REVIEW ARTICLE

JOURNAL OF PANCREATOLOGY

OPEN

Management of pancreatic fluid collections in patients with acute pancreatitis

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Abstract

Acute pancreatitis is associated with development of pancreatic fluid collections (PFCs). Acute PFCs that develop in interstitial edematous pancreatitis mostly resolve but some may persist and evolve into pseudocysts. Acute necrotic collections occurring in acute necrotizing pancreatitis generally persist and evolve into walled-off necrosis (WON) after 3 to 4 weeks. Most acute fluid collections do not require drainage unless they are large and cause compression of adjacent organs, contribute to increase in intraabdominal pressure or become infected. Acute infected collections can be managed with antibiotics and percutaneous drainage but may require necrosectomy either by minimally invasive surgical or endoscopic methods such as video-assisted retroperitoneal debridement and percutaneous endoscopic necrosectomy. Mature sterile collections, that is, pseudocyst and WON with a defined wall are best treated by internal transmural drainage which can be achieved either by per-oral endoscopic or surgical, preferably laparoscopic, method. Of late, infected PFCs are increasingly being treated with an endoscopic step-up approach that has been shown to be better than minimally invasive surgical step-up approach in terms of lesser complications. Use of lumen apposing metal stents during endoscopic drainage has emerged as an attractive option that facilitates necrosectomy in infected WON.

Keywords: Acute pancreatitis, Infected pancreatic necrosis, Necrosectomy, Pancreatic fluid collections, Walled-off necrosis

Introduction

Acute pancreatitis (AP) is an acute inflammatory condition of the pancreas that may be associated with both local and systemic complications. Two major forms of AP occur: interstitial edematous pancreatitis and necrotizing pancreatitis. Interstitial pancreatitis is a mild disease while necrotizing pancreatitis with pancreatic and/or peripancreatic necrosis generally runs a more severe course. In patients with severe pancreatitis, local inflammatory process escalates to systemic level. Systemic inflammation presenting initially as systemic inflammatory response syndrome may cause organ failure with a mortality of up to 40%.[1,2] The extent of local injury, that is, necrosis correlates with systemic injury and organ failure.[3,4]

As a part of the local inflammatory process, fluid collections may develop in and around the pancreas. The type of fluid collections are generally classified as per the revised Atlanta classification[5]: (i) acute pancreatic fluid collections (PFCs) occur in interstitial edematous pancreatitis. These may either resolve spontaneously or evolve into a pancreatic pseudocyst after around 4 weeks with a well defined mature wall. Pseudocyst contains predominantly pancreatic fluid with little or no necrotic debris and is typically extrapancreatic (ii) acute necrotic collections (ANCs) occur in early phase of acute necrotizing pancreatitis. ANC usually evolve into a localized collection termed as walled-off necrosis (WON) after around 4 weeks which is surrounded by a radiologically identifiable wall. The fluid collections, collectively termed "Pancreatic Fluid Collections" (PFCs) may remain sterile or get infected.

There has been a paradigm shift in the management of PFCs in patients with AP in the last 2 decades due to better understanding of their pathophysiology and natural course of the disease, and development in interventional endoscopy (Fig. 1). In 1980s, necrotizing pancreatitis was considered the domain of surgeons performing necrosectomy within 1 to 3 days of onset of illness.[6] A seminal paper by Bradley and Allen[7] in 1991 showed improved outcome of patients with sterile pancreatic necrosis treated with conservative therapy. Infected necrosis continued to be treated surgically until recently when conservative treatment was shown to be effective at least in a subset of patients.

The landmark study, PANTER trial by the Dutch pancreatitis group[8] demonstrated that minimally invasive approach is better than open necrosectomy in patients with acute necrotizing pancreatitis. Since then the focus has shifted to minimally invasive interventions.[9,10] We review here the current approaches for the management of PFCs.

Genesis of pancreatic fluid collections: critical location of pancreas

Pancreas is a retroperitoneal organ located posterior to the stomach. The head of the pancreas is in close contact with 1st, 2nd, and 3rd parts of the duodenum and medial border of right kidney. Body of the pancreas is separated from the stomach by the potential space "lesser sac" anteriorly and is in close contact with portal vein, inferior vena cava, and aorta posteriorly. Tail of

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Journal of Pancreatology (2019) 2:3

Published online 3 September 2019

http://dx.doi.org/10.1097/JP9.0000000000000026

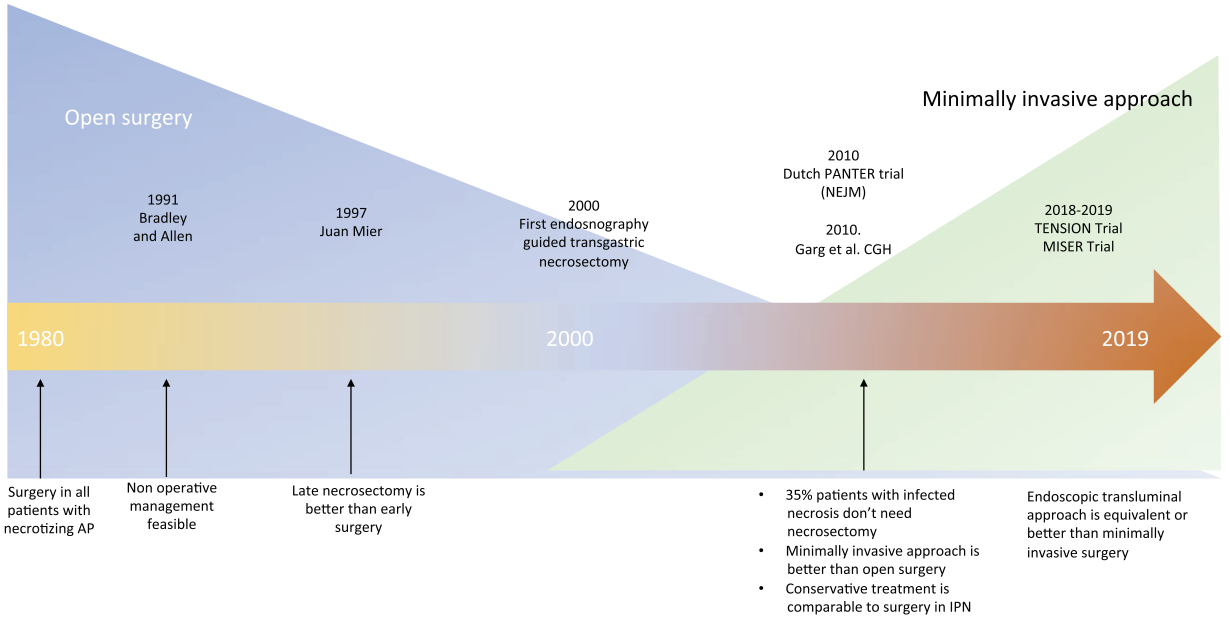

Figure 1. Paradigm shift in the management of acute pancreatitis over time.

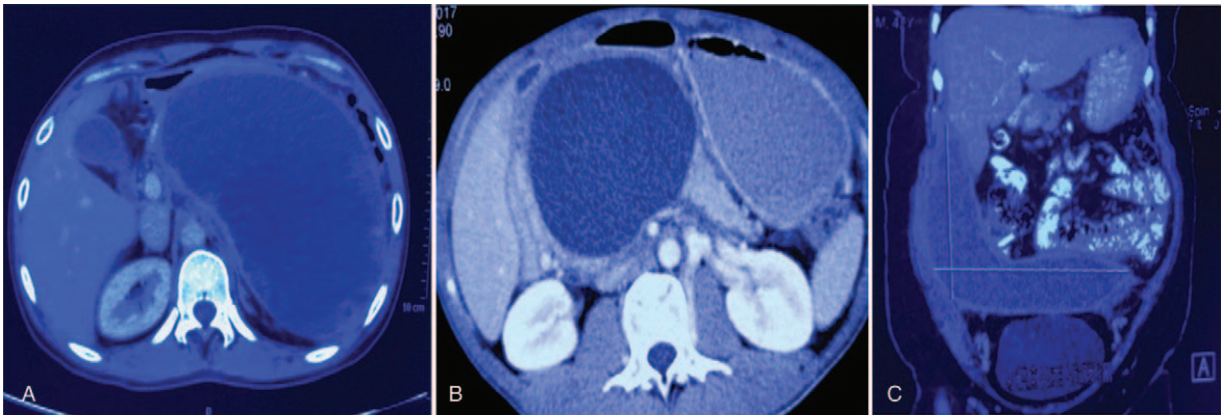

Figure 2. Location of peripancreatic fluid collections—(A) lesser sac, (B) subhepatic, (C) collections extending to paracolic gutters and pelvis.

the pancreas is in close contact with upper pole of left kidney and splenic hilum.

Smaller fluid collections develop due to inflammatory exudate, vascular leak, and possibly leak of pancreatic secretion. Large fluid collections develop primarily because of pancreatic ductal leak in necrotizing pancreatitis. The necrosed pancreatic parenchyma and/or peripancreatic fatty tissue is present within the fluid collection in WON and may gradually liquify. Fluid collections developing from body and tail of pancreas form in the lesser sac. These collections are in close proximity to posterior wall of the stomach and thus amenable for internal drainage into the stomach. PFCs may also extend to left paracolic space. Collections originating from the head and neck region are in close proximity to duodenum and may be amenable for cystoduodenostomy. At times, the collections may extend into the subhepatic space from the lesser sac through foramen of Winslow. Such subhepatic collections are intraperitoneal rather than retroperitoneal and there is a significant risk of peritoneal leak during endoscopic transmural drainage that may cause peritonitis. The collections may extend to either or both paracolic gutters retroperitoneally and at times to pelvis. These retroperitoneal collections are amenable to percutaneous drainage and necrosectomy such as through VARD (video-assisted retroperitoneal debridement) (Fig. 2).

Indications and timing of intervention in PFCs

The indications of drainage of PFCs are summarized in Table 1 and are irrespective of the route of drainage, that is, endoscopic, surgical, or radiological.

Acute necrotic collections

In the early phase of AP, sterile ANC generally do not require drainage unless there is intraabdominal hypertension. Infected ANC on the other hand, may require drainage even in early stage. Infected necrosis is diagnosed on the basis of clinical suspicion, imaging (i.e., extraluminal air in the collection on a computed

Table 1

Indications for intervention in pancreatic fluid collections (endoscopic, radiological, or surgical).

Indications
1. Clinical suspicion or documented infected necrotizing pancreatitis, preferably when necrosis has been walled off
2. In the absence of documented infection, ongoing organ failure for several weeks after the onset of acute pancreatitis, preferably when necrosis has been walled off
3. In sterile necrosis, gastric outlet, intestinal, and/or biliary obstruction due to pressure effect
4. In sterile necrosis, persistent symptoms (e.g., intractable pain, persistent unwellness) in patients with walled off necrosis
5. Disconnected Pancreatic Duct Syndrome with persisting/recurrent symptomatic collection

Adapted from Working group IAP/APA Acute Pancreatitis Guidelines.[11]

tomography scan), and culture. Clinical diagnosis of infected collection generally dictates the need for drainage rather than confirmation of infection by fine needle aspiration and culture, which has a risk of false negative result.[11] Since ANCs have mostly adherent and partially liquified debris, it is prudent to wait till the debris becomes organized and proceed with a step-up minimally invasive endoscopic or surgical approach later (usually after 4 weeks). Interventions of any kind within first few weeks may be associated with adverse outcomes and are reserved for infected necrosis in clinically deteriorating patients with AP. It is not clear whether to perform percutaneous drainage in patients with suspected infected pancreatic necrosis in the 2nd and 3rd week of illness. The general recommendation is to wait till about 4 weeks by which time the collections become walled off. However, early drainage has been shown to be effective if the clinical condition deteriorates with features of sepsis. A clinical trial is under progress at authors' institution to address this issue.

Pseudocyst and walled-off necrosis

Beyond 4 weeks of illness, symptomatic PFCs (pseudocyst/WON) require drainage. Asymptomatic PFCs do not require drainage irrespective of size, location, and extension.[12] An enlarging PFC may require drainage depending on the overall assessment of an individual patient. A mature wall is a pre-requisite for internal drainage. The wall of the collection usually matures after around 4 weeks.[11]

Early surgery is required for abdominal compartment syndrome, perforation of a hollow viscus and severe bleeding not amenable to angiographic control. Whenever exploratory laparotomy is performed for these conditions, it is prudent not to explore the lesser sac as there is a risk of introducing infection.[13]

Interventional techniques for drainage of PFCs

The management of PFCs requires a collaborative effort of a team comprising of an interventional radiologist, therapeutic endoscopist, and a surgeon. Various approaches for drainage include surgical (open surgery or VARD), endoscopic (endoscopic transmural drainage and endoscopic necrosectomy), and percutaneous drainage. A step-up approach consists of conservative treatment with antibiotics, placement of a percutaneous drain catheter followed by if required minimally invasive necrosectomy either VARD or endoscopic in patients with infected collections.[8,9] We have summarized the major studies comparing various approaches in Table 2.

Role of antibiotics

Before describing interventional techniques, let's first discuss the role of antibiotics. In patients with infected necrosis, antibiotics should be given to control infection. If signs of sepsis persist despite antibiotics after 48 to 72 h, interventional technique as described below should be considered for drainage of collections. In patients with sterile WON/pseudocyst requiring drainage, preprocedure antibiotic should be given to prevent infection of the sterile collection and it is continued usually for 3 to 5 days postprocedure. However, antibiotics should be used judiciously as development of multi-drug resistant infection is an independent predictor of mortality.[18] Prophylactic antibiotic therapy for prevention of infection in necrotizing pancreatitis should be discouraged. A meta-analysis of 7 studies comprising of 404 patients showed, no difference in mortality, infected necrosis rates and overall infection rates with and without prophylactic antibiotics.[19]

Percutaneous catheter drainage

Percutaneous catheter drainage (PCD) is generally used for draining acute collections and infected collections. PCD can be used as a primary modality, as an initial procedure in the step-up approach or as a salvage management of residual or infected collections. PCD catheter varies from 12 to 30 Fr in size and can be placed usually under computed tomograpy guidance either retroperitoneally or sometimes even transperitoneally. Retroperitoneal route is generally preferred as it avoids peritoneal contamination, bowel leaks and can be used later for VARD or percutaneous endoscopic necrosectomy. PCD is not preferred to drain sterile pseudocyst and WON because of the risk of fistula formation. The indications of drainage of acute fluid collections are raised intraabdominal pressure, pressure symptoms on adjacent organs, and infection.

A systemic review of 11 studies with 384 patients showed an overall success rate of 56% using PCD as primary drainage in patients with infected collections. Seventy percent of patients had infected necrosis and an average of 2 catheters were placed. Adverse events such as external fistulae occurred in up to 27% of patients.[20] A few studies have also shown successful outcome with conservative treatment of infected necrosis with intravenous antibiotics and selective percutaneous drainage without the need for necrosectomy.[21,22] A meta-analysis of 8 studies comprising 324 patients showed that intravenous antibiotics alone or in combination with PCD (conservative treatment approach) was successful in 64% of patients and only 26% patients required additional necrosectomy or surgery for complications.[18] In the PANTER trial,[8] 35% of patients with infected collections could be managed with PCD alone in the step-up approach arm.

Endoscopic approach

Endoscopic management of mature PFCs, that is, pseudocyst/WON is preferred in patients with AP. Endoscopic transmural

Table 2

Summary of some major studies comparing various therapeutic modalities in patients with necrotizing pancreatitis.

Author, year	Number of patients	Infected collections (%)	Timing of intervention (mean/ median days after presentation)	Intervention	Outcome and comments
1. Minimally invasive step up approach vs open necrosectomy					
a. Van Santvroot HC et al.[8] 2010 (PANTER Trial)	88	88 (100%)	29/30 Days	Open necrosectomy (45 patients) vs minimally invasive step up (43 patients) approach, RCT	Primary outcome was a composite of major complication or death which occurred in 69% in open necrosectomy vs 40% in step up approach group (risk ratio with step up approach 0.57, CI 0.38–0.87, $P=.006$) New onset multiple organ failure, incisional hernia, and new onset diabetes occurred less often in the step up approach
b. Hollemans et al.[14] 2019	73	73 (100%)		Long-term follow-up data of PANTER trial	Patients of PANTER trial were followed up for 86 months (median) 44% Patients died or had major complication in step up approach compared to 73% in open necrosectomy ($P=.005$) There was no difference in requirement of additional drainage or pancreatic surgery
2. Minimally invasive technique (VARD and endoscopy)					
a. Bakker et al.[15] 2012	22	21 (95%)	59 Days in surgical necrosectomy and 48 days in endoscopic transgastric necrosectomy	Endoscopic transgastric necrosectomy (10 patients) vs surgical necrosectomy (12 patients), RCT	Composite clinical outcome (major complication or death) was 20% in endoscopic necrosectomy vs 80% in surgical necrosectomy ($P=.03$) Post procedure IL-6 level was lower in endoscopic necrosectomy group Lesser pancreatic fistula and no new onset multiple organ failure in endoscopy group
b. Horvath K et al.[16] 2010	40	40 (100%)	49 Days	Percutaneous drain followed by VARD, prospective single arm phase 2 study	23% Patients managed with drain only and did not require surgery VARD was feasible in 60% of patients with 2.5% 30 day mortality, 7.5% bleeding, and 17.5% enterocutaneous fistula
c. Varadarajulu et al[27] 2013	40	0	NA	RCT: open surgical versus endoscopic cystogastrostomy for sterile pancreatic pseudocysts	Success rate was 95% and 100% in the endoscopy and surgery arms. Hospital stay and costs were lower in the endoscopic arm

CI = confidence interval, IPN = infected pancreatic necrosis, NA = not available, RCT = randomized controlled trial, VARD = video-assisted retroperitoneal debridement.

drainage of pseudocyst was first described in 1985.[23] Later this technique was also applied for WON in 1996 along with lavage of the cavity.[24] Endoscopic transmural necrosectomy was first described in 2000.[25] Since then this approach has been gaining momentum and is now considered first-line therapy as a minimally invasive approach whenever intervention is needed in patients with pseudocyst/WON.[11,13]

Endoscopic cystogastrostomy involves creation of a fistula with the help of cautery and balloon dilation, and placement of multiple plastic stents to facilitate drainage (Fig. 3). It has technical and treatment success rates of 89% to 100% and 82% to 100%, respectively, with <1% mortality.[17,26] Endoscopic cystogastrostomy creates a fistula of size 15 mm to 20 mm vs 60 mm in surgical cystogastrostomy and hence fistula closure is faster. However, when compared with surgery, endoscopic approach has similar efficacy but lower cost, shorter hospital stay and better physical and mental health.[27,28] Some authors advocate concomitant transpapillary pancreatic stent placement in addition to transmural drainage to bridge the pancreatic ductal leak in order to prevent recurrence.[29] A recent multicenter study, however, did not find any advantage of adding transpapillary drainage to transmural drainage of pseudocysts.[21] Recurrence of collection may be due to disconnected pancreatic duct which is mostly asymptomatic. If there is recurrence due to disconnected pancreatic duct, additional drainage interventions are required. In authors' experience most of the patients can be managed with transmural drainage alone with the requirement of transpapillary drainage only in a few cases for recurrence due to persistent duct leak.[30,31]

Direct puncture or EUS-guided drainage

Endoscopic ultrasound (EUS) guided drainage is preferred for puncture of PFCs rather than direct puncture under endoscopic vision which was being practiced earlier. EUS was associated with higher technical success (95% vs 35%–66%) and a trend toward lower adverse event rates (0%–4% vs 13%–15%) than conventional direct puncture technique in 2 randomized controlled trials.[32,33] EUS is particularly helpful for collections which do not have a visible bulge. Use of color Doppler helps avoid vessels during the puncture of the collection. After puncture of the cavity, the tract is dilated with a balloon to 12 to 20 mm followed by placement of 2 plastic stents (7–10 Fr) or a lumen apposing metal stent (LAMS) (Fig. 3). Some authors also prefer to place a nasocystic drain for continuous irrigation of the cavity.[9]

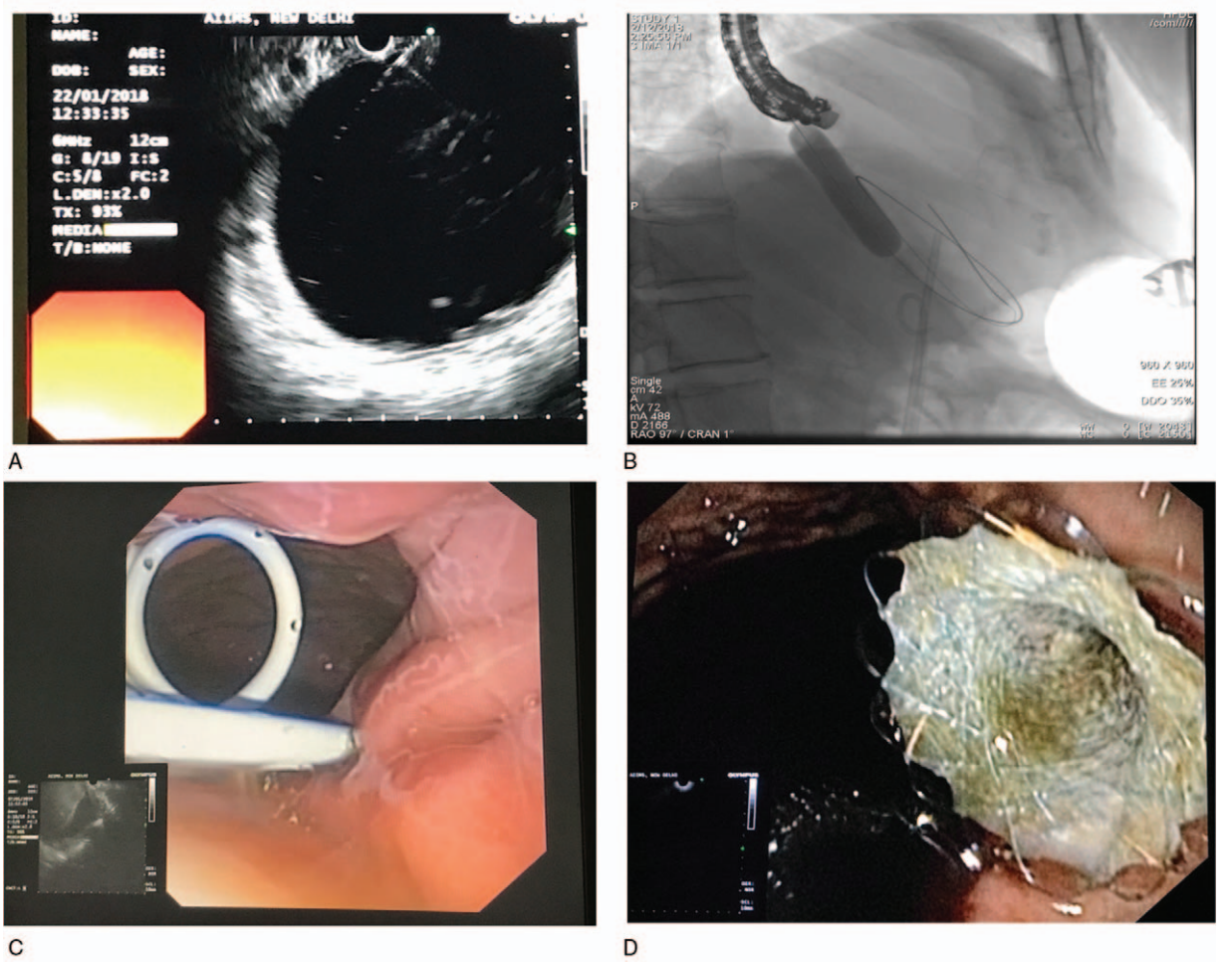

Figure 3. Endoscopic transmural drainage: (A) puncture of the pseudocyst/WON under EUS guidance and placement of guidewire, (B) balloon dilatation of the tract, (C) placement of 2 plastic stents, (D) Lumen opposing metal stent. EUS = endoscopic ultrasound, WON = walled-off necrosis.

Direct endoscopic necrosectomy

While internal drainage alone is sufficient for pseudocyst, it may result in conversion of a sterile collection to an infected one in WON which necessitates necrosectomy.[34] Over a period of time, endoscopists have ventured to perform direct endoscopic necrosectomy (DEN) in patients with WON in addition to transmural drainage alone. DEN can be performed at the index procedure but is generally performed at subsequent procedures after the liquid component has been drained. For necrosectomy, the cavity is accessed using a forward viewing endoscope, irrigated with saline and loose necrotic debris is removed using a basket, snare, or other endoscopic accessories.[35,36] The procedure may be repeated until the cavity is cleared off the debris.

LAMS or plastic stents

Of late, LAMSs are being used instead of plastic stents. LAMS having a wider diameter provides better drainage and ease of necrosectomy, and thus may be particularly helpful in WON. However, a recent randomized controlled trial showed no difference in success rate, total number of procedures performed and clinical adverse events between LAMS and plastic stents. LAMS use was associated with a higher stent related adverse events (32.3% vs 6.9%) which included bleeding and stent migration. Hence, it is recommended to remove LAMS before 3 weeks if WON has resolved.[37] Most endoscopist would prefer to place a LAMS if the amount of necrotic debris is significant, that is, >30% of the volume of the collection.

Percutaneous endoscopic necrosectomy

In patients with laterally placed collections who have undergone PCD, percutaneous endoscopic necrosectomy may be performed through the PCD tract. Initially the WON cavity can be accessed using an ultrathin endoscope if 18 to 20 Fr catheter had been placed. The cavity should be lavaged to drain the liquid pus. The catheter should be upgraded to 30 Fr after dilating the tract in 1 or 2 sessions. A metal stent may also be used (the one used for esophageal stricture). The cavity can then be accessed with a standard endoscope (diameter around 9 mm with a 2.8-mm channel) and debridement could be done using endoscopic accessories such as a snare. The procedure can be performed in the endoscopy suit under conscious sedation and also at the bedside in sick patients with organ failure.[38,39]

We have summarized the success and complications rates of various endoscopic drainage and necrosectomy procedures for WON in Table 3.

Surgical approach

Open surgery was standard of care in patients with necrotizing pancreatitis in 1980s.[6,48] The seminal paper by Bradley and Allen[7] showed that conservative approach may be justified in patients with sterile pancreatic necrosis. Surgical necrosectomy has generally been used for infected necrosis. Open necrosectomy is associated with morbidity of 34% to 95% and mortality ranging from 6% to 25%. Delayed necrosectomy (>4 weeks) is preferred over early necrosectomy decreasing morbidity and mortality.[49] Long-term complications of surgical procedure include diabetes, pancreatic exocrine insufficiency, and pancreaticocutaneous and enterocutaneous fistulae.[6,48]

Recently, minimally invasive step-up retroperitoneal approaches have been popularized and are increasingly being used to avoid complications of open surgery. A percutaneous drain is placed in the WON retroperitoneally which is subsequently enlarged via an incision (5–7 cm) and VARD is done using a rigid nephroscope or laparoscope. Another technique could be minimal access retroperitoneal pancreatic necrosectomy (MARPN) via 2 to 3 ports using a nephroscope/laparoscope without an incision.[50] Several uncontrolled series have shown that periprocedural adverse events were <5%, morbidity ranged from 10% to 30% and mortality from 0% to 20%.[16,50,51] In a randomized controlled trial, the Dutch pancreatitis group compared minimally invasive step-up approach with open necrosectomy (PANTER trial)[8] and showed that the primary endpoint (composite of major complications and death) was lower in the step-up approach (69% vs 40%,

Table 3

Summary of various studies using endoscopic methods in patients with necrotising pancreatitis.

Reference	Patients, n	IPN, n (%)	Timing of intervention (mean/median days after presentation)	Modality	Mean number of repeat interventions	Success (%)	Complication and mortality (all cause)
Baron et al[24]	11	3 (27)	50	Transmural stents + nasocystic lavage ± transpapillary stenting	2.7	9 (82)	Bleeding: 5 Perforation: 1 Infection: 4 Mortality: 0
Seewald et al[40]	13	13 (100)	NA	ETN + transmural stents + nasocystic lavage ± transpapillary stenting	7	11 (85)	Bleeding: 4 Mortality: 0
Charrnley et al[41]	13	13 (100)	27	ETN	4	9 (69)	Mortality: 2
Voermans et al[42]	25	19 (76)	84	Transmural stents + nasocystic lavage	2	23 (92)	Major bleeding: 1 Minor bleeding: 8 Perforation: 1 Mortality: 0
Papachristou et al[43]	53	26 (49)	49	ETN ± transpapillary stent ± PCD	3	43 (81)	Bleeding: 9 Gall bladder puncture: 1 Stent migration: 2 Mortality: 3
Escourrou et al[44]	13	13 (100)	28	PCD ± ETN	1.8	13 (100)	Bleeding: 3 Infection: 3 Mortality: 0
Hocke et al[45]	30	30 (100)	NA	ETN	2.7	27 (90)	Bleeding, infection and fistula in 10% Mortality: 2
Dhingra et al[39]	15	15 (100)	34	PCD + PEN	5	14 (93)	Minor bleeding: 1 Fistula: 1 Mortality: 1
Seifert et al[36]	93	50 (54)	43	ETN	6.2	75 (81)	Bleeding: 13 Perforation: 5 Fistula: 2 Infection: 1 Air embolism: 2 Mortality: 7
Gardner et al[35]	104	40 (39)	63	ETN	3	95 (91)	Major bleeding: 2 Minor bleeding: 19 Retrogastric perforation: 2 Pneumo-peritoneum: 3 Air embolism: 1 Mortality: 2
Rische et al[46]	31	24 (77)	NA	ETN + nasocystic lavage ± transpapillary stenting	4	26 (83)	Major bleeding: 1 Perforation of colon: 2 Stent dislocation to jejunum: 1 Mortality: 3
Yasuda et al[47]	57	57 (100)	50	ETN + transmural stents + nasocystic lavage	5	43 (75)	Major bleeding: 5 Perforation: 3 Air embolism: 1 Mortality: 6

ETN = endoscopic transmural necrosectomy, IPN = infected pancreatic necrosis, NA = not available, PCD = percutaneous catheter drainage, PEN = percutaneous endoscopic necrosectomy.

$P=.006$). Interestingly in the step-up approach group, 35% patients could be treated successfully with percutaneous drainage only obviating the need of VARD. There was no difference in mortality, but new onset multiple organ failure, diabetes, and incisional hernia were less in the step-up group.[8] On long-term follow-up (mean 86 months), primary endpoint was 44% in step-up group and 73% in open necrosectomy ($P=.005$).[14] In addition, pancreatic exocrine insufficiency, diabetes, and incisional hernia were higher in open necrosectomy group. There was no significant differences between the groups in proportions of patients requiring additional drainage procedures or pancreatic surgery.[14] This study probably marked almost the end of open necrosectomy and shifted the focus to minimally invasive step-up approach, whether endoscopic or VARD, in patients with necrotizing pancreatitis.

Is there still any role of open surgery? Open surgery may still be required for patients with extensive necrosis who fail minimally invasive surgery and those with complications such as bowel perforation and hemorrhage due either to pancreatitis or iatrogenic.[52] In a single-center study of 305 patients with collections associated with necrotizing pancreatitis, 193 patients underwent endoscopic interventions including endoscopic drainage alone or with necrosectomy; 7% of patients who underwent early intervention at <4 weeks required open surgery for salvage of refractory necrosis or complications such as bowel perforation.[53]

Comparison of endoscopic and minimally invasive surgical methods

Both surgical and endoscopic approaches have been shown to be effective for mature PFCs (pseudocyst/WON), the superiority of one over another needs to be studied. Recently, 3 randomized controlled trials have compared both the modalities in the management of PFCs (Table 4).

Two studies involved patients with infected collections. The TENSION trial,[9] a multicenter randomized controlled trial by the Dutch pancreatitis group, compared endoscopic step-up approach (EUS guided transmural drainage followed by endoscopic necrosectomy if required) and surgical step-up approach (PCD followed by VARD if required). The primary end point (composite of major complications or death at 6-month follow-up) was similar in both the groups (43% vs 45%). The rate of pancreatic fistula and length of hospitalization was lower in endoscopic group. Another randomized controlled trial by Bang et al[10] (MISER trial) compared minimally invasive surgery (laparoscopic or VARD depending upon the location of the infected WON) and endoscopic approach (transluminal drainage with or without necrosectomy). The primary end point (composite of major complication or death at 6-month follow-up) was higher in minimally invasive surgery group compared to endoscopic group (40.6% vs 11.8%, $P=.007$). Endoscopic group had lower cost and better quality of life. The difference in the primary outcomes between these 2 studies may be explained by (a) MISER trial included fistulae as a major complication which was not included in TENSION trial. Fistula rate was 28% in minimally invasive surgery arm in MISER trial and exclusion of this figure from the primary outcome showed comparable results in both the arms, and (b) MISER trial included laparoscopic cystogastrostomy and necrosectomy in most and VARD in a few patients compared to VARD in all the patients in the TENSION trial. Some other differences in these trials were TENSION trial included relatively stable patients with a mean sequential organ failure assessment score 0 to 1 while 29% patients had organ failure in the MISER trial at the time of intervention. The mortality in the TENSION trial was 16% while it was 8% in the MISER trial. Hopefully, minimally invasive techniques coupled with intensive care might bring down mortality in patients with infected PFCs from 15% to 39%[4,21] to a single-digit figure.

We compared laparoscopic drainage with endoscopic drainage in a randomized trial for pseudocyst and WON and showed that the overall success rates of 93.3% and 90% in the laparoscopic and endoscopic groups respectively were similar. The postoperative complications were also comparable between the groups except for higher postprocedure infection in the endoscopic group (19 vs 9; $P=.01$) requiring endoscopic reintervention.[28]

Concluding remarks

Symptomatic PFC (WON/pseudocyst) in patients with AP requires drainage. Infection in patients with necrotizing pancreatitis is an ominous development increasing morbidity and mortality. Patients with symptomatic pseudocyst can be managed

Table 4

Summary of randomized trials comparing minimally invasive techniques for drainage of PFCs.

	TENSION trial[9]		MISER trial[10]		AIIMS* trial[28]	
	Endoscopic	VARD	Endoscopic	Laparoscopic/VARD	Endoscopic	Laparoscopic
No. of patients	51	47	34	32	30	30
Percent infected collections	46 (90%)	46 (98%)	31 (91%)	30 (94%)	0	0
Successful resolution	82%	87%	91%	92%	90%	93.3%
Composite endpoint	22 (43%)	21 (45%)	4 (12%)	13 (41%)	NR	NR
New onset organ failure						
Single	7 (14%)	13 (28%)	NR	NR	2 (7%)	2 (7%)
Multiple	2 (4%)	6 (13%)	2 (6%)	3 (9%)		
Death	9 (18%)	6 (13%)	3 (9%)	2 (6%)	0	0
Major complications						
Bleeding	11 (22%)	10 (21%)	0	3 (9%)	2	0
Perforation	4 (8%)	8 (17%)	0	0	1	0
Fistula (pancreatic)	2/42 (5%)	13/42 (32%)	0	9 (28%)	0	1
New onset diabetes	10/42 (24%)	9/41 (22%)	6 (27%)	9 (28%)	NR	NR

NR = not recorded, PFC = pancreatic fluid collections, VARD = video-assisted retroperitoneal debridement.
* AIIMS = All India Institute of Medical Sciences (author's institution).

with endoscopic/laparoscopic transmural drainage with requirement of transpapillary drainage in only a few patients who have a recurrence of the collection. In patients with WON, who are otherwise stable but require drainage due to symptoms, either endoscopic or minimally invasive surgical approach would be appropriate depending upon the location and extent of collection. In patients with infected PFCs, PCD is generally preferred and results in clinical improvement stabilizing the patient before an endoscopic or minimally invasive surgical necrosectomy can be undertaken. It could by itself be a definitive treatment in one-third to half of patients. The trend may be shifting toward endoscopic transmural drainage even in infected PFCs (with matured wall) as shown in recent studies. Since infected necrosis is a heterogeneous disease, therapy should however, be tailored to an individual patient under the care of a team comprising of gastroenterologist, endoscopists, interventional radiologists, intensivists, and surgeon.

Acknowledgments

None.

Author contributions

SJM: Wrote the first draft and approved the final manuscript.
PKG: Concept and design of the review; Critical inputs and revision of the first draft, and approval of the final manuscript.

Financial support

None.

Conflicts of interest

The authors declare no conflicts of interest.

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How to cite this article: Mahapatra SJ, Garg PK. Management of pancreatic fluid collections in patients with acute pancreatitis. J Pancreatol 2019;2:82–90. doi: 10.1097/JP9.0000000000000026