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Impact of long-term transmural plastic stents on recurrence after endoscopic treatment of walled-off pancreatic necrosis

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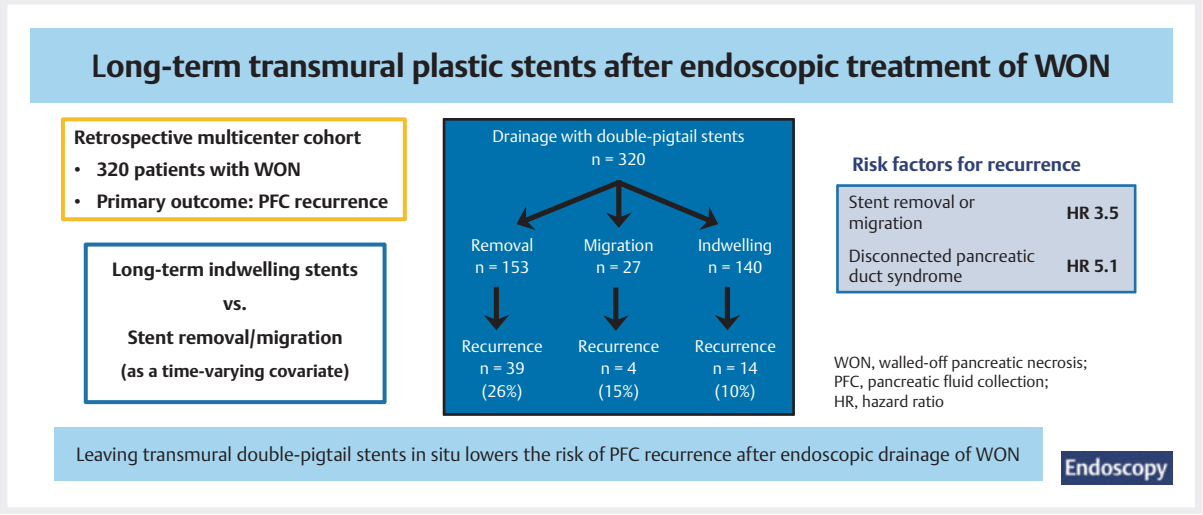
GRAPHICAL ABSTRACT



Authors
David M de Jong[1], Pauline M. C. Stassen[1], Ivo G. Schoots[2], Robert C. Verdonk[3], Marco J. Bruno[1], Rogier P. Voermans[4], Pieter Jan F. de Jonge[1]

Institutions
1 Gastroenterology and Hepatology, Erasmus MC University Medical Center, Rotterdam, Netherlands
2 Radiology, Erasmus MC University Medical Center, Rotterdam, Netherlands
3 Gastroenterology and Hepatology, St. Antonius Hospital, Nieuwegein, Netherlands
4 Gastroenterology and Hepatology, Amsterdam University Medical Center, Amsterdam, Netherlands

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Corresponding author
Pieter Jan F. de Jonge, MD, PhD, Department of Gastroenterology and Hepatology, Erasmus MC University Medical Center Rotterdam, Rotterdam, The Netherlands
p.dejonge@erasmusmc.nl

ABSTRACT

Background Endoscopic transmural drainage (ETD) using double-pigtail stents (DPSs) is a well-established treatment for walled-off pancreatic necrosis (WON). This study aimed to compare outcomes in patients undergoing ETD with DPSs left indwelling versus those where stents were removed or migrated.

‡ These authors contributed equally.

Methods This retrospective multicenter cohort study included patients with WON who underwent ETD using DPSs between July 2001 and December 2019. The primary outcome was recurrence of a pancreatic fluid collection (PFC). Secondary outcomes were long-term complications and recurrence-associated factors. Competing risk regression analysis considered DPS removal or migration as time-varying covariates.

Results Among 320 patients (median age 58; 36% women), DPSs were removed in 153 (47.8%), migrated spontaneously in 27 (8.4%), and remained indwelling in 140 (43.8%). PFC recurrence was observed in 57 patients (17.8%): after removal (n = 39; 25.5%); after migration (n = 4; 14.8%); in patients with indwelling DPSs (n = 14; 10.0%). In 25 patients (7.8%), drainage of recurrent PFC was indicated. Risk factors for recurrence were DPS removal or migration (hazard ratio [HR] 3.45, 95%CI 1.37–8.70) and presence of a disconnected pancreatic duct (HR 5.08, 95%CI 1.84–14.0).

Conclusions Among patients who undergo ETD of WON, leaving DPSs in situ seems to lower the risk of recurrent fluid collections, without any long-term DPS-related complications. These results suggest that DPSs should not be routinely removed and can be safely left indwelling indefinitely.

Introduction

Acute pancreatitis can result in walled-off pancreatic necrosis (WON) in about 20% of patients [1]. Invasive intervention can be indicated for patients with acute necrotizing pancreatitis (ANP) and clinically suspected or proven infected necrosis, in line with the European Society of Gastrointestinal Endoscopy (ESGE) guideline recommendations [2]. Other indications for invasive treatment may be organ compression or abdominal compartment syndrome. Infected pancreatic necrosis is a serious condition associated with a prolonged and severe disease course, with mortality rates reported to be as high as 40% [3]. Furthermore, the loss of viable pancreatic parenchyma can cause disruption or disconnection of the pancreatic duct, resulting in disconnected pancreatic duct syndrome (DPDS) [4]. This condition can lead to ongoing formation of peripancreatic fluid collections (PFCs) and pancreatic fistulas [5].

The ESGE guideline recommends a step-up approach for the treatment of ANP, with percutaneous or endoscopic transmural drainage (ETD) as a first step, followed by necrosectomy if necessary [2]. If technically feasible, the endoscopic approach is preferred [6, 7]. Prospective comparative studies have shown no differences in short-term outcomes for either placement of double-pigtail stents (DPSs) or lumen-apposing metal stents (LAMSs) [8, 9, 10]; however, the guideline does not provide a recommendation as to the duration that DPSs should remain in situ for patients either with or without DPDS. Studies have shown varying rates of PFC recurrence and complications (0–38%) associated with both DPS removal and leaving DPSs indwelling [2, 11, 12, 13, 14].

Our study aimed to investigate the rates of PFC recurrence in patients undergoing ETD for treatment of WON using DPSs who either had their stents removed electively/had stents that migrated spontaneously, or had stents that were left indwelling long term. In addition, possible risk factors associated with PFC recurrence were evaluated.

Methods

Study design and patient selection

A multicenter retrospective cohort study was conducted, at three Dutch tertiary referral centers for pancreaticobiliary disease, on patients who underwent ETD for the treatment of WON between July 2001 and December 2019. The patients were identified from the local endoscopy database (Endobase or Clinical Assistant), in which all endoscopic procedures and reports are prospectively registered.

WON was defined according to the revised Atlanta guidelines 2018 as a mature encapsulated collection of pancreatic and/or peripancreatic necrosis that had developed a well-defined inflammatory wall [2]. As the terminology of PFCs has changed over time, we retrospectively checked these criteria for all patients, in consultation with an experienced gastroenterologist and a radiologist experienced in hepaticopancreaticobiliary imaging, for all of the diagnostic imaging studies that were performed.

Patients with ETD for cysts other than WON, such as pseudocysts, were excluded from this study. Initial drainage by LAMS was not an exclusion criteria, as long as DPSs were placed after LAMS removal.

This study was conducted in accordance with the guidelines of the Helsinki Declaration and was approved by the ethics committee of all participating centers (MEC-2019–0116).

Intervention

Initially, ETD was performed, with step-up endoscopic necrosectomy if clinically indicated. Endoscopic ultrasound (EUS) was performed to visualize the WON, and the gastric or duodenal wall was punctured to create a fistulous tract using a cystotome or balloon dilation. Subsequently DPSs were placed under fluoroscopic guidance. The number, length, and diameter of the DPSs was left to the discretion of the treating physician. If the WON contained a significant amount of solid necrotic tissue, a nasocystic catheter was routinely placed to irrigate and stimulate liquefaction of the necrosis. Necrosectomy was performed during the first ETD if indicated or after the initial ETD, depending on whether the patient improved clinically or

whether an infection of the WON was diagnosed. During a necrosectomy, the fistulous tract was dilated to allow for access with a therapeutic gastroscope and necrotic tissue was removed.

Data collection

Data were collected from electronic patient records on demographic factors (sex, age), medical history, etiology of the pancreatitis, size of the WON, number of DPSs placed, and the number of endoscopic, radiologic, or surgical interventions for treatment of the WON. The size of the WON was measured using length, width, and height. Length was defined as the longest length in the axial plane in centimeters (cm). In the same axial plane, the longest width (in cm) was measured perpendicular to the longest length. In addition, in the frontal plane, the longest height (in cm) was measured.

In addition, long-term complications, including chronic pancreatitis, exocrine and/or exocrine insufficiency or type II diabetes mellitus, pancreatic fistula, or chronic pancreatic pain syndrome (>30 days after DPS placement), were recorded. Complications related to the DPS, such as migration and/or perforation, were also recorded. Time to migration was calculated to the date that imaging confirmed migration. Finally, the number of patients diagnosed with DPDS was recorded.

For all patients, the maximum follow-up time was based on data availability in the individual medical records (i. e. the last time of outpatient contact or death).

Cross-sectional imaging during follow up

After endoscopic treatment of WON, cross-sectional imaging was not routinely performed in every patient. Follow-up imaging after endoscopic treatment of WON was performed if there was suspicion of PFC-related symptoms or for diagnostic reasons other than detection of PFCs (for example, a computed tomography [CT] scan for pseudoaneurysm). When cross-sectional imaging or upper gastrointestinal endoscopy was performed during follow-up, this provided additional information on the status of DPSs (i. e. whether they were still left indwelling or had migrated).

Study outcomes

The study's primary end point was the recurrence of a PFC. As imaging to confirm WON resolution was not routinely performed, time to recurrence was calculated as the time from the last intervention to the date of PFC recurrence. Recurrence was defined as a PFC on imaging studies after initial successful treatment of WON, and further classified as a true recurrent PFC if it was detected at the initial site of endoscopic drainage, or as a new PFC if it was not detected at the initial site of endoscopic drainage.

The secondary end points were the factors associated with PFC recurrence. DPDS was diagnosed on magnetic resonance cholangiopancreatography (MRCP), CT, or endoscopic retrograde cholangiopancreatography, and was defined as a complete or incomplete disruption of the pancreatic duct, as judged by a radiologist experienced in hepaticopancreaticobiliary imaging.

Statistical analysis

The statistical analysis included descriptive statistics using mean and SD for normally distributed variables, and median and interquartile range (IQR) for non-normally distributed continuous variables. Categorical and dichotomous variables were described using frequencies and proportions (%).

Competing risk analysis, using cause-specific hazard regression, was performed to assess the association between several variables and PFC recurrence. In addition, a sensitivity analysis for symptomatic PFC recurrence was performed. The variables included in these analyses were based on the current literature or expert opinion. Variables included in multivariable regression were based on the statistical significance of the regression coefficients in the univariate model. In line with cause-specific hazard regression, all patients who died without a recurrence of PFC were treated as censored. DPS removal or migration of all DPSs was treated as a combined time-varying covariate. Where migration of a DPS had occurred, but at least one DPS remained in situ, this was defined as indwelling. Outcomes are presented as a hazard ratio (HR) and 95%CI. A two-sided P value of <0.05 was considered statistically significant. Statistical analyses were performed using R software, version 4.2.2.

Results

Baseline characteristics

During the study period, 320 patients (114 [35.6%] women; median age 58 years [IQR 48.0–68.0]) underwent ETD for symptomatic WON. ANP was diagnosed in 306 patients (95.6%) and acute-on-chronic pancreatitis in 14 (4.4%). Biliary stones were the most common cause of ANP, occurring in 126 patients (39.4%). In 74.0% of patients, the WON was infected prior to initial ETD. Baseline characteristics of the patients are presented in ▶ **Table 1**.

Endoscopic drainage procedures

ETD was performed via the transgastric route in the majority of patients (n = 291; 90.9%). A median of two DPSs were placed. In 29 patients (9.1%), LAMSs were exchanged for DPSs and, in three patients (0.9%), an additional LAMS was placed in a different area of WON. Following the initial ETD, a nasocystic drain was inserted in 249 patients (77.8%). An additional necrosectomy was performed in 169 patients (52.8%), with a median of three necrosectomy procedures (IQR 2–4) performed in these patients. In 33 patients (10.3%), percutaneous drainage was performed after ETD and, in 13 patients (4.1%), a surgical debridement was performed. Additional details about the ETD procedures and any other procedures performed are presented in ▶ **Table 2**.

Stents and long-term follow-up

Cross-sectional follow-up imaging was performed in 297 patients (92.8%). During a median follow-up of 23 months (IQR 5.5–66.3), a total of 57 patients (17.8%) were diagnosed with a recurrence of a PFC after initial resolution of an ETD-treated WON. In patients with a recurrent PFC, resolution of the initial

▶ **Table 1** Baseline characteristics of the 320 included patients and their walled-off pancreatic necrosis (WON).

Characteristic	n (%), unless otherwise specified
Sex, female	114 (35.6)
Age, median (IQR), years	58.0 (48.0–68.0)
WON characteristics	
Type of pancreatitis, ANP†	306 (95.6)
Etiology of pancreatitis	
▪ Alcohol	57 (17.8)
▪ Biliary stones	126 (39.4)
▪ Idiopathic	78 (24.4)
▪ Post-ERCP	21 (6.6)
▪ Other‡	38 (11.9)
WON location*	
▪ Total	94 (33.5)
▪ Head	38 (13.5)
▪ Head + body	32 (11.4)
▪ Body + tail	39 (13.9)
▪ Body	35 (12.5)
▪ Tail	43 (15.3)
Length, median (IQR), cm*	11.7 (8.6–15.2)
Volume, median (IQR), cm^3*	725.2 (402.6–1483.0)
DPDS present	55 (17.2)
Signs of infection prior to ETD*§	182 (74.0)
Interventions prior to first ETD	
▪ Percutaneous drainage	32 (10.0)
▪ Surgical procedure	5 (1.6)

IQR, interquartile range; ANP, acute necrotizing pancreatitis; ERCP, endoscopic retrograde cholangiopancreatography; DPDS, disconnected pancreatic duct syndrome; ETD, endoscopic transmural drainage.
* Missing data: WON location (n = 39); length (n = 31); volume (n = 163); signs of infection prior to ETD (n = 74).
† Remaining cases were acute-on-chronic pancreatitis.
‡ Other presumed causes of WON: L-asparaginase (n = 2), endo-barrier (n = 1), hypertriglyceridemia (n = 5), ischemia (n = 3), pancreas divisum (n = 2), pancreatic cancer (n = 3), Peutz–Jeghers polyp (n = 1), pharmacologic (n = 12), surgery (n = 5), post-partum hypercalcemia (n = 1), after single-balloon enteroscopy (n = 1), systemic lupus erythematosus (n = 1), and traumatic injury (n = 1).
§ On imaging, fine-needle aspiration, clinical presentation, or initial endoscopic findings.

▶ **Table 2** Characteristics of the drainage procedures performed for walled-off pancreatic necrosis (WON) in 320 patients.

Characteristic	n (%), unless otherwise specified
Endoscopic transmural drainage location	
▪ Duodenum/bulbus	28 (8.8)
▪ Stomach	291 (90.9)
▪ Esophagus	1 (0.3)
Number of stents at placement	
▪ 1	13 (4.1)
▪ 2	224 (70.0)
▪ ≥3	83 (25.9)
Total number of endoscopic interventions. median (IQR)	2 (1–4)
Nasocystic catheter placed	249 (77.8)
Necrosectomy performed	169 (52.8)
Infected WON	66 (20.6)
LAMS placement	
▪ Into another area of WON	3 (0.9)
▪ Before DPS placement	29 (9.1)
Interventions after first endoscopic transmural drainage	
▪ Percutaneous drainage	33 (10.3)
▪ Surgical procedure	13 (4.1)

IQR, interquartile range; DPS, double-pigtail stent; LAMS, lumen-apposing metal stent.

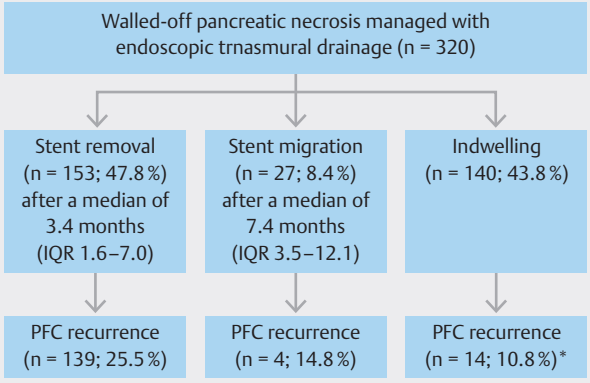
WON had been confirmed in all patients on cross-sectional imaging prior to the date the recurrent PFC was diagnosed. In 40/57 patients (70.2%), the recurrent PFC was detected at the same location as the initially drained WON. Of all detected recurrences, 36 (63.2%) were symptomatic, mostly owing to infection-related complaints. In 24 symptomatic and one asymptomatic recurrence, an additional intervention was indicated, with most of the patients undergoing ETD. The remaining PFC recurrences were managed conservatively (▶ **Table 3**).

Recurrence rates were different among the subgroups of patients who had their DPSs removed electively, had DPSs that migrated spontaneously, or had their DPSs left indwelling. During follow-up, 153 patients (47.8%) had their DPS removed after a median period of 3.4 months (IQR 1.6–7.0). The median follow-up period after stent removal was 27.1 months (IQR 4.9–79.6), with recurrence occurring in 39/153 patients (25.5%). In 27 patients (8.4%), spontaneous migration of all DPSs was documented after a median follow-up of 7.4 months (IQR 3.5–12.1). Migration of all DPSs was detected/confirmed by cross-sectional imaging in all 27 patients. In four patients, a gastroscopy to electively remove the DPSs had been previously performed, with the DPSs being found on inspection to have already migrated spontaneously, after which cross-sectional imaging was performed to confirm this finding. The median follow-up period after stent migration was 24.7 months (IQR 5.7–48.2), with recurrence after spontaneous migration of the stents occurring in 4/27 patients (14.8%). In the remaining 140 patients (43.8%), the DPSs were left in situ until the end of the follow-up period or death (▶ **Fig. 1**). After a median follow-up of 8.2 months (IQR 0.6–33.8), recurrence had occurred in 14/140 patients (10.0%).

▶ **Table 3** Long-term follow-up data for the 320 patients who underwent endoscopic transmural drainage (ETD) for walled-off pancreatic necrosis (WON).

Characteristic	n (%), unless otherwise specified
Total recurrences	57 (17.8)
▪ After removal (n = 153)	39 (68.4)
▪ After migration (n = 27)	4 (8.8)
▪ Indwelling (n = 140)	14 (24.6)
Time to recurrence, median (IQR), days	370 (198–767)
Symptomatic recurrence*	36 (63.2)
▪ Mechanical obstruction†	5 (13.9)
▪ Inflammation/infection	26 (72.2)
Recurrence in same location as initial WON*	40 (70.2)
Intervention performed*	25 (43.9)
▪ Re-ETD‡	12 (48.0)
▪ Percutaneous drainage	9 (36.0)
▪ Surgery	1 (4.0)
▪ ERCP with biliary stent placement	2 (8.0)
Total follow-up, median (IQR), days	691 (167–2005)
Death during follow-up	54 (16.9)

IQR, interquartile range; ERCP, endoscopic retrograde cholangiopancreatography.
* Missing data: symptomatic recurrence (n = 5); same location as initial WON (n = 7); intervention performed (n = 1; where intervention was performed elsewhere, so it was unclear whether this was percutaneous or re-ETD).
† Gastric outlet obstruction (n = 3), biliary duct compression (n = 2).
‡ Included one patient with asymptomatic recurrence.



▶ **Fig. 1** Outcomes of the 320 included patients. IQR, interquartile range; PFC, pancreatic fluid collection. * Stents migrated 22.7 months after recurrence was diagnosed (n = 1); stents were removed 11.5 months after recurrence was diagnosed (n = 1).

Recurrence and associated factors

In multivariate competing risk regression analysis, both the presence of DPDS (HR 5.08, 95%CI 1.84–14.0) and the DPSs being no longer in situ (HR 3.45, 95%CI 1.37–8.70) were significantly and independently associated with PFC recurrence after initial resolution of the WON (▶ **Table 4**). A sensitivity analysis for only symptomatic recurrences showed consistent results (**Table 1s**, see online-only Supplementary material).

DPS-related complications

In 28 patients, all of the DPSs seemed to have migrated spontaneously, including in one patient who had had recurrence diagnosed 22.7 months previously. In another 28 patients, at least one DPS still remained in situ after the migration of one or more DPSs. In one patient (1.8%), the DPS migrated through the WON and resulted in a perforation of the colon, which was located outside the ETD fistula. This was diagnosed 9 days after the last ETD. The patient was treated conservatively by stent removal and antibiotics. No DPS-related complications, such as occlusion or bleeding after DPS erosion, occurred in the patients with indwelling DPSs.

Discussion

In this large retrospective multicenter study of WON patients, leaving DPSs indwelling after successful ETD was associated with a significantly lower PFC recurrence rate than was seen after removal or migration of the DPSs. Severe DPS-related complications were rare. These results, which are in line with the recent literature, suggest that consideration can be given to leaving DPSs indwelling to reduce the number of PFC recurrences.

We found an overall PFC recurrence rate after successful ETD of 17.8%, with most recurrences located at the initial site of WON drainage. In the recent literature, recurrence rates have varied widely from 0 to 37% [14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27]. Arvanitakis et al. [16] compared stent retrieval versus leaving the stents indwelling, and found that retrieval was associated with higher recurrence rates, with no recurrences seen in the indwelling group; however, only 46 patients were included, who had all types of PFC, rather than WON specifically. Bang et al. [11] reported similar findings in all types of PFC. A study from 2013 reported that long-term indwelling stents are safe and effective with minimal complications [17]: in five patients (16.6%), migration of the DPS occurred, resulting in a PFC recurrence in one patient, but there were no recurrences diagnosed in the remaining 25 patients. All of the abovementioned studies were limited by their small sample sizes, relatively short follow-up, and competing risks such as death that were not accounted for.

The study of Chavan et al. [14] did however improve on many of these aspects. After successful ETD and PFC resolution, the large-caliber metal stent was removed and patients diagnosed with DPDS were randomized between DPS placement or no DPS. In the 104 patients, after 1 year of follow-up, almost 20% of patients presented with PFC recurrence. This was not

▶ **Table 4** Results from univariate and multivariate competing risk regression analysis using cause-specific hazard regression for chance of pancreatic fluid collection (PFC) recurrence.

Characteristic	Univariate analysis		Multivariate analysis	
	HR (95%CI)	*P* value	HR (95%CI)	*P* value
Age, years	0.98 (0.97–1.00)	0.03	0.99 (0.97–1.00)	0.14
Sex, female	1.26 (0.74–2.16)	0.39		
ANP, vs. acute on chronic	0.40 (0.16–1.01)	0.05		
Infected*	0.52 (0.31–0.90)	0.02	0.61 (0.35–1.05)	0.08
ETD location, vs. duodenum/bulbus				
▪ Stomach	1.40 (0.51–3.88)	0.51		
▪ Esophagus	0.00 (0.00 to infinity)	>0.99		
Nasocystic catheter	1.04 (0.54–2.02)	0.90		
Necrosectomy	1.28 (0.75–2.17)	0.37		
Percutaneous intervention	0.98 (0.49–1.94)	0.95		
Surgical intervention	1.82 (0.83–4.02)	0.14		
DPDS diagnosis	3.82 (2.26–6.45)	<0.001	5.08 (1.84–14.0)	0.002
Stent removal or migration†	2.66 (1.43–4.93)	0.002	3.45 (1.37–8.70)	0.009
ETD number (per procedure)	0.98 (0.87–1.11)	0.80		
Interaction of “stent removal or migration” and “DPDS diagnosis”			0.87 (0.26–2.88)	0.82

HR, hazard ratio; ANP, acute necrotizing pancreatitis; DPDS, disconnected pancreatic duct syndrome; ETD, endoscopic transmural drainage.
* At baseline or after ETD.
† Analyzed as a time-varying covariate.

significantly associated with plastic stent replacement on either intention-to-treat or per-protocol analysis. The trial had some limitations however, as postulated in three letters to the editor [28, 29, 30]. First, the follow-up period stopped after 1 year, potentially missing an important part of follow-up, as previous studies have shown that PFC recurrence mostly occurs in the first 2 years. Second, the per-protocol analysis was hampered by significant differential attrition bias. Third, the protocol of the study was to place a DPS 4 weeks after the initial LAMS placement, but complete resolution of the WON was not confirmed.

Several other studies have investigated the potential risk factors for PFC recurrence after initial resolution. We found DPS removal and/or migration, as well as diagnosis of DPDS, to be significantly associated with PFC recurrence. Although severely limited by their small cohort of 35 patients, Rana et al. [31] also found removal of stents and/or diagnosis of DPDS were independent risk factors for recurrence, which was in line with other recent studies. [11, 16, 26]. Gkolfakis et al. [32] found stent migration, chronic pancreatitis, and the first DPS being >6 cm in length to be independent risk factors for recurrence; however, they included all types of fluid collections and did not routinely remove stents, thereby lacking a clear comparison group.

The major limitation of all of these studies is the fact that they have not taken into account competing risks, such as death, and removal or migration of the stent as a time-varying covariate. In the current study, we have however performed these exact analyses and have confirmed that a diagnosis of DPDS and removal or migration of the DPSs are both independently and significantly associated with increased risk of PFC recurrence.

While recent studies on WON have mainly focused on LAMSs [33, 34], a recent systematic review and meta-analysis showed that LAMSs and DPSs have equivalent clinical outcomes and adverse events [35]. Recent prospective studies have also shown no significant differences [8, 9, 10]. Therefore, more studies focusing on DPS replacement after WON resolution with a LAMS are needed. The need to leave DPSs indwelling may even favor DPSs compared with LAMSs.

Compared with the aforementioned studies, our study has several strengths. To the best of our knowledge, this is the largest study evaluating the clinical outcome of patients after endoscopic treatment of WON, with regard to the removal of DPSs or leaving them in situ. First, patients were included from three expert treatment centers, thereby including a large number of patients and ensuring a high enough number of events to facilitate multivariable regression analysis. Second, with the use of competing risk analysis, the competing event of mortality could be taken into account. Third, time-varying covariates

are more suited for such complex situations, where the status of the stent changes over time, then stratification based on what happened during follow-up.

With its retrospective design, some inherent limitations are however also worth noting. Long-term follow-up was not available in several patients as they had been referred back to another hospital or had died shortly after; we took these factors partially into account by performing competing risk analysis. Second, the definitions of WON were not as well formulated before the Atlanta guidelines, so potential patients could have been missed owing to misclassification [2]. To obtain our total cohort, all endoscopically treated PFCs were retrospectively analyzed using the most recent guidelines. Third, the recurrence rate is likely an underestimation as not all patients underwent routine follow-up imaging to assess for recurrence, as is shown by the high rate of recurrences that were not managed by re-ETD; however, this is likely not to be clinically relevant as these patients would have self-presented with symptoms. In addition, it is difficult to assess whether a PFC is an actual recurrence, or a PFC/WON at another location. Fourth, the rate of spontaneous migration of indwelling DPSs may have been an underestimation as follow-up imaging was not routinely performed. Finally, the choice to remove or leave the DPSs indwelling changed over time and differed between the treatment centers.

In conclusion, in this largest study to date on the effect of removal of DPSs after ETD on PFC recurrence rates, our results suggest that DPSs can be left indwelling indefinitely in order to lower the risk of (symptomatic) recurrence. The effect of removing or leaving the DPSs indwelling should be included in future randomized controlled trials with long-term follow-up and larger patient cohorts to enable vast multivariable regression analyses.

Conflict of Interest

M.J. Bruno received research support from Boston Scientific, Cook Medical, Pentax Medical, Mylan, ChiRoStim and acts as a consultant/lecturer for Boston Scientific, Cook Medical, Pentax Medical and AMBU. R.P. Voermans received research funding for investigator initiated studies from Boston Scientific and Prion Medical. He is a consultant with speakers fee for Boston Scientific. PJ.F. de Jonge received research support from FujiFilm. He received speakers fee for Boston Scientific and Cook Medical. D.M. de Jong, P.M.C. Stassen, I.G. Schoots and R.C. Verdonk declare that they have no conflicts of interest.

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