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EXPERT REVIEW OF GASTROENTEROLOGY & HEPATOLOGY
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ORIGINAL RESEARCH

Endoscopic drainage versus percutaneous drainage for the management of infected walled-off necrosis: a comparative analysis

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ABSTRACT

Background: Comparative data on percutaneous catheter drainage (PCD) vs EUS-guided drainage (EUS-D) for management of symptomatic walled-off-necrosis (WON), specially infected WON with/without organ failure(OF) is limited.

Methods: Patients with symptomatic WON were divided into two groups of PCD and EUS-D, depending on the modality of drainage. Resolution of OF, adverse events, and other outcome measures were recorded. The two modalities were compared among infected WON sub-cohort and also degree of solid component (SC).

Results: 218 patients (175 males; 80.3%) were included who underwent either PCD (n = 102) or EUS-D (n = 116). Clinical success was significantly higher in the EUS-D group (92.1% vs 64.6%; p < 0.0001) and even for infected WON (n = 128) (p = 0.004), with higher (p = 0.007) and faster (p < 0.0001) OF resolution. Other outcome measures including mortality were significantly higher in the PCD group. Among subgroups, PCD with >40% SC had the worst clinical success/OF resolution rates, while EUS-D with <40% SC had the best outcomes.

Conclusion: EUS-D should be preferred over PCD in the management of WON, infected or otherwise, for higher clinical success, and higher/faster resolution of OF. PCD should be avoided in WON with>40% SC.

ARTICLE HISTORY

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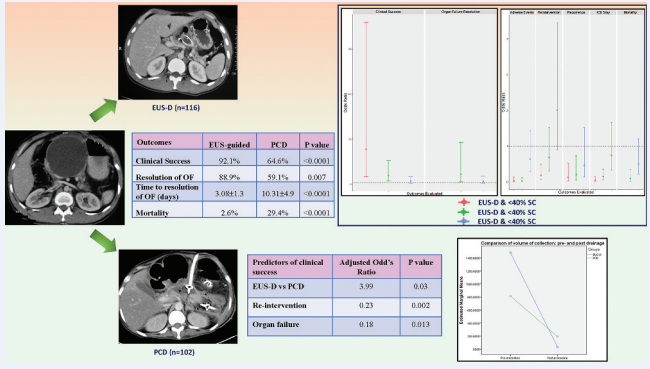
KEYWORDS

Pancreatic fluid collections; endoscopic ultrasound; percutaneous catheter drainage; pancreatitis; direct endoscopic necrosectomy

GRAPHICAL ABSTRACT



1. Introduction

Pancreatic fluid collections (PFCs) are abnormal collections of fluid and/or debris in and around the pancreas. While 5%–15% of acute pancreatitis (AP) develop pseudocysts (PPs) [1], 15% of severe AP will develop walled-off-necrosis (WON) [2]. Post-operative PFCs are noted in 15%–30% of cases after distal pancreatic resections [3,4]. Drainage of PFCs may be required if they cause pressure symptoms, pain or gets secondarily infected. This drainage can be performed either surgically, radiologically by percutaneous catheter (PCD) or by endoscopic techniques. Surgical drainage has been shown to have a high mortality and morbidity with higher complication rates of 40% to 80% [5–9]. PCD and endoscopic drainage using endoscopic ultrasound guidance (EUS-D) have been more commonly used with

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Supplemental data for this article can be accessed here

Table 1. Procedural steps and protocol.

Protocol for ultrasound/CT-guided percutaneous catheter drainage
(1) Performed under CT guidance or ultrasonography (USG) with fluoroscopy.
(2) Location of the WON identified including its size, amount of necrotic contents and possible interposition of blood vessels or other vital organs. The amount of necrotic components was calculated as percentage of solid echogenic debris noted as a percentage of the total collection.
(3) Skin and subcutaneous tissue anesthetized with 2% lidocaine layer by layer.
(4) Initial access obtained using an 18 G needle and a small aliquot of fluid aspirated for Gram's stain and culture sensitivity.
(5) Seldinger technique was used to dilate the tract over a 0.035" stiff guidewire.
(6) Either a pigtail or Malecot catheter was placed. The initial size used was 10–12 Fr.
(7) Catheter flushed with sterile normal saline 20–50 ml. twice daily to maintain the patency.
(8) The decision for upsizing or removal was based on the size of the collection on subsequent imaging, drain output and clinical condition.
Protocol for EUS-guided drainage
(1) Carried out using a linear array echoendoscope (EG-3870UTK, Pentax Medical, USA).
(2) Done under moderate sedation using pentazocine and midazolam. Need for deeper sedation was assessed by an experienced anesthetist and induced accordingly.
(3) IV antibiotic administered peri-procedure if the patient was not already receiving it.
(4) Diagnostic scanning was done to measure the size of the collection, the amount of solid debris and to look for any intervening blood vessels. The amount of necrotic component was calculated as percentage of solid echogenic debris noted as a percentage of the total collection.
(5) WON punctured using a 19 G EUS-FNA needle (EchoTip® Ultra, Cook Medical, USA or EZ Shot3 Plus, Olympus Medical, Japan).
(6) Aliquot of the fluid was aspirated for culture sensitivity.
(7) A 0.035' guidewire then passed through the needle and allowed to loop adequately inside the cyst cavity as confirmed on EUS view or fluoroscopy.
(8) Tract dilated with a coaxial diathermy dilator, cystotome 8.5 Fr (CYSTO085U, G-Flex, Belgium) using dry cut mode.
(9) Placement of bi-flanged metallic stents (BFMS; 16 mm X 20/30 mm) (Taewoong Niti-S Nagi™ Stent, Taewoong Medical, South Korea) done.
(10) For plastic stents, the tract was further dilated with controlled radial expansion balloon (CRE™ wire-guided balloon dilatation catheters, Boston Scientific, USA) till 12–15 mm, followed by placement of two or more plastic stents (10 Fr X 3/5 cm).
Post-procedure care
(1) Post drainage, the patients were observed for symptomatic improvement, and documented for improvement in organ failure, fever and other symptoms.
(2) Oral fluids were allowed 6 hrs after the EUS-D.
(3) Antibiotics were continued for 2–3 days and switched to oral if improvement occurred.
(4) For non-improvement/deterioration, antibiotics were upgraded or changed as per the microbial spectrum and sensitivity pattern of the aspirated fluid.
(5) Imaging (USG/CT) was done 72 hrs after the drainage to assess for adequacy of drainage in the form of reduction of collection size.
(6) The 'step-up' approach was used for upgradation of PCD, need for additional PCD or for the need for additional procedures such as DEN for the EUS-D, after a multi-disciplinary team discussion.
(7) Patients with infected WON were monitored till symptom or OF resolution.
(8) If there was no improvement with these measures in the two arms, the patients were taken up for minimally invasive necrosectomy.
Technique of DEN
(1) Carried out using a gastroscope (Olympus GIF HQ190, Olympus Medical, Japan) with water-jet facility.
(2) Cavity was entered either through the BFMS or after removing the plastic stents.
(3) Debridement carried out using snares, nets and forceps.
(4) Post debridement, new plastic stents were placed in the plastic stents arm.
(5) 7 Fr naso-cystic drain (NCD) sometimes was placed in both, plastic and BFMS groups, for irrigation, depending on the debris content.

Abbreviations: CT computed tomography; EUS-D Endoscopic ultrasound guided drainage; Won Walled-off-necrosis; DEN Direct endoscopic necrosectomy; PCD Percutaneous catheter drainage; BFMS Bi-flanged metallic stent

comparable efficacy. Comparison between the two modalities exists, but such studies are few and heterogeneous. While some have compared them in patients with only PPs [10,11], others have compared in patients with all PFCs [12,13] and some others in post-operative collections [14,15].

While PPs have minimal or no solid debris, WON is a sequela of acute necrotizing pancreatitis (ANP) with significant solid debris. Thus, management of WON, specifically those secondarily infected, are different and difficult. Although some studies have shown similar clinical success rates for PPs between PCD and EUS-D [10,13], the same might not hold true for WON. Only a single small study of only 24 patients [16] had dedicatedly looked into the outcome of WON using the two modalities. Moreover, infected WON with/without organ failure (OF) is a still more difficult cohort to manage and the two modalities have never been compared in this subgroup of patients. The advent of direct endoscopic necrosectomy (DEN) has widened the spectrum further [17].

This study was aimed at comparing the efficacy and safety of PCD and EUS-D in the management of WON and more so for infected WON. The two modalities were also compared for efficacy in terms of the content of solid debris in WON.

2. Methodology

This is a retrospective analysis of a prospectively collected database of patients who presented at our center between January 2018 and February 2020, with symptomatic WON and underwent EUS-D or PCD. The inclusion criteria were: i) age more than 18 years; ii) having WON as per revised Atlanta classification [18]; iii) symptomatic with pain abdomen, pressure symptoms in

the form of gastric outlet obstruction, early satiety/vomiting, biliary obstruction secondary to WON or features suggestive of infected WON with fever, sepsis with/without OF; iv) WON amenable for drainage by both endoscopic and PCD techniques. The exclusion criteria include: i) ANC < 4 weeks; ii) PPs or post-operative PFCs; iii) pregnant/ lactating women; iv) previous intervention or drainage; v) distant collection not amenable for EUS-D; vi) lack of informed consent. The decision for EUS-D or PCD was taken after a multi-disciplinary team decision comprising of gastroenterologist, intensivist, radiologist and surgeons. The study was approved by the Institute Ethics Committee (INT/IEC/2020/Spl-1213, Dated 02/09/2020).

2.1. Procedural steps

The procedural steps and institute protocol followed have been outlined on Table 1.

2.2. Definitions

Various study definitions used are:

a. **Technical Success**: Successful placement of the intended internal or external drain in the intended position as assessed endoscopically or radiologically.
b. **Clinical success: I**mprovement of the symptoms and resolution of the collection radiologically without the need for alternative drainage techniques such as salvage PCD for EUS-D, need for necrosectomy or death.
c. **Radiological resolution**: Reduction in WON < 2 cm on follow-up CECT abdomen.
d. **Reintervention**: Need for additional measures after the index procedure such as: i) upgradation of PCD, additional placement of PCD for the PCD group or ii) need for DEN or need for additional EUS-D for the EUS-D group.
e. **Recurrence**: Reappearance of significant collection radiologically after complete resolution of the index collection.
f. **Organ failure**: Defined by Modified Marshal scoring system [18].
g. **Systemic inflammatory response syndrome**: Defined by presence of any 2 of the criteria, namely tachycardia (heart rate >90 beats/min), tachypnea (respiratory rate >20 breaths/min), fever or hypothermia (temperature >38 or <36°C), and leukocytosis, leukopenia, or bandemia (white blood cells >1,200/mm3, <4,000/mm3 or band cells > 10%) [19].
h. **Infected WON (suspected/confirmed)**: defined as culture positivity of the aspirated fluid, presence of gas in the WON on imaging or persistent SIRS with/ without OF without any extra-pancreatic source of infection [20].

2.3. Follow Up

The patients were admitted for at least 48–72 h post-procedure. Patients with infected WON with/without OF were monitored in-hospital till symptom or OF resolution. Patients were asked to follow up after 3 weeks and subsequently 3 monthly or anytime earlier in case of recurrence of symptoms. Any catheter related adverse events were asked to report immediately. All patients underwent a magnetic resonance cholangio-pancreaticography (MRCP) and all BFMS were removed after 3 weeks. In patients with disconnected pancreatic duct syndrome (DPDS), the transmural plastic stents were left indefinitely. For BFMS, it was replaced with plastic stents. In cases with external pancreatic fistula (EPF), endoscopic retrograde pancreatography (ERCP) was carried out for pancreatic stenting. Patients were followed up for 6 months for recurrence of collection.

2.4. Outcome measures

The primary outcome measures were clinical and technical success. The various other outcome measures analyzed were reintervention rates, adverse event rates, recurrence of collection, resolution of OF, ICU need, length of hospital stay, need for surgery and mortality.

2.5. Statistical analysis

All the data were entered into a spreadsheet and analyzed using the SPSS (version 21.0, SPSS Inc; Chicago, USA) software. Continuous variables were expressed as mean ± standard deviation or median (interquartile range). Dichotomous variables were compared using the Chi-square test/Fischer's exact test. The p-value of less than 0.05 were taken as statistically significant. Sub-group analysis was done for patients with infected WON and/or OF.

Outcome measures were compared between patients undergoing PCD, EUS-D with plastic stents and EUS-D with bi-flanged metallic stents (BFMS). The cohort was further divided into four groups based on the type of drainage (EUS-D vs PCD) and the solid component (<40% vs >40%). Patients undergoing PCD drainage with >40% solid component (PCD + >40% SC) was expected to have the worst outcome and taken as a reference arm to calculate adjusted Odds' ratio (aOR) for the various outcome measures and a forest plot was constructed.

3. Results

Of the 296 patients screened, 78 patients were excluded (Figure 1) and 218 patients (175 males; 80.3%) were included in the study and categorized into two groups depending on the mode of drainage into those undergoing PCD (n = 102) (Figure 2) and those undergoing EUS-D (n = 116) (Figure 3). Most of the patients had alcohol (129; 59.2%) or gall stone disease (44; 20.2%) as the etiology of AP (Table 2).

3.1. Baseline characteristics of WON (*Table 2*)

EUS-D group had significantly larger collection compared to the PCD group (p = 0.001). Reduction in the volume of the collection on day 3 of assessment was significantly higher in the EUS-D group (p = 0.001) (**Suppl**. Figure 1).

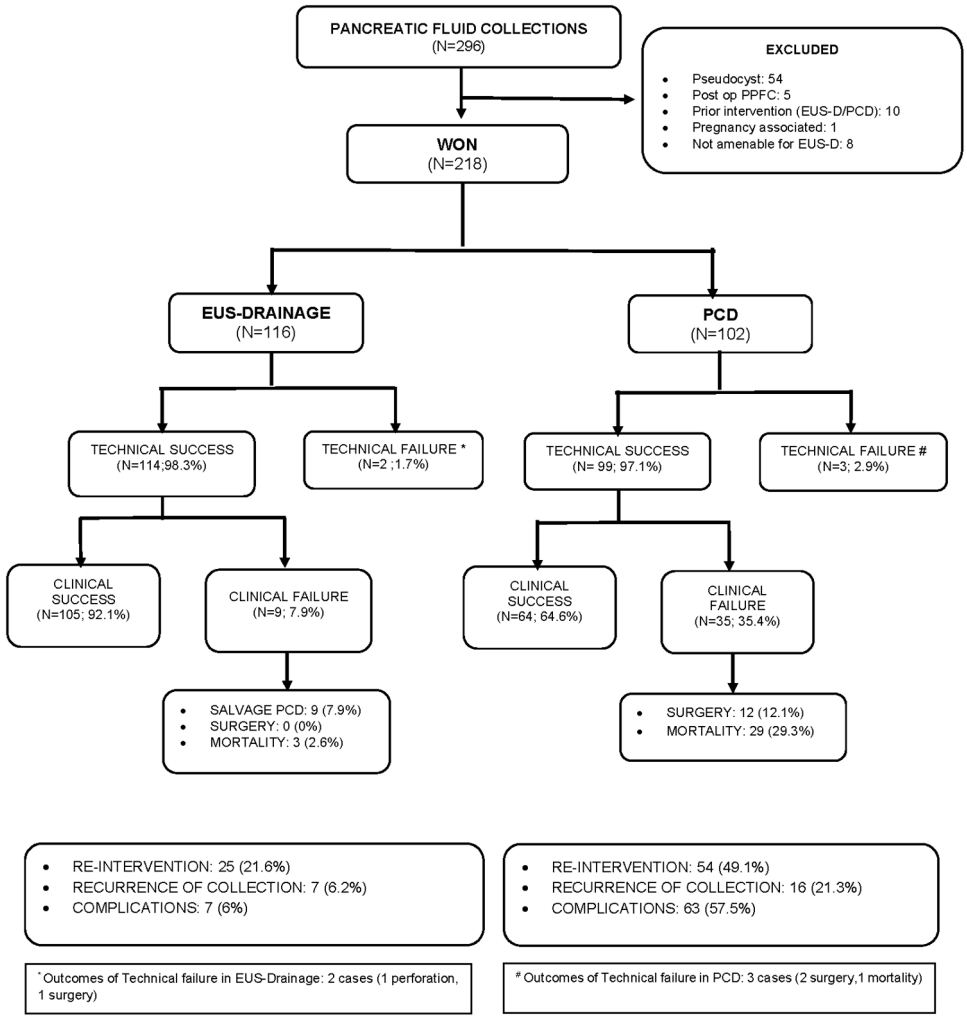

Figure 1. Flowchart of the study. Abbreviations: WON walled-off-necrosis; EUS-D endoscopic ultrasound guided drainage; PCD percutaneous catheter drainage; PPFC peri-pancreatic fluid collection.

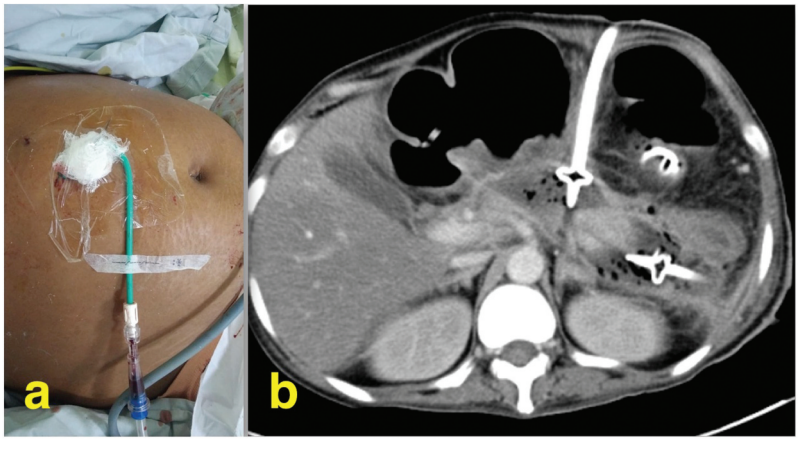

Figure 2. Percutaneous catheter drainage: a) clinical image depicting percutaneous catheter drain in a patient; b) computed tomography imaging post-drainage.

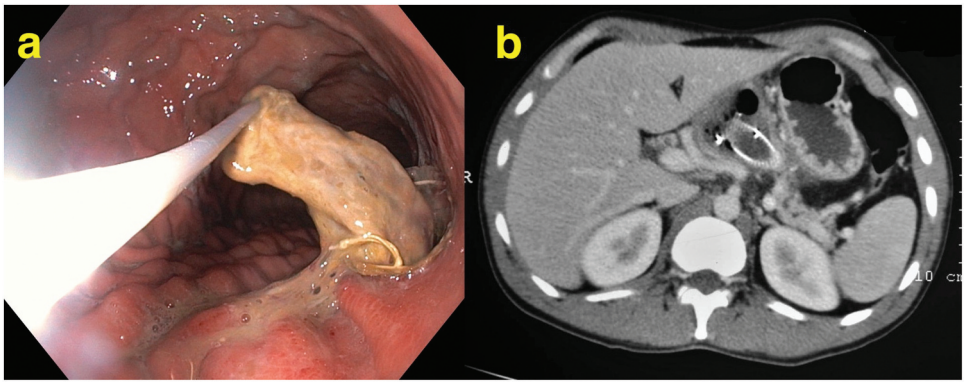

Figure 3. EUS guided drainage: a) direct endoscopic necrosectomy carried out; b) computed tomography imaging post-drainage.

Table 2. Demographic profile and baseline characteristics of WON.

	EUS -D (n = 116)	PCD (n = 102)	P value
Age (years) (mean ± SD)	39.10 ± 14.5	40.84 ± 13.0	
Sex Male	97 (83.6%)	78 (76.5%)	
Female	19 (16.4%)	24 (23.5%)	
Etiology Alcohol	67(57.8%)	62 (60.8%)	0.353
Gall stones	21 (18.1%)	23 (22.5%)	
Others	28 (24.1%)	17 (16.7%)	
Solid component			
<40%	60 (51.7%)	52 (51.0%)	0.913
>40%	56 (48.3%)	50 (49.0%)	
Collection Size (cm^3) (median; IQR)	972.03 (450.25–1833.75)	456.05 (236.4–906.0)	**0.0001**
Change in volume (cm^3) (median; IQR)	845.70 (355.5–1689.0)	292.13 (105.7–1935.6)	**0.001**
Growth on 1st culture	45 (38.8%)	41 (40.2%)	0.833

Abbreviations: WON walled-off necrosis; EUS-D EUS-guided drainage; PCD percutaneous catheter drain; SD Standard deviation; IQR Inter-quartile range

Table 3. Outcome measures between EUS-D and PCD groups.

	EUS -D (n = 116)	PCD (n = 102)	P value
Technical Success	114 (98.3%)	99 (97.1%)	0.667
Clinical Success	105 (92.1%)	64 (64.6%)	**<0.0001**
Reintervention	25 (21.6%)	51 (50.0%)	**<0.0001**
Adverse events	7 (6.0%)	58 (56.9%) #	**<0.0001**
Slippage/Migration	1 (0.9%)	22 (21.6%)	**<0.0001**
Perforation/Fistula	1 (0.9%)	12 (11.8%)	**0.001**
Bleeding	5 (4.3%)	16 (15.7%)	**0.005**
Recurrence of collection	7 (6.2%)	15 (21.7%)	**0.002**
Resolution of OF	24/27 (88.9%)	39/66 (59.1%)	**0.007**
Time to resolution of OF (days) (median; IQR)	3.00 (2.0–4.0)	10.00 (8.0–12.0)	**<0.0001**
ICU need	17 (14.7%)	62 (60.8%)	**<0.0001**
ICU stay (days) (Median; IQR)	4.00 (2.5–8.0)	11.00 (5.00–18.75)	**0.001**
Ventilator need	3 (2.6%)	36 (35.3%)	**<0.0001**
Ventilator days (median)	6.00*	5.50 (3–10)	0.720
Hospital stay in days (Median; IQR)	8.00 (2–12)	28.00 (18.75–41.25)	**<0.0001**
Surgery	1 (0.9%)	14 (13.7%)	**<0.0001**
Mortality	3 (2.6%)	30 (29.4%)	**<0.0001**

#29 patients had EPF; *only 3 cases in EUS arm had ventilator stay, hence IQR could not be calculated. Abbreviations: EUS-D EUS-guided drainage; PCD percutaneous catheter drain; OF organ failure; IQR Inter-quartile range

3.2. Overall outcome measures between PCD and EUS-D

While technical success was similar, clinical success was significantly higher in the EUS-D group (92.1% vs 64.6%; p < 0.0001) compared to the PCD group (Table 3). Reintervention rates (p < 0.0001), adverse events (p < 0.0001) and recurrence of collection (p = 0.002) were higher in the PCD group. PCD group had greater need for ICU admission (p < 0.0001), ventilator support (p < 0.0001) with more prolonged ICU stay (11 days vs 4 days; p = 0.001) and hospital stay (28 days vs 8 days; p < 0.0001) compared to EUS-D. Requirement for surgery (13.7% vs 0.9%; p < 0.0001) and mortality (29.4% vs 2.6%; p < 0.0001) were also higher in the PCD group.

Table 4. Sub-group analysis of patients with infected WON.

	EUS-D (n = 45)	PCD (n = 83)	P value
Technical Success	45 (100%)	82 (98.8%)	1.000
Clinical success	39 (86.7%)	51 (62.2%)	**0.004**
Adverse events	2 (4.4%)	46 (55.4%) *	**<0.0001**
Bleed	2 (4.4%)	13	0.083
Slippage/Migration	0 (0%)	(15.7%)	**<0.0001**
Perforation/Fistula	0 (0%)	18	**0.05**
		(21.7%)	
		7 (8.4%)	
Reintervention	17 (37.8%)	43 (51.8%)	0.l29
Recurrence of collection	2 (4.8%)	12 (22.6%)	**0.019**
Resolution of OF	24/27 (88.9%)	39/66 (59.1%)	**0.007**
Time to resolution of OF (days) (mean ± SD)	3.08 ± 1.3	10.31 ± 4.9	**<0.0001**
Hospital stay (days) (mean ± SD)	10.31 ± 6.3	31.92 ± 17.4	**<0.0001**
ICU need	14 (31.1%)	55 (66.3%)	**<0.0001**
ICU stay (days) (mean ± SD)	4.57 ± 2.8	13.3 ± 9.9	**<0.0001**
Ventilator need	3 (6.7%)	32 (38.6%)	**<0.0001**
Surgery	0 (0%)	11 (13.3%)	**0.008**
Mortality	3 (6.7%)	27 (32.5%)	**0.001**

*23 patients had EPF.Abbreviations: WON Walled-off necrosis; EUS-D EUS-guided drainage; PCD percutaneous catheter drain; OF Organ failure; ICU intensive care unit

3.3. Outcome in patients with infected WON

On sub-group analysis of patients with infected WON, clinical success was significantly higher in EUS-D group (86.7% vs 62.2%; p = 0.004) compared to the PCD group (Table 4). Adverse events rate (p < 0.0001) and recurrence of collection (p = 0.019) were significantly higher in the PCD group. Higher rate of resolution of OF (88.9% vs 59.1%; p = 0.007) with faster resolution (median 3 days vs 10 days; p < 0.0001) was noted in the EUS-D group. All other outcome measures such as need for ICU or ventilator

Table 5. Multivariate model for prediction of clinical success in infected walled-off necrosis.

			95% confidence interval		
	Beta coefficient	aOR	Lower	Upper	P value
Age	0.02	1.02	0.99	1.06	0.26
EUS-D vs PCD	1.38	3.99	1.12	14.13	**0.03**
Solid component	−1.04	0.36	0.13	0.98	0.05
Adverse events	0.35	1.42	0.54	3.74	0.48
Re-intervention	−1.48	0.23	0.09	0.59	**0.002**
Organ failure	−1.74	0.18	0.04	0.69	**0.013**

Abbreviations: EUS-D EUS-guided drainage; PCD percutaneous catheter drain; aOR adjusted odds' ratio

support, length of ICU or hospital stay, surgery and mortality were significantly higher in the PCD group.

3.4. Outcome in patients of infected WON with organ failure

Further analyzing the cohort of infected WON patients with OF only, similar results were noted in favor of EUS-D with significantly higher clinical success (85.2% vs 53.8%, p = 0.005), lower adverse events rate (p < 0.0001), and lower need for surgery (p = 0.05) and mortality (p = 0.002) (**Suppl** Table 1).

3.5 Outcome measures between EUS-guided plastic stents, metal stents and PCD for infected WON with/without organ failure

Comparison of PCD with the two sub-groups of EUS-D with plastic stents (PS) and BFMS (**Suppl**. Table 2), showed that EUS-D with BFMS fared better than EUS-D with PS with higher resolution of OF (p = 0.015 vs p = 0.193) and lower need for ICU admission (p < 0.0001 vs p = 0.115).

3.6. Predictors of clinical success in infected WON

A multivariable model for prediction of clinical success in patients with infected WON (Table 5) showed that reintervention (p = 0.002) and presence of OF (p = 0.013) were significant negative predictors while EUS-D was a significant positive predictor (aOR = 3.99; p = 0.03) for clinical success.

3.7. Outcome measure comparison based on mode of drainage and degree of solid component

The PCD with >40% solid component (SC) (n = 50) evidently had the worst clinical success and OF resolution rates with higher adverse events, reintervention rates, ICU stay, mortality and recurrence rates (Figure 4**; Suppl**. Table 3), while EUS-D with <40% SC (n = 60) had the best outcomes. Patients in the EUS-D with >40% SC (n = 56) and PCD with <40% SC (n = 52) had outcomes intermediate between the above two.

4. Discussion

This study encompasses one of the largest data comparing the outcomes of PCD and EUS-D in selected patients with WON and showed that EUS-D had significantly higher clinical success. EUS-D not only had lower adverse events, reintervention and recurrence rates but also had higher and faster resolution of OF compared to PCD. Even the challenging sub-cohort of infected WON patients with OF showed better clinical success.

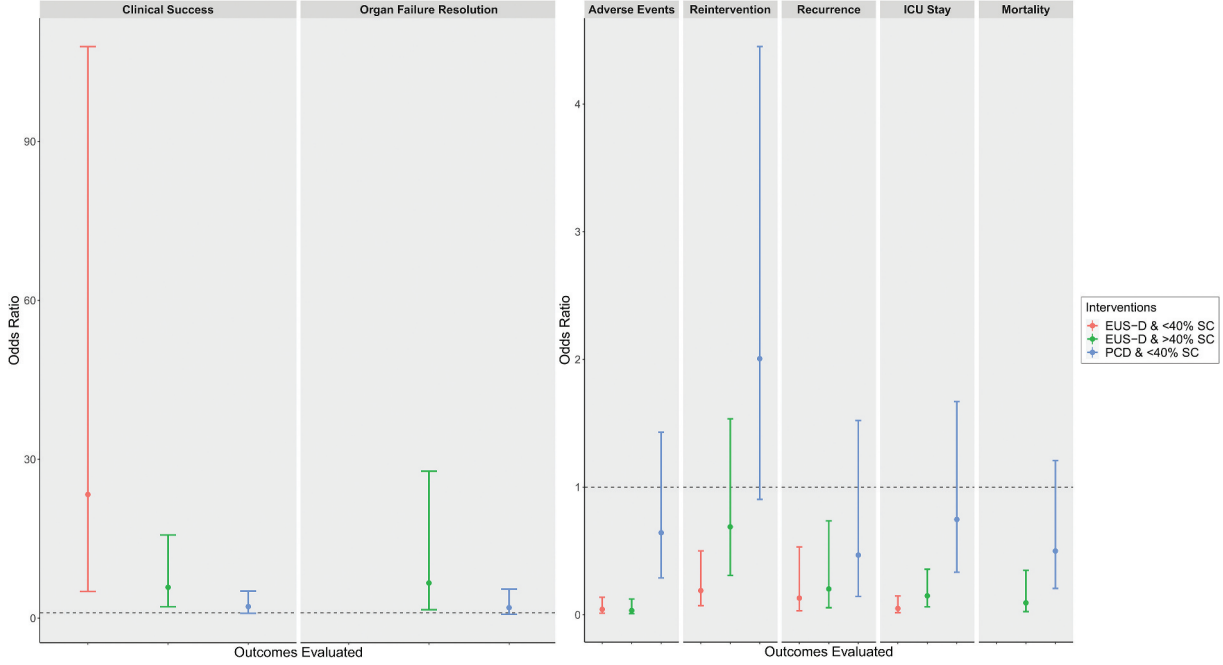

Figure 4. Forest plot of the adjusted Odd's ratio for the various outcome parameters compared between the four groups based on modality of drainage and percentage of solid component in the walled-off-necrosis: a) comparison for clinical success and organ failure resolution; b) comparison for adverse events, re-intervention, recurrence, ICU stay and mortality. (PCD with >40% solid component is taken as the reference arm). Abbreviations: ICU intensive care unit; EUS-D endoscopic ultrasound guided drainage; PCD percutaneous catheter drainage; SC solid component.

Endoscopic drainage and PCD have become the first-line interventional method for drainage of symptomatic PFCs [21]. However, the data comparing the two modalities are few and heterogeneous. While Johnson et al [11] and Akshintala et al. [10] have compared the two modalities in patients with PPs, others have studied post-surgical PFCs [14,15]. These studies found similar clinical efficacy of the two approaches [10,14,15]. However, the major drawbacks of these studies were small sample size and heterogeneous technique of drainage [10,14]. Two other studies with substantial sample size [12,13] had heterogeneous study population. Only Kumar et al [16]. had dedicatedly compared the two in infected WON, but the sample size was small. Thus, the current study has specifically looked into the outcome of drainage by the two modalities in patients of WON alone.

The dynamics of PPs and WON are quite different. PPs are seen in AP and chronic pancreatitis cases [22] and contain only liquid component without any solid debris. On the other hand, WON is a sequela of ANP [18] and contains variable amount of solid debris. Thus, while PPs requires drainage, WON requires debridement. Moreover, secondarily infected WON is still more difficult to treat as it can precipitate secondary OF [23]. Thus, a dedicated study for WON, such as our study, would be able to better assess the efficacy of the two modalities of drainage.

The clinical success of PCD for the management of WON as reported in studies ranges from 35% to 71% [9,24–26]. Our study had a similar success rate of 53% (in the sub-cohort with OF) to 63.6% (overall). The EUS-D group, in the current study, had a clinical success of 85.2% (sub-cohort of OF) to 90.5% (overall). This corroborates with the available meta-analysis data with a success rate of 81% – 92% [27–29]. The higher success rate in the EUS-D group for WON can be explained by the fact that endoscopic techniques enable to achieve a greater diameter of drainage port compared to PCD with added advantage of DEN. While PCD enables an initial drain portal of 14/16 Fr, EUS-D provides a diameter of at least 12 mm (36 Fr) for plastic stents to 16 mm (48Fr) for BFMS at the first go. The narrow diameter of the PCD and clogging of the channel with necrotic material leads to poor efficacy. Our study results clearly showed that this clinical advantage of EUS-D over PCD was noted even in the cohort of patients with infected WON and also in sicker patients with OF, although the success rates were lower. Infected collections are known to have poor clinical success compared to sterile ones [30,31].

One of the key findings of our study was the impact of drainage modality on the resolution of OF. EUS-D not only had a higher rate of OF resolution (88.9% vs 59.1%) but also a more rapid resolution (3 days vs 10 days). Unlike the inflammatory surge of primary OF noted in the initial stages of AP [32], secondary OF in infected WON is due to sepsis. Sepsis leads to a dysregulated immune response leading to organ dysfunction [33,34]. Drainage leads to not only removal of infective material but also decrease in cytokines. PCD placement has been shown to cause decrease in cytokine levels such as CRP, IL-6 and IL-10 [35]. Moreover, the reduction in volume of collection has been found to be an independent predictor for organ resolution [36]. Similarly, DEN has also been shown to reduce IL-6 levels and improve outcome [5]. We have conclusively shown that there is more rapid reduction of collection in EUS-D group on day 3 compared to PCD. Thus, with faster resolution of OF, shorter ICU/hospital stay and better survival can be easily explained.

Reintervention rates were found to be significantly higher in the PCD group compared to EUS-D (50.0% vs 21.6%; $p < 0.0001$), like other studies [10,12,13]. This high rate is due to the difficult maintenance of drain position and patency. Besides cumbersome maintenance of external catheters, there is need for regular flushing to maintain patency, chances of accidental slippage and peri-catheter leakage. On the contrary, EUS-D is devoid of such requirements. A fraction of WON can improve just by endoscopic drainage without the need for DEN [5,37]. In our study 78.4% of EUS-D did not require additional intervention. Additionally, external drain always increases the risk of secondary infection [24]. Development of external pancreatic fistula (EPF), a complication unique to PCD only, can occur in up to 15% to 100% [24]. In the current study, 29 (28.4%) cases had EPF.

In fact, our study showed that EUS-D was a significant positive predictor with a four times higher chance ($p = 0.03$) for clinical success in patients with infected WON, while presence of OF and need for reintervention were expected negative predictors. Greater the solid component, more difficult is the management. We divided the study cohort into four groups based on the extent of solid component and the mode of drainage and objectively proved, for the first time, that use of PCD in cases of WON with >40% SC had the worst outcomes. EUS-D use in cases with >40% SC had better outcomes than even the sub-group of PCD with <40% SC. This reiterates the fact that EUS-D performs better than PCD in any WON, irrespective of the extent of solid debris. Subgroup analysis showed some added benefit of use of BFMS over plastic stents in the EUS-D group, akin to previous studies [38,39].

There are several strengths of the study. This is a large study comparing the two drainage modalities of EUS-D and PCD group. The study cohort is homogeneous, including only WON and for the first time, critically analyzed the sub-cohort of infected WON with OF, which is the most challenging subset of patients. Resolution of OF, which is one of the key outcome measures, has also been systematically analyzed. We objectively established that use of PCD in WON cases with >40% SC have the worst outcomes and using EUS-D even in higher degree of solid debris edges over use of PCD with lesser solid debris.

However, there are a few limitations of the study. This is a retrospective single center study. Site and extent of WON might have precluded inclusion of cases not amenable for EUS-D leading to selection bias. With the advent of more data on the benefit of EUS-D, more sick infected WON patients can be taken upfront for EUS-D rather than PCD.

5. Expert opinion

Symptomatic PFCs require drainage and the two first line modalities are PCD and EUS-D. While data exist comparing the two for PFCs, homogenous data analysing the two modalities for drainage of the difficult-to-treat sub-cohort of WON is limited. Our data, one of the largest studies, showed that

EUS-D, wherever can be performed, should be preferred over PCD in the management of WON.

Infected WON with/without OF is a still more difficult cohort to manage and has not been specifically studied. Our data categorically analysed and showed that WON, infected or otherwise, drained by EUS-D has higher clinical success, higher and faster resolution of OF with lower rates of reintervention, adverse events, recurrence and better survival with lower need for surgical necrosectomy.

The amount of debris is a key factor deciding outcome of WON, including need for reinterventions, an effect not studied specifically earlier. We showed objectively that while EUS-D should be preferred in all cases of WON, PCD should be avoided in WON cases with >40% solid debris. Larger randomised studies focussing on the efficacy of the drainage modalities on OF resolution and the effects of solid debris content are needed to further clarify this conundrum.

Author contributions

J Samanta: conception and design, data interpretation, data analysis, drafting the work, patient care and doing the procedure and final approval. J Dhar: data acquisition, data interpretation, patient care, intellectual review of the work, final approval. G Muktesh data interpretation, patient care, intellectual review of the work, final approval. P Kumar-M and A Das: data interpretation, intellectual review of the work, patient care, final approval. P Gupta, R Agarwala and BL Bellam: data acquisition, patient care, intellectual review of the work, final approval. R Chuahan, H Kumar, TD Yadav and V Gupta: data interpretation, intellectual review of the work, patient care, final approval. SK Sinha and R Kochhar: data interpretation, critical review of the work, final approval. A Facciorusso: data interpretation, data analysis, critical review of the work, final approval.

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