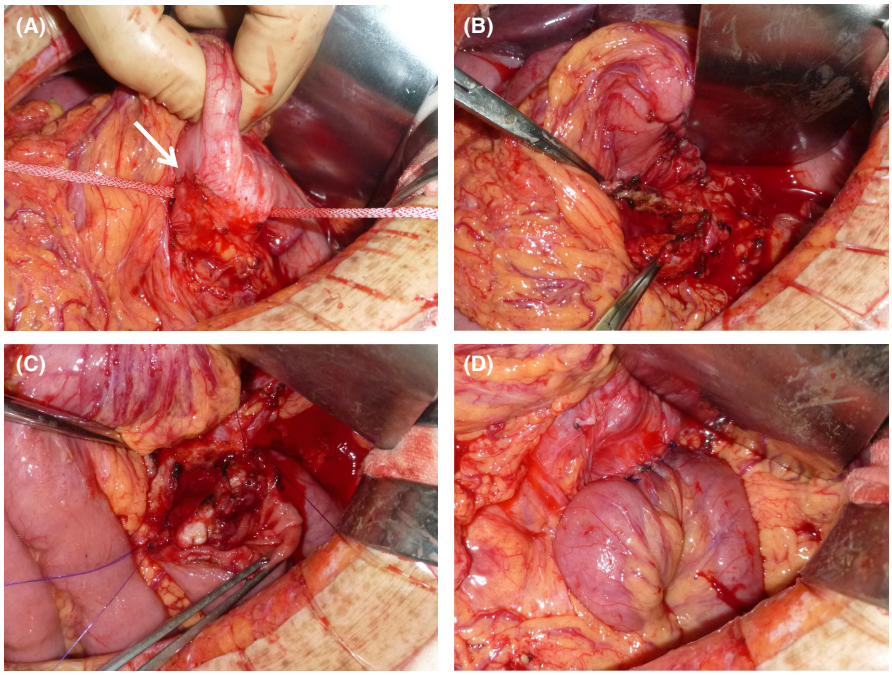

FIGURE 2 The surgical procedure of longitudinal pancreaticojejunostomy (LPJ) after pancreaticoduodenectomy. (A) Pancreaticogastrostomy is carefully identified and dissected (white arrow). (B) The main pancreatic duct is opened longitudinally, leftward toward the tail. (C) Anastomosis of the inferior side is completed. (D) LPJ is completed

sutures in the inner layer and interrupted sutures in the outer layer. Full-thickness suturing was used in the jejunum, and partial thickness was used for the pancreatic parenchyma without incorporating the pancreatic ductal epithelium in the inner layer. Seromuscular layer suturing was used in the jejunum, and partial thickness was used for the pancreatic parenchyma in the outer layer. After completion of LPJ (Figure 2D), a closed silicon drain was placed along LPJ.

2.4 | Definition of postoperative complications and pain relief

Postoperative complications were evaluated using a modified Clavien–Dindo (CD) grading system.[8] Postoperative pancreatic fistula (POPF) was defined by the classification system of the International Study Group on Pancreatic Fistula (ISGPF) as the amylase level in the fluid collected on the third postoperative day (POD) > 3-fold the serum amylase level.[9] POPF was assigned to one of three categories according to the ISGPF clinical criteria: biochemical leak, grade B, or C. The amylase levels in the drainage fluid on POD 3 were measured in all patients.

Information on pain relief was extracted from the medical records at the time of the latest outpatient visit during the study period. Complete pain relief was defined as no pain killer use at all times. Partial pain relief was defined as occasional use of painkillers. No pain relief was defined as painkiller use at any time.

2.5 | Statistical analysis

The collected data are expressed as median (range). Daily insulin requirement was expressed as the mean (standard deviation). The paired Student's *t*-test was used to compare daily insulin requirements before and after LPJ. All analyses were performed using JMP 13.0 for Macintosh (SAS Institute, Cary, NC).

3 | RESULTS

3.1 | Patient characteristics and postoperative complications of the first operation

Patient characteristics and postoperative complications during the first operation are shown in Table 1. There were 13 men and five women with a median age of 58 y (range, 41–82). Pathological diagnoses after PD were intraductal papillary mucinous neoplasm in six patients, pancreatic cancer in four, ampulla of Vater cancer in four, and other diagnoses in the remaining four patients. The pancreaticodigestive tract anastomosis was reconstructed with PG in 16 patients and PJ in two patients. Overall morbidity (Clavien classification grade II or higher) after the first operation was observed in five of 15 (33%) patients (unknown in three patients). Two patients (13%) developed biochemical leaks and one (7%) developed clinically relevant POPF grade B. Other complications included delayed gastric emptying (grade II) in three patients (20%), chyle ascites (grade II) in one patient (7%), bile leak in one patient (7%), and portal vein thrombosis in one patient (7%).

3.2 | Preoperative patient characteristics of LPJ

The preoperative patient characteristics of LPJ are shown in Table 2. The median age of the patients was 66 y (range, 43–84). The median

TABLE 1 Patient characteristics and postoperative complications of the first operation

Age (y; median; range)	58 (41–82)
Sex	
Male	13
Female	5
Primary disease	
IPMN	6
Pancreatic cancer	4
Ampulla of Vater cancer	4
Chronic pancreatitis	3
Duodenal neuroendocrine tumor	1
Type of operation	
SSPPD	14
PPPD	2
PD	1
DPPHR	1
Type of pancreaticodigestive tract anastomosis	
PG	16
PJ	2
Pancreatic fistula, ISGPF grade	
None	12
Biochemical leak	2
Grade B	1
Grade C	0
Unknown	3
Other complications	
Delayed gastric emptying	3
Chyle ascites	1
Bile leak	1
Portal vein thrombosis	1

Abbreviations: DPPHR, duodenum preserving pancreas head resection; IPMN, intraductal papillary mucinous neoplasm; ISGPF, International Study Group on Pancreatic Fistula; PD, pancreaticoduodenectomy; PG, pancreaticogastrostomy; PJ, pancreaticojejunostomy; PPPD, pylorus-preserving pancreaticoduodenectomy; SSPPD, subtotal stomach-preserving pancreaticoduodenectomy.

time from the initial operation to LPJ was 2.0 y, range, 0.4–25.8 y. Ten patients had recurrent obstructive pancreatitis. Rapid deterioration of glucose tolerance with rapidly increasing HbA1c and fasting blood sugar levels was observed preoperatively in nine patients. Three patients had both obstructive pancreatitis and deterioration of glucose tolerance. Two patients experienced severe steatorrhea. In all patients, preoperative MDCT revealed an anastomotic stricture with MPD dilatation. The median diameter of the MPD was 7.0 mm (range, 5.0–15.0 mm). Before LPJ, endoscopic ultrasound (EUS)-guided PG was performed in two patients. However, the effect was temporary owing to repeated stent obstruction. The endoscopic intervention was attempted in another two patients; however, this failed for technical reasons.

3.3 | Operative data and postoperative complications of LPJ

Operative data and postoperative complications of LPJ are shown in Table 3. The median operation time and intraoperative blood loss were 179 min (range, 145–353 min) and 201 mL (range, 49–926 mL), respectively. One patient required intraoperative blood transfusion.

TABLE 2 Preoperative patient characteristics of LPJ

Age (y; median; range)	66 (43–84)
Previous endoscopic intervention for the anastomotic stricture	
None	14
Yes	2
Technical failure	2
Time from the first operation to LPJ (y; median; range)	2.0 (0.4–25.8)
Symptoms	
Obstructive pancreatitis	10
Rapid deterioration of glucose tolerance	9
Severe diarrhea	2
Diameter of the MPD (mm; median; range)	7.0 (5.0–15.0)

Abbreviations: LPJ, longitudinal pancreaticojejunostomy; MPD, main pancreatic duct.

TABLE 3 Operative data and postoperative complications of LPJ

Operation time (min; median; range)	179 (141–353)
Blood loss (mL; median; range)	201 (49–926)
Blood transfusion	
None	18
Yes	1
Additional procedure	
None	14
Yes	4
Mortality	0
Morbidity (Clavien–Dindo classification)	
None or I	15
II	3
≥IIIa	0
Pancreatic fistula, ISGPF grade	
None	17
Biochemical leak	1
B or C	0
Other complication	
Delayed gastric emptying	1
Wound infection	2
Portal vein thrombosis	1
Adrenal insufficiency	1
Duration of postoperative hospital stay (d)	11 (7–33)

Abbreviations: ISGPF, International Study Group on Pancreatic Fistula; LPJ, longitudinal pancreaticojejunostomy.

Four patients required additional procedures at the time of the operation, namely, pancreatic cystectomy for a cystic lesion of the pancreatic tail, partial hepatectomy for a liver tumor, re-anastomoses of concurrent stricture of hepaticojejunostomy, and gastrojejunostomy. Overall morbidity (grade II) was observed in three (20%) patients; however, there was no mortality. One patient developed a biochemical leak. However, no clinically relevant grade B or C POPF was observed. The median duration of postoperative hospital stay was 11 d (range, 7–33 d).

3.4 | Symptom relief and long-term outcome after LPJ

During the median follow-up period of 39 mo (range, 4–126 mo) after LPJ, preoperative symptoms improved in 16 patients (89%). Nine of 10 patients (90%) with obstructive pancreatitis achieved complete relief of pain. However, one patient achieved no pain relief. One patient required readmission due to recurrent pancreatitis during the follow-up period. All nine patients who had rapid deterioration of glucose tolerance had improved glucose control and endocrine function. The changes in serum HbA1c levels before and after LPJ in these patients are shown in Figure 3. Serum HbA1c levels rapidly increased before LPJ and decreased after LPJ. Mean doses of daily insulin before and after LPJ were 11.6 ± 3.3 units and 3.4 ± 4.3 units, respectively. The daily insulin requirement significantly decreased after LPJ ($P = .0239$). Although seven patients required insulin before LPJ, four were free of insulin after LPJ. One patient required re-LPJ 7 mo after LPJ owing to increased HbA1c levels (Figure 3). Although the patient required 20 units of daily insulin just before re-LPJ, the patient was free of insulin after re-LPJ.

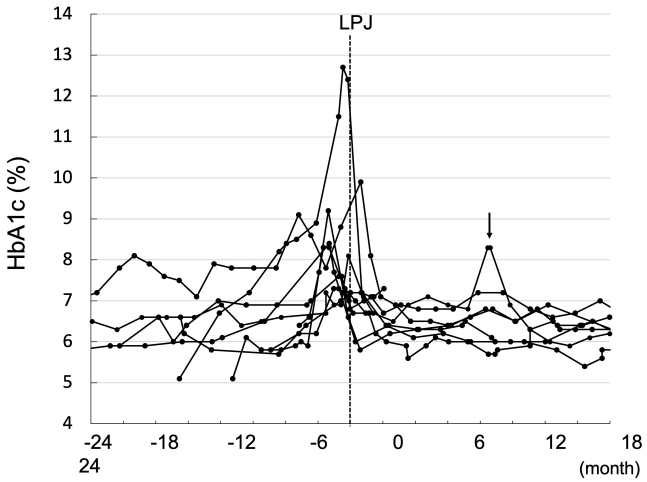

FIGURE 3 Changes of serum hemoglobin (Hb) A1c levels before and post-longitudinal pancreaticojejunostomy (LPJ) in patients with rapid deterioration of glucose tolerance. Serum HbA1c levels are rapidly decreased after LPJ. One patient required re-LPJ 7 mo after LPJ owing to increased HbA1c (black arrow). Serum HbA1c levels rapidly decreased, and the patient is free of insulin after re-LPJ

4 | DISCUSSION

A pancreaticodigestive tract anastomotic stricture can be a problematic late complication after PD. However, little is known about the pancreaticodigestive tract anastomotic stricture, and the optimal treatment has not yet been defined. The results of previous studies are summarized in Table 4.[10-14] Three studies demonstrated that the occurrence rate of pancreaticojejunostomy (PJ) stricture after PD was 2.0%–11.3%. On the other hand, our study showed that the occurrence rate of PG stricture was 2.4% (9/373). To the best of our knowledge, this is the first report describing surgical techniques and outcomes in detail for patients with PG stricture after PD. Demirjian et al[12] reported that the occurrence rate of PJ stricture after PD was 2.0% (7/357). The rate of patients who required surgical intervention due to PG stricture after PD was similar to that of PJ stricture. Our study also showed that there was no significant difference in the occurrence rate of anastomotic stricture between PG and PJ (2.9% vs 0.7%, $P = .134$; Table 4). Reid-Lombardo et al[10] reported that the cumulative probability of PJ stricture after PD for benign disease at 1 and 5 y was 2.8% and 4.6%, respectively. In their report, surgical intervention was required in two of four (50%) patients. However, detailed surgical techniques and outcomes have not been described. Mucci-Hennekinne et al[15] described the surgical intervention in detail. In their report, two patients were successfully treated with LPJ and re-anastomosis of the PG. Morgan et al[11] reported a high incidence rate (11.3%) of PJ stricture after PD for benign disease. They discussed that the discrepancy between their results and others might reflect the larger proportion of patients in their series with chronic pancreatitis (68%). Moreover, chronic pancreatitis was found to be a risk factor for PJ stenosis (68% overall vs 89% in the anastomotic stricture group; $P < .04$). Demirjian et al[12] reported that POPF occurred in six of seven patients who developed PJ stricture. They discussed that the occurrence of PJ stricture was most affected by the development of clinically relevant POPF, which induced aggressive local inflammation and an accentuated repair response marked by development of the fibrosis. In our study, however, only one patient developed clinically relevant POPF grade B. PG stricture occurrence after PD appeared to be independent of the original pathological diagnosis and POPF in our study.

In general, surgeons may prefer to avoid reoperation for this benign disease situation due to operative risks. However, our study clearly showed that LPJ can be performed safely. The overall morbidity rate after reoperation for PJ stricture after PD was reported to be 22%–29%.[11,12] In our study, overall morbidity (CD grade II) was observed in three (17%) patients, and no patients developed CD grade ≥ III complications. None of the patients developed clinically relevant POPF (grade B or C), as the remnant pancreas was hard in all patients. Our surgical procedure may be technically easier and safer, probably because PG is a pancreaticodigestive tract anastomosis after PD in most patients. At the time of reoperation for PJ stricture, LPJ was performed using the same limb of the small bowel

TABLE 4 Reported studies of revision surgery for pancreaticodigestive tract anastomotic stricture after PD

Year	Authors	Occurrence rate (Number of surgeries for anastomotic stricture / total number of PDs)	Type of anastomosis after PD	Postoperative pancreatic fistula after PD	Median time to revision surgery (mo, range)	Postoperative complication after revision surgery	Pain relief	Median follow up time after revision surgery (mo, range)
2007	Reid-Lombardo et al[10]	3.3% (4/122)	PJ	25%	3 (1–56)	N/A	100%	N/A
2010	Morgan et al[11]	11.3% (27/237)	PJ	15%	12 (2–99)	22%	23%	56 (23–126)
2010	Demirjian et al[12]	2.0% (7/357)	PJ	86%	10 (8–120)	29%	57%	18 (12–57)
2016	Cioffi et al[13]	2.2% (27/1175)	PJ	22%	46 (4–269)	26%	78%	30 (3–96)
2017	Wagle et al[14]	1.3% (4/308)	PG (n = 1) PJ (n = 5)	0%	62 (48–120)	50%	83%	36 (16–84)
	Present study	2.9% (14/468) 0.7% (1/137)	PG (n = 16) PJ (n = 2)	7% 0%	25 (5–308) 61 (21–101)	14% 0%	93% 100%	43 (5–126) 13 (7–18)

Abbreviations: PD, pancreaticoduodenectomy; PG, pancreaticogastrostomy; PJ, pancreaticojejunostomy.

in most cases (24/27).[11] This might sometimes be complicated and is difficult to perform LPJ with sufficient lengths of the small bowel under a good operative field.

In our study, the long-term results were favorable. Preoperative symptoms improved in 16 of 18 (89%) patients during a median follow-up period of 39 mo. It is worth noting that all nine patients who had rapid deterioration of glucose tolerance improved glucose control and endocrine function with decreasing serum HbA1c levels and doses of daily insulin requirement after LPJ. Four of the seven patients who required insulin achieved being insulin-free after LPJ. However, previous studies did not describe the surgical indication or outcome of the revision for pancreaticodigestive tract anastomotic stricture with deterioration of glucose tolerance. To the best of our knowledge, this is the first report showing that decompression of increased pressure of the main pancreatic duct recovers and preserves the endocrine function of the remnant pancreas after PD. Our findings suggest that some patients present with a rapid deterioration of glucose tolerance with an anastomotic stricture. In most cases, the endocrine function of the remnant pancreas was potentially reversible by decompression of the increased pressure of the MPD. On the other hand, many patients present with normal or slow deterioration of glucose tolerance. However, the pathophysiology of glucose tolerance with increased and/or decompression ductal pressure is not well understood. This is a future research question that needs to be addressed. Our study also showed that nine of 10 patients (90%) with obstructive pancreatitis achieved complete relief of pain. However, previous studies have shown that long-term pain relief was unsatisfactory. Demirjian et al[12] reported that only four of seven patients achieved pain relief at a mean follow-up of 25 mo. Morgan et al[11] reported that six of 23 survivors achieved pain relief at a median follow-up of 56 mo. The discrepancy between our results and those of others might be as follows. First, reoperation for PJ stricture may be technically difficult, as mentioned above. As LPJ was performed using the same limb of the small bowel, it may be challenging to perform LPJ with sufficient lengths of the small bowel. This situation may cause insufficient decompression of the increased ductal and parenchymal pressures. Demirjian et al[12] reported that four of seven patients underwent re-PJ and only two patients underwent LPJ using the same limb of the small bowel. Second, the indications for LPJ should be carefully selected. We performed LPJ in 10 patients with intractable abdominal or back pain due to duct obstructive pancreatitis. Importantly, all 10 patients showed increased serum amylase levels when they experienced pain and decreased postoperatively. Previous studies did not mention the preoperative serum amylase levels. Additionally, it has previously been shown that pancreatic duct and parenchymal drainage with LPJ is unsuccessful for pain relief in patients with small duct chronic pancreatitis (pancreatic duct diameter <7 mm in diameter).[16] In our preoperative imaging evaluation, the median diameter of the MPD was 7.0 mm (range 5.0–15.0 mm). In contrast, Morgan et al[11] showed that the preoperative median diameter of the MPD was 3.5 mm and long-term pain relief was achieved in only six of 26 (26%) patients. In patients

with an outflow obstruction of the pancreatic duct due to strictures, it is hypothesized that pain arises from increased ductal and parenchymal pressure.[17] As pain syndrome is complex and often multifactorial, the selection of patients who will benefit from LPJ is highly important. Patients with preoperative increased serum amylase levels and MPD dilatation might be a good indication for LPJ. Patency of pancreaticodigestive tract anastomosis is an important factor affecting pancreatic function.[1-4] Therefore, we believe that this early surgical intervention, which decompresses the increased ductal and parenchymal pressure, may mitigate disease progression, achieve pain control, and preserve pancreatic function. The procedure can manage pain, preserve the greater part of the endocrine and exocrine function still present, reduce or avoid insulin and opioid use, and restore quality of life. In our study, eight patients with cancer, including four patients with pancreatic cancer, received LPJ. We consider that the risk of cancer recurrence alone is not excluded from the indication of LPJ, as LPJ can be performed safely and effectively.

Endoscopic intervention, which is less invasive than surgical intervention, may be another treatment of choice. Several reports have described EUS-guided PG with pancreatic duct stenting in pancreaticodigestive tract anastomotic stricture after PD.[18-21] However, this procedure is technically challenging and has a success rate of only ~50%.[18] Moreover, its long-term efficacy has not yet been reported. Two of four (50%) patients failed this procedure before LPJ in our cases. The remaining two patients required several hospital admissions owing to repeated pancreatic stent obstruction. Several randomized control trials and meta-analyses have shown that surgical drainage is superior to endoscopic techniques in controlling symptoms in patients with chronic pancreatitis.[22-25] Therefore, we recommend early surgical intervention for patients with symptomatic pancreaticodigestive tract anastomotic stricture after PD. However, a recent systematic review showed that EUS-guided pancreatic stent placement for PJ stenosis after PD resulted in high technical and clinical success rates of 72% and 79%, respectively.[26] It should be noted that the reported data are likely to come from expert centers and present only the most successful case series. A prospective randomized trial comparing endoscopic and surgical interventions will be required in the future.

Our study had several limitations. First, this was a single-center retrospective study with a small number of subjects and without a control group. Although the patient selection and surgical indication were decided in multidisciplinary meetings according to our criteria, patient selection bias may still have been present. Second, pain relief was not evaluated using visual analog scales or Izbicki pain scores. Therefore, it may be challenging to reach a definitive conclusion. A prospective, large-scale multicenter data collection using standardized outcomes is needed to determine the true efficacy of the procedure.

In conclusion, LPJ is a safe and effective surgical procedure for symptomatic patients with stricture of pancreaticodigestive tract anastomosis after PD.

DISCLOSURE

Ethical approval: The protocol for this research project was approved by a suitably constituted Ethics Committee of the institution, and it conforms to the provisions of the Declaration of Helsinki. Informed consent was waived owing to the retrospective nature of the study. The opt-out recruitment method was applied to all patients with an opportunity to decline to participate. The Ethics Committee of the Kindai University Faculty of Medicine, Approval No. 28-230.

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ORCID

Ippei Matsumoto https://orcid.org/0000-0003-3965-3693
Dongha Lee https://orcid.org/0000-0001-6796-1891

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