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An audit of percutaneous drainage for acute necrotic collections and walled off necrosis in patients with acute pancreatitis

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ABSTRACT

Background and objectives: Percutaneous catheter drainage (PCD) is used as a first step in the management of symptomatic fluid collections in patients with acute pancreatitis (AP). We aimed to compare the outcome of patients with acute necrotic collection (ANC) and those with walled-off necrosis (WON), who had undergone PCD as a part of management of AP.

Methods: Consecutive patients of AP with symptomatic ANC or WON undergoing PCD were evaluated. Primary outcome measures were need for additional surgical necrosectomy and mortality. Secondary outcome measures were need for up-gradation of first PCD, need for additional drain, in-hospital as well as total duration of PCD and length of hospital stay.

Results: Indications of PCD in 375 patients (258 with ANC and 117 with WON) were suspected infected pancreatic necrosis (n = 214), persistent organ failure (n = 117) and pressure symptoms (n = 44). Need for additional surgical necrosectomy was seen in 14% patients with ANC and in 12% of patients with WON (p = 0.364) and mortality was 19% in patients with ANC as compared to 13.7% in those with WON (p = 0.132). There was no significant difference in the secondary outcome parameters between patients who underwent PCD for ANC or WON. Complications of PCD were comparable between patients with ANC and WON except development of external pancreatic fistula which occurred more often in patients with WON than in those with ANC (24.4% versus 34.2% respectively, p = 0.034).

Conclusion: Persistent organ failure in more often an indication of PCD in patients with ANC than in WON and suspected infection is more commonly an indication in WON than in ANC. Early PCD is as efficacious and safe as delayed PCD.

1. Introduction

Acute pancreatitis (AP) is an acute inflammatory disease of pancreas with involvement of both local tissues and distant organs. Overall 15–20% patients have necrotizing pancreatitis and depending on the presence of persistent organ failure, necrotizing pancreatitis is considered moderately severe or severe, with mortality exceeding 30% in severe AP [1–4]. Percutaneous catheter drainage (PCD) of symptomatic fluid collections in patients with AP is a minimally invasive alternative to surgical treatment and it can also be performed in very sick patients. There has been a paradigm shift in management of pancreatic fluid collections from open necrosectomy to minimally invasive treatment. Most of the centres have now adopted the "step up" approach for management of symptomatic fluid collection in pancreatitis, the first step being the percutaneous or endoscopic catheter drainage [5]. Meta-analyses have shown that the non-operative approach with percutaneous drainage is successful in up to 50% of patient with infected necrosis [6]. Surgical necrosectomy could be avoided in over half of the patients when PCD is used for infected necrosis and the overall mortality rate was lower [7]. Patients failing to recover with medical management and percutaneous drainage need stepping up in the approach of treatment in the form of single or multiport percutaneous endoscopic necrosectomy or video-assisted retroperitoneal debridement (VARD) [5,8]. Patients not responding to these minimally invasive necrosectomy techniques will ultimately

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require surgical necrosectomy which can have high mortality [9].

Most of the current guidelines recommend against invasive intervention until the collection is walled off, a process which takes atleast 4 weeks after the onset of pancreatitis [2,3,10,11]. The morbidity and mortality of patients undergoing late surgical necrosectomy in walled-off collection stage is far less than in patients undergoing early necrosectomy [12,13]. As the management of symptomatic fluid collections in AP patients has shifted from surgical necrosectomy to PCD, the question remains whether catheter drainage should be delayed till encapsulation. The median time of diagnosis of infection in pancreatic necrosis is 3–4 weeks and postponement of catheter drainage until encapsulation stage could in fact hamper recovery [14,15]. Early catheter drainage of symptomatic fluid collections in AP can lead to removal of pancreatic necrotic and/or infected tissue and decrease in intra-abdominal pressure resulting in interruption of the inflammatory cascade. This could have the potential to improve outcome, but evidence for the same is lacking [16,17].

The present study was undertaken to do an audit of PCD looking at the indications, outcomes and complications among patients who had undergone PCD for pancreatic collections at the stage of ANC and WON in a tertiary care centre.

2. Patients and methods

2.1. Patients

This retrospective study is based on patients who had undergone PCD as part of their management of AP at a tertiary care centre in North India between January 2011 and December 2017. The study was approved by Institutional Ethics Committee and informed consent was taken from each patient. Patients with evidence of chronic pancreatitis (CP) were excluded from the study. Patient who had undergone any prior endoscopic/radiological/surgical intervention or PCD outside of our centre were also excluded from the study. Patients with known severe pre-existing co-morbid illnesses like chronic kidney disease, cirrhosis, chronic obstructive airway disease, bronchial asthma, congestive heart failure and malignancy were also excluded.

2.2. Treatment protocol

The diagnosis of AP was made on the basis of revised Atlanta criteria [2]. Severe acute pancreatitis was defined by the presence of persistent organ failure (OF) and moderately severe pancreatitis defined as local/systemic complications without persistent organ failure, based on modified Marshall scoring system [18]. A score of $\geq$2 in the modified Marshall scoring system for organ dysfunction was defined as presence of organ failure and if organ failure resolved within 48 h labelled as transient and when it persisted >48 h labelled as persistent organ failure [2,18]. All patients were managed according to standard recommendations which included fluid resuscitation, organ system support, pain alleviation and nutritional support (enteral or parenteral) [19,20]. Nutritional support was primarily provided by naso-jejunal tube feeding which was instituted as soon as the patient was stabilised to undergo endoscopy.

Contrast-enhanced computed tomography (CECT) was done within 5–7 days after onset of pain or after initial evaluation in patients referred from other centres for pancreatic/extra-pancreatic necrosis and fluid collections. Antibiotics were used for extra-pancreatic infections and suspected pancreatic necrosis infection. Infected necrosis was suspected by the patient's worsening clinical course or by the presence of gas within the necrosis seen on CECT. Infection of pancreatic necrosis was established by culture of drain fluid.

2.3. Percutaneous catheter drainage (PCD)

2.3.1. Procedure

The fluid collections were characterized as ANC and WON as per revised Atlanta criteria [2]. The indications for PCD were persistent organ failure, suspected infected necrosis and/or pressure symptoms (persistent pain, biliary obstruction, gastric outlet obstruction). The site, route and image guidance (computed tomography/ultrasonography) of PCD were chosen by interventional radiologist based on the location, size and extent of the pancreatic collections (Figs. 1 and 2). Pre-procedure optimization of coagulation parameters (platelet count of at least 100,000/μL and international normalized ratio (INR) less than 1.5) was done. The techniques used for PCD was either Tandem trocar or Seldinger technique depending on the size and site of collection(s) and an initial size of 10 Fr catheter was used for PCD [21,22]. The first aspirated fluid sample was transferred to bacteriology laboratory in a sterile container for culture. Catheter was left for gravity drainage and flushed with normal saline at least once a day.

2.3.2. Post PCD follow-up

Post-procedure, patients were monitored for improvement in organ failure, control of infection and relief of pressure symptoms. In the event of no improvement within 72 h, the catheters were upsized to a maximum of 16 Fr or additional drainage was placed for any residual collection(s). After the drainage procedure, antibiotic therapy was modified according to the culture sensitivity report and continued for at least 10–14 days. All patients were followed up clinically and radiologically (ultrasonography or computed tomography) till discharge and thereafter imaging repeated at 2–4 weeks till resolution or surgery/death. Patients who failed to recover or worsened with medical management and PCD were subjected to open surgical necrosectomy.

2.3.3. Complications

Complications related to PCD like external pancreatic fistula (EPF), slippage and blockade of catheter and bleeding through PCD were noted. External pancreatic fistula (EPF) was diagnosed when clear pancreatic secretion of $\geq$100 ml per day persisted through PCD beyond 3 weeks of insertion of PCD, adopted from International Study Group of Postoperative Pancreatic Fistula definition [23]. Patients with EPF were managed conservatively for 1–2 weeks and in the event of persistence of drainage, considered for pancreatic duct stenting. Patients with slippage and blockade of catheter were readmitted and managed with reintroduction of PCD. Bleeding from PCD site was investigated and managed as per the indication.

2.3.4. Statistical analysis

All data were entered on a personal computer in Microsoft Excel (2010) and SPSS software. The data was analysed using SPSS software (version 23.0, IBM). Data was explored for any outliers, errors and missing values. Quantitative or numerical variables were represented with measures of central location like mean with measures of dispersion i.e. standard deviation. Categorical variables between ANC and WON were compared using Chi-square test. Comparison of mean between ANC and WON was done with student t-test. The p value of less than 0.05 was statistically significant.

3. Results

3.1. Patient characteristics

Of the 650 patients with AP admitted to our centre between the study period 375 underwent PCD as a part of their management.

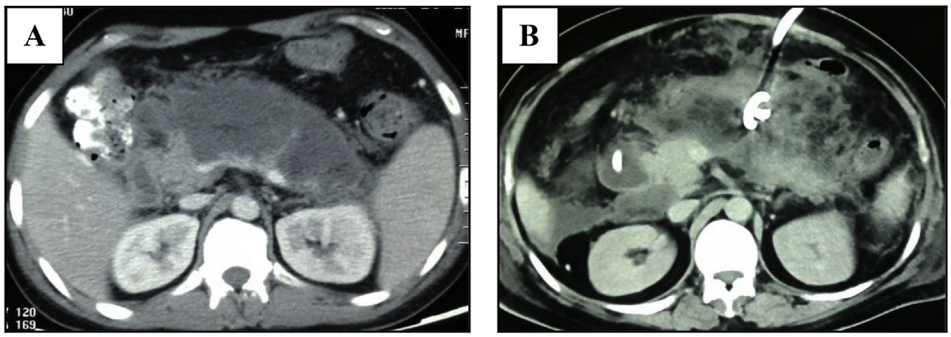

Fig. 1. CECT abdomen; A) Before PCD, B) 15 days after PCD for ANC.

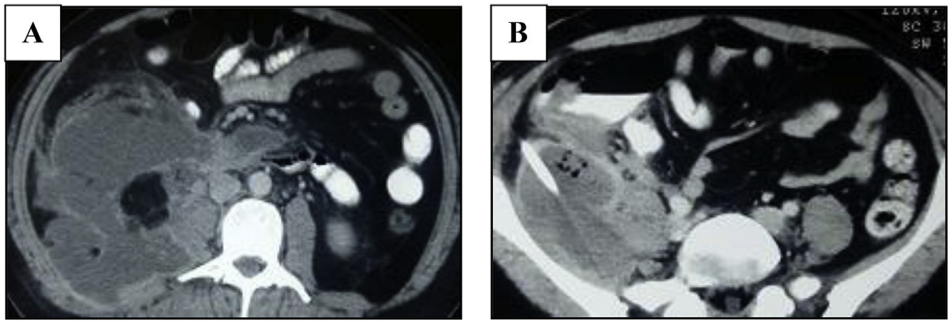

Fig. 2. CECT abdomen; A) Before PCD, B) 11 days after PCD for WON.

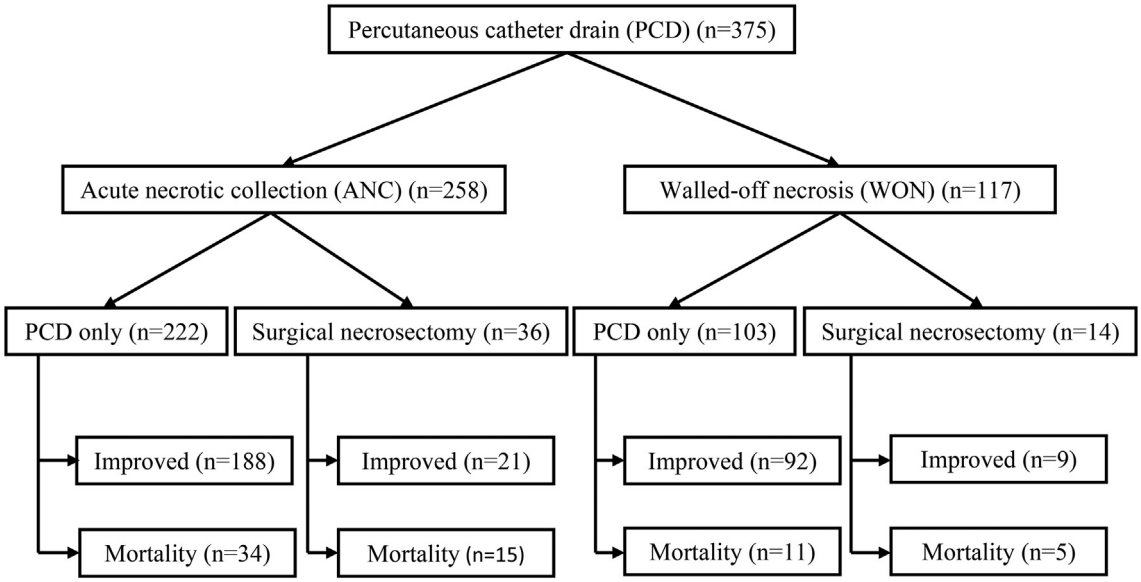

Fig. 3. Outcome of PCD for ANC and WON.

The mean age was 38.58 ± 12.28 years and 71.5% patients were males. Out of the 375 patients who underwent PCD, 258 (68.8%) patients underwent PCD for ANC and 117 (31.2%) for WON (Table 1). The underlying etiology was alcohol in 51.5%, biliary in 35.5%, idiopathic in 9.1% and other identifiable etiology in 3.9% of patients without any difference in patients having ANC or WON. The mean time to admission to our hospital was 10.47 ± 9.82 days and 36.79 ± 30.69 days in patients who underwent PCD for ANC and WON respectively.

3.2. Percutaneous catheter drainage (Figs. 1–3)

The indications for PCD were suspected infected necrosis, persistent organ failure, and pressure symptoms (Table 2). Though the commonest indication for PCD in ANC as well as WON was suspected infection of pancreatic necrosis, persistent organ failure was an indication for PCD in a significantly higher number of patients with ANC as compared to those with WON (38% vs 16.2% respectively). Pressure symptoms formed the indication for PCD in

Table 1
Clinical parameters of 375 patients.

Characteristics		Total (n = 375)	Acute necrotic collection (ANC) (n = 258)	Walled-off necrosis (WON) (n = 117)	Significance (p)
Age, Years (mean ± SD)		38.58 ± 12.28	37.42 ± 12.20	41.13 ± 12.15	0.007
Gender	Male	268 (71.5%)	179 (69.4%)	89 (76.1%)	0.113
	Female	107 (28.5%)	79 (30.6%)	28 (23.9%)	
Etiology	Alcohol	193 (51.5%)	134 (51.9%)	59 (50.4%)	0.914
	Gallstones	133 (35.5%)	88 (34.1%)	45 (38.5%)	
	Others	15 (3.9%)	11 (4.3%)	4 (3.4%)	
	Idiopathic	34 (9.1%)	25 (9.7%)	9 (7.7%)	
Pain-to-admission interval (days)		18.68 ± 22.53	10.47 ± 9.82	36.79 ± 30.69	0.001
Infected pancreatic necrosis		221 (58.9%)	146 (56.6%)	75 (64.1%)	0.104

Table 2
Comparison of PCD parameters between patients with ANC and WON.

Characters		Total	Acute necrotic collection (ANC)	Walled-off necrosis (WON)	Significance (p)
Indication	Suspected infection	214 (57.1%)	135 (52.3%)	79 (67.5%)	0.001
	Persistent organ failure	117 (31.2%)	98 (38.0%)	19 (16.2%)	
	Pressure symptoms	44 (11.7%)	25 (9.7%)	19 (16.2%)	
PCD up-gradation		201 (55.2%)	150 (58.1%)	57 (48.7%)	0.056
Additional PCD		151 (40.3%)	106 (41.1%)	45 (38.5%)	0.358
Duration of in hospital PCD (days)		22.30 ± 13.24	22.02 ± 13.55	22.93 ± 12.55	0.536
Total duration of PCD (days)		28.94 ± 22.55	28.38 ± 20.72	30.16 ± 26.20	0.479
Mean number of PCDs		1.50 ± 0.68	1.50 ± 0.66	1.50 ± 0.72	0.915

PCD: Percutaneous catheter drainage; ANC: Acute necrotic collection; WON: Walled-off necrosis.

9.7% patients with ANC and 16.2% with WON. Infection of pancreatic necrosis was proven with culture of drain fluid in 146 (56.6%) patients with ANC and 75 (64.1%) patients with WON (p = 0.104). PCD was placed under radiological guidance (ultrasound or computed tomography), endosonographic guidance was not used in any of the patients.

One PCD was placed in 152 (58.9%) patients with ANC and 72 (61.5%) patients with WON whereas 106 (41.1%) patients with ANC and 45 (38.5%) patients with WON required ≥ 2 PCDs with a mean of 1.50 ± 0.66 and 1.50 ± 0.72 PCDs per patient respectively (Table 2). The first PCD was upgraded in 150 (58.1%) patients with ANC and 57 (48.7%) patients with WON. The mean in-hospital PCD duration was 22.02 ± 13.55 days and 22.93 ± 12.55 days for ANC and WON respectively. The total duration of PCD for patients with ANC was 28.38 ± 20.72 days in comparison to 30.16 ± 26.20 days for patients with WON.

3.3. Complications

A total of 204 complications occurred in 375 patients with AP who underwent PCD as part of their management with, external pancreatic fistula (EPF) being the most common (n = 103), followed by blockade of PCD catheter (n = 46), slippage of PCD catheter (n = 41), and bleed through PCD catheter (n = 14) (Table 3). The rate of complications was comparable between patients who underwent PCD for ANC and WON, except for development of EPF. A majority of patients with ANC and WON and EPF underwent successful endoscopic pancreatic stenting with resolution of fistula (43/63; 68.3% and 32/40; 80% respectively) and rest of the patients with EPF were managed conservatively. Patients with blockade or slippage of PCD catheter were readmitted and repositioning of catheter was done. Bleeding from PCD site was investigated and managed as per indication. Pseudoaneurysms were identified in 11 patients and managed successfully with endovascular coil/glue embolization, while in 3 patients no bleeding site could be identified on imaging or angiography and they were managed with surgical packing.

3.4. Outcome

Of the 375 patients required PCD as part of management subsequent opensurgical necrosectomy was required in 50 (13.3%) patients and the overall mortality was 65 (17.3%). The need for additional surgical necrosectomy and mortality were similar in patients who underwent PCD for ANC and WON (Table 3). Subgroup analysis was done for patients with proven infected pancreatic necrosis for open surgical necrosectomy and mortality. The rate of open surgical necrosectomy after PCD for patients with proven infected necrosis and ANC was 19.9% in comparison to 16% with WON (p = 0.306) and mortality was 22.6% and 17.3% respectively (p = 0.232).

4. Discussion

We retrospectively analysed data of 375 patients with AP having symptomatic fluid collections who underwent PCD as a part of their management and compared the data between the patients who underwent PCD for symptomatic ANCs and WONs. The need for upgradation and additional PCD, duration of in-hospital PCD, total duration of PCD and average number of PCDs were similar between the two groups. Need of additional surgical necrosectomy and mortality were also similar in patients who underwent PCD for ANC and WON.

The natural history of AP suggests that nearly 90% of severe necrotizing pancreatitis patients develop ANC, of whom 70% go on to develop WON [24]. Open surgical necrosectomy had been the mainstay of management of patients not responding to conservative treatment. A number of studies have shown that delayed necrosectomy had better outcome than when it was done early [12,13,25]. Evidence based guidelines recommend that open necrosectomy should preferably be postponed till 4 weeks after the onset of disease [2,3,10,11]. But even delayed necrosectomy carries significant mortality [13]. Percutaneous or endoscopic drainage with or without endosonographic guidance of necrotic fluid collections has emerged as an alternative to open necrosectomy in the

Table 3
Complications and outcome of percutaneous catheter drainage.

Characters		Total	Acute necrotic collection (ANC)	Walled-off necrosis (WON)	Significance (p)
Complication	EPF	103 (27.5%)	63 (24.4%)	40 (34.2%)	0.034
	Bleed	14 (3.7%)	8 (3.1%)	6 (5.1%)	0.247
	Blockade	46 (12.3%)	29 (11.2%)	17 (14.5%)	0.231
	Slippage	41 (10.9%)	18 (10.9%)	13 (11.1%)	0.534
PD stenting for EPF		75 (72.8%)	43 (68.3%)	32 (80.0%)	0.013
Surgery		50 (13.3%)	36 (14.0%)	14 (12.0%)	0.364
Mortality		65 (17.3%)	49 (19.0%)	16 (13.7%)	0.132

EPF: External pancreatic fistula; PD: Pancreatic duct.

last 15–20 years. These minimally invasive procedures are associated with lower morbidity and mortality as compared to open necrosectomy and are the preferred treatment option now [26,27]. It has been suggested that even these interventions should be delayed as much as possible [28]. The Dutch Pancreatitis Study Group had reported that longer the time between admission and intervention (both surgical and non-surgical), the lower the risk of mortality: 56% within 0–14 days; 26% within 14–29 days; 15% after 29 days [27]. The rationale for delayed percutaneous or endoscopic drainage is that some patients might improve with antibiotics only [29] and catheter drainage might be easier in the WON as collections become more liquefied with time [30] and endoscopic transmural drainage may have better results in patients with walled-off collection. However, data on the impact of timing of PCD is limited [17,31]. In the current study we have carried out PCD under radiologic guidance and endosonography was not used.

In our study, of the 375 patients undergoing PCD, 258 had the procedure done in the first 4 weeks i.e. they had ANC, while 117 had PCD beyond 4 weeks for WON. Previous studies have reported a widespread time interval of 9–75 days after the onset of pancreatitis for first catheter drainage procedures [22,26,27,32–41]. However in none of the studies, a distinction has been made between patients having ANC and WON. Baudin et al., reported that among patients who underwent PCD, those who ultimately survived had onset-to-PCD interval of 23 ± 18.7 days, compared to those who died having onset-to-PCD interval of 13 ± 7.5 days ($p = 0.04$) [32]. Sugimoto et al., had contrary results with less mortality (10%) in their patients who had PCD done within a median of 23 days as compared to the patients in "PANTER" trial who had the PCD done after 30 days with mortality of 40% [42]. The Dutch Pancreatitis Study Group have done sub-analysis of "PANTER" trial patients and concluded that there was no difference in mortality among patients undergoing first surgical or non-surgical intervention for infected necrosis within or beyond 28 days [43]. In a systematic review of 14 studies, van Grinsven et al. have also reported no evident relation of outcome of PCD with timing of first catheter placement with mortality ranging from 0% to 29% [17].

Percutaneous catheter drainage works as a definite treatment or "bridge therapy" to surgical necrosectomy [26]. However, data on relationship of subsequent requirement of surgical necrosectomy and the timing of PCD are contradictory [26,32,40]. Baudin et al. reported that need for additional surgical necrosectomy was 26.5% when PCD was placed within 24 days of hospitalization as compared to none when PCD was placed after that period [32]. However, Tong et al. reported that the mean time of onset-to-PCD in patients who improved with only PCD (30.74 days) was similar to that in patients who required additional open necrosectomy (27.80 days, $p = 0.153$) [40]. Wronski et al. also reported that the median time to PCD in patients successfully treated (33 days) was similar to that patients who failed to improve with PCD (25 days, $p = 0.29$) [26]. The rate of surgical necrosectomy after first intervention with PCD in our study was 13.3%, without any difference between the two group of ANC and WON (14% and 12%, respectively). Van Grinsven et al. in their systematic review also reported a wide range of 0%–100% of requirement of necrosectomy after PCD without any relation with timing of first intervention [17].

There is heterogeneity in the reported data on relationship between time of first intervention and complication rates. The Dutch Pancreatitis Study Group had reported that longer the time between admission and intervention (surgical and non-surgical), lower the risk of complications [27]. The same group had reported that there was no difference in complication rates among patients undergoing first surgical or non-surgical intervention for infected necrosis within or beyond 28 days [43]. We also did not find any difference in complications between patients undergoing PCD for ANC and WON, except for development of EPF. The overall development of EPF in our study was 27.5% and it was significantly higher when first PCD placement was done for WON. The rate of development of EPF in our study was greater than the previously reported figure of 10–24% [32,37,44]. There is no standardised definition for EPF and previous studies have not mentioned the criteria for its diagnosis. We have adopted the criteria from International Study Group of Postoperative Pancreatic Fistula definition 2016 [23]. We do not have a clear explanation for development of more EPF with delayed drainage. We speculated that patients with WON have a mature encapsulation and tissues are more organised which might result in slower closure of the PCD track. The rate of bleeding complications in our study was 3.7% without any relation to the time of first PCD. A systematic review of 11 studies had reported bleeding rates varying from 0% to 50% with no correlation to the timing of intervention [17]. The readmission rate due to blockage and slippage of catheter was 23.2% in our study without any evident relation to the timing of intervention and it was much lower than the reported rate of up to 53% [41]. We believe that proper counselling and instructions and meticulous follow up resulted in low readmission rate in our study patients.

Our study thus shows that timing of PCD does not in any way impact the outcome. PCD can be safely done in patients with ANC, with equal safety and efficacy as in patients with WON. We can speculate that waiting for the collections to mature dose not accrue any additional benefit. It has been suggested that, early and proactive PCD provides control of extravasated pancreatic secretions by maintaining a patent drain at the site of leakage, allowing necrotic cavity collapse over a period of time [42]. The opinion of experts is equivocal on the timing of intervention [31]. In an international expert survey, 55% of pancreatologists agreed to postpone PCD in infected necrosis using antibiotics, whereas the other 45% agreed to drain immediately [31]. Although the step-up approach was routinely used by 87% of pancreatologists, the timing of intervention varied markedly, especially for PCD [31]. Disagreement was most notable when infected necrosis was diagnosed in second or third weeks of pancreatitis, which is the period between the inflammatory phase and encapsulation.

The strength of this study is that it included a large number of patients treated with predefined management strategy of indications, up-gradation and monitoring of PCD. Limitations of our study are that our centre has a strong bias towards image guided drainage in the management of pancreatic fluid collections and we being a tertiary referral centre, there is an inherent bias towards more severe disease. As most of the patients with WON had been referred from other hospitals, with a mean pain-to-admission interval of 36.7 days, we did not have all the details of previous treatment. We had excluded patients with prior PCD or surgery, though. Additionally, like many of the studies on PCD, details about the size and site of collections were not analysed.

We have thus shown that the indications of PCD are somewhat different when it is done for ANC, when compared to WON. Persistent organ failure in more often an indication in ANC than in patients with WON and suspected infection is more commonly an indication in WON than in ANC. The outcome of PCD is however, similar in patients with ANC and WON. Apart from EPF which is more common in WON, other complications are similar. Our data, thus, suggests that PCD should be done for the specific need or indication irrespective of duration of fluid collection. Waiting for the fluid collection wall to mature is unlikely to yield any advantage.

Conflicts of interest

The authors declare that they have no conflict of interest.

Contributions

BM: Acquisition and analysis of data, Initial draft of the manuscript, Approval to final version.

ND: Acquisition and interpretation of data, Approval to final version.

PG: Acquisition and interpretation of data, Intellectual content, Approval to final version.

AG: Acquisition and interpretation of data, Approval to final version.

SM: Acquisition and interpretation of data, Approval to final version.

SKS: Conception and design of study, Intellectual content, Approval to final version.

TDY: Intellectual content, Approval to final version.

VK: Intellectual content, Approval to final version.

RK: Conception and design of study, Intellectual content, Revision and approval to final version.

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