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Endoscopic Management of Pancreatic Fluid Collections: An Update

Zaheer Nabi and D. Nageshwar Reddy

Abstract

Pancreatic fluid collections (PFCs) are a frequent complication of acute pancreatitis. PFCs have been categorized according to their content and duration after an episode of pancreatitis. Acute collections (<4 week) and asymptomatic late collections (>4 weeks) can be usually managed conservatively. Late collections including walled off necrosis (WON) and pancreatic pseudocysts (PP) have a well-defined wall. Consequently, it is easier and safer to drain these collections when required. The most common indication to drain PFCs is infection and the available means of drainage include surgical, endoscopic, and percutaneous. Open surgical interventions carry a high risk of morbidity and mortality. Therefore, in the current era, a step up approach is preferred to minimize morbidity over the more aggressive surgical treatments. Endoscopic step-up approach is effective and favored over minimally invasive surgical or percutaneous drainage due to reduced risk of organ failure and external pancreatic fistula. However, the approach to PFCs should be individualized for optimal outcomes. A small subgroup of patients does not respond to endotherapy or percutaneous interventions and requires open surgical debridement. Similarly, not all PFCs are amenable to endoscopic drainage and demand alternative modalities like percutaneous or minimally invasive surgical drainage.

Keywords: pancreatitis, pseudocyst, walled off necrosis, drainage, endoscopy

1. Introduction

Acute pancreatitis is mild in majority of the cases and categorized as interstitial edematous pancreatitis. About 15–20% of cases develop necrotizing pancreatitis involving necrosis of variable proportion of pancreatic parenchyma. Pancreatic fluid collections (PFCs) are a common local complication of acute pancreatitis. PFCs have been classified according to the revised Atlanta criteria based on duration (<4 or >4 weeks) and contents of fluid collection [1]. Acute collections include acute pancreatic or peri-pancreatic fluid collections (APFCs) and acute necrotic pancreatic fluid collections (ANPFCs) which develop after acute interstitial and acute necrotizing pancreatitis, respectively (**Figure 1**). APFCs and ANPFCs get walled off after about 4–6 weeks into pseudocysts and walled off necrosis (WON), respectively. By definition, pseudocysts have clear contents and WON consists of variable amount of necrotic debris (**Figures 2 and 3**).

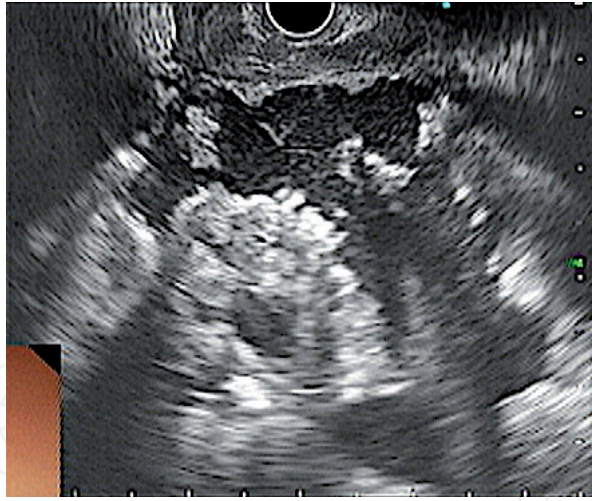


Figure 1.
Endosonographic image of acute necrotic pancreatic fluid collections. Note the ill-defined boundaries and the solid component within the fluid collection.

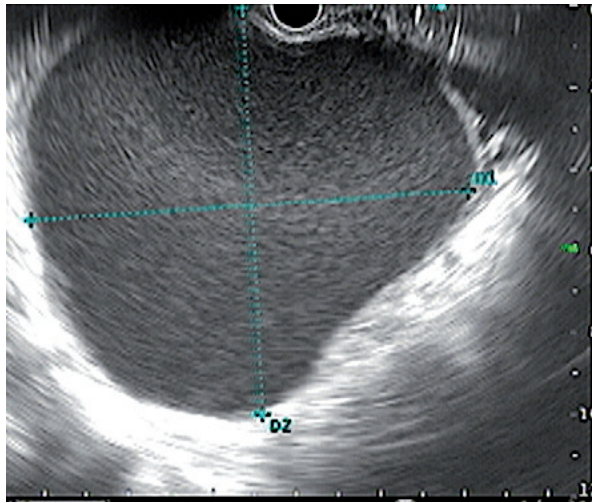


Figure 2.
Endosonographic image in a case with pancreatic pseudocyst. Note the well-defined boundaries without any echogenic debris in the cyst cavity.

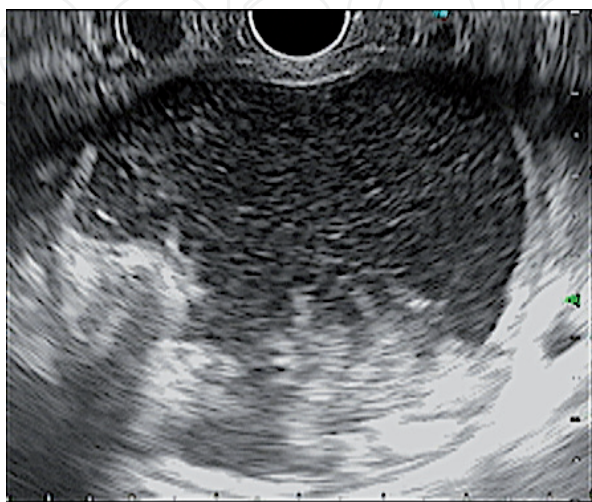


Figure 3.
Endosonographic image in a case with walled off necrosis. Note the well-defined boundaries with echogenic necrotic debris in the cyst cavity.

1.1 Natural history of pancreatic fluid collections

APFCs develop in about 20–40% of patients after acute interstitial pancreatitis [2–4]. Majority (~90%) of APFCs resolve and do not transform into pseudocyst. Moreover, majority of the pseudocysts resolve or reduce in size with time and therefore, do not require an intervention [4]. On the other hand, majority (90–100%) of the patients with acute necrotizing pancreatitis develop ANPFCs. Nearly half of the patients with ANPFCs develop walled off necrosis (WON) [2, 3]. The natural history of WON is not well known and appears to be more unpredictable than pseudocysts. An intervention may be required in one quarter to more than half of the patients with WON [2, 3].

2. Management of pancreatic fluid collections

The options of drainage for PFCs include surgery, percutaneous catheter drainage, and endoscopic transmural drainage (ETD). Open necrosectomy is associated with substantial rates of new onset multiple organ failure as compared to minimally invasive surgical step up approach (see later) [5]. Subsequent studies comparing endoscopic necrosectomy to open as well as minimally invasive surgical debridement concluded the superiority of endoscopic approach [6, 7]. Reduced mortality, less frequent new onset multiple organ failure, and the development of pancreatic fistulas are distinct advantages of endoscopic necrosectomy [8, 9]. In the current era, a step up approach is preferred for its obvious benefits in reducing a pro-inflammatory response and prevention of new onset organ failure. In the ensuing sections, we would discuss endoscopic approach to PFCs and its advantages over surgical and percutaneous drainages.

2.1 Endoscopic drainage of PFCs

Characterization of PFCs into pseudocysts and WON is important prior to ETD. WON has variable amount of necrotic debris and therefore, has a protracted course and more frequent requirement of re-interventions as compared to pseudocysts (**Figures 2 and 3**). Computed tomography is frequently used to localize the site of collection. However, it may not accurately differentiate between the solid and liquid contents of the collection (**Figures 4 and 5**). Magnetic resonance imaging (MRI)

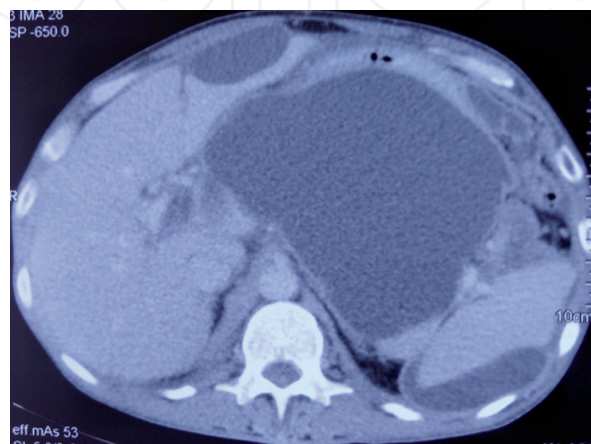


Figure 4.
CT image in a case of pancreatic pseudocyst. Note the well-defined boundary and clear contents of the cyst.

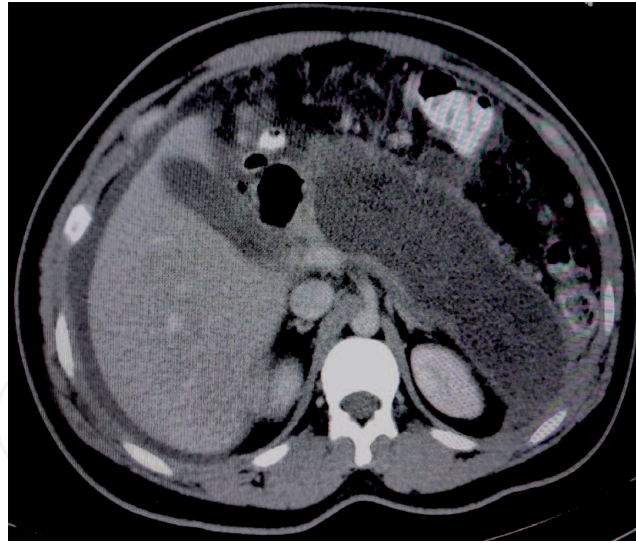


Figure 5. *CT image in a case of walled off necrosis replacing almost entire pancreas. Note that the necrotic contents of the cyst cavity are not obvious in CT image.*

and endoscopic ultrasound (EUS) are better imaging modalities for qualitative assessment of PFCs. We perform both CECT and EUS to define the anatomical relation of PFCs to the lumen and characterize them into pseudocyst or WON, respectively.

The technique of endoscopic drainage of PFCs involves the following steps: puncture of the cysto-gastric or cysto-duodenal wall using a 19 gauge needle and aspiration of cyst contents, coiling of guidewire within the cyst cavity under fluoroscopy guidance, dilatation of the tract using cystotome and balloon and deployment of plastic or metal endoprostheses. EUS guided drainage is preferred to endoscopic approach as intervening vessels can be avoided and non-bulging collections can be targeted under vision [10].

The success rate of ETD with or without endoscopic necrosectomy ranges from 80 to 95% in recent studies [11–19] (**Table 1**). The outcomes of ETD of PFCs is variable in literature presumably due to heterogeneity in the nature of collection, that is, pseudocyst or WON, type of stent used, and whether necrosectomy is performed or not [20]. In addition, the presence of disconnected pancreatic duct (DPD) may impact the outcomes of ETD. The requirement of hybrid treatment, re-interventions, recurrences, and rescue surgery appear to be higher in the patients with DPD [21].

ETD of PFCs is safe, and major complications are uncommon. Complications related to ETD occur in 10–40% of patients with WON [22]. Supra-infection of the cyst cavity is the most common significant complication associated with ETD. Occlusion of the stent with necrotic debris and inadequate drainage may lead to sepsis. In such situations, de-clogging of the metal stent, cyst lavage with saline or diluted hydrogen peroxide and direct endoscopic necrosectomy (DEN) are often helpful. Other complications associated with ETD include bleeding and perforation. Recent studies have drawn attention towards the relatively high incidence of bleeding especially with the use of large caliber metal stents (LCMS) [23–25]. Since, majority of the bleeding episodes occurred ≥ 3 weeks after the deployment of LCMS, the current trend is to remove LCMS between 2 and 3 weeks in cases of resolution of PFC [24].

2.2 Endoscopic transmural drainage: choice of stents

Endoscopic drainage of PFCs can be performed using pigtail plastic stents or metal stents. Plastic stents have been effectively used for the drainage of PFCs for

	N	PFC	Type of stent	Success	Recurrence	Adjuvant PCD or Sx	Complications
Walter et al. [11]	61	PC 15 WON 46	LAMS (AXIOS)	93% 81%	NR	Sx 6.5%	Infection 6.5% Perforation 1.6%
Siddiqui et al. [12]	82	PC 12 WON 68	LAMS (AXIOS)	100% 88.2%	1.2%	PCD 5%	Stent mal-deployment 2.5% Bleeding 7.5%
Sharaiha et al. [13]	124	All WON	LAMS (AXIOS)	86.3%	4.8%	10.5%/2.4%	Infection 3.2% Stent occlusion 4% Stent migration 2.4% Bleeding 1.4%
Lakhtakia et al. [14]	205	All WON	Biflanged (Nagi)	96.5%	2.4%	1%/1%	Bleeding 2.9% Perforation 1%
Venkatachalapathy et al. [15]	116	PC 46 WON 70	LAMS (AXIOS)	94%	0.86%	2.5%/–	Sepsis 6% Stent occlusion 0.86% Migration 0.8% Bleeding 0.86% Death 1.7%
Dhir et al. [16]	88	All WON	Biflanged (Nagi)	80.7%	9.1%	Sx 1.1%	Fever 13.6% Stent migration 2.3% Bleeding 3.4%
Yang et al. [17]	122	PC 58 WON 64	LAMS (AXIOS)	96.5% 62.3%	NR	Sx: 3.3% WON	Bleeding 3.3% Infection 4.8%
Kumta et al. [18]	192	PC 41 WON 151	LAMS (AXIOS)	92.6%	3.7%	7.3%/3.1%	Bleeding 5.7% Perforation 2.1% Infection 2.1%
Teoh et al. [19]	59	PC 20 WON 39	LAMS (SPAXUS)	100%	3.4%	None	Bleeding 5.1% Perforation 1.7%

PFC, pancreatic fluid collection; PC, pseudocyst; WON, walled off necrosis; Sx, surgery; PCD, percutaneous drainage; NR, not reported; LAMS, lumen apposing metal stent.

Table 1.
Outcome of endoscopic transmural drainage in pancreatic fluid collections using large caliber metal stents.

several decades now. The proposed advantages of plastic over metal stents include lower cost, less risk of delayed bleeding, and ability to keep them for long term in cases with DPD. On the other hand, metal stents have wider lumen, allowing efficient drainage of the necrotic material and endoscopic necrosectomy when required. Conventional fully covered metal stents used initially were suboptimal due to their longer lengths and lack of lumen apposing properties. The development of novel LCMS has widened the therapeutic armamentarium for ETD of PFCs. Newly developed LCMS have either lumen apposing (AXIOS, Xlumena, Mountain View, CA, United States and Niti-S SPAXUS, TaeWoong Medical Co., Ltd., Ilsan, South Korea) properties or flared ends (NAGI, Taewoong Medical Co, Ilsan, South Korea) to prevent stent migration [10]. As compared to the conventional metal stents, the use of LCMS is associated with superior outcomes in terms of number of procedures required for the resolution of WON [26]. Similarly, better clinical outcomes and reduced requirement of endoscopic necrosectomy have been found with the use of metal stents as compared to plastic stents in several studies [27–30]. In a large, multicenter study including 189 patients with WON, the use of LCMS was associated with higher clinical success (80.4 vs. 57.5%), shorter procedure time, lower need for surgery (5.1 vs. 16.1%), and lower rate of recurrence as compared to plastic stents [31]. However, the superiority of LCMS is not uniform across the published studies. In a randomized trial, there was no significant difference in the treatment outcomes including the total number of procedures performed, treatment success, and readmissions between LCMS and plastic stent groups in patients with WON [24]. In addition, the treatment cost (LCMS: US\$12155 vs. plastic stents: US\$6609) and stent related adverse events were higher in the LCMS group (32.3 vs. 6.9%, $p = 0.01$) [24]. Several systematic reviews and meta-analyses draw conflicting conclusions while comparing plastic stents vs. metal stents for ETD of PFCs [32–37]. In three of the published systematic reviews and meta-analyses, metal stents were found superior to plastic stents for both pseudocysts as well as WON in terms of clinical success and adverse events [34, 36, 32]. On the contrary, two other systematic reviews and meta-analyses did not find a difference in the outcomes between metal or plastic stents [33, 37]. It must be emphasized that the paucity of randomized trials is the major limitations of these reviews.

The current trend is to use metal stents for WON with significant debris. These cases may require more frequent re-interventions including endoscopic necrosectomy for which LCMS are ideal. Whereas, plastic stents are a cost effective alternative in pseudocysts or WON with minimal necrotic contents. Randomized trials are warranted before concluding the superiority of metal stents for the management of PFCs.

2.3 Endoscopic necrosectomy

Endoscopic necrosectomy essentially comprises of endoscopic debridement of necrotic debris within the cyst cavity using a variety of methods including DEN and naso-cystic lavage with saline and or diluted hydrogen peroxide (3%, 1:10 dilution). DEN involves the passage of endoscope within the cyst cavity followed by mechanical removal of necrotic tissue using forceps, polypectomy snares, and retrieval nets [38]. With the availability of LCMS (≥ 15 mm), multiple sessions of DEN can be performed with relative ease. However, there is no dedicated device or accessory for DEN and therefore, the process is cumbersome and time consuming. Recent development of new devices to facilitate endoscopic debridement is likely to make DEN less cumbersome and more efficacious [39, 40].

DEN is safe and effective in about 80–90% of patients with WON. However, DEN may be associated with substantial complications. In a systematic review, the

overall rate of adverse events and mortality associated with endoscopic necrosectomy were 22% and 5%, respectively. The complications reported with DEN include air embolism (0.4%), bleeding (11%), and perforation (3%) [41]. Therefore, DEN is usually performed in cases with no improvement after ETD alone.

Our group re-defined the endoscopic step-up approach in patients with WON. This approach includes cyst cavity lavage using nasocystic catheter and de-clogging of the metal stent as intermediate steps after transmural placement of metal stent and before proceeding to endoscopic necrosectomy [14]. With this approach, endoscopic necrosectomy can be avoided in the vast majority of patients with WON.

2.4 Step-up approach for walled of necrosis

Open surgery is associated with a high morbidity and mortality in patients with WON. Consequently, minimally invasive surgical or endoscopic approaches have virtually replaced open necrosectomy in these patients [6]. The available evidence favors a step-up approach over the conventional techniques [7, 42–44]. In general, minimally invasive surgical step-up approach consists of percutaneous drainage followed by (if necessary) video assisted retroperitoneal debridement (VARD). Whereas, endoscopic step up approach includes ETD followed by (if necessary) endoscopic necrosectomy. Percutaneous catheter drainage can be used as an adjunct to ETD in cases with incomplete response or large collections with extension into paracolic gutter (**Figure 6**).

Several trials have compared endoscopic versus minimally invasive surgical methods of drainage in cases with WON [7, 45]. In a randomized trial by the Dutch Pancreatitis Study Group, there was no difference in the incidence of major complications or mortality between the endoscopic or minimally invasive surgical step-up approach (endoscopy: 43% vs. surgery: 45%, $p = 0.88$) [7]. However, the rate of



Figure 6.
Large pancreatic fluid collection extending into pelvis.

pancreatic fistulas (5 vs 32%, $p < 0.01$) and the length of hospital stay were lower in the endoscopy group [7]. In another randomized trial including 66 patients with infected WON, ETD was associated with significantly reduced major complications (0.15 vs. 0.69), lowered costs (75,830 \$ vs. 117,492 \$), lower incidence of pancreatic fistula (0 vs. 28.1%), and increased quality of life as compared to minimally invasive surgery [45]. In a recent systematic review including two randomized trials and four observational studies, ETD was associated with lower mortality, risk of major organ failure, adverse events, and length of hospital stay [44]. These trials suggest that endoscopic step-up approach should be preferred over minimally invasive surgical step-up approach for the management of PFCs.

2.5 Endoscopic vs. surgical drainage: pseudocysts

Endoscopic and surgical cyst-gastrostomy have been compared in several studies [46–50]. Initial non-randomized trials found surgical drainage to be superior to endoscopic drainage of pseudocysts [50]. However, subsequent randomized studies concluded that endoscopic drainage achieves similar outcomes as compared to surgical drainage [46, 49, 47]. In addition, EUS guided cyst-gastrostomy is less invasive, cost saving, and associated with a shorter length of a post procedure hospital stay when compared with surgical cyst-gastrostomy [46, 47]. In a recent systematic review and meta-analysis including six studies (342 patients), there was no significant difference between surgical and endoscopic treatment success rates, adverse events, and recurrence for pancreatic pseudocysts [51]. To conclude, the current evidence suggests that endoscopic drainage is as efficacious as surgical cyst-gastrostomy for pseudocysts with shorter hospital stay and reduced costs.

2.6 Endoscopic vs. percutaneous drainage

Percutaneous catheter drainage remains an important modality even in the era of minimally invasive endoscopic or surgical treatments. In different studies, percutaneous drainage alone was successful in 35–50% of cases with WON [52]. Percutaneous drainage can be used as an adjunctive to endoscopic drainage in selected cases with large PFCs extending into paracolic gutters or pelvis. In addition, percutaneous drainage is useful in acute or ill-defined PFCs (<4 weeks) where endoscopic drainage may not be feasible. Percutaneous tract can also be utilized for endoscopic and VARD [43]. Having described all the major advantages of percutaneous catheter drainage, the major limitation remains the development of external pancreatocutaneous fistula which may be difficult to treat.

As compared to percutaneous approach, endoscopic drainage is associated with significantly better clinical success, a lower re-intervention rate, and a shorter hospital length of stay [53]. Therefore, percutaneous drainage is only performed in cases where either endoscopic drainage is not available or not feasible (ill-defined or distantly located collections).

2.7 Dual modality drainage

Dual modality drainage (DMD) involves the simultaneous or sequential use of endoscopic and percutaneous approaches for symptomatic PFCs. Several studies have concluded the utility of DMD in symptomatic PFCs especially WON [54, 55]. The proposed advantages of this technique include a quicker recovery and reduced chances of forming an external pancreato-cutaneous fistula. In the study by Gluck et al., the use of DMD was associated with reduced length of hospital stay, and less requirement of radiological or endoscopic interventions [55].

This technique may be especially useful in cases with large WON especially those extending into the paracolic gutters [56]. In these cases, transmural approach alone may not provide adequate drainage in these patients (**Figure 6**).

2.8 Trans-papillary drainage of PFCs

Trans-papillary drainage (TPD) of PFCs may be useful in certain scenarios as follows: (a) small size of cyst (<5 cm) communicating with main pancreatic duct (PD), (b) as an adjunct to ETD in cases with PD leak or disconnected PD, (c) chronic pancreatitis with an obstructed PD communicating with a pseudocyst, and (d) management of external pancreatic fistula after percutaneous or surgical drainage [22]. When used as a primary modality, TPD provides the path of least resistance for the pancreatic juice, thereby diverting it away from the cyst. There is a potential of cyst infection with TPD and therefore, antibiotics should be routinely given to these patients. TPD may be useful in preventing recurrences of PFCs following ETD in cases with PD leak and disconnected PD [57]. We do not routinely perform TPD as an adjunct to ETD in all the cases. In our practice, we evaluate the PD anatomy using an magnetic resonance cholangiopancreatogram (MRCP) prior to removal of stents placed during ETD. In cases with a PD stricture, leak or disconnection we attempt placing a trans-papillary PD stent. Subsequently, trans-papillary stents are removed or exchanged (as per the PD morphology) after 4–6 weeks. However, trans-papillary stenting may not be always feasible especially in cases with a disconnected PD. In these cases, transmural plastic stents can be left in situ and metal stents can be exchanged with plastic stents [58]. However, the latter approach needs to be substantiated by high quality randomized studies. Nevertheless, metal stents should be removed between 2 and 4 weeks irrespective of the PD anatomy due to the risk of buried stent syndrome and delayed bleeding.

2.9 Endoscopic drainage of PFC in children

The literature regarding the efficacy of endoscopic drainage of PFCs in children is sparse. Unlike adults, the feasibility of drainage using an adult duodenoscope or EUS scope is questionable in smaller children. Nevertheless, emerging data indicates that EUS-guided drainage is feasible and effective in children with PFCs [59–63]. Our group evaluated the long-term outcomes in 30 children with PFCs using pigtail plastic stents [60]. Clinical success was documented in 93% of children at a median follow up of 829 days. The use of novel metal stents has also been described in pediatric age group [62, 61]. Nabi et al. used novel bi-flanged metal stents in 21 children with WON. Metal stents could be successfully placed in all the children, and clinical success was achieved in 95% of children [62].

3. Recent advancements

The technique of ETD of PFCs using metal stents requires a series of steps including needle puncture, coiling of guidewire in the cyst cavity, balloon dilatation of the cystogastric tract, and finally, deployment of stent. With the availability of electrocautery-enhanced delivery systems, the deployment of metal stents can be achieved in a single step [64, 65]. Therefore, the drainage of PFCs using these “Hot Devices” is quicker and simpler. Currently, the electrocautery-enhanced delivery system is available with lumen apposing (Hot *AXIOS*) as well as biflanged metal stents (Hot *NAGI*).

4. Individualized approach to pancreatic fluid collections

The management of PFCs requires an individualized approach based on their maturity (acute or well defined), contents, and anatomical location in relation to gastroduodenal wall (**Figure 7**). Asymptomatic PFCs do not require drainage irrespective of their size. Similarly, symptomatic and ill-defined APFCs are managed conservatively with antibiotics (if necessary), nutritional support, and analgesics initially. In non-responders, percutaneous drainage is a reasonable next step in acute collections.

Mature PFCs with a well-defined wall and in close proximity to gastroduodenal wall can be managed endoscopically using plastic or metal endoprostheses in majority of the cases. We prefer LCMS in PFCs containing substantial necrotic debris identified on EUS or MRI. Occasionally, the PFC is situated away (>1–1.5 cm) from the gastroduodenal wall and not amenable to endoscopic drainage. In these cases, percutaneous or minimally invasive surgical drainage (e.g., VARD) are alternatives.

Subsequent interventions are carried in a step-up fashion based on the persistence of significant symptoms. Endoscopic or percutaneous necrosectomy is performed in non-responders who underwent ETD or percutaneous drainage, respectively, as the primary mode of drainage. We prefer intermediary steps including naso-cystic lavage and de-clogging of LCMS before proceeding to DEN. In our experience, only a minor fraction of cases require DEN with this approach [14]. Some cases do not respond to the aforementioned minimally invasive step-up approach and require an open surgical debridement.

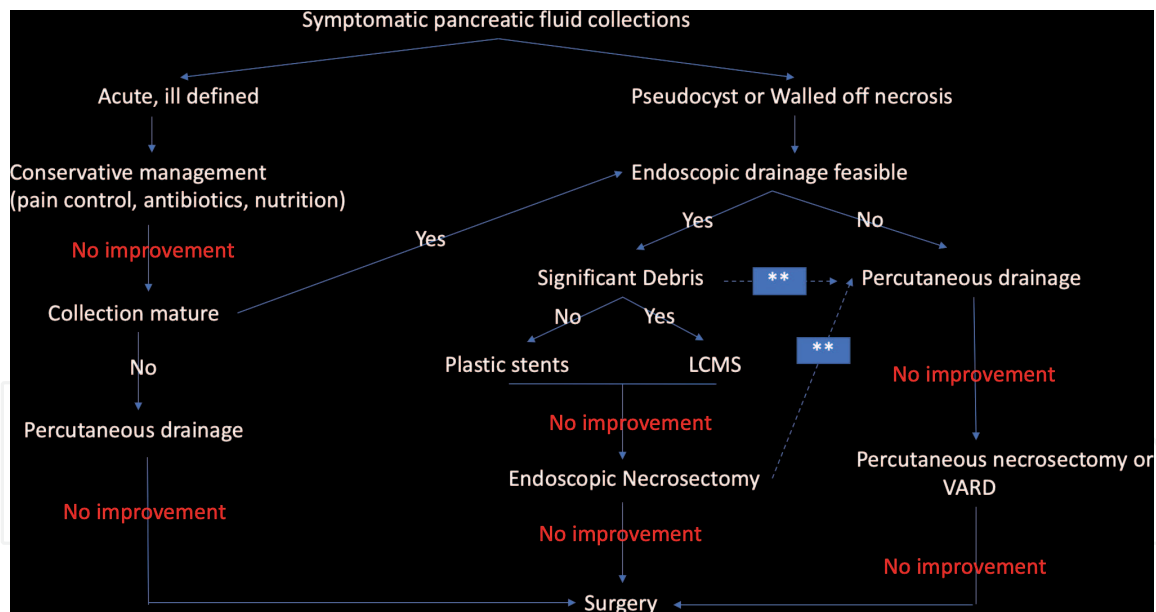


Figure 7.

*Approach to symptomatic pancreatic fluid collections. VARD, video-assisted retroperitoneal debridement; LCMS, large caliber metal stent; **percutaneous drainage can be performed either simultaneously with endoscopic transmural drainage or sequentially in non-responders.*

5. Conclusions

The management of PFCs requires a multidisciplinary approach involving experienced endoscopists, interventional radiologists, pancreatic surgeons, and nutritionists. Endoscopic drainage is the preferred first line approach to symptomatic and infected PFCs. Percutaneous drainage is useful in selected scenarios and can complement the benefits of endotherapy in large collections extending toward

pelvis. The approach to PFCs should not be rigid and should be individualized for each patient. In general, a step-up approach minimizes the morbidity associated with open surgical drainage and is usually successful in majority of the patients. However, some cases do require open surgical debridement despite of all the recent advancements in endotherapy.

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