



Review

The Role of EUS-Guided Drainage in the Management of Postoperative Fluid Collections after Pancreatobiliary Surgery

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Abstract: Postoperative fluid collection (POFC) is a challenging complication following pancreatobiliary surgery. Traditional treatment with surgical drainage is associated with significant morbidity, while percutaneous drainage is associated with a higher rate of recurrence and the need for repeated interventions. Studies have shown that endoscopic ultrasound (EUS)-guided drainage may offer a promising solution to this problem. There are limited data on the ideal therapeutic protocol for EUS-guided drainage of POFC including the timing for drainage; type, size, and number of stents to use; and the need for endoscopic debridement and irrigation. Current practices extrapolated from the treatment of pancreatic pseudocysts and walled-off necrosis may not be applicable to POFC. There are increasing data to suggest that drainage procedures may be performed within two weeks after surgery. While most authors advocate the use of double pigtail plastic stents (DPPSs), there have been a number of reports on the use of novel lumen-apposing metal stents (LAMSs), although no direct comparisons have been made between the two.

Keywords: endosonography; endoscopic ultrasound; EUS; drainage; postoperative complication; postoperative fluid collection; pancreatobiliary surgery; pancreatectomy; bile duct surgery



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1. Introduction

Postoperative fluid collections (POFCs) are well-recognised adverse events following pancreatobiliary surgery and significantly increase morbidity and mortality. Most commonly, they are due to leaking pancreatic fluid after pancreatectomy [1]. The reported incidence of pancreatic leak varies depending on the type and indication of surgery. It can be as high as 20% after pancreaticoduodenectomy to 40% after distal pancreatectomy [2]. The leaking pancreatic fluid can lead to POFC or more severe consequences such as pseudoaneurysms, bleeding, tissue necrosis, and abscess formation. Small, asymptomatic POFC may be managed conservatively by long-term jejunal feeding, total parenteral nutrition, octreotide, and/or antibiotics [3]. Drainage of the accumulated pancreatic fluid remains the cornerstone in management of symptomatic or complicated POFC.

Traditionally, symptomatic POFCs have been managed with percutaneous or surgical drainage. Surgical reoperations are associated with significant morbidity and mortality [3]. While percutaneous drainage (PD) is associated with good success (80–100%) and low mortality rates (1.4–1.5%) [4], percutaneous catheters require daily care and can be problematic for the patients and their caregivers. They can also cause local skin irritation, infection, and fistula formation, compromising patients' quality of life [3,4].

EUS-guided management of POFC has the advantages of obviating the need for additional external drainage catheters, minimising the risk of external pancreatic fistulae, and reducing fluid and electrolyte loss. However, data remain limited, and there has been no randomised trial on the use of EUS-guided drainage in the management of POFC. There are also no data on the ideal therapeutic protocol to optimise outcomes and reduce

complications. This review article summarises the existing evidence and recommendations for EUS-guided drainage of POFC and aims to provide directions for future research.

2. Materials and Methods

This is a review article. A search was made of English-language, human studies in the PubMed database, EMBASE, and Cochrane Library from earliest inception to April 2021. Keywords used in the search include “endosonography”, “endoscopic ultrasound”, “EUS”, “drainage”, “post-operative complication”, “post-operative fluid collection”, “pancreatobiliary surgery”, “pancreatectomy”, and “bile duct surgery” alone or in combination. References of identified articles were also searched for potentially relevant studies. Studies that did not include EUS-guided drainage, case reports, duplicated data, and data published only as an abstract at academic meetings were excluded.

The quality of studies included in comparative analyses was assessed using a modified Newcastle–Ottawa score. Studies that scored 6 or higher were deemed high-quality, whereas studies scoring fewer than 4 points were deemed low-quality. The detailed assessment of study quality is given in Table 1.

Table 1. Modified Newcastle–Ottawa score of studies.

Studies Included in Early versus Delayed Drainage of POFC										
Study	Selection			Comparable			Outcome		Score	Quality
	Representative	Cohort Size	Info. on Tech. and Clinical Success	Outcome Not Present at Start	Factors Comparable between 2 Groups	Type of Surgery, Patients' Comorbidities and Condition	Follow-Up Long Enough for Outcomes to Occur	Adequacy of Follow-Up		
	Population-based: 1 Multicentre: 0.5 Single-centre: 0	≥40: 1 20–39: 0.5 <20: 0	Yes: 1 No: 0	Not present: 1 Present: 0			Yes: 1 No: 0	100%: 1 ≥50%: 0.5 <50%: 0	Max = 8	>6: high 4–6: med. <4: low
Tilara A, 2014	0	0.5	1	1	0	0	0	1	3.5	Low
Caillol F, 2018	0	1	1	1	0	0	1	1	5	Med.
Storm AC, 2020	0	1	1	1	1	1	1	1	7	High
Oh D, 2021	0	1	1	1	0	0	1	1	5	Med.
Fujimori N, 2019	0	1	1	1	1	0	1	1	6	Med.
Studies Included in EUS-Guided Drainage versus Percutaneous Drainage in Early POFC										
Study	Selection			Comparable			Outcome		Score	Quality
	Representative	Cohort Size	Info. on Tech. and Clinical Success	Outcome Not Present at Start	Factors Comparable between 2 Groups	Type of Surgery, Patients' Comorbidities and Condition	Follow-Up Long Enough for Outcomes to Occur	Adequacy of Follow-Up		
	Population-based: 1 Multicentre: 0.5 Single-centre: 0	≥40: 1 20–39: 0.5 <20: 0	Yes: 1 No: 0	Not present: 1 Present: 0			Yes: 1 No: 0	100%: 1 ≥50%: 0.5 <50%: 0	Max = 8	>6: high 4–6: med. <4: low
Futagawa Y, 2017	0	0.5	1	1	1	0	0	1	4.5	Med.
Tamura T, 2019	0	1	1	1	1	1	1	1	7	High

Info.: information. Tech.: technical. Med.: medium.

3. Current Evidence

3.1. Indications for POFC Drainage

The well-accepted indications for POFC drainage are symptomatic and/or enlarging collection. The most common symptoms are fever, abdominal pain, nausea and vomiting, and leucocytosis [2,5–7]. In a large study performed in a single centre in South Korea, 602 (79.7%) out of 755 patients who developed fluid collection after laparoscopic distal pancreatectomy were treated successfully with observation only [8]. In this study, patients who required drainage procedures were more often symptomatic and had higher serum white blood cell (WBC) count compared to the patients who were treated conservatively. The authors noted that size of the collection alone was not an indication for intervention, although patients with fluid collection ≥ 8 cm and rapid increase in size of ≥ 2 cm/month were more likely to require intervention. Other authors have advocated a collection of at least 4 cm [9,10] prior to EUS-guided drainage. There is no specified upper limit to the size of the collection and collections larger than 20 cm in diameter have been successfully drained endoscopically [4]. Although many studies have reported the size of the POFC prior to drainage, there are no studies to our knowledge that reported the wall thickness of the POFC.

3.2. Timing for POFC Drainage

In the management of pancreatic walled-off necrosis, many studies recommend waiting four weeks for the collection to become well-encapsulated to reduce the risk of adverse events [11–13]. Earlier studies for EUS-guided drainage of POFC have followed this recommendation [10,14,15]. However, patients who are septic or at risk of serious sequelae of pancreatic leaks may not have the luxury of waiting for encapsulation to occur.

Tilara et al. first demonstrated that early drainage within 30 days after surgery had similar technical success rates, as well as adverse events, compared to delayed drainage [7]. Two more recent studies comparing early drainage and delayed drainage then showed comparable clinical success and adverse events between the two groups [16,17]. Subgroup analysis in one of these studies even demonstrated no significant difference in terms of clinical outcomes or complications for patients undergoing acute drainage within 14 days of surgery [17]. These results were then replicated in dedicated studies comparing acute EUS-guided drainage within two weeks of surgery to those performed after two weeks [18,19]. These studies are summarised in Table 2 below.

Table 2. Summary of studies comparing early versus delayed drainage of POFC.

Author (Year)	Timing of Drainage	Sample Size	Mean Diameter of POFC	Technical Success	Clinical Success	Adverse Events
Tilara (2014) [7]	≤ 30 days	17	NR	100%	80%	3%
	> 30 days	14		100%	100%	3%
Caillol (2019) [16]	≤ 25 days	22	NR	100%	86%	45% ¹
	> 25 days	19		100%	100%	47% ²
Storm (2020) [17] ³	≤ 30 days	42	77 \pm 35 mm	100%	93%	21.4%
	> 30 days	33	79 \pm 32 mm	100%	94%	30.3%
Oh (2021) [18] ⁴	≤ 14 days	29	NR	100%	96.6%	6.8%
	> 14 days	19		100%	94.7%	0%
Fujimori (2021) [19] ⁴	≤ 15 days	14	66.1 \pm 7.3 mm	100%	93%	7.1%
	> 15 days	16	78.8 \pm 6.8 mm	100%	100%	6.3%

NR: not reported. ¹ Global morbidity. Specific morbidity of EUS-guided drainage is 22%. ² Global morbidity. Specific morbidity of EUS-guided drainage is 21%. ³ Subgroup analysis of patients who underwent drainage within 14 days after surgery showed a clinical success rate of 95% and adverse events rate of 15%. ⁴ All patients in these studies had early drainage within four weeks of surgery.

Interestingly, Storm et al. found that fewer patients had solid necrosis in the group that underwent early EUS-guided drainage (26.2%) compared to those who underwent delayed EUS-guided drainage (63.6%) [17]. They postulated that early intervention and removal of pancreatic enzyme-rich fluid from the surgical bed resulted in decreased subsequent tissue necrosis by the same enzymes.

3.3. EUS-Guided versus Percutaneous Drainage of POFC

A recent systematic review and meta-analysis of 13 retrospective studies comparing EUS-guided drainage and PD of postoperative pancreatic fluid showed that EUS-guided drainage is associated with significantly better clinical success (93.2% vs. 79.8%) and lower recurrence of POFC (9.4% vs. 25.7%) [20].

While EUS-guided drainage is now considered standard of care for management of inflammatory pancreatic fluid collection, guidelines still recommend PD where early drainage is required before the collection is well-encapsulated [21,22]. In terms of POFC, an earlier Japanese study first showed that early EUS-guided drainage had similar technical success (92% vs. 100%), clinical success (92% vs. 100%), and complication rates (both 0%) compared to PD [23]. A more recent study in a propensity-scored matched cohort by Tamura et al. then showed that EUS-guided drainage was associated with lower reintervention rates (15.3% vs. 50%), fewer reinterventions, and shorter time to clinical resolution of the collection (14 vs. 25 days) compared to PD for treatment of POFC within 28 days of surgery [24]. Table 3 summarises these two studies.

Table 3. Summary of studies comparing EUS-guided drainage and PD in early POFC.

Author (Year)	Type of Drainage	Sample Size	Number of Days after Surgery (Median (Range))	Diameter of POFC (Mean, mm) *	Technical Success	Clinical Success	Adverse Events
Futagawa (2017) [23]	EUS	12	11.5 (4–71) ¹	80 × 50 × 57	92%	92%	0%
	PD	21	14 (7–35) ²	85 × 46 × 90	100%	100%	0%
Tamura (2019) [24] ³	EUS	13	14.5 ± 7.3	75.3 ± 19.6	100%	100%	7.7%
	PD	28	11.0 ± 4.9	72.6 ± 23.6	100%	100%	10.7%

* Differences in size were not statistically significant. ¹ 92% of procedures performed within 30 days postoperative. ² 86% of procedures performed within 30 days postoperative. ³ All patients in this study had early drainage within four weeks of surgery.

3.4. Type, Size, and Number of Stents for POFC Drainage

The most common type of stent inserted for POFC drainage is a double-pigtail plastic stent (DPPS). Out of 19 studies reviewed (see Table 4), 15 studies had between one and three 7–10-French DPPSs inserted as the initial form of drainage for some or all of their patients [2–4,6,7,9,10,14–19,25,26]. Most authors follow a standard protocol for EUS-guided drainage. In brief, a therapeutic linear echoendoscope is inserted into the stomach or duodenum and a 19-gauge EUS needle is used to puncture the luminal wall and gain access to the POFC. Fluid is then aspirated and contrast may be injected to confirm the correct target for drainage. A 0.025–0.035-inch guidewire is placed and coiled in the cavity under fluoroscopic guidance. The tract is then dilated using various devices including a cystotome and biliary or oesophageal balloon dilators before the DPPSs are inserted.

Table 4. Summary of studies utilising DPPS.

Author (Year)	Sample Size	Size of POFC	No. of Stents	Size of Stents	No. of Sessions	Technical Success	Clinical Success	Adverse Events
Al Efishat (2018) [2]	39 ¹	NR	1–3	7/10 F	2 †	100%	66.7%	12.8%
Kwon (2013) [3]	12 ²	89 mm *	1–3	7/10 F	2 †	100%	100%	8.3%
Télliez-Ávila (2015) [4]	13	65 mm †	2	7 F	1 †	100%	100%	7.7%
Donatelli (2018) [6]	32 ³	50–100 mm (53%) ⁴	1 (69%) 2 (31%) 1 (13%)	7/10 F	NR	100%	93.4%	12.5%
Tilara (2014) [7]	31	85 × 60 mm *	2 (81%) 3 (6%)	7/10 F	1 †	100%	93%	6%
Varadarajulu (2011) [9]	20	78.5 × 56.6 mm * 80 × 43.6 mm †	1 (15%) 2 (85%)	7 F	1 †	100%	100%	0%
Varadarajulu (2009) [10] ⁵	10	91.4 mm *	1 2	10 F 7 F	1 †	100%	90%	10%
Onodera (2012) [14]	5 ⁶	71 mm †	1	7 F	1 †	100%	100%	0%
Azeem (2012) [15]	15	70 mm †	1–3 1 (23.7%)	7/10 F	2 †	100%	80%	9.4%
Caillol (2019) [16]	41	76 mm *	2 (73.7%) ⁷ 3 (2.6%)	NR	1 †	100%	93%	46%
Storm (2020) [17]	75	79 mm *	2 (83%) ⁸	7 F (89%) ⁸	2.2 *	100%	93%	25.3%
Oh (2021) [18]	41	NR	1–3	7 F	NR	100%	100%	0%
DPPS	6	NR	1	NR	NR	100%	95.1%	4.9%
SEMS								
Fujimori (2021) [19]	30 ⁹	69.5 mm †	1	7 F	1 †	100%	97%	6.9%
Jürgensen (2019) [25]	39 ¹⁰	4 †	1 †	NR	1 †	NR	85%	NR
Gupta (2012) [26]	43 ³	96 mm *	1 †	7/8.5 F	1 †	96%	80%	19.5%

NR: not reported. * Mean. † Median. SEMS: self-expanding metal stent. ¹ Only includes patients who underwent primary EUS-guided drainage. ² Including 3 patients who had EUS-guided drainage after failed PD. ³ Including patients who developed POFC after non-pancreatobiliary surgery. ⁴ Thirty-one percent of patients had POFC smaller than 50 mm, and 16% of patients had POFC larger than 100 mm. ⁵ In this study, either a single 10F or two 7F DPPS would be used. ⁶ Excluding one patient who only had a dilated main pancreatic duct but no POFC. ⁷ Excluding two patients who had LAMS and one patient who had a nasocystic drain. ⁸ This study included 38 patients who had LAMS and 2 patients who had SEMS. The number and size of stents in this table are only given for DPPSs. The number of sessions, technical and clinical success, and adverse events are the overall result of both metal and plastic stents as they were not separately compared. ⁹ Including four patients with LAMS and three patients without any drains inserted (aspiration only). There were 12 patients who also had nasocystic drains on top of DPPS or LAMS. ¹⁰ Only including EUS-guided drainage performed for patients with POFC. Includes 3 patients who had SEMS.

The main limitation of the DPPS is its relatively small calibre which predisposes to stent blockage if the collection contains a lot of debris. Additional procedures may then be required to change the blocked stents and improve drainage. It is also impossible to access a collection for debridement via a DPPS. Dedicated lumen-apposing metal stents (LAMSs) for transluminal drainage of pancreatic fluid collections were developed to overcome these problems [27]. Newer LAMSs with an electrocautery-enhanced delivery system also allow EUS-guided drainage to be performed without multiple changes of guidewires and instruments, thereby reducing procedural time [28]. Most studies involving LAMSs were performed in pancreatic walled-off necrosis. Data from a randomised controlled trial did not show a significant difference in the overall clinical outcome and adverse events when compared to placing multiple plastic stents for pancreatic walled-off necrosis [29]. However, two meta-analyses published in 2021 seemed to suggest that LAMSs may be superior to plastic stents in terms of clinical success, recurrence of pancreatic fluid collection, need of additional intervention, and adverse events [30,31].

There are only three studies (see Table 5) examining the use of LAMSs in patients with POFC that had more than 30 patients [5,17,32]. Two other studies only utilised LAMSs in fewer than five patients, and therefore, no meaningful conclusions can be drawn [16,19]. The technical and clinical success rates of the larger studies range from 93.6% to 96.8% and from 89.3% to 91.9%, respectively [5,32]. Total adverse events range from 10.6% to 12.9% and include stent migration, bleeding, perforation, and infection. Storm et al. noted that metal stent was not an independent risk factor for adverse events [17]. There are no studies that directly compared the outcomes of LAMSs and DPPSs in the management of POFC.

Table 5. Summary of studies utilising LAMS.

Author (Year)	Sample Size	Size of POFC	Type of LAMS	Size of LAMS	No. of Sessions	Technical Success	Clinical Success	Adverse Events
Yang (2019) [5]	62 ¹	51–100 mm (62.9%) ²	AXIOS “Hot” (87.1%) “Cold” (12.9%)	10 mm (32.3%) 15 mm (67.7%)	1.6 *	96.8%	91.9%	12.9%
Storm (2020) [17] ³	75	79 mm *	AXIOS “Hot” (52.6%) “Cold” (47.4%)	10 mm	2.2 *	100%	93%	25.3%
Mudireddy (2018) [32]	47 ¹	78.6 mm *	AXIOS “Hot” (76%) “Cold” (24%)	10 mm (30%) 15 mm (70%)	1 †	93.6%	89.3%	10.6%

NR: not reported. * Mean. † Median. ¹ Includes patients who developed POFC after non-pancreatobiliary surgery. ² In this study, 9.7% of patients had POFC 50 mm or smaller, and 27.4% of patients had POFC larger than 100 mm. ³ This study included 35 patients who had DPPS and two patients who had SEMs. The number of sessions, technical and clinical success, and adverse events are the overall result of both metal and plastic stents as they were not separately compared.

3.5. The Use of Nasocystic Drainage and Irrigation

There are currently two methods in which nasocystic drains are being used for the treatment of POFC. The first is the exclusive use of nasocystic drains as the initial drainage for POFC. This method is only described in two Japanese studies [23,24]. The authors then internalise the drain about one week after the initial procedure. The second method is the selective use of nasocystic drains only if there was necrotic debris or purulent fluid with poor drainage [10,15,18,19,26]. The routine use of nasocystic drains runs counter to the original intention of EUS-guided drainage to reduce external drains and their associated problems. In addition, patients who only had nasocystic drains as the first procedure appear to have a longer hospital stay after drainage (median 15 days) [23] compared to patients who had DPPS (median 2 to 4 days) [10,15]. However, this does not take into account inherent differences in patient population, clinical parameters, type and size of collection, and local practices. There are currently no data on whether nasocystic irrigation or drainage improves clinical outcomes in the management of POFC.

There are also reports of adjunctive techniques to improve the efficacy of endoscopic debridement in patients with walled-off pancreatic necrosis. Methods of irrigation with normal saline [33] or hydrogen peroxide [34] have been described, but their effectiveness and benefit are not very clear [35]. There are no studies on their use in POFC.

4. Discussion and Recommendations

POFCs are well-recognised adverse events after pancreatobiliary surgery and can occur despite the best efforts to prevent them. Traditional treatments of surgical drainage and PD are associated with increased morbidity and reduced quality of life, respectively [20]. EUS-guided internal drainage avoids these problems and results in less fluid and/or electrolyte loss and fewer infective complications [3].

While there are no randomised trials on this subject, a recent meta-analysis has shown that EUS-guided drainage is superior to PD in terms of clinical success and recurrence of POFC [20]. This result and recommendation must be interpreted with care as these studies were mostly performed in tertiary centres by experienced and expert proceduralists. The meta-analysis is also limited by the heterogeneity of the included studies and could not answer the questions of the optimal timing for drainage and the type and number of stents to use.

A number of studies have demonstrated the safety and efficacy of early EUS-guided drainage for POFC. EUS-guided drainage in some of these studies was performed within two weeks of surgery and sometimes even as early as three days after surgery [19]. These studies are limited by their retrospective nature, small sample sizes, and potential for selection bias [7,16–19,23,24]. In addition, three out of the five studies comparing early and

delayed EUS-guided drainage did not report the size of the POFC prior to drainage, and none of the studies provided details of the patients' condition prior to intervention.

It is unlikely that a randomised trial can be conducted to compare early and delayed EUS-guided drainage directly due to the ethical considerations of delaying life-saving treatment for a patient. Patients who are amenable to delayed drainage may fundamentally be very different compared to those who require early intervention. However, a future area of research may be in the wall thickness of POFC prior to intervention. The rationale for delaying intervention is to allow encapsulation to occur in order to reduce the risk of adverse events [11–13]. It is interesting that despite this reason, no authors have measured or reported the thickness of the pseudocapsule of the POFC, especially when comparing early and delayed drainage, as this may be a confounding factor in the results. A well-conducted, propensity-matched cohort study of early versus delayed drainage, which includes the wall thickness of POFC and patients' condition (e.g., Acute Physiology and Chronic Health Evaluation II score) will help to answer some of the pressing questions. A larger, randomised, prospective study of PD versus EUS-guided drainage specifically in the early (within 30 days) and acute (within two weeks) postoperative period would also help to elucidate the ideal treatment for patients who develop POFC.

Based on the available evidence, the ideal candidate for EUS-guided drainage of POFC is a symptomatic patient with a well-encapsulated collection of at least 40 mm in size. Early, nonencapsulating collections within two weeks of surgery can also be drained endoscopically, but patients should be carefully selected and the expertise, resources, and support to manage all forms of complications should be available. PD is an alternative if there is no expert endoscopist.

At this moment, most authors recommend the use of DPPSs for the drainage of POFC. Some authors feel that the softer, more pliable plastic stents are less likely to cause trauma to surrounding structures and may be safer for patients [6,19]. Although three retrospective studies have demonstrated the safety and clinical efficacy of LAMSs for the drainage of POFC, there is a lack of a prospective trial comparing the outcomes of LAMSs versus DPPSs. In addition, the majority of studies (see Table 3) showed that the median number of procedures need to treat POFC is 1 even when DPPSs are used. The supposed advantages of LAMSs (better drainage and easier access for endoscopic debridement) may not be as important if early drainage of POFC is truly associated with less solid necrosis and thus easier resolution of collection even with smaller plastic stents. We recommend the use of DPPSs for the drainage of POFC until larger randomised trials comparing DPPSs and LAMSs in POFC demonstrate the superiority of LAMSs over DPPSs.

We do not recommend the routine use of nasocystic drains for the drainage or irrigation of POFC. There are currently limited data on its use and it may potentially prolong hospital stay and reduce patient's quality of life. Further studies are required on its efficacy, safety, and effect on patient's satisfaction.

5. Limitations

Our review is limited to the management of postoperative fluid collection after pancreatobiliary surgery, and hence, it is applicable only to a very small patient population. Within the scope of our review, we are further limited by the paucity of large, prospective, randomised studies pertaining to the management of POFC. The studies included in this review are all of a retrospective nature, thereby contributing to selection bias. They are also mostly done in tertiary referral centres, and hence, their results may not be generalisable to all centres. Nevertheless, this review can serve as a summary of available evidence and as a guide for future research.

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