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# Effect of the Crushing and Ligation Technique During Pancreatectomy in Decreasing the Incidence of Postoperative Pancreatic Fistula

Kyohei ABE, Tomoyoshi OKAMOTO, Michinori MATSUMOTO, Yasuro FUTAGAWA, Takeshi GOCHO, Shinji ONDA, Kenei FURUKAWA, Koichiro HARUKI, Shuichi FUJIOKA, Katsuhiko YANAGA, and Toru IKEGAMI

*Department of Surgery, The Jikei University School of Medicine*

*ABSTRACT*

*Background*：The prevention and treatment of postoperative pancreatic fistulas (POPFs) are crucial problems associated with pancreaticoduodenectomy (PD) and distal pancreatectomy (DP). The objective of the present study was to determine the outcomes of the crushing and ligation (CL) technique and the conventional ultrasonically activated scalpel (UAS) technique for liver dissection during PD and DP procedures.

*Methods*：Outcomes of PD or DP were evaluated in patients who had undergone pancreatic dissection with the CL technique (44 patients) or with the UAS technique (44 patients). Compared between CLgroup and UAS group were operative duration, blood loss, length of hospital stay, incidence of POPFs (grade BC), and postoperative drainage amylase fluid level.

*Results*：The incidence of POPF (grade BC) was significantly higher in the PD-UAS group (44.8%, 13 patients) than in the PD-CL group (8.0%, 2 patients；$p < 0.01$). The maximum amylase levels in drainage fluid was significantly lower ($p = 0.04$), the operative duration was significantly longer ($p = 0.04$), and the postoperative length of hospital stay was significantly shorter ($p = 0.02$) in the PD-CL group than in the PD-UAS group. The incidence of POPFs (grade BC) was significantly lower in the DP-CL group (10.5%, 2 patients) than in the DP-UAS group (46.7%, 7 patients).

*Conclusion*：When pancreatic dissection is performed, the CL technique leads to better outcomes and fewer complications than does the UAS technique. (Jikeikai Med J 2023；70：39-46)

Key words：pancreatectomy, pancreatic dissection, pancreatic fistula, pancreaticoduodenectomy

## INTRODUCTION

Pancreatic ductal adenocarcinoma (PDAC) is the 10th most common cancer diagnosed in the United States, with 62,210 new cases in 2022[1]. In addition, PDAC is the third leading cause of cancer death and has a high mortality rate and a poor prognosis[1]. To achieve long-term survival in patients with PDAC, surgical treatment is considered most effective[2]. Two types of pancreatectomy are pancreaticoduodenectomy (PD) and distal pancreatectomy (DP)[3]. With advances in systematic chemotherapy and surgery, the indications for pancreatectomy have become more diverse. However, pancreatectomy and reconstruction still have unresolved complications.

The most serious complication of PD and DP is a postoperative pancreatic fistula (POPF). This complication has a high incidence (2% to 35%)[4-7] and can be fatal when associated with intra-abdominal hemorrhage[8]. Among the compli-

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阿部　恭平，岡本　友好，松本　倫典，二川　康郎，後町　武志，恩田　真二，古川　賢英，春木孝一郎，藤岡　秀一，矢永　勝彦，池上　徹
Mailing address：Kyohei ABE, Department of Surgery, The Jikei University School of Medicine, 3-25-8, Nishi-Shinbashi, Minato-ku, Tokyo 105-8461, Japan
E-mail：kyoheiabe@jikei.ac.jp

cations of PD and DP, POPF remains difficult to prevent and treat. Although several preventative pharmacotherapies and surgical strategies have been reported, none have been identified as a decisive treatment for managing POPF[9–19]. The incidence of POPF has been shown to be significantly reduced by external drainage and the use of a transanastomotic stent in PD[17]. However, POPF remains a common complication of PD and DP, in many institutions, the method of pancreatic dissection is the traditional ultrasound coagulation incision.

Because we have focused on the branch ducts of the resected pancreas as a cause of POPF, when dividing the pancreatic parenchyma during all pancreatic resections at our hospital we use the crushing and ligation (CL) method, which has become widely used in hepatectomies[20–24]. The effectiveness of this technique in preventing POPF has not previously been reported. Therefore, in this study, we compared the results of the CL technique employed in our institution for PD and DP with those of the conventional ultrasonically activated scalpel (UAS) technique.

## Methods

This retrospective comparative study was conducted from January 2012 through December 2017 at our hospital and includes patients who had undergone PD or DP. All procedures performed in this study and the protocol for this research project were approved by the Ethics Committee of The Jikei University School of Medicine, approval no. 27-177(8062)(2015.10.10), and it conforms to the provisions of the Declaration of Helsinki. Verbal informed consent for inclusion in the study was obtained from the patients. Patients were excluded for the following criteria : performance status 3 or 4, active infections, uncontrolled diabetes, concomitant cancers in areas other than the pancreas, and a platelet count $< 100{,}000/\mu$L. The work has been reported in line with the STROCSS (Strengthening the Reporting of Cohort Studies in Surgery) criteria[25]. The International Study Group of Pancreatic Fistula[4] defines a pancreatic fistula as "a drainage amylase level on postoperative day 3 that is at least three times the upper limit of normal for serum amylase, regardless of drainage volume." The grades are defined as follows : Grade A, no clinical symptoms ; Grade B, signs of infection but can be treated conservatively, and Grade C, severe pancreatic fistula, such as intra-abdominal bleeding or sepsis that requires management in the intensive care unit or reoperation[4]. In the present study, pancreatic fistulas of Grade A, which has little clinical significance, were not included. Pancreatic fistulas of Grades B and C were counted and their relationship with the method of pancreatic resection was investigated.

The CL technique involves the use of mosquito forceps to crush the pancreatic parenchyma and ligation of the remnant tissue using 4-0 polydioxanone sutures (Ethicon, Johnson & Johnson K.K., Tokyo, Japan) (Fig. 1a, 1b). Ligation was performed with the aim of sealing all visible ( $\geq 1$ mm) vessels and pancreatic ducts, including the parenchyma. The other method of dissecting the pancreas involved the use of an ultrasonically activated scalpel (UAS).

The surgery performed was PD if patients had lesions of the pancreatic head or the region of the distal bile duct. The surgical procedure involved conventional PD or subtotal stomach-preserving PD in addition to lymph node dissection in accordance with the pathological presentation, and reconstruction in all cases was performed with the Child-II method and Braun anastomosis. Pancreatojejunostomy was performed with the modified Kakita method. The drains were placed in the foramen of Winslow and at the pancreatojejunostomy site. If the postoperative course was uneventful, oral intake was started on postoperative day (POD) 4. If the case did not meet the criteria[4] for POPF, the drains were removed on PODs 5 through 7. Similarly, the external drainage tube of the pancreatic duct was removed on POD 21.

All patients who had a POPF (grade BC) underwent percutaneous drainage (including drain replacement) or transgastric drainage, with fasting and antimicrobial therapy if necessary. After a POPF had been confirmed, via blood sampling and computed tomographic examinations, to have resolved, feeding was resumed, antimicrobial therapy was stopped, and the drain was removed. The patient was discharged with stable food intake, normalized blood test findings, and good activities of daily living.

The surgery performed was DP if patients had lesions of the pancreatic body or tail. The surgical procedure included DP in addition to lymph node dissection in accordance with the pathological presentation. Drains were placed at the resection stump of the pancreas and the right subdiaphragmatic region. Postoperative management was generally the same as that for PD. In addition, all pancreatic

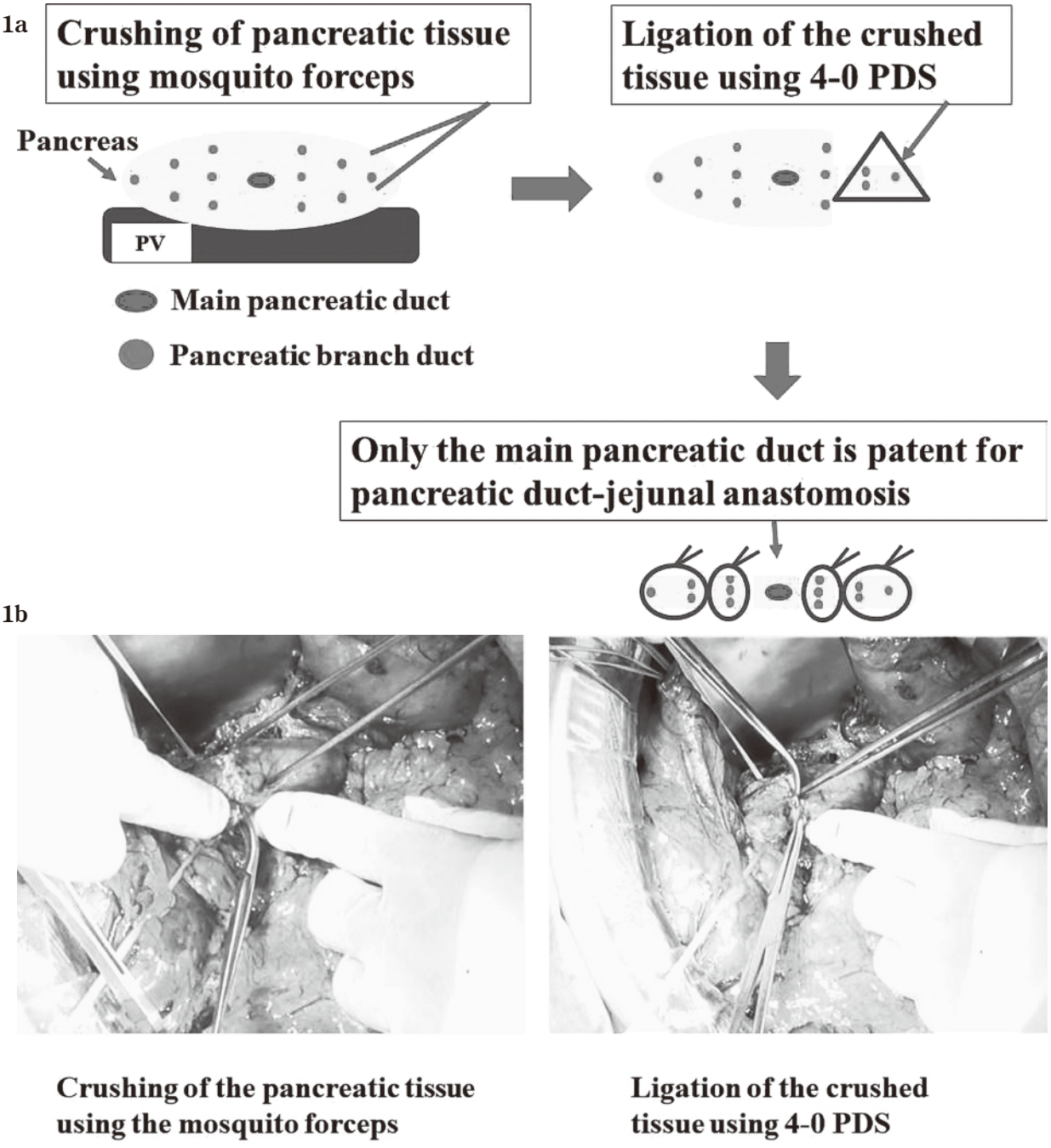


Fig. 1. Schematic of the protocol (a) and intraoperative photos (b) for the crushing and ligation (CL) method. Branches of pancreatic duct are identified by crushing the pancreatic parenchyma. The branches are ligated using 4–0 polydioxanone sutures (PDSs). PV, portal vein

resections were performed via laparotomy, and laparoscopic surgery was not included.

Outcomes of PD were compared between patients in whom the CL method was used (PD-CL group, 25 patients, 2015–2017) and patients in whom the UAS method was used (PD-UAS group, 29 patients, 2012–2014 ; historical control). Similarly, outcomes of DP were compared between patients in whom the CL method was used (DP-CL group, 19 patients, 2015–2017) and patients in whom the UAS method was used (DP-UAS group, 15 patients, 2012–2014 ; historical control). The primary outcome measures were the incidence of POPF and the amylase level of postopera-

tive drainage fluid (amylase level on POD 3 and maximum level during the postoperative course), and the secondary outcome measures were the reoperation rate, in-hospital death rate, surgical site infection rate, operative duration, blood loss, and length of hospital stay (LOS).

## Statistical Analysis

Data are expressed as a median (interquartile range). All evaluation items were compared via the Mann-Whitney U test or the $\chi 2$ test. Univariate and multivariate analyses were performed with logistic regression analysis. All $p$-values were considered statistically significant when the associated probability was $< 0.05$. These analyses were performed with the software program IBM SPSS Statistics version 20.0 (IBM Japan Ltd., Tokyo, Japan).

## Results

*Background characteristics of patients*

Although body mass index differed significantly between the PD-CL and PD-UAS groups (Table 1), no significant differences were found in other variables between the groups.

Also, there were no significant differences in patient background between the DP-CL and DP-UAS groups (Table 2).

*Analysis within the PD groups*

Among patients who had undergone PD, the incidence of POPFs (grade BC) was significantly higher ($p < 0.01$) in the PD-UAS group (44.8%, 8 patients) than in the PD-CL group (8.0%, 2 patients). The maximum amylase level in the drainage fluid on POD 3 was significantly lower ($p = 0.04$) in PD-CL group than in the PD-AUS group. Operative duration was significantly longer for the PD-CL group ($p = 0.04$), and postoperative LOS was significantly longer for the PD-UAS group ($p = 0.02$) (Table 3). Although the main pancreatic duct could not be identified in 2 patients of the PD-UAS group, these ducts were identified in all patients of the PD-CL group. In the 2 patients in whom the main pancreatic duct could not initially be identified, after an addi-

Table 1. Background characteristics of patients who underwent pancreaticoduodenectomy

| Factors | | Crushing and ligation group ($N = 25$) | Ultrasonically activated scalpel group ($N = 29$) | $p$-value |
|---|---|---|---|---|
| Sex, | Male : female | 13 : 12 | 19 : 10 | 0.31 |
| Age, years* | | 66 (59-69) | 70 (64-78) | 0.09 |
| Body mass index, kg/m$^2$* | | 20 (19-23) | 22 (20-25) | 0.04 |
| ASA-PS | 1 : 2 : 3 | 9 : 14 : 2 | 9 : 17 : 3 | 0.90 |
| Disease | Pancreatic cancer : other | 13 : 12 | 11 : 18 | 0.30 |
| Soft pancreas | | 12 (48%) | 16 (55%) | 0.60 |
| Diabetes mellitus | | 9 (36%) | 4 (13%) | 0.06 |
| Chronic pancreatitis | | 4 (16%) | 5 (17%) | 0.42 |

*median (interquartile range) ; ASA : American Society of Anesthesiologists physical status

Table 2. Background characteristics of patients who underwent distal pancreatectomy

| Factors | | Crushing and ligation group ($N = 19$) | Ultrasonically activated scalpel group ($N = 15$) | $p$-value |
|---|---|---|---|---|
| Sex | Male : female | 9 : 10 | 6 : 9 | 0.74 |
| Age, years* | | 64 (60-70) | 65 (60-69) | 0.97 |
| Body mass index, kg/m$^2$* | | 21 (19-25) | 19 (16-23) | 0.08 |
| ASA-PS | 1 : 2 : 3 | 7 : 11 : 1 | 4 : 11 : 0 | 0.50 |
| Disease | Pancreatic cancer : other | 12 : 7 | 7 : 8 | 0.49 |
| Soft pancreas | | 10 (53%) | 6 (40%) | 0.51 |
| Diabetes mellitus | | 8 (42%) | 5 (33%) | 0.12 |
| Chronic pancreatitis | | 3 (16%) | 2 (13%) | 0.61 |

*median (interquartile range) ; ASA, American Society of Anesthesiologists physical status

tional 1 cm of the pancreatic parenchyma was resected, the main pancreatic duct was identified, and the cases were reconstructed of pancreatic jejunal anastomosis as usual.

*Analysis within the DP groups*

The incidence of POPFs (grade BC) was significantly lower ($p = 0.03$) in the DP-CL group (13.3%, 2 patients) than in the DP-UAS group (46.7%, 7 patients). The amylase level of drainage fluid on POD 3 was slightly higher in the DP-CL group than in the DP-UAS group, but the difference was not significant ($p = 0.49$) (Table 4). Furthermore, the operative duration, blood loss, and LOS did not differ significantly between the DP-CL group and the DP-UAS group.

Univariable analyses revealed that risk factors for POPF were a soft pancreas and resection via the UAS method. Multivariate analysis identified the UAS method as an independent risk factor for POPF ($p = 0.05$) (Table 5).

## Discussion

A major complication after pancreatectomy is POPF, for which suggested risk factors include a soft pancreas, a

Table 3. Outcomes of patients undergoing pancreaticoduodenectomy

| Factors | Crushing and ligation group ($N = 25$) | Ultrasonically activated scalpel group ($N = 29$) | $p$-value |
|---|---|---|---|
| Repeated surgery | 0 (0%) | 1 (3%) | 0.35 |
| In-hospital death | 1 (4%) | 0 (0%) | 0.28 |
| Surgical site infection | 2 (8%) | 13 (45%) | <0.01 |
| Operative duration, minutes* | 432 (330-487) | 395 (3,265-474) | 0.04 |
| Blood loss, mL* | 685 (285-810) | 740 (330-830) | 0.74 |
| Length of hospital stay, days* | 24 (20-30) | 31 (26-39) | 0.02 |
| Postoperative day 3 drainage amylase level, U/L* | 650 (300-1,050) | 7,155 (3,010-12,500) | 0.09 |
| Maximum postoperative drainage amylase level, U/L* | 1,909 (515-2,500) | 11,881 (6,020-18,050) | 0.04 |
| Postoperative pancreatic fistula | 2 (8%) | 13 (44.8%) | <0.01 |
| Clavien-Dindo grade III | 2 (8%) | 3 (10%) | 0.35 |
| Abscess | 4 (16%) | 4 (14%) | 0.45 |
| Postoperative bleeding | 0 (0%) | 1 (3%) | 0.35 |
| Delayed gastric empty | 5 (20%) | 5 (17%) | 0.61 |
| Rehospitalization | 1 (4%) | 2 (7%) | 0.24 |

*median (interquartile range)

Table 4. Outcomes of patients undergoing distal pancreatectomy

| Factors | Crushing and ligation group ($N = 19$) | Ultrasonically activated scalpel group ($N = 15$) | $p$-value |
|---|---|---|---|
| Repeated surgery | 0 (0%) | 1 (7%) | 0.44 |
| In-hospital death | 0 (0%) | 0 (0%) | 0.28 |
| Surgical site infection | 3 (15%) | 3 (20%) | 1.00 |
| Operative duration, minutes* | 259 (230-292) | 261 (230-301) | 0.94 |
| Blood loss, mL* | 364 (205-580) | 640 (230-770) | 0.13 |
| Length of hospital stay, days* | 17 (13-21) | 21 (14-28) | 0.42 |
| Postoperative day 3 drainage amylase level, U/L* | 1,738 (880-2,980) | 1,182 (500-2,250) | 0.49 |
| Maximum postoperative drainage amylase level, U/L* | 16,214 (4,850-19,800) | 4,406 (2,150-7,020) | 0.15 |
| Postoperative pancreatic fistula | 2 (10.5%) | 7 (46.7%) | 0.03 |
| Clavien-Dindo grade III | 2 (10.5%) | 7 (46.7%) | 0.03 |
| Abscess | 4 (21%) | 5 (33%) | 0.55 |
| Postoperative bleeding | 0 (0%) | 0 (0%) | 0.79 |
| Delayed gastric empty | 2 (11%) | 2 (15%) | 0.64 |
| Rehospitalization | 1 (6%) | 1 (7%) | 0.43 |

* median (interquartile range)

Table 5. Univariate/multivariate analysis

| Variables | Univariate analysis | | Multivariate analysis | |
|---|---|---|---|---|
| | Odds ratio (95% confidence index) | *p*-value | Odds ratio (95% confidence index) | *p*-value |
| Male sex | 1.11 (0.43–2.88) | 0.83 | | |
| Age > 73 years | 0.89 (0.39–2.07) | 0.80 | | |
| Body mass index > 22 kg/m$^2$ | 0.93 (0.39–2.16) | 0.93 | | |
| ASA-PS, 2 or 3 | 1.12 (0.6–2.08) | 0.73 | | |
| Nonpancreatic cancer | 2.72 (0.68–10.8) | 0.16 | | |
| Soft pancreas | 2.41 (1.23–4.71) | 0.01 | 1.83 (0.98–3.42) | 0.07 |
| No diabetes mellitus | 1.33 (0.60–2.93) | 0.47 | | |
| No chronic pancreatitis | 2.45 (0.51–11.77) | 0.26 | | |
| Ultrasonically activated scalpel transection | 2.61 (1.43–4.78) | <0.01 | 2.28 (1.26–4.15) | 0.02 |

ASA, American Society of Anesthesiologists physical status

high body mass index, blood transfusion, an increase in intraoperative blood loss, and a longer operative time. However, the incidence of POPF is reportedly not correlated with numerous other factors, including disease type, octreotide administration, a medical history of diabetes mellitus or chronic pancreatitis, splenectomy, multiorgan resection, ligation of the main pancreatic duct, preoperative serum albumin levels, coverage with polyglycolic acid felt, dissection of enlarged lymph nodes, or the procedure used to perform the pancreatectomy[26,27].

Although crushing the parenchyma has come into widespread use when dissecting the liver[20–22,24,28], few studies have investigated its use for pancreatic resection ; thus, its efficacy for pancreatic resection is unknown[29]. The merits of the CL technique are as follows : 1) ligation is possible of most branches of the pancreatic duct other than the main pancreatic duct, 2) intraoperative blood loss is reduced during pancreatic resection, and 3) ligation is not affected by the hardness (texture) of the pancreatic parenchyma.

Whether pancreatic tissue can be successfully crushed appears to depend on the surgeons and the facilities. The aim of ligating all visible (> 1 mm) vessels and pancreatic ducts in the remaining tissue in this study seems to have yielded good results. Investigation of the results obtained in our PD showed that the CL method significantly reduced the incidence of POPF, maximal amylase levels in the drainage, and postoperative LOS. However, the CL group with DP showed significant superiority only in terms of the incidence of POPF. Therefore, we suspect that the significant differences in other outcomes between the PD-CL and PD-AUS groups were due to the larger number of patients. Another advantage of the CL technique was that the pancreatic duct could be identified during pancreatic dissection. If the conventional UAS method was used, a main pancreatic duct with a small diameter was sealed during pancreatic dissection.

Although the CL technique has advantages, it might also have several disadvantages. The present study found that of patients who had undergone PD, those in the CL group had a significantly longer duration of the operation than did those in the UAS group ; this result was not surprising because PD, unlike DP, consists of many procedures in addition to parenchymal dissection. The duration of PD appeared to be affected by other parts of the procedure upon completion. Additionally, the CL method was difficult to apply to the resection of additional tissue, as indicated by the intraoperative pathologic examination of frozen tissue sections. Currently, laparoscopic surgery is becoming a more common method for pancreatic resection. The same CL method of pancreatic resection is considered to be applicable to laparoscopic surgery for PD, in which a mid-to-small incision is made, and for DP, in which the pancreatic parenchyma is crushed with forceps and treated with small clips.

The present study had several limitations. The first is that the number of patients was small : therefore, the 2 homogeneous groups could not be compared and propensity score matching, although ideal, was not possible. A second limitation is that because PD and DP were performed in different time frames, patient selection might have been biased owing to differences in the historical background of surgery. When the results are divided by age, the learning

effect might lead to better results in the second half of the year. A second limitation is that the surgeries (PD and DP) were performed at different times, so the results may differ due to the different historical backgrounds of the surgeries. A third and final limitation is that the present study was retrospective.

## Conclusion

The present study has found that the use of the CL technique reduces pancreatic fluid leakage and prevents the development of POPF in patients who undergo PD or DP. Because the study has indicated that the CL technique is superior to the AUS technique, we believe that future large-scale prospective randomized controlled clinical trials are required to verify our results.

## Abbreviations

POPF, postoperative pancreatic fistula ; PD, pancreaticoduodenectomy ; DP, distal pancreatectomy ; POD, postoperative day ; LOS, length of hospital stay ; CL, crushing and ligation ; UAS, ultrasonically activated scalpel ; PDAC, pancreatic ductal adenocarcinoma

Authors have no conflicts of interest.

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