Endoscopic Ultrasound-Guided Drainage in the Management of Postoperative Pancreatic Fistula After Partial Pancreatectomy

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ABSTRACT

Background: *Postoperative pancreatic fistula (POPF) is the most frequent and harmful complication following pancreatic surgery. Traditional management includes conservative treatment, percutaneous drainage (PD), and reoperation. The objective of the present study was to evaluate the safety and effectiveness of EUS (Endoscopic ultrasound)-guided drainage by using nasocystic tubes combined with single or 2 stents for POPF.*

Methods: *Patients who had POPF after surgery and then underwent EUS-guided drainage, from October 2016 to October 2019, were enrolled in this study. Technical success was defined as successful transgastric puncture of the peripancreatic fluid collection (PFC) and deployment of the nasocystic tube and stents. Clinical success was defined as symptomatic improvement and the resolution of the fluid collection on follow-up CT scan.*

Results: *A total of 15 patients received EUS-guided drainage. In 13 patients, a nasocystic tube was placed in the PFC combined with a double-pigtail plastic stent. In the remaining 2 patients, a nasocystic tube and 2 stents each were inserted in place. Technical success was achieved in 15 of 15 patients (100%). Clinical success was achieved in 14 of 15 patients (93.3%). In one case, the stent was blocked on the 10th day after the procedure. The median time between surgery and EUS-guided drainage was 10 (5-32) days. The median time of hospital stay after EUS-guided drainage was 16 (11-48) days. Operation-unrelated death occurred in 1 patient (7%) during follow-up.*

Conclusion: *EUS-guided drainage with a nasocystic tube and double-pigtail stents appears to be safe and technically feasible, and could be an alternative treatment for patients with POPF.*

Keywords: *Postoperative pancreatic fistula, peripancreatic fluid collection, endoscopic ultrasound-guided drainage, endoscopic nasocystic tube, double-pigtail plastic stent, percutaneous drainage*

INTRODUCTION

Despite the development of surgical approaches, postoperative pancreatic fistula (POPF) is still regarded as the most frequent and harmful complication after pancreatic operation, with a reported incidence of 20-35%.[1,2] In patients undergoing distal pancreatectomy, the rate is even higher. The pancreatic fluid in the leakage can rapidly lead to fever, abdominal pain, nausea, and other symptoms, as well as a series of adverse events including pseudoaneurysm leading from the erosion of surrounding arteries, gastric outlet obstruction, and necrosis, abscess, and sepsis formation in surrounding tissue, which is considered a life-threatening complication.[3] In 2005, the International Study Group (ISGPS) gave the first standardized definition of POPF (i.e., an abnormal communication between the pancreatic ductal "system" and another epithelial surface containing pancreas-derived, enzyme-rich fluid). The diagnostic criteria included any measurable volume of drainage fluid on or after postoperative day 3 with amylase level > 3 times the upper limit of serum amylase activity.[4] In this article, the ISGPS divided patients with POPF into grades A, B, and C based on clinical conditions, imaging changes, reintervention treatment, etc. In addition, the POPF classification is a main determinant of postoperative morbidity and mortality and plays a core role in postoperative hospital stay and economic impact. Thus, in 2016, the ISGPS updated the concept and grading of POPFs. Grade A POPF with no clinical significance was redefined as a "biochemical leak," and patients with grade A POPFs had identical prognoses to patients without fistulas. The criteria for grade B and C POPFs were also made stricter and more distinctive (Table 1).[1] Patients with grade B and C POPFs need further invasive

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Table 1. Definition of POPF Grading

Event	BL (NO POPF)	Grade B POPF	Grade C POPF
Increased amylase activity >3 times upper limit Institutional normal serum value	Yes	Yes	Yes
Persisting peripancreatic drainage>3 weeks	No	Yes	Yes
Clinically relevant change in management of POPF	No	Yes	Yes
POPF percutaneous or endoscopic specific interventions for collections	No	Yes	Yes
Angiographic procedures for POPF-related bleeding	No	Yes	Yes
Reoperation for POPF	No	No	Yes
Signs of infection related to POPF	No	Yes, without organ failure	Yes, with organ failure
POPF-related organ failure	No	No	Yes
POPF-related death	No	No	Yes

management, in addition to persistent surgical drainage, which gives rise to extended hospitalization and increased health-care burden.[5,6]

Conservative management of biochemical leaks may include enteral nutrition support, antibiotics, and somatostatin analogs, as well as persistent surgical drainage. For grade B-C POPFs, the selection of treatment of further drainage management or reoperation depends on wound site, comorbidity, the patient's general condition, center-specific expertise, and the patient's preference.[3] Although no standardized treatment option has been suggested, all further treatments are to ensure smooth drainage of the leakage. Reoperation will aggravate the patient's surgery-related injuries, and it is associated with considerable morbidity and mortality.[7,8] However, Elena Rangelova et al.[9] suggested that reoperation remains an undeniably valuable choice for severe POPF. Thus, this method would be chosen only for patients with severe conditions or those who have undergone failed treatments. Currently, drainage management mainly includes image-guided (B-ultrasound or CT) percutaneous (external) and endoscopic (internal) drainage.[10] The former is a minimally invasive procedure for POPF treatment. It offers satisfying results, but in certain patients, the pancreatic fluid collection is located in the lesser omentum or posterior peritoneum, making it difficult to approach those positions without injuring the surrounding visceral organs by percutaneous drainage (PD). In addition, the external drainage tube requires daily care and regular irrigation of the catheter. Electrolytes maybe lost, which also affects the quality of life and prolongs the duration of treatment. A permanent cutaneopancreatic fistula may develop in 5-25% of patients after PD. [11-13]

In this decade, endoscopic intervention has been used to manage POPF, including endoscopic retrograde pancreatography (ERP)-guided drainage and EUS (endoscopic ultrasound)-guided drainage. ERP improves drainage by pancreatic sphincterotomy and pancreatic stent placement to reduce the pressure in the pancreatic duct and facilitate the drainage of pancreatic juice. In 1993, Saeed et al. inserted pancreatic stents for 5 patients with POPF.[14] In another study, the treatment success rate was 71%, but the procedure-related complication rate was 9%, mainly including postoperative pancreatitis.[15] Other procedures were also reported, such as injecting tissue adhesive or fibrin glue into the fistula.[16,17] However, their safety and effectiveness remain controversial. EUS-guided drainage was the same as that used for a peripancreatic fluid collection after necrotic pancreatitis, and its safety and effectiveness have been evaluated by various large case-controlled reports.[18] Some studies have suggested that EUS-guided drainage with single or multiple double-pigtail stents for POPF drainage is safe and effective.[19] Other patients underwent self-expanding metal stent insertion for drainage.[20] However, reports of interventional management with a nasocystic tube are scarce. In our experience, in the first few days after endoscopic drainage, the volume of drainage needs to be known to evaluate the effect of the drainage. Thus, we report our experience with EUS-guided drainage using a nasocystic tube combined with double-pigtail stents for the treatment of POPF. It is worth noting that some patients with POPF did not undergo mature capsular wall-wrapped fluid collection early in the postoperative period. Therefore, scholars proposed the concept of EUS-guided treatment of non-wrapped postpancreatic fluid collections, and the results were also encouraging.[21] In the present study, we also performed EUS-guided management on these

patients in the early postoperative period, and this article will also discuss this issue.

PATIENTS AND METHODS

Patients

This study was conducted as a retrospective analysis. Patients with POPF undergoing EUS-guided procedures were enrolled in our hospital, from October 2016 to October 2019. In these patients, conservative treatment and permanent surgical drainage were ineffective, and no patients received PD or surgery unless EUS-guided drainage failed. Adjusting the position of the surgical drainage tube was also tried in all patients, but the drainage effect was limited. Therefore, further drainage treatment was needed. In other words, EUS-guided drainage was considered the primary choice for the treatment of POPF in this study. All patients underwent an abdominal CT scan to assess the accessibility of the POPF before management (Figure 1). EUS-guided drainage was forbidden for patients who had coagulation dysfunction and abdominal aortic aneurysm and for those who could not tolerate endoscopic procedures. Notably, patients with multilocular fluid collection were excluded to reduce patient heterogeneity. This study was approved by the Ethics Committee of the First People's Hospital of Changzhou (2020-029). All patients provided written informed consent for undergoing the procedure.

Definition

Postoperative pancreatic fistula was defined according to the 2016 ISGPS definitions. Technical success was defined as successful transgastric puncture for the peripancreatic fluid collection (PFC) and deployment of the nasocystic tube and stent. Clinical success was defined as meeting all the following 4 points: (1) a resolution of clinical symptoms after management, including the relief of abdominal pain, fever, nausea and vomiting within a week; (2) an improvement in leukocytosis and the CRP level; (3) radiographic improvement after the procedure (maximal diameter of PFC less than 2 cm); and (4) a resolution of the PFC without the need for further alternative drainage techniques.

Procedure

All EUS-guided procedures were performed with therapeutic linear array echoendoscopes (UCT-260, Olympus, Tokyo, Japan) under conscious sedation anesthesia by two experienced endoscopists. Peripancreatic fluid collection was localized by ultrasound endoscopy. After excluding the presence of local blood vessels by using color Doppler, a 19G puncture needle (ECHO-19, Cook Ireland Ltd., Limerick, Ireland) was used to puncture through the gastric wall and into the fluid collection under EUS-guidance. Fluid was aspirated to confirm that the needle tip was in the cavity. A 0.035-inch guidewire (Jagwire, Boston Scientific Corporation, United States) was introduced through the needle and coiled within the fluid collection under fluoroscopic guidance. Then, the puncture needle was withdrawn, and a Cook cystotome (CST-10, Cook Ireland Ltd.) was used to puncture the gastric wall and dilate the sinus along the guidewire. Another guidewire was inserted along the cystotome. A 7Fr-7 or 7Fr-3 double-pigtail plastic stent (Zimmon® Biliary Stent, Cook Ireland Ltd.) was deployed. The distal end of the stent was gently pushed into the cystic cavity. Next, a nasocystic tube (NBDS-B-7/250-P, Micro-Tech (Nanjing) Co., Ltd., Nanjing, China) was inserted into the cavity. If another stent was needed, one more guidewire was inserted, and the nasocystic tube was usually inserted after stent insertion (Figure 2).

After the procedure, the drainage fluid was tested for amylase activity and bacterial culture. Patients were required to fast for approximately 24 hours. Parenteral

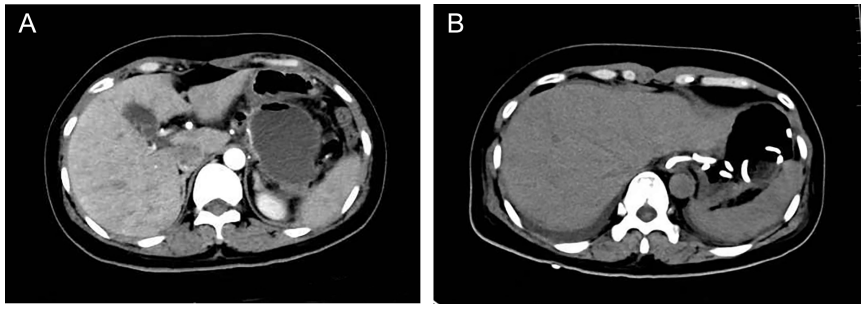

Figure 1. (A) Abdominal CT revealing pancreatic fluid collection after laparoscopic distal pancreatectomy measuring 7.1 × 5.1 cm; (B) Follow-up CT showing significant resolution of the POPF 14 days after EUS-guided drainage.

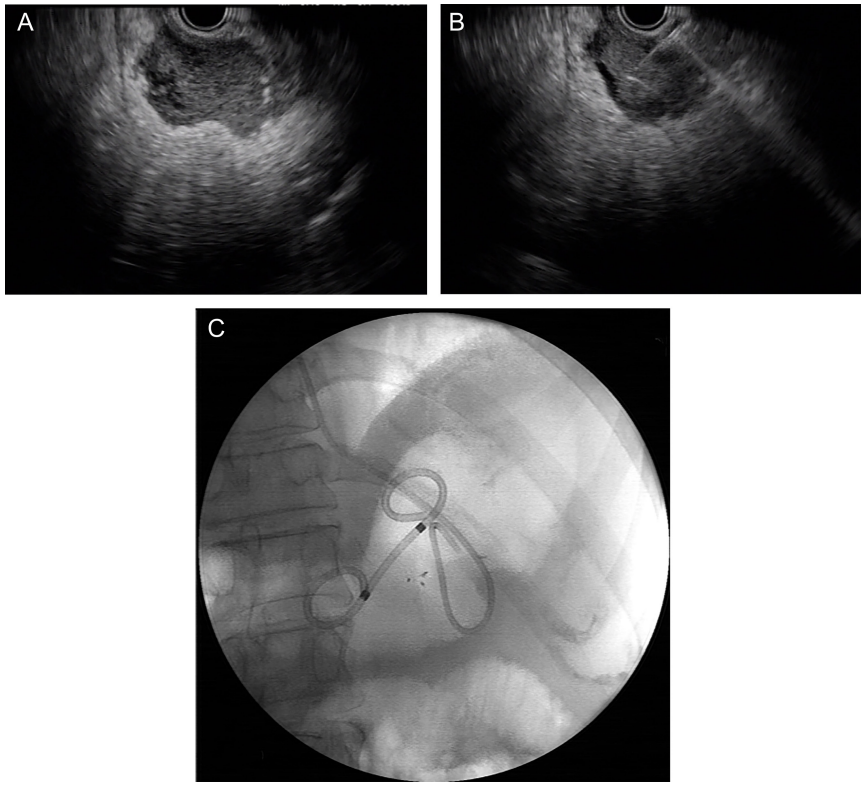

Figure 2. (A) The drainage was visualized adjacent to the stomach by EUS; (B) Puncture of the PFC with a 19G needle; and (C) The drainage was completed with a nasocystic tube and a double-pigtail stent from the stomach into the drainage canal.

nutrition support, antibiotics, proton-pump inhibitors (PPIs), and somatostatin analogs were used in all patients. The volume of drainage, fever, and the level of abdominal pain were recorded daily. The white blood cell count and CRP level were tested every 2-3 days. A repeat abdominal CT was obtained at approximately 72 hours to evaluate the drainage response. Afterwards, an abdominal CT was done weekly. When an encapsulating wall was defined on CT, more than 1 month after the primary pancreatectomy, the nasocystic tube was flushed twice per day using saline or metronidazole solution. If any new-onset clinical presentations occurred, blood tests and CT scans were conducted at any time. Patients were discharged from the hospital when their symptoms disappeared, their test results dropped to the normal level, and the maximal diameter of the PFC reduced to less than 2 cm on a CT scan. The stent and nasocystic tube were removed at the time of patient discharge. The surgical drainage tubes were removed when there was no drainage fluid and the symptoms disappeared, and the tubes were removed before nasocystic tube and stent removal.

Follow-up

All patients received abdominal CT during outpatient clinic visits at 4 weeks after discharge to evaluate the extent of recovery from the POPF. Patients with a partial decrease in the fluid collection needed further CT scanning 4 weeks later.

Statistical Analysis

SPSS 23 statistical software was used for data analysis. The χ^2 test and the Fisher's exact probability test were used to compare categorical variables. The Student's *t*-test was used to compare continuous variables. Non-normally distributed variables are expressed as medians (range). Nominal variables are expressed as frequencies and percentages. A *P*-value < .05 was considered statistically significant.

RESULTS

From October 2016 to October 2019, 15 patients underwent EUS-guided drainage for POPF in our center, with a median age of 59 (40-76) years. These 15 patients underwent surgery for pancreatic adenocarcinoma (5,

33%), pancreatic cystic neoplasm (5, 33%), distal bile duct tumor (2, 13%), neuroendocrine tumor (1, 7%), metastases (1, 7%), and solid pseudopapillary neoplasm of the pancreas (1, 7%). The surgical methods included distal pancreatectomy (8, 54%) and pancreaticoduodenectomy (7, 46%). During the surgery, 2 to 3 drainage tubes were routinely placed near the surgical anastomosis. Patient characteristics are summarized in Table 2.

Before the procedure, fever, abdominal pain, and elevated amylase levels in the drainage occurred in all cases (15, 100%). The majority of patients' laboratory examinations showed leukocytosis (15, 100%) and a higher level of CRP (14, 93%). Abdominal CT showed a PFC, without pancreatic necrosis. Fourteen patients (93%) were grade B POPF. The other patient (7%) had septic shock and renal insufficiency after surgery. Thus, he was diagnosed with a grade C POPF.

The median time from surgery to EUS-guided drainage was 10 (5-32) days. In 13 patients, one double-pigtail stent was inserted into the cavity, followed by nasocystic tube deployment (87%). In the remaining 2 patients, another stent was needed because the PFC was large and difficult to aspirate from the nasocystic tube (13%). The median procedure time was 32 (22-50) minutes.

Table 2. Main Characteristics of Patients with POPF

Total patients, n	15
Male, n (%)	5 (33)
Age, years	59 (40-76)
Pathology, n (%)	
Pancreatic adenocarcinoma	5 (33)
Pancreatic cystic neoplasm	5 (33)
Distal bile duct tumor	2 (13)
Neuroendocrine tumor	1 (7)
Metastases	1 (7)
Solid pseudopapillary neoplasm of the pancreas	1 (7)
Surgical approach, n (%)	
Distal pancreatectomy	8 (54)
Pancreaticoduodenectomy	7 (46)
POPF grade, n (%)	
Grade B POPF	14 (93)
Grade C POPF	1 (7)
Count of white blood cell (10^9/L)	18.4 (11.5-25.1)
CRP level (mg/L)	81(4.1-167)
Maximal diameter of PFC (mm)	67.6 (55.6-100.0)

The bacterial culture of the intraoperative fluid drainage was positive in 11 patients (73%). Approximately 1 week after the procedure, improvement in presentation occurred in all patients. The fever of all patients was relieved. Three patients complained of persistent abdominal pain, which eventually resolved. The preoperative white blood cell count was 18.4 (11.5-25.1) $\times$ 10^9/L, and the postoperative white blood cell count was 7.3 (3.8-13.5) $\times$ 10^9/L ($P < .05$). The preoperative CRP level was 81 (4.1-167) mg/L and the postoperative CRP level was 19.9 (3.8-53.5) mg/L ($P < .05$). The preoperative maximal diameter of the PFC was 67.6 (55.6-100.0) mm, and the postoperative maximal diameter of the PFC was 23.1 (13.7-35.5) mm ($P < .05$) (approximately 10 days after the procedure).

One patient (7%) underwent 7 Fr double-pigtail plastic stent blockage, on the 10th day after the procedure. He complained of recurrent abdominal pain and fever, and the nasocystic drainage had less fluid than before. Therefore, the blocked stent was removed by using a snare, and another 10 Fr stent (Zimmon® Biliary Stent, Cook Ireland Ltd., Limerick, Ireland) was inserted under EUS guidance. The nasocystic tube was aspirated, but not flushed. In the following days, the symptoms resolved, and all the test results improved. No bleeding or POPF recurrence occurred in this study. At the time of discharge, the PFC disappeared in 13 patients, and the PFC persisted in 2 patients (maximal diameter less than 2 cm).

The median time of hospital stay after EUS-guided drainage was 16 (11-48) days. The median follow-up time was 21 (10-48) months. The 2 patients who had a persistent PFC underwent further CT scans monthly; the PFC of one patient disappeared at the first follow-up, and the PFC of the other disappeared at the second follow-up. One patient (1, 7%) died of a metastatic liver tumor 152 days after discharge that was not related to the POPF or endoscopic operation. The subsequent clinical course of the remaining patients was non-eventful. The technical success rate of EUS-guided drainage reached 100%, and the clinical success rate was 93.3% (Table 3).

DISCUSSION

Percutaneous drainage is the most widely used interventional treatment for POPF, and it generally achieves satisfactory results in most cases. Smits suggested that

PD, as the first choice for severe pancreatic fistula after pancreatoduodenectomy, may lead to a better clinical outcome than reoperation.[7] On the other hand, there are also some limitations of PD. The most serious problem with the PD technique is the difficulty in approaching the PFC without injuring the surrounding visceral organs in some patients with POPF, especially when the lesion is located in the lesser omentum or posterior peritoneum. In addition, PD does not allow the evacuation of necrotic tissue. Furthermore, external catheters require daily care, which affects the quality of life and even increases the risk of cutaneous pancreatic fistulas.[11-13] Reoperation can aggravate the patient's surgery-related injuries, and some patients may not be able to tolerate the reoperation. Surgeons only choose surgery if other treatments are ineffective or fail, with serious complications.[22]

EUS-guided drainage for POPF may be an alternative method in some studies. All reports of EUS-guided treatment of POPF suggested that this technique was safe and effective, and our research was no exception. The success rate of this technique was 100% in all reports, with the clinical success rate ranging from 79% to 100%. The first reported study by Varadarajulu et al.[23] showed a safe and effective technique for the treatment of POPF. Ten patients received 1 or 2 stent insertions, with a clinical success rate of 90%. They also introduced a nasocystic tube in addition to stenting in 1 patient. This patient had a peripancreatic abscess and a necrosis-type PFC with failed transmural drainage. In another study, in 2011, the technical success rate and clinical success rate of EUS-guided drainage were both 100% in 20 patients, without any complications or reoperations.[24] In the following years, some case-controlled studies were published. A multicenter retrospective study by Jürgensen et al.[3] analyzed patients with a PFC or POPF. In the study, the median time of EUS-guided drainage leading to resolution was 8 days, while that of PD and surgery was 25 days and 248 days, respectively. The success rate of the main treatment method of EUS-guided drainage was 85%, which was higher than that for PD (64%) and surgical treatment (41%).[3] Tamura compared EUS-guided drainage with PD for non-encapsulated POPFs. In the EUS group, reintervention occurred in 2 patients (15.3%), while in the patched PD group, reintervention occurred in 14 patients (50%).[21] Both controlled studies showed that EUS-guided drainage led to a more rapid resolution and reduced reintervention rate. The safety and effectiveness of EUS-guided drainage determined that it is suitable for patients with grades B and C POPFs, especially for patients whose PFC was difficult to approach by PD. There were no special contraindications for EUS-guided procedures in this study, except for general conditions (patients with coagulation dysfunction or abdominal aortic aneurysm, or those who could not tolerate endoscopic procedures).

Table 3. Technical Data and Clinical Outcomes of the Patients Who Underwent EUS-Guided Drainage of POPF

Technical success, n (%)	15 (100)
Clinical success, n (%)	14 (93)
The interval between surgery and procedure (days)	10 (5-32)
Drainage process, n (%)	
Nasocystic tube combined with 1 stent	13(87)
Nasocystic tube combined with 2 stents	2 (13)
Procedure duration (minutes)	32 (22-50)
Count of white blood cell after 7 days (10^9/L)	7.3 (3.8-13.5)
CRP level after 7 days (mg/L)	19.9 (3.8-53.5)
Maximal diameter of PFC after 10 days (mm)	23.1 (13.7-35.5)
Hospital stay after EUS-guide drainage (days)	16 (11-48)
Duration of tube insertion (days)	16 (11-48)
Complications, n (%)	
Stent blockage	1 (7)
Hemorrhage	0 (0)
Recurrence, n (%)	0 (0)

The complications included hemorrhage and the recurrence of PFC. In most studies, repeat drainage was needed in some patients because of insufficient drainage or relapse.[25,26] In our study, one patient also received repeat drainage because of stent blockage. This complication was fixed by a reinsertion of another stent and did not affect patient prognosis. Hemorrhage was also reported in some studies. Caillol reported hemorrhage due to arterial injuries (splenic artery and gastroduodenal artery) during the drainage procedures that occurred in 3 patients within 25 days following the procedure (day 4, day 6, and day 25).[25] In our opinion, POPF may also result in an erosion of the surrounding arteries and cause a pseudoaneurysm, which may lead to life-threatening bleeding. Using our method, the draining fluid is bloody if hemorrhage occurs in the cavity. In these patients, the reason for hemorrhage remains unclear, and may include primary surgery and drainage procedures.

At present, most reports on EUS-guided treatment of POPF have been performed using single or multiple double-pigtail plastic stents for drainage. In another study, a self-expanding metal stent was also used for drainage in some patients whose CT or EUS images suggested a large amount of necrotic tissue in the PFC.[3] In our research, the imaging of patients suggested no solid necrotic tissue in the PFC. Therefore, we did not select metal stents for drainage. The main feature of our procedure was the use of a nasocystic tube combined with stents for drainage. The nasocystic tube was used for evaluating the drainage volume in the following days and for flushing into the cavity when the cystic cavity matured. The nasocystic tube had several advantages: First, the culture of drainage fluid was positive in 11 patients. Therefore, double-pigtail stents directly placed in peripancreatic fluid collection for intestinal drainage might cause digestive tract infection and stent obstruction. The placement of a nasocystic tube for external drainage could reduce the flow of infectious effusion and thus reduce the occurrence of such events. Second, the amount of drainage fluid needs to be known daily, especially in the first few days following the procedure. On the other hand, cystic cavity hemorrhage can be noticed in time. Third, in addition to drainage, the nasocystic tube could also be periodically flushed if the drainage fluid is viscous (to prevent infection spread, flushing was not recommended if the capsule wall is immature). Finally, some scholars have reported that external drainage may reduce the potential risk of gastrointestinal fluid backflow from the digestive tract into the abdominal cavity.

Some scholars have also used nasocystic tubes for drainage for PFC after pancreatitis. In a study by Futagawa et al.,[27] 11 patients had nasocystic tubes placed under endoscopic guidance. The difference was that they replaced the nasocystic tube with double-pigtail stents 8 (6-10) days after the procedure. In Tamura's research, a nasocystic tube was placed in 13 patients with POPF. Subsequently, the nasocystic tube was cut as an internal drainage tube and left in the stomach in 2 patients (15%).[21] The duration of the nasocystic tube in place in our study was 21 (7-61) days compared with 8 (6-10) days for Futagawa and 8 (6-13) days for Tamura. The appropriate time for removing drainage tubes in our study was more conservative. The drainage tube was not removed until the patient's clinical symptoms disappeared, and the maximal diameter of the PFC was reduced to less than 2 cm on CT imaging. Therefore, the nasocystic tube and stents were placed longer than in the other 2 studies. We believe that it could reduce the rate of reintervention. The diameter of the nasocystic tube is approximately 7 Fr, which is fine and may not effectively drain fluid. Thus, 1 or 2 stents were inserted as well. Fluid and debris appeared to drain not only through the stents but also through the space between the tubes in the cystogastrostomy tract.

Choosing the appropriate time for drainage was also important. In early reports, the researchers excluded patients whose fluid collections were less than 4-weeks old because of the lack of a mature wall.[24] In theory, fluid collection in the early stage, without a thick encapsulating wall, will develop intraperitoneal infection spread during transmural drainage. However, in recent reports, the researchers explored early EUS-guided drainage, and the success rate was high as well.[3] In some patients, after severe pancreatitis, pancreatic necrosis is a severe complication. There was a great deal of necrosis in the pancreatic cystic cavity, which needed not only EUS-guided drainage but also necrosectomy. These researchers usually insert self-expanding metal stents first and then perform necrosectomy.[20] However, considering the potential for stent migration and procedure-related complications, the efficiency is still controversial. In other studies, researchers introduced a novel lumen-apposing metal stent or transmural nasocyst continuous irrigation (TNCCI) for drainage and necrosectomy. We will welcome these excellent apparatuses to China as soon as possible.[28-30] In this study, we performed the drainage procedure during the early stages of POPF, when there was little tissue necrosis in the cyst. The mean time from surgery to EUS-guided drainage was 10 (5-32) days. None of these patients had an encapsulated PFC or much necrosis on CT images at the time of the procedure. In our opinion, it was too late to wait for the capsule wall to mature because of the acute severe presentation and subsequent life-threatening complications. Early drainage would quickly relieve the clinical symptoms, shorten the hospital stay, and prevent more dangerous complications. After early drainage and reduction of pressure in the cystic cavity, the peripancreatic cystic cavity tended to be reduced. The results were consistent with those of former reports, mainly because of the relatively higher pressure and local packing in the cystic cavity. Futagawa et al. also reported that the median time for EUS-guided drainage in 12 patients was 11.5 days after surgery, and no related adverse events occurred.[27]

In Varadarajulu's study in 2009, they excluded patients with the PFCs measuring less than 4 cm on CT scan.[23] In

their opinion, stent insertion into the correct place may be difficult if the PFC is too small. However, we think that patients with high amylase levels and clinical presentations all need further intervention. On the other hand, the PFC with a short diameter may be absorbed and dissipated by itself. Only a larger PFC may lead to clinical presentation and sepsis. Therefore, the size of the PFC was not the assessment indicator for further treatment in our study.

The median time of hospital stay after EUS-guided drainage was 16 (11-48) days. This was similar to the multicenter retrospective study of Jürgensen et al.[3] However, the length of hospital stay was longer than that in some other reports. This mainly resulted from internal drainage patients being allowed to leave the hospital with the drainage tube. The appropriate time for removing the external drainage tube was during the hospital stay. In our study, the external drainage tube required daily care and leaving the hospital with an external drainage tube may cause accidental detachment of the tube or retrograde infection. Premature removal of the drainage tube may increase the recurrence rate of POPFs. Due to slow persistent pancreatic ductal leakage after pancreatectomy, recurrences of PFCs may occur after EUS-guided drainage, which is not uncommon in some reports of EUS-guided drainage.[3,31] However, in our study, no PFCs relapsed during the subsequent outpatient follow-up. We speculate that the reasons include the use of internal drainage combined with external drainage and the more conservative timing of removal of the drainage tube.

There were some limitations in this study. First, above all, the quality of life of patients was reduced when using nasocystic tubes. Second, there was no control group in this study, and a controlled study with PD and reoperation is lacking. Finally, the number of subjects in our study was small, and more patients are needed to further evaluate the effectiveness of EUS-guided drainage.

CONCLUSION

EUS-guided drainage with a nasocystic tube and double-pigtail stents appears to be safe and technically feasible and could be an alternative treatment for patients with POPF. This minimally invasive method should be evaluated in larger prospective studies.

Ethics Committee Approval: This study was approved by the Ethics Committee of the First People's Hospital of Changzhou (2020-029).

Informed Consent: All patients provided written informed consent for undergoing the procedure.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – C.B.; Design - D.Y., Z.Y.; Supervision C.B.; Resource - W.L.; Materials - C.B., D.Y.; Data Collection and/or Processing - W.L., Z.Y.; Analysis and/or Interpretation - Z.Y.; Literature Search - Z.Y.; Writing - W.L.; Critical Reviews - C.B.

Conflict of Interest: The authors have no conflict of interest to declare.

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