

Endosonographic drainage of pancreatic fluid collections and walled-off necrosis



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ARTICLE INFO

Article history:

Received 24 August 2017

Accepted 6 November 2017

Keywords:

Endoscopic ultrasound

Pseudocyst

Endoscopic necrosectomy

Lumen-apposing stents

ABSTRACT

Endosonographic drainage of pseudocysts and walled-off necrosis (WON) has not been standardized. Drainage of pseudocysts via endosonographic guidance has high rates of technical success via the transmural approach. Alternative modalities including transpapillary endoscopic retrograde pancreatography with pancreatic duct sphincterotomy and pancreatic duct stent placement are options for patients with small pseudocysts and in the presence of pancreatic duct disruption. Drainage of WON has a variety of approaches and may require a combination of endoscopic or percutaneous techniques to achieve the optimal outcome. Endosonographic drainage of WON has lower rates of mortality and morbidity compared to surgical intervention. Several options regarding stent placement exist including the use of fully covered self-expandable metal stents and lumen-apposing metal stents. Depending upon their properties, each type of stent carries its own risk including the risk of migration. The endoscopist performing drainage of these fluid collections must take into account the number and size of these collections as well as the presence and amount of necrotic debris in order to choose the most appropriate technique and equipment in order to achieve optimal outcomes.

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1. Introduction

Pancreatic pseudocysts and walled-off necrosis (WON) are frequent complications of acute and chronic pancreatitis. It is estimated approximately 20% of individuals with acute pancreatitis will develop necrosis with secondary infection occurring in 30% of these patients [1,2]. Management of pancreatic pseudocysts and WON is increasingly being performed via endoscopic methods owing to lower rate of adverse events including shorter hospital stays and comparable successful outcomes when compared to surgically treated patients [3]. However, the technique used to drain pancreatic fluid collections have not been standardized owing to lack of comparative randomized trials and specifically for WON. However, a randomized trial comparing endoscopic and surgical drainage for pseudocysts documented shorter hospital stays, improved quality life, and equivalent recurrence at 2 years [4]. For WON and necrotizing pancreatitis, a multicenter randomized trial found decreased rates of pancreatic fistula, shorter

hospital stays, and reduced health care costs with endoscopic drainage compared to a step-up approach of percutaneous drainage with or without video assisted retroperitoneal debridement [5]. Furthermore, complications and mortality were the same in both groups illustrating the overall challenge in management of these patients [5]. In this review, we will focus on the technique for accessing and draining pancreatic pseudocysts and WON with the use of endosonography. In addition, we will review the various drainage devices used, overall success, adverse events, and limitations of the particular modalities and approaches.

1.1. Pseudocysts

1.1.1. Background

Pseudocysts are fluid collections that are extrapancreatic and present for more than 4 weeks and usually without solid debris. After 4 weeks, a well-circumscribed fluid collection is often formed and amenable to drainage if needed. The indication for drainage of pseudocysts include symptom management that can occur with compression of the stomach and biliary tree or enlarging cysts [6,7]. Previous guidelines regarding drainage of pseudocysts greater than 6 centimeters has fallen out

The author reports no direct financial interests that might pose a conflict of interest in connection with the submitted manuscript.

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<https://doi.org/10.1016/j.tgie.2017.11.002>

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of favor, though, cysts greater than 6 centimeters tend to be symptomatic [8,9].

1.1.2. Preprocedural preparation

Preprocedural preparation including discontinuation of anti-coagulant and antiplatelet medications are required to prevent acute and delayed bleeding. Antibiotic prophylaxis is also given and often includes a fluoroquinolone or cephalosporin though this has not been substantiated by randomized trials [10]. Often deep sedation or anesthesia is used owing to the complexity of the cases. Carbon dioxide as opposed to air is for used for gas insufflation as it is thought to minimize risk of air embolus; a potentially fatal complication.

1.1.3. Endoscopic technique

There are 2 main endoscopic approaches for pseudocyst drainage: transpapillary or transmural.

Endoscopic transpapillary approach requires stent placement with or without pancreatic duct sphincterotomy using endoscopic retrograde pancreatography. This approach is most effective to treat small pseudocysts which are in communication with the main pancreatic duct. The stent allows for bridging of the ductal disruption and the proximal end of the stent can reside directly into the pseudocyst [3]. Advantages of the transpapillary approach include evaluation of the pancreatic duct and decreased risk of bleeding or perforation when compared to the transmural technique [3]. Disadvantages of this approach include the risk of pancreatitis, infection of the cyst, and the inability to adequately drain large fluid collections [11,12]. Occasionally a combined transpapillary and transmural approach will need to be taken if there is a persistent fluid collection, despite transmural drainage, which could indicate pancreatic duct disruption.

The endoscopic transmural approach for pseudocysts can be performed with or without the use of endoscopic ultrasound (EUS). EUS facilitates evaluation of cyst morphology as well as an estimation of the distance between the intestinal lumen and fluid collection. In addition, the use of color Doppler ultrasound is used to identify surrounding blood vessels. EUS obviates the need for luminal indentation. The transmural approach can be performed by creating a cystgastrostomy or cystduodenostomy depending upon the location of the pancreatic fluid collection. After evaluation of the pseudocyst a 19-gauge needle is used to puncture the pseudocyst followed by a 0.025 or 0.035-in guidewire introduced through the needle and coiled within the pseudocyst under fluoroscopic guidance [13]. The fistula track can be dilated with the use of biliary balloons to facilitate insertion of plastic or metals stent(s) into the pseudocyst. Technical success of EUS-guided drainage compared to non-EUS have been demonstrated to vary between 82%–100% and 62%–97%, respectively [14]. A prospective randomized trial of 30 patients comparing EUS and non-EUS transmural drainage of pseudocysts found significantly greater technical success with the use of EUS (100% vs 33%) and this was substantiated even when adjusting for luminal compression [15]. In addition, all patients who had failed endoscopic drainage had successful drainage when using EUS with 2 patients who underwent drainage via endoscopy suffering major procedure related bleeding [15]. An additional benefit of EUS is the ability to differentiate between benign and malignant cysts [16,17]. A study by Varadarajulu et al, found 5% of patients referred for pancreatic pseudocyst drainage had a mucinous neoplasm [16]. Though technical success of EUS compared to non-EUS drainage has been previously demonstrated, long-term resolution of pseudocyst is not significantly different when using either modality [16,18]. However, often these studies are limited to 30 days or 6-month follow-up [15,18].

Several studies evaluating procedural complication rates of EUS and non-EUS-guided drainage have not found significant differences [15,18]. Overall complication rates of endoscopic-guided drainage are estimated between 5% and 35% [13]. Most common complications include secondary infection, bleeding, and pneumoperitoneum. In addition, stent placement carries its' own risk of adverse events and the risk profile differ between the type of stent placed. Factors influencing the type of stent used will be discussed later.

The benefits of EUS are many and allows for real-time location of the fluid collection(s) and its superiority in the absence of luminal compression is well known [15]. The distance between the gastric wall and the pseudocyst is able to be accurately assessed and allow for safe pseudocyst drainage. In addition, the use of EUS can help facilitate drainage of pseudocysts located in the pancreatic tail which may otherwise may not be feasible to drain via the non-EUS approach [13]. Also, the ability to complement direct visualization with color Doppler mitigates the risk of bleeding as it can assess for perigastric varices and collateral blood flow before needle puncture. In addition, the endoscopist can abort the procedure if intracyst hemorrhage begins to take place. For patients who have chronic pancreatitis as well as coexisting portal hypertension the ability to avoid gastric vessels is paramount. Owing to the significant percentage of patients in whom EUS can change management along with higher rates of technical success, the American Society of Gastrointestinal Endoscopy (ASGE) recommends EUS be pursued if there is absence of luminal compression, an unusual location of the pseudocyst, evidence of portal hypertension, or, after failed conventional endoscopic approach [3].

1.2. Walled-off necrosis

1.2.1. Background

According to the 2013 revised Atlanta Classification WON is an encapsulated collection of nonviable pancreatic tissue that may contain liquid and solid components and may be intrapancreatic or extrapancreatic (Figure 1) [19]. On cross-sectional imaging walled-off necrosis is often seen as a heterogeneous fluid collection with or without loculations. The presence of gas bubbles in the fluid collection or fevers without an alternative etiology may signify infected necrosis. Indications for intervention in WON include suspected infection, ongoing organ failure after onset of acute pancreatitis, disconnected pancreatic duct, as well as symptomatology related to compression of the gastric outlet or biliary system. The presence of necrotic debris can result in the need for several endoscopic procedures to facilitate adequate drainage and prevent subsequent infection. Endoscopic drainage of organized necrosis has a higher failure rate than drainage of pseudocysts. A retrospective review of a multicenter study found successful resolution of 75% of patients treated with endoscopic



Fig. 1. An anechoic lesion measuring with a thick outer wall and evidence of internal debris or necrotic material within the fluid-filled cavity.

necrosectomy with a median of 5 endoscopic sessions performed [20]. Given the morbidity associated with surgical necrosectomy, an endoscopic approach may be taken in select patients in a setting with highly skilled endoscopists and support staff available [21].

1.2.2. Preprocedural preparation

Similar to preparing the patient for endoscopic drainage of pseudocysts, antiplatelet and anticoagulant medication should be discontinued several days before the procedure. Patients with WON may already be on antibiotics given concern of infected necrosis and if not, should be given preprocedural antibiotics. Given the complexity and varying degrees of technical success for endoscopic drainage of WON, these procedures should be performed with other consulting services available including surgery, critical care, and interventional radiology.

1.2.3. Endoscopic technique

The transmural approach is the standard endoscopic therapy for WON. The advantage of using the echoendoscope is the ability to identify in real-time if there are any remaining loculations as well as debris that would require further drainage and debridement. There is considerable variability in the endoscopic technique used as there are a paucity of comparative studies regarding different techniques including the type and number of stents used to facilitate drainage [22]. Access to the WON is gained using the same approach for pseudocysts and given the fibrotic nature of mature necrotic fluid collections the endoscopist can choose to use a needle knife to gain access. Often drainage is performed before necrosectomy. However, in a study of 12 patients comparing direct endoscopic necrosectomy vs a step-up approach for WON, higher rates of resolution as well as lower rates of health care utilization with the use of initial necrosectomy were found [23]. Drainage can be performed with placement of plastic or metal stents(s) and currently, there is no standard approach in regards to the size, number, and type of stent used. Adequate drainage often takes 5–7 days and can be demonstrated on subsequent cross-sectional imaging. After satisfactory drainage is achieved necrosectomy can be pursued.

1.2.4. Endoscopic necrosectomy

A meta-analysis evaluating drainage only without necrosectomy for infected WON demonstrated a 59% success rate [24]. The endoscopic technique for necrosectomy varies and includes the possibility of dilation of the fistula tract after stent placement in order to facilitate direct endoscopic insertion into the fluid collection (Figure 2) [22]. The fistula tract is often dilated with

the use of 8–15 mm biliary balloon. In addition, there is an assortment of options to extract debris including the use of a Roth Net, snares, baskets, and extraction balloons (Figure 3). Necrotic debris that has remained after drainage can result in stent occlusion and clinical deterioration if not removed (Figure 4). However, endoscopic necrosectomy is challenging and complications can range from 26%–35% with mortality estimated at 6%–7% [25]. Also, direct endoscopic necrosectomy inherently carries the risk of stent migration and the risk is dependent upon the type of stent used as detailed below.

2. Stents

After gaining access to the pancreatic fluid collection via the transmural approach, the endoscopist has the ability to use double pigtail plastic stents, fully covered biliary metal stents, and fully covered self-expandable metal stents (FCSEMS) including lumen-apposing metal stents (LAMS) for pseudocysts and WON.

2.1. Plastic vs fully covered metal stents

A study of 122 patients found overall treatment success of 94% with use of plastic stents for pancreatic pseudocysts and no difference in the number of interventions needed with the use of 7-Fr and 10-Fr plastic stents [26]. A randomized study of 50 patients comparing plastic and metal stents found no significant difference in terms of clinical success (91% vs 87%) and adverse events [27]. Of note, procedure times were significantly shorter with the use of metal biliary stents (15 minutes vs 29.5 minutes) [27].

A systematic review of seventeen studies using plastic and metal stents used for transmural drainage for pseudocysts found no significant difference in overall treatment success for both pseudocysts (81% vs 82%) and WON (70% vs 78%), respectively [28]. The majority of patients with metal stents were treated using fully covered biliary metal stents. Overall there has been no significant difference in adverse events and recurrence between plastic and metal stents [28]. However, fully covered stents have been shown to have an advantage over plastic stents given the need for fewer stents for pseudocyst drainage [29]. In addition, metal stents have been used with the idea that a greater stent diameter would facilitate improved drainage. The need for improved drainage is apparent when examining the utility of plastic stents for WON. Varadarajulu, et al [30] demonstrated an almost 30% reduction in success when using plastic stents for WON (63%) as compared to pseudocysts (93%). Also, adverse events in endoscopic drainage of



Fig. 2. Walled-off necrosis with necrotic material being accessed through a cystogastrostomy. (Color version of figure is available online.)

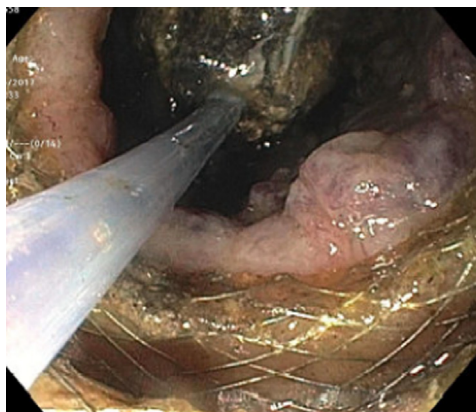


Fig. 3. A lumen-apposing metal stent (AXIOS) in place via cystogastrostomy into an area of walled-off necrosis through which endoscopic necrosectomy is performed. (Color version of figure is available online.)

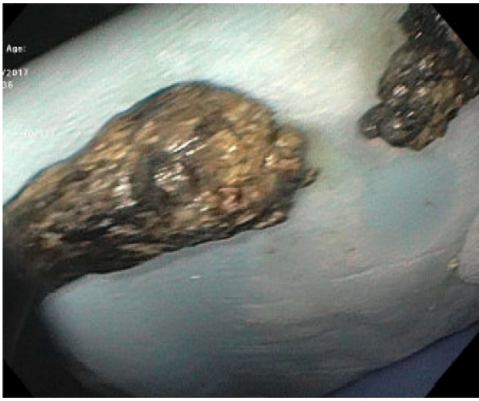


Fig. 4. Necrotic debris removed via endoscopic necrosectomy. (Color version of figure is available online.)

necrosis were significantly greater than when drainage of pseudocysts were pursued (15.8% vs 5.2%) secondary to rates of postprocedural infection, bleeding, and perforation [31]. The disadvantage of biliary metal stents is the risk of stent migration which have been reported to be as high as 15% [32].

2.1.1. Lumen-apposing metal stents

LAMS in comparison to covered self-expanding biliary metal stents have antimigratory features which are thought to reduce the chance of migration. There is a large flange at both ends of the stent (Figure 5). The stent is placed with one set of phalanges inside the fluid collection and other in the stomach or small intestine. LAMS are short in length and were specifically designed for purposes of draining fluid collections, whereas covered self-expanding metal stents are predominantly covered biliary metal stents designed for biliary drainage. The advantage of LAMS over covered biliary stents include the large working diameter of 10–15 mm which allows for manual extraction of necrotic debris [31]. A retrospective study evaluating the effectiveness of FCSEMS including biliary and lumen-apposing stents in both pseudocysts and WON found overall technical success in 97% of patients with overall adverse events of 21% including infection (11%), bleeding (7%), and stent migration, or perforation (3%) [33]. Different types of FCSEMS did not seem to effect clinical outcome [33]. It is not surprising that LAMS were not found to be superior to metal biliary stents or even plastic stents given the already high rate of success of pseudocyst drainage with the latter 2 modalities.

However, the utility of LAMS is perhaps more apparent when examining its performance in WON. A randomized trial comparing LAMS to two 7-Fr double pigtail stents in WON found greater rate

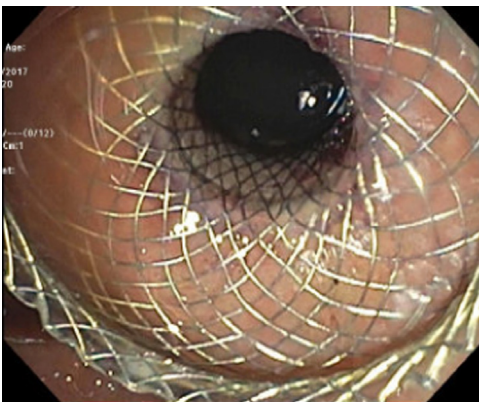


Fig. 5. A lumen-apposing metal stent (AXIOS) was placed into the cyst through a cystogastrostomy. (Color version of figure is available online.)

of adverse events in patient who had LAMS (50% vs 0%) [34]. Adverse events included delayed bleeding, buried stent syndrome, and obstructive jaundice secondary to stent-induced biliary stricture [34]. It has been theorized that the relative immobility and short length (10 mm) of LAMS compared to plastic stents likely lends itself to these greater complications [34]. However, in a larger study evaluating LAMS in both WON and pseudocysts, found the stent-related adverse event rate to be 10.3% in patients with WON [35]. There were no cases of delayed hemorrhage [35]. In addition, Sharaiha et al [36] demonstrated LAMS had high technical and clinical success for patients with WON with an overall adverse event of 18.5%. Stent migration only occurred in 5% of patients and all occurred during necrosectomy [36]. Multivariate analysis demonstrated clinical success to be six times more likely if a larger stent diameter was used (15 mm) [36]. Another potential advantage of LAMS over plastic stents is the significant shorter procedure times (25 minutes vs 43 minutes) [37]. Though high rates of technical and clinical success with LAMS has been demonstrated the different rates of procedural related complications for LAMS require standardization of endoscopic technique including number and size of fluid collections, diameter of stents used, and percentage of necrotic debris to allow for comparison between trials.

3. Multimodal techniques to facilitate drainage and debridement

3.1. Nasocystic irrigation

Before the advent of LAMS nasocystic drain placement was used in conjunction with plastic stents to facilitate extraction of necrotic debris as well as for pseudocyst drainage albeit with low quality of evidence. A retrospective study examining the use of nasocystic drainage with plastic stents vs plastic stents alone demonstrated increased short-term success (85% vs 63%) and decreased stent occlusion rates (13% vs 33%) in WON when using both modalities [38]. In this small case series, hydrogen peroxide was the fluid used for irrigation. The practice of nasocystic drainage for pseudocysts was analyzed by a Cochrane review but study results were limited by few trials and high risk of bias. Nonetheless, they found patients who underwent EUS-guided and nasocystic drainage had fewer adverse events, shorter hospital stays, and lower need for additional invasive procedures as compared to EUS-guided drainage alone [39]. Consequently, the use of nasocystic drainage along with plastic stents for pseudocysts seems to be based on local expertise and institutional norms than high-quality evidence. Given the greater stent diameter of LAMS the need for nasocystic drainage for WON will require re-evaluation but is still being performed given the lack of comparative and randomized trials.

3.1.1. Multiple transluminal gateway technique

For WON, and specifically if there is presence of necrotic debris, the need for improved drainage is paramount. Varadarajulu et al [40] demonstrated the benefits of multiple transluminal gateway technique (MTGT) for WON which included the creation of 2–3 transmural tracts. One tract was used for irrigation of normal saline via a nasocystic catheter while multiple plastic stents were placed in the other tracts [40]. Patient who underwent MTGT had improved overall success when compared to conventional transmural drainage via plastic stents for WON (92% vs 52%) [40]. In addition, there were no adverse events in the MTGT group compared to a 10% complication rate in the conventional group [40]. MTGT may result in a reduced need for endoscopic necrosectomy and requires further study.

4. Conclusion

Transpapillary endoscopic retrograde pancreatography drainage as well as conventional transmural drainage of pseudocysts can be performed safely and with high rates of technical success but mainly for small pseudocysts. However, EUS drainage has been shown to be of benefit even in the presence of luminal compression over non-EUS-guided drainage [15]. EUS-guided drainage can improve technical success in the absence of luminal compression, atypical location of pseudocysts, and decrease bleeding especially in patients with portal hypertension [3]. In addition, EUS-guided drainage can confirm the presence of a pseudocyst in real time as well help discern between a pseudocyst and a potential malignant fluid collection. In WON, the benefit of EUS include the ability to ascertain the presence of loculated collections as well as necrotic debris that may lead to further therapeutic procedures such as endoscopic necrosectomy.

Endoscopic drainage of WON is a complex endeavor with reduced rates of technical success as compared to pseudocysts, however, is an option for patients in part because of the increased morbidity and mortality of pursuing surgical drainage [41]. Endoscopic drainage of pseudocysts and WON have not been standardized and newer devices including LAMS have the potential to decrease the number of interventions needed, procedure times, and hospital days. Plastic stents for WON have lower rates of success as compared to metal biliary stents and LAMS, however, LAMS carry a higher rate of stent migration and stent complications as compared to plastic stents. Whether the use of concomitant nasocystic drainage should be performed or is safer than LAMS use solely has yet to be determined. Newer techniques including MTGT have the potential to decrease the need for direct endoscopic necrosectomy and may be beneficial for patients with minimal necrotic debris. Further comparative trials and standardized patient groups are required before particular endoscopic techniques or stents can be considered customary practice.

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