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Editorial board member of *World Journal of Gastroenterology*, Oya Yucel, PhD, Associate Professor, Pediatric Department, Baskent University, Istanbul Teaching and Medical Research Hospital, Istanbul 34662, Turkey

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World Journal of Gastroenterology (*World J Gastroenterol*, *WJG*, print ISSN 1007-9327, online ISSN 2219-2840, DOI: 10.3748) is a peer-reviewed open access journal. *WJG* was established on October 1, 1995. It is published weekly on the 7th, 14th, 21st, and 28th each month. The *WJG* Editorial Board consists of 1375 experts in gastroenterology and hepatology from 68 countries.

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World Journal of Gastroenterology (*WJG*) is now indexed in Current Contents[®]/Clinical Medicine, Science Citation Index Expanded (also known as SciSearch[®]), Journal Citation Reports[®], Index Medicus, MEDLINE, PubMed, PubMed Central, Digital Object Identifier, and Directory of Open Access Journals. The 2015 edition of Journal Citation Reports[®] released by Thomson Reuters (ISI) cites the 2015 impact factor for *WJG* as 2.787 (5-year impact factor: 2.848), ranking *WJG* as 38 among 78 journals in gastroenterology and hepatology (quartile in category Q2).

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NAME OF JOURNAL
World Journal of Gastroenterology

ISSN
 ISSN 1007-9327 (print)
 ISSN 2219-2840 (online)

LAUNCH DATE
 October 1, 1995

FREQUENCY
 Weekly

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PUBLICATION DATE
 April 21, 2017

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Endoscopic management of pancreatic fluid collections- revisited

Zaheer Nabi, Jahangeer Basha, D Nageshwar Reddy

Zaheer Nabi, Jahangeer Basha, D Nageshwar Reddy, Department of Gastroenterology, Asian Institute of Gastroenterology, Somajiguda 6-3-661, Hyderabad, India

Author contributions: All authors equally contributed to this paper with conception and design of the study, literature review and analysis, drafting and critical revision and editing, and final approval of the final version.

Conflict-of-interest statement: No potential conflicts of interest.

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Manuscript source: Invited manuscript

Correspondence to: Dr. D Nageshwar Reddy, Asian Institute of Gastroenterology, Asian Institute of Gastroenterology, Somajiguda 6-3-661, Hyderabad, India. zaheernabi1978@gmail.com
Telephone: +91-40-23378888

Received: January 3, 2017

Peer-review started: January 4, 2017

First decision: February 10, 2017

Revised: February 27, 2017

Accepted: March 21, 2017

Article in press: March 21, 2017

Published online: April 21, 2017

Abstract

The development of pancreatic fluid collections (PFC) is one of the most common complications of acute severe pancreatitis. Most of the acute pancreatic fluid

collections resolve and do not require endoscopic drainage. However, a substantial proportion of acute necrotic collections get walled off and may require drainage. Endoscopic drainage of PFC is now the preferred mode of drainage due to reduced morbidity and mortality as compared to surgical or percutaneous drainage. With the introduction of new metal stents, the efficiency of endoscopic drainage has improved and the task of direct endoscopic necrosectomy has become easier. The requirement of re-intervention is less with new metal stents as compared to plastic stents. However, endoscopic drainage is not free of adverse events. Severe complications including bleeding, perforation, sepsis and embolism have been described with endoscopic approach to PFC. Therefore, the endoscopic management of PFC is a multidisciplinary affair and involves interventional radiologists as well as GI surgeons to deal with unplanned adverse events and failures. In this review we discuss the recent advances and controversies in the endoscopic management of PFC.

Key words: Endotherapy; Pseudocyst; Pancreatic necrosis; Necrosectomy

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Core tip: The management of pancreatic fluid collections has revolutionised over last several decades. New devices and techniques have evolved which have largely obviated the need for surgery in these patients. The differentiation of nature of fluid collections into pseudocyst and walled off necrosis has enabled the endoscopist to plan management strategies. With the introduction of dedicated metal stents, the task of endoscopic necrosectomy has become easier. However, all patients with pancreatic fluid collections cannot be managed in the same way. Therefore, the management of pancreatic fluid collections (PFC) requires multidisciplinary and individualised approach.

In this review, we describe the recent advances and controversial issues in the endoscopic management of PFC.

Nabi Z, Basha J, Reddy DN. Endoscopic management of pancreatic fluid collections-revisited. *World J Gastroenterol* 2017; 23(15): 2660-2672 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v23/i15/2660.htm> DOI: <http://dx.doi.org/10.3748/wjg.v23.i15.2660>

INTRODUCTION

Acute pancreatitis is an acute inflammatory process involving pancreas, characterized by upper abdominal pain and more than three-fold rise in pancreatic enzymes^[1,2]. The development of pancreatic fluid collections (PFCs) is a common complication of severe acute pancreatitis. The revised Atlanta classification categorizes PFC into four sub-types- acute pancreatic fluid collections (APFC), acute necrotic collections (ANC), pseudocysts and walled off necrosis (WON)^[3]. The differentiation of these collections is mainly based on the duration (< or > 4 wk) and nature of collections (necrotic or non-necrotic). APFC (\leq 4 wk) develop after an episode of interstitial edematous pancreatitis (IEP) and may evolve into pseudocyst after 4 wk. Whereas, ANC (\leq 4 wk) develop after acute necrotizing pancreatitis and subsequently transform into WON after 4 wk. By definition, pseudocysts have clear contents and WON have variable amount of solid necrotic debris^[3]. The present classification of fluid collections and severity of acute pancreatitis has important implications on the management as well as clinical outcomes in these patients^[4-7].

Acute collections (APFC or ANC) usually do not require any intervention for drainage as most improve with conservative management. However, a substantial proportion of symptomatic WON and pseudocysts require some drainage intervention. With the development of technical innovations in interventional endoscopy, invasive surgical procedures can be avoided in majority of these patients. New techniques and devices have emerged to improve the efficacy and safety of endoscopic drainage of PFCs. In this review we shall highlight the recent advances and controversies in the endoscopic management of PFCs.

NATURAL HISTORY OF PANCREATIC FLUID COLLECTIONS

The clinical outcome and requirement of an intervention in patients with PFCs is largely determined by the knowledge of their behavior with due course of time. The evolution and behavior of APFC and ANC may be different. A prospective multicenter study analyzed

the clinical course of PFCs in acute pancreatitis. Out of 302 patients with acute pancreatitis, 129 patients (42.7%) had APFC. Majority (70%) of these APFC resolved spontaneously, while about 15% developed pseudocysts. On subsequent follow-up about a quarter of pseudocysts disappeared completely^[1]. The nature of PFC (pseudocyst or walled off necrosis) and its influence on the natural history were not depicted in this study. In a prospective cohort study including majority of patients with ANP, about half of the ANC transformed into WON. In more than 50% cases, WON resolved spontaneously without requirement of an intervention. Therefore, in about 3/4th cases ANC resolved before or after evolving into WON^[8]. In a more recent study including 189 patients, 153 patients (81%) were classified as ANP and 36 (19%) with interstitial oedematous pancreatitis (IEP). About 22% patients with IEP developed APFC of which only one patient subsequently advanced to pseudocyst. In contrast, majority of patients with ANP developed ANC. Of these, about 55% patients developed WON of which 63% required an intervention^[9].

It can be concluded that majority of APFC resolve spontaneously and only a minority transform into pseudocyst, whereas a sizeable proportion of ANC transform into WON.

DRAINAGE OF PFCs - EVOLUTION OVER THE LAST DECADE

Over the last few decades, few critical observations have been made regarding the management of PFCs. First, the outcome of any drainage intervention is better if an intervention is performed after the collection gets walled off (> 4 wk) or encapsulated. Second, minimally invasive management of PFCs is better than the conventional surgical approach^[10-13]. Third, the outcomes of endoscopic drainage depend on the nature of PFCs, *i.e.*, pseudocyst or WON^[14].

The foundation of minimally invasive management of PFCs (especially WON) was laid by two landmark studies. The first study concluded that step-up surgical approach (*i.e.*, per-cutaneous drainage followed by minimally invasive retroperitoneal necrosectomy) resulted in less major complications and mortality as compared to the open necrosectomy group^[11]. In the second study, endoscopic necrosectomy reduced the pro-inflammatory response as well as new onset organ failure as compared to surgical necrosectomy in patients with infected necrotizing pancreatitis^[10].

The concept of step-up approach has now gained world-wide acceptance. Initial management of symptomatic PFCs constitutes antibiotics and nutritional support, followed by minimally invasive drainage (endoscopic, percutaneous or surgical) if symptoms persist. Necrosectomy (endoscopic or surgical) should be considered only if there is no response to these measures.

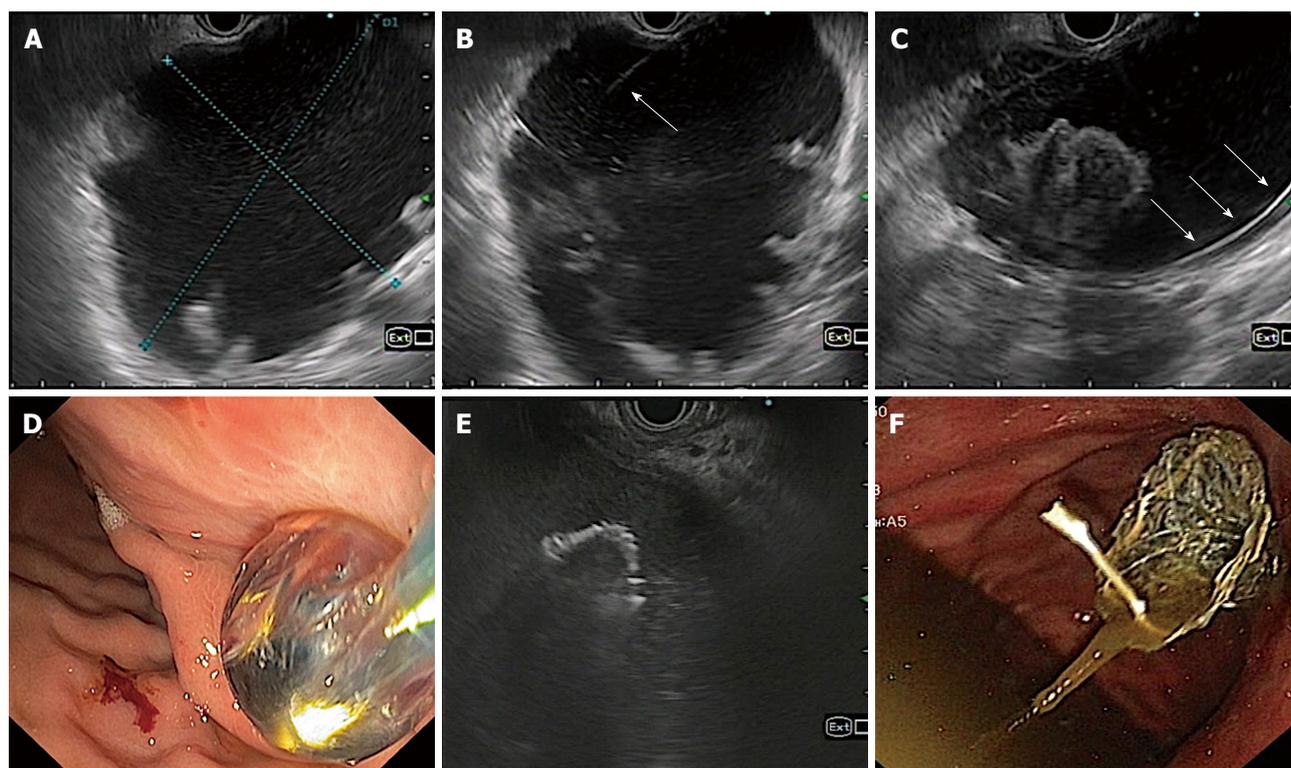


Figure 1 Technique of endoscopic ultrasonography guided drainage of pancreatic fluid collection. A: EUS evaluation of pancreatic fluid collection; B: Puncture of pancreatic fluid collections (PFC) wall with 21 G fine needle aspiration needle; C: Coiling of guidewire inside PFC cavity; D: Enlarging the cysto-gastric tract with balloon; E: Placement of stent under EUS-guidance; F: Final position of stent after placement.

ENDOSCOPIC DRAINAGE OF PFCs - CONVENTIONAL OR EUS GUIDED

Endoscopic transmural drainage (ETD) has been used effectively for over two decades' now. However, certain drawbacks are noteworthy with ETD. First, it requires an endoluminal bulge for it to be successfully performed. However, some PFCs like those located in the tail of pancreas usually do not produce a luminal compression. Second concern is the risk of bleeding due to presence of intervening vessels or collaterals which may not be taken care of in ETD. Endoscopic ultrasound guided transmural drainage (EUS-TD) enables the drainage of non-bulging PFCs, provided they are at a reasonable distance (< 1.5 cm) from the gastric wall^[15]. In a RCT, the technical success with EUS-TD was significantly higher than conventional-ETD even after adjusting for luminal compression. There were two bleeding episodes in the conventional group vs none in EUS-TD group^[16]. EUS-TD, therefore is not only more effective but also appears to be safer as it allows the visualization of any intervening vessels. In addition, the amount of necrotic debris can be assessed for deciding appropriate management strategies. While, Contrast CT is often utilized as the initial imaging modality in these patients, it is suboptimal in picturing debris inside the cyst cavity. EUS and magnetic resonance imaging (MRI) are superior for qualitative as well as quantitative assessment of

contents of PFCs^[17-19].

At this juncture, it can be concluded that when available EUS-TD is preferable for drainage of PFCs^[20].

ENDOSCOPIC DRAINAGE OF PANCREATIC FLUID COLLECTIONS

Endoscopic drainage of PFCs is accomplished by placing cysto-gastric stents (plastic or metal). The technique involves standard sequence of steps as follows - identification of ideal puncture site under EUS guidance, needle puncture of PFC wall, coiling of guidewire inside the cyst cavity, dilatation of cysto-gastric tract (cystotome and balloon) and finally placement of stents (Figure 1). The identification of the nature of PFCs is crucial in determining the outcome of endoscopic drainage. WON have variable amount of necrotic debris as compared to pseudocysts which may preclude complete drainage (Figure 2). Therefore, the success rate of endoscopic drainage is relatively lower and requirement of repeated endoscopic interventions is frequent as compared to pseudocysts^[14]. Additional measures like placement of a naso-cystic tube for irrigation and direct endoscopic necrosectomy (DEN) have been utilized to improve the success rates. Despite of all the efforts, the overall success rate of endoscopic drainage is lower in WON (63%-81%) as compared to that in pseudocysts (86%-100%)^[17].

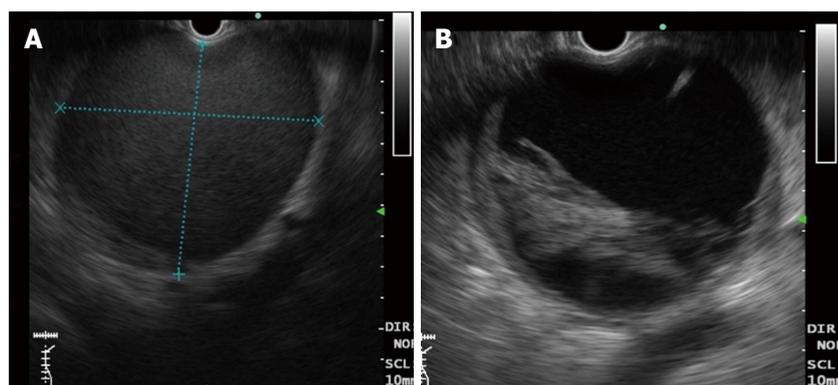


Figure 2 Differentiation of pancreatic fluid collections on endoscopic ultrasonography after 4 wk. A: Pseudocyst - note the clear contents of a pseudocyst (without solid debris); B: Walled off necrosis- note the presence of debris inside the cyst cavity.

ENDOSCOPIC DRAINAGE OF PSEUDOCYSTS

EUS-TD was initially described in early 1990's. Since then numerous studies have been published revealing excellent outcomes of endoscopic drainage of pseudocysts. Endoscopic drainage of pseudocysts is successful in about 86%-100% of cases^[17]. The advantages of EUS-TD over ETD have been described earlier in this review. Endoscopic drainage of pseudocysts is accomplished by placing one or more pigtail plastic stents (7 or 10 Fr). The size and number of plastic stents probably do not play a role in the successful outcome of endoscopic drainage of pseudocysts. In a recent retrospective study, there was no relation between the treatment outcome and stent characteristics (number and size - 7 or 10 Fr) in patients undergoing endoscopic drainage of uncomplicated pancreatic pseudocysts^[21]. However, the results may not apply to WON or complex pseudocysts where larger stents or multiple stents may prove to be beneficial.

Several studies have compared the outcomes of endoscopic drainage with surgical cysto-gastrostomy and percutaneous drainage^[13,22-24]. The only RCT conducted by Varadarajulu *et al.*^[13] concluded that both the modalities are equally effective with shorter hospital stay and lower costs in the endoscopic group. However, surgical drainage was performed by open procedure rather than laparoscopic cysto-gastrostomy. In another study, laparoscopic cysto-gastrostomy outperformed endoscopic drainage. But, the clinical success was unusually low in the endoscopic group (51.1%) in this study, in contrast to most of the published literature (86%-100%)^[17]. Therefore, more RCTs are required to determine the superiority of one approach over the other.

The literature comparing endoscopic and percutaneous drainage is limited. In one retrospective study, both the modalities were found to have equal efficacy. However, percutaneous drainage group had higher rates of re-intervention and longer length of

hospital stay^[24]. The development of troublesome external pancreatic fistula and infection are major drawbacks associated with percutaneous drainage. External pancreatic fistula is the most common complication and develops in about 8.2% patients undergoing percutaneous drainage for infected pancreatic necrosis^[25]. A recent systematic review compared endoscopic, percutaneous and surgical pancreatic pseudocyst drainage. The authors concluded that both endoscopic and surgical drainage are equally effective, with shorter hospital stay, less cost and better quality of life in the endoscopic group. Nevertheless, surgical or percutaneous drainage may be considered in patients with disapproving anatomy^[26].

ENDOSCOPIC DRAINAGE OF WON

The standard endoscopic drainage technique has yielded satisfactory clinical outcomes in pseudocysts. However, the same has been sub-optimal for efficiently draining WON. Therefore, a complementary procedure is frequently required to improve the results in patients with WON. The innovations in devices and techniques in this regard include - use of naso-cystic catheter (NCT) for irrigation, multiple transluminal gateway technique, DEN, development of novel metal stents, dual modality drainage and the endoscopic step up approach^[27-35].

The placement of NCT allows irrigation of the cyst cavity with saline or hydrogen peroxide and facilitates the drainage of viscous contents in WON. In a retrospective study, the clinical success was significantly higher and stent occlusion lower in the combination group (NCT + plastic stents) when compared to plastic stent only group^[35].

In the multiple transluminal gateway technique, 2 or 3 transmural tracts are fashioned between the necrotic cavity and the GI tract. One of the tracts is used for irrigation *via* a NCT and multiple plastic stents are arrayed in other tracts to assist drainage of necrotic debris^[27]. Multiple tracts enable rapid and efficient drainage in cases of large WON^[36].

Table 1 Studies revealing outcomes of pancreatic fluid collections with newly designed metal stents

Study	n	Stent used	Size (cm)	Technical success, %	Clinical success, %	Necrosectomy, %
Walter <i>et al</i> ^[49] , 2015	61	AXIOS	9.0	98.0	PC-93 WON-81	43.0
Shah <i>et al</i> ^[48] , 2015	33	AXIOS	9 ± 3.3	91.0	93.0	33.0
	47	NAGI	10.0	98.0	76.6	19.2
Siddiqui <i>et al</i> ^[34] , 2016	82	AXIOS	11.8	97.5	PC-100 WON-88	All WON
	124	AXIOS	9.5	100.0	86.3	62.9
	93	Hot AXIOS	10.0	98.9	PC-100 WON-90.4	59.6
Lakhtakia <i>et al</i> ^[65] , 2016	211	NAGI	10.8	99.0	96.5	9.2
Vazquez-Sequeiros <i>et al</i> ^[50] , 2016	211	FCMS-139	9.3	97.0	94.0	17.0
		AXIOS-72				

PFC: Pancreatic fluid collection; WON: Walled off necrosis; PC: Pseudocyst; FCMS: Fully covered metal stent; BFMS: Bi-flanged metal stent; LAMS: Lumen apposing metal stent; PS: Plastic stent; AE: Adverse events.

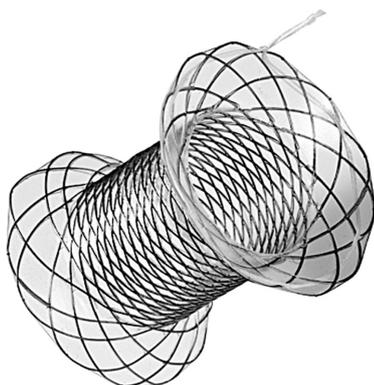


Figure 3 Specially designed bi-flanged metal stent (Nagi stent, Taewoong Medical Co, Ilsan, South Korea) for drainage of pancreatic fluid collection.

EVOLUTION OF METAL STENTS - PAST, PRESENT AND FUTURE

The “bigger” the “better” theory has been optimally utilised at various luminal territories in GI tract. The motive behind the use of metal stents is to overcome the problem of sub-optimal drainage efficiency of plastic stents in WON^[37]. Metal stents have larger diameter and permit for endoscopic necrosectomy. In the initial small studies, covered biliary metal stents and to a lesser extent esophageal stents were used for trans-enteric drainage^[38-42]. Although these stents provided efficient drainage, few inherent limitations precluded their widespread use. Biliary metal stents have anti-migration features (like anti-migratory fins) which are not suitable for cysto-enteric drainage. Therefore, pigtail plastic stents were used to anchor these stents across the cysto-gastric tract to prevent migration^[40]. These stents are long with relatively small lumen which increases the chances of erosions

or ulceration over gastric or retroperitoneal side and hindrance for DEN^[43]. Nevertheless, it would be unfair to criticize biliary stents, as they were designed for biliary drainage rather than drainage of PFCs.

The unmet gap of a dedicated metal stent for trans-enteric drainage has largely been filled with the availability of novel metal stents. These stents have been specially designed for the drainage of PFCs and have either lumen apposing property like Axios stent (Xlumena, Mountain View, CA, United States), Niti-S SPAXUS stent (TaeWoong Medical Co., Ltd., Ilsan, South Korea) or are bi-flanged like Nagi stent (Taewoong Medical Co, Ilsan, South Korea), Aixstent (Leufen Medical, Aachen, Germany) and the Hanarostent BCF (M.I. Tech. Co., Inc., Seoul, South Korea) to offset migration rates especially during debridement (Figure 3)^[44]. The stents are fully covered with silicone membrane to minimize tissue ingrowth and difficulty in removal. The efficacy and safety of these dedicated metal stents has been proven unequivocally in multiple recent studies^[33,34,43,45-50] (Table 1).

Newly designed metal stents are easy to deploy with technical success of > 90% in recent studies. In a retrospective case-control study, the median procedural duration was significantly shorter for lumen apposing metal stents (LAMS) as compared to plastic stents (8.5 vs 25 min, *P* < 0.001)^[51]. Procedural duration is proportional to the difficulty of technique and matters the most in sick patients.

Clinical success is impressive with new metal stents ranging from 76%-100%. The common adverse events (AE) include- bleeding (1%-7%), perforation (1%-2%), stent migration (1%-6%) and infection (1%-11%). In a multicentre study, Siddiqui *et al*^[34] found metal stents could be successfully placed in 97.5% patients. PFC resolution was achieved in all cases (100%) with

Table 2 Selected studies comparing the outcomes between plastic and metal stents

Study	PFC type	n	Success	AE	Conclusion
Lee <i>et al</i> ^[55] 2014	WON-14	PS-25	90.9%	8%	Efficacy equal
	PC-36	FCMS-25	87%	0	Re-intervention: FCMS = PS AE: FCMS = PS
Mukai <i>et al</i> ^[53] 2015	WON	PS-27	92.6%	18.5%	Efficacy and AE: BFMS = PS
		BFMS-43	97.7%	7%	Re-intervention: BFMS < PS AE: BFMS = PS
Sharaiha <i>et al</i> ^[54] 2015	PC	PS-118	89%	31%	Efficacy: FCMS > PS
Siddiqui <i>et al</i> ^[52] 2016	WON	FCMS-112	98%	16%	AE: FCMS < PS
		PS-106	81%	7.5%	Efficacy: FCMS, LAMS > PS
		FCMS-121	95%	1.6%	Re-intervention: LAM < FCMS < PS
		LAMS-86	90%	9.3%	AE: LAMS = PS > FCMS
Bapaye <i>et al</i> ^[76] 2016	WON	PS-61	73.7%	36.1%	Efficacy: BFMS > PS
		BFMS-72	94%	5.6%	Re-intervention: BFMS < PS AE: BFMS < PS

PFC: Pancreatic fluid collection; WON: Walled off necrosis; PC: Pseudocyst; FCMS: Fully covered metal stent; BFMS: Bi-flanged metal stent; LAMS: Lumen apposing metal stent; PS: Plastic stent; AE: Adverse events.

pseudocyst and 88.2% of cases with WON. There was no incidence of endoscopic debridement related stent migration. In a large Spanish study including 211 patients with PFCs (pseudocyst-53%, WON-47%), straight biliary metal stents and new LAMS were utilized. Both stents fared equally with respect to clinical success and adverse events. The overall rate of adverse events was 21%, including infection, bleeding, stent migration and perforation^[50]. Another study comparing fully covered self expanding metal stent (FCSEMS) with LAMS, reported that although clinical outcomes were similar in both the groups, significantly fewer interventions were required in LAMS group^[52].

CHOICE OF STENT - METAL OR PLASTIC

Large comparative studies between metal and plastic stents are lacking. Limited data suggests that in WON metal stents are more efficacious, easier to deploy with shorter procedural duration and associated with lower AE in patients with WON (Table 2)^[52-55]. Siddiqui *et al*^[52] retrospectively compared plastic stents with FCSEMS and LAMS in patients with WON. Metal stents (FCSEMS or LAMS) fared better in terms of clinical success and AE. LAMS was better than FCSEMS with respect to the number of procedures required for resolution of WON. In another retrospective study comparing plastic stents with metal stents (covered biliary stents) for pancreatic pseudocysts, procedure related adverse events were significantly higher in the plastic stent group^[54]. In contrast, few studies conclude otherwise with no difference in clinical outcomes between metal and plastic stents. Bang *et al*^[51] compared plastic stents with LAMS retrospectively. The clinical outcomes were similar in both the groups, but costs significantly higher in the LAMS group. In the only randomized study (50 patients), Lee *et al*^[55] concluded that both FCSEMS and plastic stents have equal efficacy for PFCs. However, metal stents were easier to deploy with shorter procedure time than plastic stents. In a

systematic review, the pooled success rates and AE for endoscopic drainage of pseudocysts and WON were comparable using plastic or metal stents. However, newly designed metal stents (Axios in two studies, Nagi in one study) were used in only three studies in this review^[56]. Moreover, the studies using metal stents included small number of patients. More recent studies display excellent outcomes with less technical difficulty or procedure duration while using novel metal stents in PFCs^[53,55]. This is especially important in sick patients and when there is high likelihood of re-intervention for debridement or necrosectomy. Large randomized trials are required to prove the efficacy of metal stents over plastic stents for WON.

One distinct advantage of plastic over metal stents is that they can be left in situ for prolonged duration in cases of non-resolving PFCs or disconnected pancreatic duct (PD)^[57,58]. Metal stents need to be removed after a finite duration as stent impaction due to tissue ingrowth or overgrowth is a possibility^[46].

DIRECT ENDOSCOPIC NECROSECTOMY

Open necrosectomy is associated with high mortality and morbidity and therefore, has largely been replaced by minimally invasive necrosectomy^[59]. Minimally invasive retroperitoneal necrosectomy has been shown to be superior as compared to surgical necrosectomy in a randomized study^[11]. In the present era, endoscopic necrosectomy is preferred over open or minimally invasive surgical necrosectomy. A number of studies have established the safety and efficacy of DEN^[60-62]. Endoscopic necrosectomy is associated with reduced formation of pancreatic fistula as compared to surgical drainage^[10]. DEN is probably more efficacious (81% vs 61%) with less mortality (6% vs 13%) and reduced occurrence of pancreatic fistulae (5% vs 17%) than minimally invasive surgery (VARD)^[63].

The technique of DEN involves dilatation of the cysto-gastric tract with a balloon, followed by advancement of the endoscope into the cavity of WON (Figure

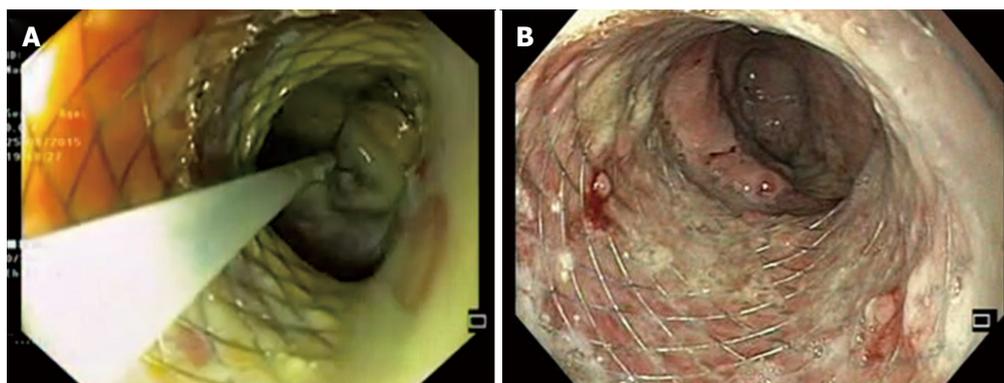


Figure 4 Direct endoscopic necrosectomy. A: Removal of necrotic debris with a snare; B: After completion of endoscopic necrosectomy.

4). Subsequently, the cavity is lavaged with normal saline and necrotic debris are removed under direct vision using snares or baskets. Hydrogen peroxide can be used with the advantage of loosening up of necrotic tissue to facilitate its easy removal in between the sessions of DEN. Several sessions may be required for completing the DEN procedure. Unfortunately, there is no dedicated device designed for endoscopic necrosectomy and retrieval of necrotic material. Snares, forceps or baskets are used to remove the necrotic tissue, but appear to be suboptimal.

The clinical success of DEN in multicentre studies ranges from 75%-91%^[60-62]. Overall complication rates range from 14%-33% with mortality in up to 11% patients. The most common complication of DEN is bleeding followed by perforation and infection^[60-62]. Air embolism has also been described with DEN, therefore it is imperative to use CO₂ for insufflation during the complete procedure^[63].

With the development of novel metal stents, the task of DEN has become relatively easy. These stents have wide lumen and allow multiple sessions of DEN without the need of repeated dilatations of cysto-gastric tract.

DEN may be associated with significant complications and therefore should not be performed unless indicated. A conservative approach is reasonably efficacious to begin with. A recent systematic review and meta-analysis supports the concept of initial conservative approach for the management of infected pancreatic necrosis. About 2/3rd patients (64%) with infected pancreatic necrosis could be managed with conservative approach alone (percutaneous drainage)^[64]. In case an endoscopic drainage is required, DEN can be avoided in majority of cases with a step up approach^[65]. In a large single center study including 205 patients, bi-flanged metal stents were used and a step up approach utilized for the management of WON. In about 75% patients, clinical success was achieved by placing bi-flanged SEMS alone without any additional intervention. The next steps included de-clogging of SEMS followed by placement of NCT and finally DEN. With this approach DEN was required only in 9.2% cases to achieve an overall success rate of 96.5%^[65].

TRANSPAPILLARY DRAINAGE

Transpapillary drainage (TPD) of PFCs involves placement of pancreatic ductal stent, in cases with small collections (< 6 cm) communicating with the pancreatic duct^[17]. Therefore, TPD is not beneficial if bridging of PD disruption is not achieved or the collection is large and non-communicating. In addition, there is risk of infecting the PFC with TPD. In the current era, TPD is usually not performed alone and often combined with transmural drainage (TMD) when indicated.

COMBINED VS TRANSMURAL DRAINAGE

- THE ROLE OF ERCP?

The occurrence of pancreatic ductal disruption is well known after acute severe pancreatitis^[66,67]. It is logical to believe that the severity of pancreatitis or extent of necrosis would be proportional to the incidence of PD disruption. In a retrospective study, PD disruption was documented in 38% of patients with acute necrotizing pancreatitis^[68]. More patients in the extensive necrosis group had complete disruption as compared to those in the partial disruption group. The recurrence of PFCs was also high in complete disruption group^[68]. Therefore it seems prudent that PD disruption should be addressed prior to the removal of cysto-gastric stents to prevent recurrence. PD stent may be placed at the time of index endoscopic drainage or before removing cysto-gastric stent. The current literature is divergent regarding the benefits of combined drainage over transmural drainage alone^[47,66,67,69-71]. In a retrospective study including 110 patients, Trevino *et al*^[67] concluded that combined drainage (TPD + TMD) has a positive impact on the resolution of PFCs. Interestingly, there was no difference in the recurrence rates of PFCs in trans-papillary stenting vs no stenting group. In a small prospective single center study, TPD in selected cases allowed early removal of FCSEMS and prevented the recurrence of PFCs. PD leak or disruption was an independent factor affecting PFC resolution at 3 wk^[47]. In contrast to the above mentioned studies, the results of several studies failed

Table 3 Adverse events in selected studies evaluating endoscopic ultrasonography drainage of pancreatic fluid collections with metal stents

Study	n	Perforation, %	Bleeding, %	Migration, %	Infection, %	Overall complications, %
Walter <i>et al</i> ^[49] , 2014	61	1.6	6.5	4.9	6.5	9.0
Chandran <i>et al</i> ^[46] , 2015	54	-	5.5	20.4	4.0, 7.4	Early-7.4 Late-11.1
Bapaye <i>et al</i> ^[43] , 2015	19	-	5.3	5.3	-	10.5
Rinninella <i>et al</i> ^[45] , 2015	93	2.1	1.1	1.1	1.1	5.4
Vazquez-Sequeiros <i>et al</i> ^[50] , 2016	211	3.0	7.0	3.0	11.0	21.0
Siddiqui <i>et al</i> ^[34] , 2016	82	1.2	7.3	-	6.1	9.8
Sharaiha <i>et al</i> ^[33] , 2016	124	-	Early-1.6 Late-0	Early-2.4 Late-3.2	Early-3.2 Late-2.4	Early-11.3 Late-7.2
Lakhtakia <i>et al</i> ^[65] , 2016	205	1.0	2.9	2.4	-	3.9

to show any benefit of combined drainage over TMD alone^[69,71]. In a retrospective study, there was higher albeit non-significant recurrence of PFCs in combined group as compared to TMD group alone. The authors proposed that placement of a trans-papillary stent hinders the maturation of cyst-enterostomy fistula^[69]. However, the study population was heterogeneous and included patients with acute collections, necrotic collections, abscess and pseudocysts (acute and chronic). In a more recent multicenter study inclusive of a homogeneous study population (pancreatic pseudocysts), the authors concluded that there was no difference in the long-term radiological resolution of pseudocysts in combined (62%) vs trans-mural drainage group (69%). Moreover, on multivariate analysis - TPD was the only factor negatively associated with long-term radiological resolution of PFC^[71].

The success rate of endoscopic bridging of complete PD disruption or disconnection is much lower than that of TPD in case of partial PD disruptions^[66]. If disruption cannot be bridged the benefit is likely to be marginal if any. In a retrospective analysis, there was no additional benefit of TPD in complete PD disruptions (9/17, as compared to cyst-enterostomy or percutaneous drainage alone (52.9% vs 70.6%, $P = 0.61$)^[70].

At this moment the role of TPD in the management of PFCs remains ambiguous. In cases of suspected disruption or disconnection it seems rational to bridge the gap with a plastic stent. Cysto-gastric plastic stents can be left in place in case PD leak cannot be bridged to reduce recurrences^[57,58,72,73]. However, randomized trials are required to clear the prevailing dilemma.

ADVERSE EVENTS

Endoscopic drainage of PFCs is safe and major AE are uncommon. AE include - bleeding, perforation, infection and stent migration (Table 3). Rarely, air embolism and intestinal obstruction due to stent migration have also been reported after endoscopic drainage.

The incidence of AE depends on several factors including - endoscopic vs EUS guided drainage, nature of collections (pseudocyst vs WON), DEN performed

or not and type of stent used (plastic vs metal). Complications may be higher while draining WON as compared to pseudocysts. In a large retrospective study including 211 patients, complications were encountered in 17 patients (8.5%) and were higher for drainage of necrosis than pseudocyst or abscess (15.8% vs 5.2%, $P = 0.02$)^[37]. Similarly DEN is associated with higher AE (see above). In few studies where endoscopic drainage was combined with DEN, up to one-fourth of patients suffered some complication^[74,75].

In recent studies comparing plastic with metal stents - the AEs were either similar or lower in the metal stent group (Table 2)^[52-55,76]. Metal stents can tamponade the edges of cysto-gastrostomy site, thereby reducing the occurrence of bleeding from puncture site. Larger size allows better drainage and less chances of occlusion and sepsis. In contrast, higher than expected delayed AE were encountered in the interim analysis of an ongoing RCT (plastic vs LAMS) in patients with WON. These AE included - delayed bleeding (3 patients, 3-5 wk), buried LAMS (2 patients, 5-6 wk) and biliary stricture (5 wk)^[77]. Therefore, early removal of metal stents may be considered if the PFC has resolved.

OPTIMAL DRAINAGE OF PFCs - PLEA FOR MULTIDISCIPLINARY APPROACH

The development of endoscopic drainage techniques has led to decline in the use of percutaneous and surgical drainage of PFCs. However, large WON and complex pseudocysts like those extending into paracolic gutters may be inadequately drained by endoscopic techniques alone. In addition, endoscopic drainage is not feasible if the PFC is situated at a distant location from the GI lumen. Therefore, in selected cases percutaneous drainage may complement the benefits of endoscopic drainage and help in circumventing the need of surgical necrosectomy. About 1/3rd to 2/3rd patients with WON improve with percutaneous drainage alone^[11]. Dual modality drainage (endoscopic + percutaneous) appears safe and appealing and may reduce the chances of pancreatico-cutaneous fistula also^[28,32]. In addition, other hybrid technique involves percutaneous endoscopic necrosectomy with or without endoscopic

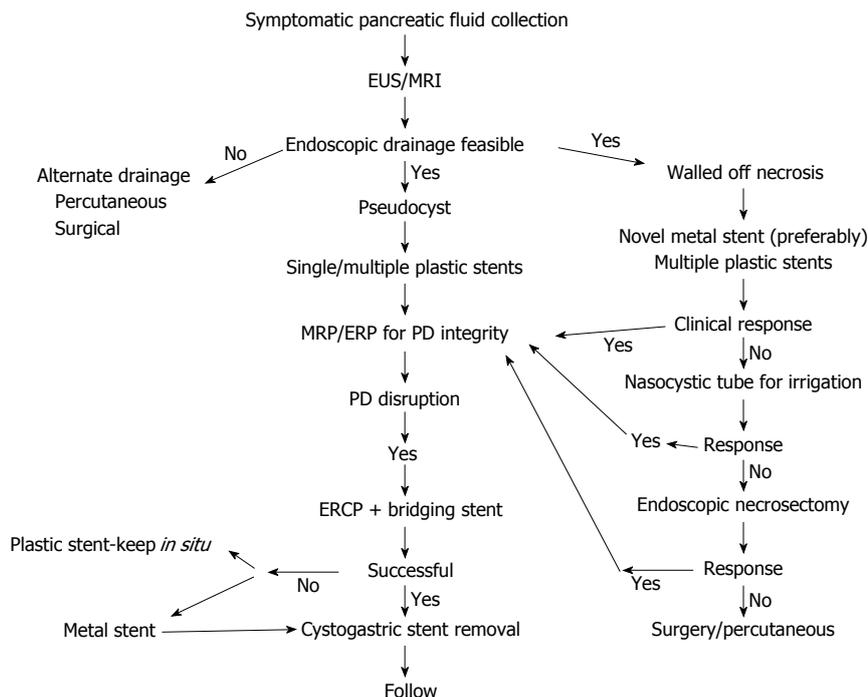


Figure 5 Algorithmic approach to the management of pancreatic fluid collections. EUS: Endoscopic ultrasound; MRI: Magnetic resonance imaging; PD: Pancreatic duct; ERCP: Endoscopic retrograde cholangiopancreatography.

drainage^[78-80]. The data on safety and efficacy of these novel approaches is limited. Studies in future should clarify their role in difficult to manage PFCs.

MANAGEMENT OF PFCS IN PAEDIATRIC POPULATION

The data for minimally invasive endoscopic management of PFCs is limited in children. The size of a standard adult EUS scope (about 14 mm) may be prohibitive for its use in small children (< 15 kg). Therefore, caution is advised while performing EUS-drainage in small children (< 15 kg)^[81].

The available evidence (small case series) suggests that endoscopic drainage is safe and efficacious in paediatric age group^[82-84]. More recently, the use of novel bi-flanged metal stent has been reported in children with WON^[85,86]. Nabi *et al.*^[86] utilized bi-flanged metal stents in twenty-one children with WON. Technical success was achieved in all and clinical success documented in 95% of children. There were no major complications.

CONCLUSION: INDIVIDUALIZED APPROACH TO PFCS - "ONE SIZE DOES NOT FIT ALL"

The management of PFCs needs to be tailored for each patient. The endoscopist should justify answers to several questions before attempting the drainage procedure. The first and foremost is the indication of

drainage procedure. Asymptomatic collections need not be drained irrespective of their size. Second, is it the right time to drain. Acute collections usually resolve and endoscopic drainage is performed only under exceptional circumstances. Third, what would be the ideal route for draining the PFC in question. PFCs situated > 1.5 cm from the lumen are not usually amenable to endoscopic drainage and therefore alternate routes should be sought. Likewise, large collections extending into the paracolic gutters may require combined approach (endoscopic and percutaneous) for optimal results. Fourth, the nature of PFCs should be identified by suitable imaging (EUS or MRI). Characterisation of PFCs into pseudocyst and WON have critical therapeutic complications. WON have debris and therefore are more demanding than pseudocysts with clear contents. However, it should be acknowledged that sometimes the distinction between WON and pseudocyst is blurred. The decision to proceed is then dictated by the amount of debris in the cyst cavity. Lastly, appropriate endoprosthesis should be chosen for draining PFCs. The choice of stent is largely dependent on nature of PFCs and the possible need for re-interventions or DEN. Endoscopic drainage using one or more plastic stents seems to be good enough for pseudocysts. In contrast, WON should be drained with multiple plastic stents or newly available metal stents if multiple sessions of DEN are expected. Placement of a NCT in addition may be useful for irrigating the cavity. Subsequently, DEN should be performed only in cases with no improvement in symptoms (Figure 5).

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P- Reviewer: Garcia-Flórez LJ, Maluf-Filho F **S- Editor:** Qi Y
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ISSN 1007-9327

