

## Strategy to Treat Pancreatic Fistula Using Comprehensive Endoscopic Procedures Together with Percutaneous Methods

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### Abstract

**Objective:** Pancreatic fistula (PF) is an early complication after pancreatoduodenectomy. PF occurs because of disruption to the pancreatodigestive tract anastomosis with stricture or occlusion. A strategy to treat PF using interventional methods is proposed.

**Methods:** We treated a total of 6 patients with PF by endoscopic ultrasound (EUS)-guided or percutaneous pancreatic duct drainage. In this paper, these patients are reviewed based on the applied treatment for PF.

**Results:** At the time of introduction to our department, all the patients, except for one, had a percutaneous drainage tube implanted prior to surgery. In 2 patients undergoing pancreatojejunostomy within 3 months of the previous surgery, percutaneous introduction of a guidewire into the anastomosed jejunum, via the disrupted anastomosis, through the percutaneous fistula and the implantation of a percutaneous jejunal tube for 6 weeks was an effective PF treatment. There were 4 patients (3 pancreatojejunostomy, 1 pancreatogastrostomy) with more than 3 months of PF, with an occluded anastomosis and the pancreatic juice flow had to be rerouted by making another pancreatodigestive tract anastomosis using percutaneous or EUS-guided puncture of the pancreatic duct.

**Conclusions:** The optimal treatment for PF is considered to be the recanalization of the stricture or occluded anastomosis, or rerouting of the pancreatic juice flow by making another anastomosis. Considering our experiences in the treatment of PF, EUS-guided puncture of the pancreatic duct near the occluded anastomosis using a convex-type EUS endoscopy is the most preferable method to treat PF. In patients for whom it is difficult to introduce the endoscope into the afferent loop in the pancreatojejunostomy, various methods, including percutaneous approaches, are feasible to treat PF.

**Keywords:** Pancreatic fistula; Pancreatoduodenectomy; Pancreatojejunostomy; Acute recurrent pancreatitis

### Introduction

Pancreatic fistula (PF) and acute recurrent pancreatitis (ARP) are the respective early and late stage complications after pancreatoduodenectomy (PD). The frequency of PF is low in patients with pancreatogastrostomy, with a rate of 0-12% [1], while it is more frequent among pancreatojejunostomy patients, with a rate of 10 to 20% [1]. Another study has reported that 14% of patients with pancreatoduodenectomy have suffered from PF [2]. The disruption of the anastomotic site is the cause of PF and is associated with stricture or occlusion of the anastomosis at early stages after PD. In contrast, the frequency of ARP is low with the ratio of 2% in pancreatogastrostomy [1], and 1.6% [1] to 2.2% [2] in pancreatojejunostomy. The strictured or occluded anastomosis at the late stage post-PD causes ARP [3].

These disorders cause the patients to stay in the hospital for longer periods of time without any oral intake, consequently reducing the quality of life. Although surgeons are frequently reluctant to perform surgery, due to an increased susceptibility to postoperative adhesion or a physical burden to the patients, surgical treatment is associated with good results [3].

Pancreatic duct drainage is the optimal treatment for these disorders. Recently, endoscopic procedures have been adapted to treat ARP, and the endoscopic ultrasound (EUS)-guided method was reported to be useful for such treatment [4-7]. Yet, symptomatic treatments using EUS-guided drainage of the collected fluid have been reported on several occasions [8,9], while there are only a few reports on draining a pancreatic duct [10,11]. We treated a total of 6 patients with PF by EUS-guided or percutaneous pancreatic duct drainage. In

this paper, these patients are reviewed based on the applied treatment for PF, and a strategy is proposed.

### Methods

For 10 years, starting from 2005, 6 patients (mean age, 71-year-old (46-82); male: female, 4:2) with PF were introduced to our hospital for its treatment. The initial diseases which showed evidence of PD were bile duct cancer in 3, as well as acinar cell cancer, chronic pancreatitis with pancreatic stones, and multiple aneurysms of the pancreas head, one in each patient (Table 1). Reconstruction was completed through pancreatogastrostomy and pancreatojejunostomy in 1 (Case 3) and 5 patients, respectively. PF was recognized immediately after the previous surgery in 5 patients. The remaining 1 patient (Case 2) suffered from PF shortly after radiological interventional treatment for hemorrhage caused by the pseudoaneurysm occurring 52 days after the previous surgery. In 5 patients, a percutaneous tube had been placed near the anastomosis during the prior surgery, and in 1 after treating pseudoaneurysm using IVR (Case 2). In this case, it had been

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Case	Age	Sex	Previous disease	Reconstruction	Onset of PF	Period suffering PF (days)
1	71	F	PMA	PJ	Immediately after sur.	43
2	82	M	BC	PJ	After IVR for pseudoaneurysm	33 (85 after the prior surgery)
3	46	M	CP	PG	Immediately after sur.	156
4	71	M	BC	PJ	Immediately after sur.	93
5	78	F	AC	PJ	Immediately after sur.	361
6	71	M	BC	PJ	Immediately after sur.	134

PF: Pancreatic Fistula; PMA: Pancreas Multiple Aneurysm; BC: Bile Duct Cancer; CP: Chronic Pancreatitis; AC: Acinar Cell Cancer; PJ: Pancreatojejunostomy; PG: Pancreatogastrostomy; IVR: Interventional Radiology; Sur: Surgery

**Table 1:** Patient Characteristics.

implanted after the treatment for draining the fluid collected around the pancreas due to PF.

At the time of introduction, every patient did not have the sign of infection, but kept with nothing by mouth with support by total parenteral nutrition, whose PF were classified to Grade B of ISGPF definition [12] according to the duration of persistent PF over 3 weeks. The drained volume through the percutaneous tube changed depending on the day, but kept more than 100 ml with the maximum volume of 200 ml a day.

The time from the onset of PF to its treatment using endoscopic or percutaneous procedures was 43, 33, 156, 93, 361, and 134 days in each case. The patient suffering from hemorrhage because of the pseudoaneurysm (Case 2) had the period of 33 days, and the treatment was performed 85 days after the former surgery.

The percutaneous tube was removed when effectiveness of the treatments for disappearance of PF was recognized. After removing the percutaneous tube, recurrence of PF was examined by computed tomography or ultrasonography.

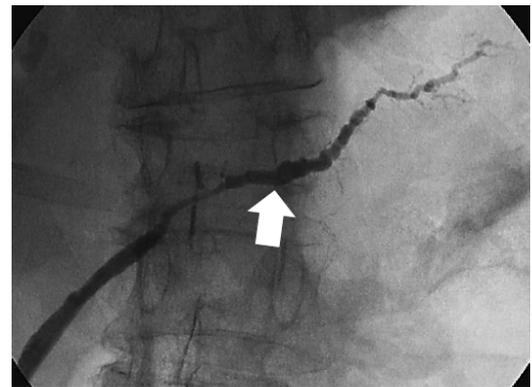
## Results

Through the percutaneously implanted tube, contrast medium injection revealed the remnant pancreatic duct, but not the anastomosed jejunum in all patients (Figure 1).

In the 2 patients suffering from PF for 45 days (Case 1) and 33 days, or specifically 85 days after the previous surgery (Case 2), a 0.025-inch guidewire (GW) (Radifocus, Terumo, Japan) was introduced through the percutaneous tube and advanced into the anastomosed jejunum via the disrupted pancreatojejunostomy (Figure 2). A 7-Fr percutaneous jejunal tube through the pancreatojejunostomy was placed over the GW (Figure 3). PF was cured, and the percutaneous tube was removed on the 27th and 49th day after the treatment without recurrence of PF, respectively.

In 4 patients suffering from PF for over 3 months, a GW introduced through the percutaneous drainage tube could not pass through the disrupted anastomosis into the anastomosed digestive tract. In 3 patients (Case 4, 5, 6) with pancreatojejunostomy, the anastomosis was not recognized by an endoscope introduced into the anastomotic site. Endoscopic or percutaneous treatments mentioned below were performed, and PFs were cured in all 4 patients by making another pancreatojejunostomy (Table 2).

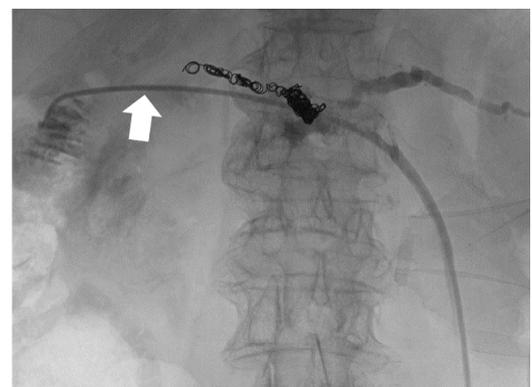
A 46-year-old man suffered from PF for 156 days after PD with pancreatogastrostomy due to chronic pancreatitis with pancreatic stones. Using a duodenoscope, the pancreatogastrostomy was identified at the posterior wall of the lower gastric body (Figure 4). Endoscopic retrograde cholangiopancreatography (ERCP) was attempted through the anastomosis, but failed as a result of the occluded anastomosis. The dilated pancreatic duct was identified from the stomach using a miniature sonographic probe near the anastomosis, and the dilated pancreatic duct was punctured from the stomach using an electric needle knife (KD-10Q-1, Olympus, Japan) under the fluoroscope. A



**Figure 1:** Contrast medium injection via the percutaneous drainage tube reveals the remnant pancreatic duct (arrow), but not the anastomosed jejunum.



**Figure 2:** A. Contrast medium injection via the percutaneous drainage tube reveals the remnant pancreatic duct (arrow). B. A 0.025-inch guidewire, introduced through the percutaneous tube (arrow), advanced into the anastomosed jejunum via the disrupted pancreatojejunostomy (Case 2).

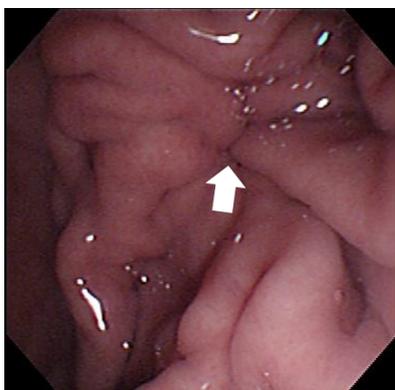


**Figure 3:** A percutaneous jejunal tube (arrow) through the pancreatojejunostomy was placed over the guidewire (Case 2).

Case	Method of treatment	Technical success	Period of percutaneous PF drainage tube removal after the treatment (days)	PF recurrence
1	Percutaneous GW insertion	Yes	27	No
2	Percutaneous GW insertion	Yes	49	No
3	Transgastric puncture	Yes	25	No
4	Transjejunal puncture	Yes	21	No
5	Percutaneous puncture	Yes	29	No
6	Transjejunal puncture	Yes	16	No

GW: Guide wire; PF: Pancreatic Fistula

**Table 2:** Method of treatment for PF and results.



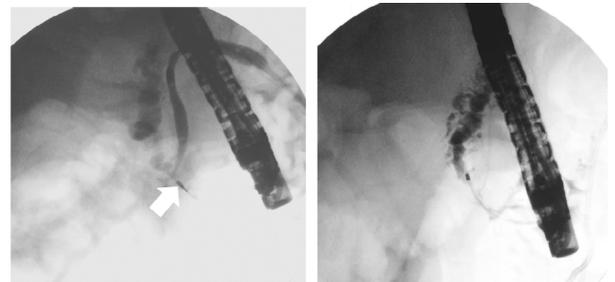
**Figure 4:** Using a duodenoscope, the pancreaticogastrostomy (arrow) was identified at the posterior wall of the lower gastric body (Case 3).

pancreatography was made (Figure 5), and a 0.025-inch guidewire (Jagwire, Boston, Japan) was introduced into the pancreatic duct through the catheter with the placement of a 7-Fr 7-cm pancreatic stent (Olympus, Japan) after dilating the puncture route (Figure 6), which was another pancreaticogastrostomy. The percutaneous tube was removed on the 25th day after the treatment without recurrence of PF (Case 3).

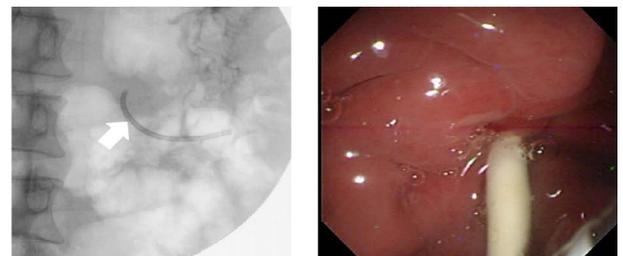
A 71-year-old man suffered from PF for 93 days after PD with pancreatojejunostomy due to bile duct cancer. Abdominal ultrasonography clearly revealed the dilated main pancreatic duct (MPD), and a percutaneous puncture of the MPD was performed by implanting a percutaneous pancreatic duct drainage tube. A 0.025-inch GW was placed through the implanted tube, which could not pass through the anastomosis. Introducing a forward-viewing endoscope to the anastomotic site through the anastomosed jejunum, the pancreatic duct was revealed using a miniature sonographic probe. Under the fluoroscope, the pancreatography carried out by the injection of contrast medium through the percutaneous pancreatic duct drainage tube and the pancreatic duct was punctured from the jejunum using a 19G needle (Echo-tip, Wilson-Cook, USA) (Figure 7). A 0.025-inch GW was introduced into the pancreatic duct to dilate the puncture route. Through the percutaneous pancreatic duct drainage tube, a 0.025-inch GW was introduced into the anastomosed jejunum via the dilated puncture route and a 5-Fr percutaneous tube was implanted into the jejunum via the pancreatic duct and the dilated route (Figure 8). Making another pancreatojejunostomy was achieved. The percutaneous tube was removed on the 21th day after the treatment without recurrence of PF (Case 4).

A 73-year-old woman suffered from PF for 361 days after PD with pancreatojejunostomy due to duodenal papillary cancer. Abdominal ultrasonography clearly revealed the dilated pancreatic duct and the anastomosed jejunum (Figure 9). We percutaneously punctured the anastomosed jejunum through the pancreatic duct near the anastomosis using a 21G needle (Hanaco, Japan) (Figure 10). Introducing a 0.018-inch GW (Hanaco, Japan) and placing a percutaneous tube through the pancreatic duct into the anastomosed jejunum (Figure 11), another pancreatojejunostomy was made. The percutaneous tube was removed on the 25th day after the treatment without recurrence of PF (Case 5) [10].

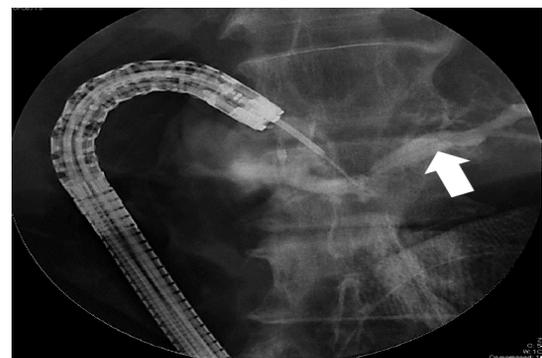
A 71-year-old man suffered from PF for 93 days after PD with pancreatojejunostomy due to bile duct cancer. A convex-type EUS endoscopy for puncture (GF type UCT260, Olympus, Japan) was introduced into the anastomotic site of the anastomosed jejunum.



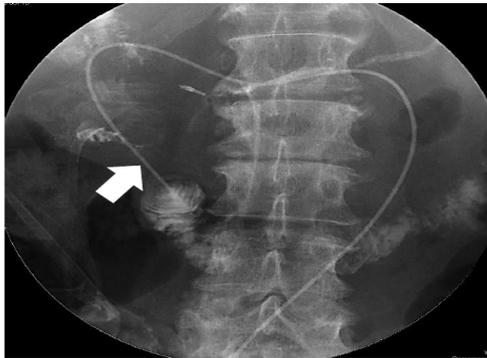
**Figure 5:** A. The dilated pancreatic duct was puncture from the stomach using an electric needle knife (arrow) under the fluoroscope. B. A pancreatography was made (Case 3).



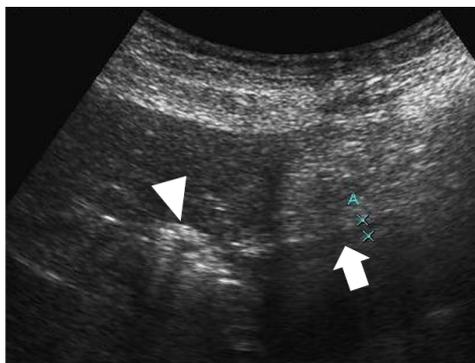
**Figure 6:** After dilating the puncture route, a 7-Fr 7cm pancreatic stent (arrow) was implanted. A, X-ray image; B, Endoscopic image (Case 3).



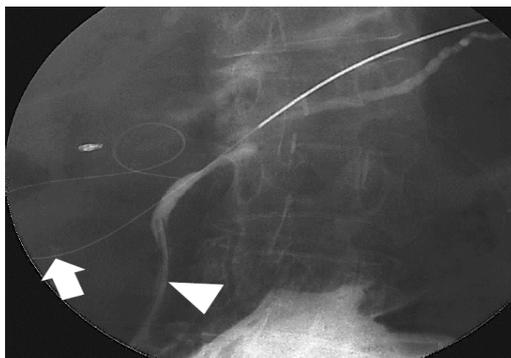
**Figure 7:** Under the fluoroscope, the pancreatic duct was punctured from the jejunum with pancreatography through the percutaneous pancreatic drainage tube (arrow) (Case 4).



**Figure 8:** Through the percutaneous route, a 5-Fr percutaneous tube was placed into the jejunum via the pancreatic duct and the dilated route (Case 4).



**Figure 9:** Abdominal ultrasonography reveals the dilated pancreatic duct (arrow) and the anastomosed jejunum (arrow head) (Case 5).



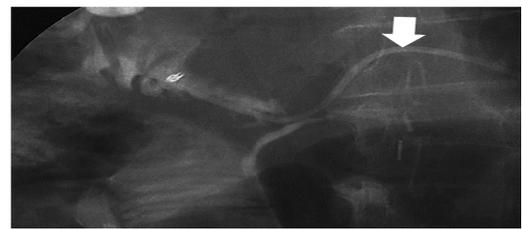
**Figure 10:** The anastomosed jejunum was punctured percutaneously through the pancreatic duct near the anastomosis and the guidewire (arrow) was introduced into the jejunum. Arrowhead shows the percutaneous drainage tube (Case 5).

Using EUS, the dilated MPD was clearly visible (Figure 12) and punctured using a 19G needle (Sonotip, Medi-Globe, Germany). After the pancreatography (Figure 13), a 0.025-inch GW was introduced into the pancreatic duct and a tapered 5-Fr pancreatic stent was implanted (Figure 14) to make another pancreatojejunostomy. The percutaneous tube was removed on the 16th day after the treatment without recurrence of PF (Case 6) [11].

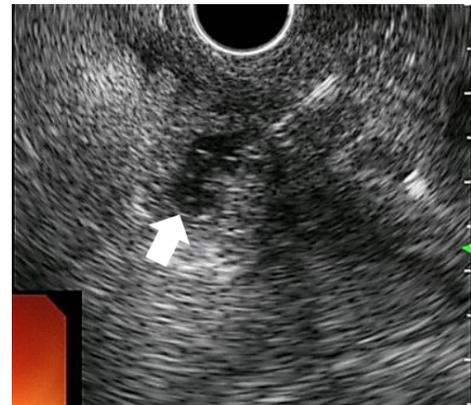
## Discussion

Post-operative PF is diagnosed by elevated amylase concentration

in the drained fluid, and the grade is defined [12]. Grade A is a transient PF, while grade B and C have persistent drainage over 3 weeks. These patients require clinical intervention or an operation preventing the patient from consuming anything by mouth, meaning they are supported with partial or total parenteral or enteral nutrition and an extended hospital stay [12]. Intra-drainage of pancreatic juice, instead of extra-drainage, could lead to patient discharged with per-oral intake. Further, EUS-guided cyst-gastrostomy, by placing a stent between the gastric cavity and the fluid collection, was reported to be the method with preferable results [8,9]. However, the method is just a symptomatic treatment, as it allows for draining of the collected fluid leaking from the pancreatic duct, but does not treat PF itself. Not treating PF has the risk of repeated fluid collection after removing the implanted stent [13]



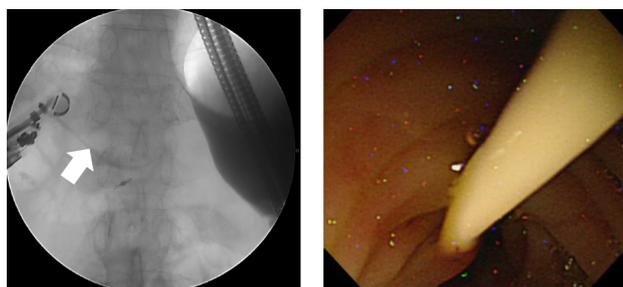
**Figure 11:** A percutaneous tube (arrow) was placed through the pancreatic duct into the anastomosed jejunum (Case 5).



**Figure 12:** Convex-type EUS endoscopy for puncture was introduced into the anastomotic site of the anastomosed jejunum. Using EUS, the dilated MPD (arrow) is revealed (Case 6).



**Figure 13:** Pancreatography was made (Case 6).



**Figure 14:** A tapered 5Fr pancreatic stent (arrow) was implanted. A, X-ray image; B, Endoscopic image (Case 6).

or as a result of implanted stent dysfunction in patients with persistent pancreatic juice leakage. Moreover, many patients with PF were introduced to the department of gastroenterology with a percutaneous tube, which had been implanted during the previous operation. In these cases, the fluid collection cavity was absent for continuous drainage by the tube, and EUS-guided transmural cyst drainage was not feasible. The optimal treatment for PF is considered to be internal pancreatic duct drainage by reopening the occluded pancreatodigestive tract anastomosis or making a new one.

According to our experience treating PF, the state of the disrupted anastomosis changed at about 3 months after the onset of PF. In patients at the early stage, before 3 months (Case 1, 2), the disrupted anastomosis was easily passed through by a GW, and dilatation with percutaneous tube placement could treat PF. The reason why implantation of a percutaneous tube through the disrupted anastomosis is a treatment for PF is discussed below. The jejunal side of the anastomosis becomes stenotic and obstructed pancreatic juice flow induces disruption of the anastomosis. However, the stenotic jejunal side of the anastomosis is not organized, and percutaneous tube placement contributes to the dilation of the stenotic portion to recover the pancreatic juice flow into the jejunum.

On the other hand, patients suffering from PF for more than 3 months had an organized occluded anastomosis, and opening an occluded anastomosis or making another pancreatojejunostomy was needed. To treat an occluded anastomosis, the anastomosis needed to be punctured from the pancreas side using a needle knife introduced through the EUS-guided route from the stomach [14]. This method is an attractive and a novel procedure, but also hazardous, as reaching the anastomosed GI tract is not guaranteed and vessels lying along the direction of the puncture are not excluded. Pancreatogastrostomy by implanting a stent between the pancreatic duct and the stomach is an alternative method to treat the obstructed pancreatic duct. However, hemorrhage during stent placement, slipping down of the placed stent, or abscess formation after the procedure has been experienced [15]. Therefore, this method is considered to be feasible, but not preferable. As a result, a new stent for pancreatogastrostomy was developed [16]. However, introducing a GW into the anastomosed jejunum through the pancreatojejunostomy is necessary to implant the stent between the pancreatic duct and the stomach. Further, it is not feasible in patients with PF due to the occluded anastomosis.

In Case 3 and Case 4 of our study, we treated PF with the obstructed anastomosis using a miniature EUS probe to identify the pancreatic duct and decide the direction of the puncturing needle for making another pancreatodigestive tract anastomosis. When these treatments had been performed, a EUS endoscope for puncture had

not been introduced to our hospital and the treatment for a strictured anastomosis using EUS had been scarcely reported. However, now, these treatments could be accomplished using a EUS endoscope for puncture in patients with pancreatogastrostomy [17], and also in patients with pancreatojejunostomy, if the endoscope could be introduced into the anastomotic site [11]. Moreover, the percutaneous method used to treat PF in Case 5 can also be treated using a EUS endoscope for puncture, if the endoscope can be introduced into the anastomotic site.

## Conclusions

The optimal treatment for PF is considered to be recanalization of the stricture or occluded anastomosis, or the rerouting of the pancreatic juice flow by making another anastomosis. While the regular treatment has not been established, percutaneous introduction of a guidewire into the anastomosed jejunum via the disrupted anastomosis through the percutaneous fistula to place a percutaneous jejunal tube could be effective within 3 months after the onset of PF and the previous surgery. Further, EUS-guided transmural puncture near the occluded anastomosis from the anastomosed jejunum in pancreatojejunostomy and the anastomosed stomach in pancreatogastrostomy is feasible to implant a stent after the 3-month period. In patients where it is difficult to introduce the endoscope into the afferent loop in pancreatojejunostomy, various methods, including percutaneous methods described above, are feasible to treat PF.

## Conflict of Interest

The authors declare that they have no conflict of interest.

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