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ORIGINAL ARTICLE

Safety and clinical outcomes of early dual modality drainage (< 28 days) compared to later drainage of pancreatic necrotic fluid collections: a propensity score-matched study

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Abstract

Background Necrotizing pancreatitis can be complicated by Necrotic Fluid Collections (NFC). Guidelines recommend waiting for 4 weeks from the onset of acute pancreatitis (AP) before considering endoscopic drainage. We aimed to compare outcomes and safety in patients undergoing early versus late drainage of NFC.

Methods We performed a retrospective review of all patients who underwent Dual Modality Drainage (DMD) [combined endoscopic and percutaneous drainage] for NFC from January 2007 to December 2020. Patients were stratified into the "early" group (DMD < 28 days from AP onset) and were matched to "late" (DMD ≥ 28 days) drainage group using propensity- core-matching. Primary outcomes of interest were technical success and adverse events. Secondary outcomes included clinical success, late complication rates, and mortality.

Results We identified 278 patients who underwent DMD for NFC. Thirty-nine belonged to the early group and were matched to 174 patients from the late group. Technical success was similar in both early and late groups (97.4% vs 99.4%: $P = 0.244$) as were the procedural and early post-procedural (< 14 days) adverse events rates (23.1% vs 27.6%: $P = 0.565$). Clinical success (92.3% vs 93.1%; $P = 0.861$) and late complication rates (23.1% vs 31.6%; $P = 0.294$) were similar. There were 2 deaths (5.7%) in the early vs. 9 (5.2%) in the late group, $P = 0.991$.

Conclusions When performed in a tertiary care center with expertise in therapeutic endoscopic ultrasound, early drainage of NFC appears to be feasible and safe. Further studies are needed to validate our results.

Keywords Acute pancreatitis · Necrotic fluid collections · Walled off pancreatic necrosis · Dual modality drainage

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Acute pancreatitis (AP) is frequently complicated by pancreatic fluid collections (PFC). Based on the duration of the collections, necrosis and contents, and degree of encapsulation, they can be classified as either "Acute pancreatic fluid collections" or "acute necrotic collections" (ANC) which usually develop within 4 weeks of the onset of pancreatitis and "pancreatic pseudocyst" or "walled-off necrosis" (WON) which usually develop after 4 weeks [1]. ANC and WON are associated with necrotizing pancreatitis which develops in approximately 10–20% of acute pancreatitis [2]. Infected necrotic fluid collections (NFC) are associated with a mortality of up to 20–30% [2].

Asymptomatic NFCs are generally managed conservatively. The most common indications for invasive treatments of NFCs are proven or suspected infection, persistent organ failure, and symptoms due to compression of adjacent vital structures [3]. International guidelines recommend waiting for at least 4 weeks from the onset of AP before any invasive therapy which allows time for the collections to form adequate encapsulation and for the necrotic material to organize [3–5]. However, these guidelines were extrapolated mainly using data from studies involving patients who underwent surgical intervention and have shown worse outcomes with early surgical intervention [6–9]. Furthermore, NFCs have been shown to become infected prior to 28 days [10] with associated significant symptomatology or deterioration despite conservative management, which requires some form of early definitive invasive therapy. Data on outcomes of early endoscopic intervention of NFCs are limited. Some studies have evaluated the feasibility and outcomes of earlier endoscopic drainage, but the data is sparse [11–13].

A "step-up" approach has been accepted as the standard of care for the treatment of symptomatic NFCs and involves initial treatment with percutaneous or endoscopic drainage followed by more invasive approaches such as minimally invasive or open surgical debridement only if needed [3, 14]. Furthermore, there has been a paradigm shift in the treatment approach from surgical necrosectomy toward minimally invasive approaches such as video-assisted retroperitoneal debridement (VARD) or endoscopic necrosectomy which has facilitated the endoscopic "step-up" approach to evolve as a first line treatment for these patients wherever expertise is available [2, 15]. Our center, has adopted a technique of combination drainage with percutaneous and endoscopic drainage simultaneously called dual modality drainage (DMD) with excellent clinical outcomes [16, 17]. The basis of this technique is to use the benefits of percutaneous drainage for irrigation and combined with an internal drain to reduce the risk of enterocutaneous fistula.

To date, there have been no studies comparing the efficacy and safety of performing early DMD (< 28 days). We performed a propensity-score matched study, comparing patients who underwent DMD before 28 days with patients who had DMD after 28 days.

Methods

We performed a retrospective, propensity-score matched study comparing the safety and clinical outcomes of patients who underwent DMD before 28 days versus the patients who had the procedure after 28 days. The study was approved by the Institutional Review Board of Virginia Mason Franciscan Health, Seattle.

Patients, inclusion, and exclusion criteria

A retrospective review of all patients who underwent DMD for NFC at our institution between January 2007 and December 2020 was performed. Patients were identified from electronic medical records as well as endoscopic and scheduling databases by using appropriate keywords and ICD codes. Clinical parameters and outcomes were analyzed via thorough chart review.

Based on the timing from the onset of symptoms until DMD, the patients were allocated into two groups based on the drainage interval—(1) "Early drainage" (ED) if the DMD was within 28 days of symptom onset or (2) "Late drainage" (LD) if DMD was at 28 days or later. Extrapolating from prior data on surgical debridement [7, 18], most endoscopist try to delay drainage of necrotic fluid collections for 4 weeks from onset of pancreatitis. However, with the current minimally invasive endoscopic and percutaneous interventions, the physiological stress and the inflammatory response is much lesser than a surgical procedure and hence the delaying of drainage until a fixed milestone of 28 days might not be as important as previously believed. Hence, we aimed to evaluate the outcomes of patients who had earlier DMD compared to those who had the intervention beyond 4 weeks. Patients were included if: (1) AP was diagnosed as per clinical, radiological, and laboratory findings as per International Association of Pancreatology (IAP)/American Pancreatic Association (APA) guidelines, (2) Necrotizing pancreatitis and NFC was confirmed by contrast enhanced computer tomography scan (CECT), and (3) DMD for NFC was performed within 28 days of symptom onset. Patients were excluded from the study if: (1) Date of onset of symptoms was unclear, (2) In the setting of chronic/recurrent pancreatitis with prior fluid collections and treatment, (3) Patients who were transferred from an outside facility with an existing percutaneous drain or any prior interventions for NFC, (4) Patients with only single modality drainage (either only percutaneous or endoscopic drainage) or only surgical management or (5) Lost follow-up prior to resolution of the fluid collections.

Imaging

Computer Tomography Severity Index (CTSI) scores are analyzed based on points provided for pancreatic necrosis (None = 0, ≤ 30% = 2, > 30–50% = 4, > 50% = 6) and grading of pancreatitis (Normal pancreas = 0, Enlarged or expanded pancreas = 1, Stranding/edema in pancreas and peripancreatic fat = 2, Single peripancreatic fluid collection = 3, 2 or more peripancreatic collections = 4). CTSI score constitutes the sum of these 2 factors with a maximum score of 10 [19]. CECT images of the patients prior to DMD, when available, were reviewed independently by a radiologist to evaluate the degree of encapsulation of NFC and contents of the fluid collections. The degree of encapsulation was categorized as complete if there was 100% encapsulation around the NFC or incomplete if less than 100%. The content of the largest collection was classified by its appearance on CT as (1) homogenous fluid, (2) non-homogenous fluid with visible debris and/or septations and/or visible fat, and (3) collections containing gas. These features were analyzed and compared between the ED and LD groups. Patients who had CT scans without IV contrast prior to DMD or CECT done at outside facility with unavailable images for review were excluded from this analysis.

Dual modality drainage (DMD)

The full description of DMD has been previously published [16, 17]. In summary, patients have both percutaneous drainage by interventional radiology (IR) and endoscopic drainage on the same day. The steps involved in DMD are illustrated in Fig. 1. An external drain is directed by computed tomography (CT) (Fig. 1A, B). The entry of the catheter into the collection is directed toward the dependent area of the collection (Fig. 1C). If the CT scan shows multiple areas of NFC, then multiple percutaneous catheters are placed. The patient is then transferred from the IR area to our endoscopy unit for an endoscopic ultrasound (EUS). Transluminal puncture is then performed with an EUS-guided needle access (Fig. 1D). Transgastric or transenteric stents are placed into the necrotic cavity which is in closest proximity to the GI tract. Transluminal drainage is achieved using either two 7 French (Fr) double pigtail stents or a lumen apposing metal stent (LAMS) (Fig. 1E). The location of the necrogastrostomy or necroduodenostomy is confirmed with fluoroscopy. Contingent upon imaging studies suggesting a pancreatic duct (PD) leak, an endoscopic retrograde cholangiopancreatography (ERCP) was performed to study the PD (Fig. 1F). A pancreatic duct stent was placed in the case of a pancreatic leak. An antibiotic plan is set up if appropriate, and patients are trained how to flush their drains with 10–20 mL of sterile saline 3 times per day prior to discharge.

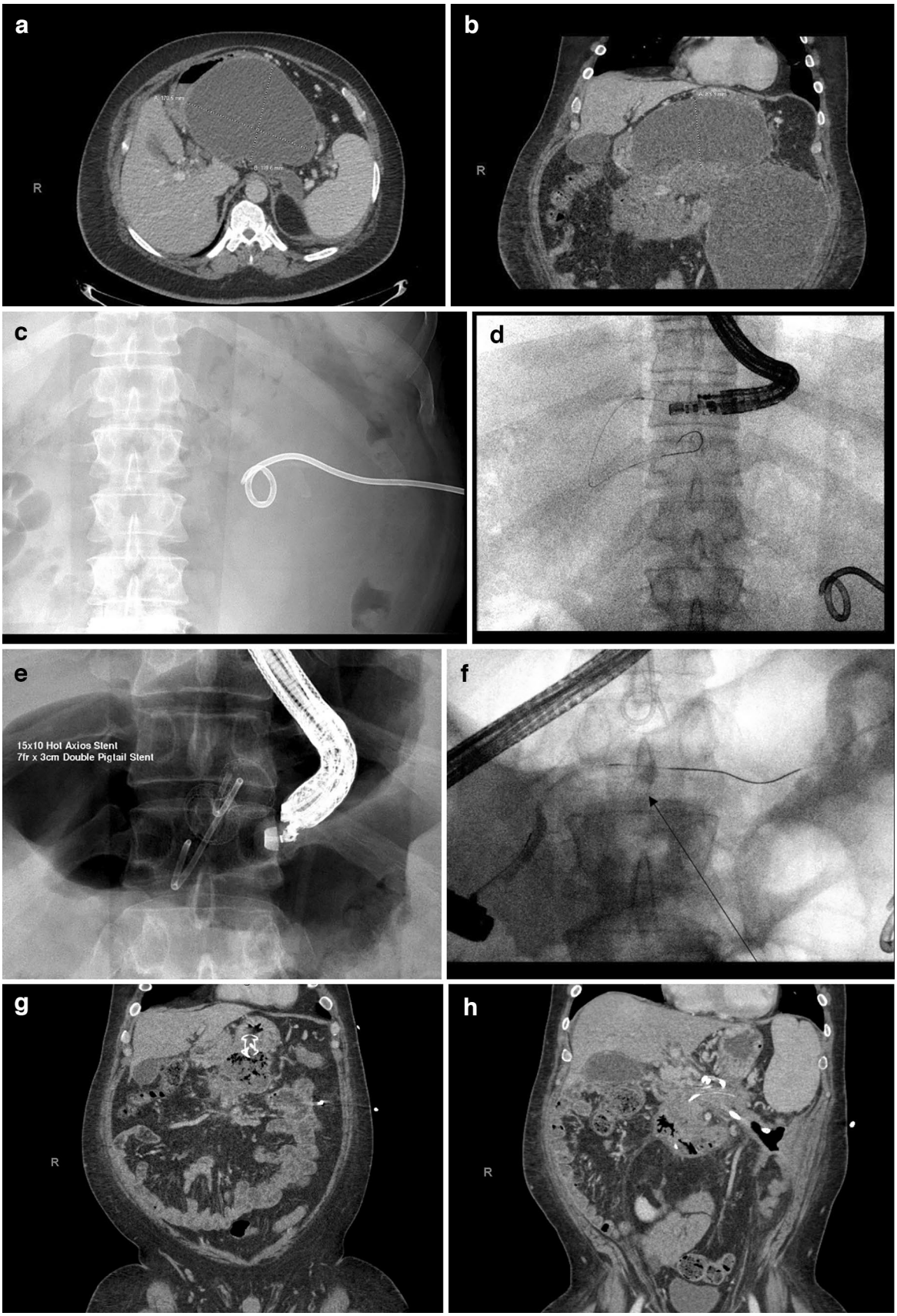
After discharge, a CT scan and IR tube check are arranged for 1–2 weeks post-discharge (Fig. 1G, H). CT scans and drain checks are dictated by the patient's course. Subsequent tube checks are typically done every 3 weeks. If necessary, the external drains are upsized. If there is no evidence of a residual fluid collection, then the drain is capped. If there is no recurrence of the fluid collections in the following 2 weeks, then the drain is removed. If there is no evidence of disconnected duct syndrome (DDS), the endoscopic stents are also removed. Transluminal pigtail stents are left in place indefinitely if there is evidence of DDS, and further work-up is performed for determination of need for surgical intervention.

Outcomes assessed

Primary outcomes of interest were technical success and early procedural or post-procedural adverse events (AE) [≤ 14 days from DMD]. Technical success was defined as successful endoscopic transluminal drainage of NFC with placement of endoscopic stents along with a percutaneous drain placement to complete DMD. Secondary outcomes of interest included clinical success, late complications (> 14 days from DMD), length of hospital stay (LOS) after drainage, time from DMD to resolution of fluid collections, requirement for endoscopic necrosectomies, requirement of surgical intervention and death. Additionally, radiological findings from CECT, when available, were compared between the early vs late group. Clinical success was defined as complete or near complete resolution (< 3 cm) of NFC resulting in removal of drains/stents without the need for surgical intervention. Adverse events/complications were classified as early (≤ 14 days) and late (> 14 days) and were recorded as per the American Society for Gastrointestinal Endoscopy ASGE lexicon [20].

Statistical analysis

All analyses were performed using Stata, Version 14.2 (Statacorp, College Station, TX). Comparison was done using Student's *t test* for continuous variables and χ^2 test for categorical variables. Statistical significance was defined as a P value < 0.05. Nearest neighbor M: 1 [variable] propensity-score matching was performed to match cases to controls on age, sex, and CTSI score resulting in matches ranging from 1:1 to 7:1.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◂**Fig. 1** Steps involved in dual modality drainage. **A**, **B** Transverse, and coronal images of the walled-off pancreatic necrosis with gastric compression. **C** Fluoroscopic image of a left-sided percutaneous drain. **D** Endoscopic ultrasound with wire access of the WOPN. **E** Fluoroscopic image of a lumen-apposing metal stent (LAMS) and a transgastric pigtail stent. **F** Endoscopic retrograde cholangiopancreatography with demonstration of a main pancreatic duct (MPD) leak (arrow). **G**, **H** Coronal images of the significantly improved WOPN with no further compression of the stomach

Results

Two hundred and seventy-eight patients who underwent NFC drainage with DMD from 2007 to 2020 were identified. Twenty-six patients were excluded for having a prior percutaneous drain from a transferring facility. Of the remaining 252 patients, 47 patients were found to have undergone early DMD < 28 days. Among the 47 patients, 3 were excluded for unclear date of onset of symptoms, 3 were excluded for history of recurrent pancreatitis episodes with prior intervention for fluid collections, 1 was excluded for inadequate imaging data, and 1 was excluded due to lost follow-up. Thirty-nine patients were included in the early DMD group. With propensity-score matching, 174 patients were matched to be included in the late DMD group, and the rest were excluded.

Baseline characteristics of the 213 patients involved in the study have been outlined in Table 1. Patients in the ED group were found to have higher BMI than the LD (32.5 ± 7.7 vs 28.7 ± 6.9, $P = 0.003$). Gallstone pancreatitis was the main etiology in both groups (61.5% vs 47.7%, $P = 0.118$). The American Society of Anesthesiologists (ASA) physical status classification was statistically similar in both groups [21]. However, most of the patients belonged to ASA class III and IV in the ED group vs class II and III in the LD group. Nearly 54% of the patients in the ED required ICU stay compared to 41% in the LD group, but this was statistically insignificant. The NFC and drainage characteristics have been outlined in Table 2. Infection was the most common indication for drainage in the ED group. The median interval between onset of pancreatitis and DMD was 22 days (10–27) in the early group compared to 52 days (28–420) in the LD group. The transgastric route was most common route used for transluminal drainage, and LAMS usage was found to be higher in the LD group.

The clinical outcomes of patients undergoing early DMD vs late has been described in Table 3. The technical success was similar in both ED vs LD groups (97.4% vs 99.4%; P value = 0.244), the procedural and early procedural adverse events (< 14 days) were similar in both the groups (23.1% vs 27.6%; P value = 0.565). One patient in the ED group did not achieve technical success due to inadequate encapsulation noted on the EUS and cystogram studies, and 1 patient in the LD group had technical failure as EUS at the attempted DMD showed 90% of the collection to be solid material in the necrosum, and therefore the procedure was aborted. Furthermore, there were 9 (23.1%) patients in the ED group and 55 (31.6%) patients in the LD group that had left paracolic gutter extension of their pancreatic fluid collections. Similarly, 4(10.2%) and 20 (11.5%) patients had right paracolic gutter extension in the ED and LD group respectively. It is important to note that, in our DMD protocol, in addition to DMD of the NFCs adjacent to gastric or duodenal lumen, additional percutaneous drainage of fluids not amenable to endoscopic drainage was allowed. This allows a patient to have multiple percutaneous drains at different locations in addition to endoscopic drainage.

Secondary outcomes of interest which included clinical success, late complications (> 14 days from DMD), time from DMD to resolution, requirement of endoscopic necrosectomies, requirement of surgical interventions, and death were similar in both groups (Table 3). Median length of hospital stay was found to be higher in the ED than the LD group (14 (3–98) vs 6 (1–95) days; P value = 0.033). Only 7.7% of patients in ED and 11% in the LD group required subsequent endoscopic necrosectomies. One patient in the LD group required surgery due to a bleeding complication with hemorrhage into the necrotic cavity that could not be managed by endoscopic or radiologic interventions. Patient underwent an exploratory laparotomy with ligation of bleeding vessel and surgical cystgastrostomy. None of the patients required surgical necrosectomies. Details of the AEs among both the groups are described in Table 4. At 6 months' interval, 2 patients had died in the ED group. One patient died 4 months after DMD due to septic shock and ventilator dependent respiratory failure due to multifocal pneumonia which was complicated by cirrhosis and hepatic encephalopathy. One other patient died 3 months later at an outside nursing facility with a suspected mucous plug and subsequent respiratory arrest.

Independent review of the available CECT images of patients prior to DMD showed that nearly 44% of patients had complete encapsulation of NFC before 28 days while 61% of the patients in the LD group had complete encapsulation. Homogenous fluid was the main content of the dominant collection in 37.5% of patients in ED and 28.5% in LD group (P value = 0.310). The remaining patients had non-homogenous fluids with debris and or fat. The technical success, clinical success, and adverse event rates did not differ among patients with complete vs incomplete encapsulation (Table 5).

Discussion

Historically, surgery or percutaneous drains were the mainstay of therapy in the management of NFCs. Studies have shown poor outcomes in patients undergoing definitive

Table 1 Demographic characteristics of patients involved in the study

Patient characteristics	< 28 days, $n=39$	≥ 28 days, $n=174$	*P* value
Age, m ± SD	55.2 ± 16.6	54.1 ± 15.1	0.697
Sex—male, *n* (%)	27 (69.2)	124 (71.3)	0.801
BMI, m ± SD	32.5 ± 7.7	28.7 ± 6.9	0.003
Etiology			
Gallstones, *n* (%)	24 (61.5)	83 (47.7)	0.118
EtOH, *n* (%)	5 (12.8)	45 (25.9)	0.082
Hypertriglyceridemia, *n* (%)	2 (5.1)	12 (6.9)	0.687
Other, *n* (%)	8 (20.5)	38 (21.8)	0.856
C-reactive protein, m ± SD	142.8 ± 79.4	138.2 ± 92.4	0.845
ASA score	–	–	0.219
ASA I, *n* (%)	0 (0.0)	1 (0.6)	
ASA II, *n* (%)	5 (13.5)	51 (29.5)	
ASA III, *n* (%)	25 (67.6)	98 (56.6)	
ASA IV, *n* (%)	7 (18.9)	23 (13.3)	
Disconnected duct syndrome, *n* (%)	22 (56.4)	94 (54.0)	0.787
ICU stay, *n* (%)	21 (53.8)	72 (41.4)	0.156

BMI body mass index, *EtOH* ethyl alcohol, *ASA* The American Society of Anesthesiologists, *ICU* intensive care unit

Table 2 Characteristics of necrotic fluid collections and drainage in early vs late groups

NFC and drainage characteristics	< 28 days, $n=39$	≥ 28 days, $n=174$	*P* value
Indication for drainage			
Obstruction (gastric outlet, biliary), *n* (%)	9 (23.1)	34 (19.5)	0.619
Infection, *n* (%)	27 (69.2)	82 (47.1)	0.013
Pain, *n* (%)	6 (15.4)	70 (40.2)	0.003
Pancreatitis to drain interval (days), median [range]	22 [10–27]	52 [28–420]	< 0.001
Type of endoscopic drain/stent			0.023
LAMS	4 (10.3)	48 (27.6)	
Pigtail	35 (89.7)	126 (72.4)	
Route			0.532
Transgastric, *n* (%)	37 (94.9)	160 (91.9)	
Transduodenal, *n* (%)	0 (0.0)	9 (5.2)	
Transgastric followed by transduodenal, *n* (%)	2 (5.1)	5 (2.9)	
Collection size (cm), m ± SD	13.8 ± 3.7	12.8 ± 4.5	0.232
Discrete collections, m ± SD	1.9 ± 0.9	2.1 ± 0.9	0.299
Disconnected duct syndrome, *n* (%)	22 (56.4)	94 (54.0)	0.787
Pancreatic duct stent among those with disconnected ducts	10/22	32/94	0.334

NFC necrotic fluid collections, *LAMS* lumen-apposing metal stent

surgical management in the early phases of the disease [6–9]. Guidelines have, hence, recommended waiting for 4 weeks before any invasive interventions for NFC [3–5]. This time allows the collections to organize and a wall to be formed around the necrotic fluid collections to become WON. Over the years, the PENGUIN and TENSION trials have shown the benefit of endoscopic necrosectomy and endoscopic "step-up" therapy which has made endoscopic treatments the main therapeutic modality for NFC [2, 22]. However, clinicians are faced with the dilemma of selecting the appropriate treatment approach when there is evidence of early NFC. Early infection can happen in nearly one third of patients with necrotizing pancreatitis. Historically, mortality of infected necrosis has approximated around 30%, and, in the presence of organ failure, mortality reaches up to 43% [23]. We performed this study to compare the safety and clinical outcomes of patients who underwent early DMD, based on clinical indications,

Table 3 Outcomes of early vs late dual modality drainage of necrotic fluid collections

Outcomes	< 28 days, $n = 39$	≥ 28 days, $n = 174$	*P* value
Technical success, *n* (%)	38 (97.4)	173 (99.4)	0.244
Clinical success, *n* (%)	36 (92.3)	162 (93.1)	0.861
Hospital days after drainage, median [range]	14 [3–98]	6 [1–95]	0.033
Drain interval until resolution, median [range]	64 [15–185]	67 [10–386]	0.302
Procedural/post procedural adverse events < 14 days, *n* (%)	9 (23.1)	48 (27.6)	0.565
Readmit w/in 30 days, *n* (%)	11 (28.9)	57 (32.8)	0.581
# Of CT scans until resolution, median	7 [3–19]	6 [1–30]	0.301
# Tube checks until resolution, median [range]	6 [1–15]	5 [0–26]	0.208
New onset diabetes 6 months after pancreatitis, *n* (%)	9 (23.1)	28 (16.1)	0.298
Endoscopic necrosectomies, *n* (%)	3 (7.7)	19 (10.9)	0.549
Required surgery for management of necrotic fluid collection, *n* (%)	0 (0.0)	1 (0.57)	0.635
Total endoscopies until resolution, median [range]	2 [0–5]	2 [1–17]	0.964
Late complications, *n* (%)	9 (23.1)	55 (31.6)	0.294
Death within 6 months, *n* (%)	2 (5.7)	9 (5.2)	0.991

Table 4 Adverse events associated with early and late DMD

Adverse events	Early group (< 28 days), $n = 39$	Late group (≥ 28 days), $n = 174$
Early procedural/post procedural adverse events [≤ 14 days after procedure] *n* (%)	9 (23.1)	48 (27.6); *P* value = 0.565
Readmission requiring PD upsizing/change due to suspected infection or PD malfunction	5 (12.8)	24 (13.8)
Bleed	2 (5.1)	16 (9.2)
Perforation	0 (0.0)	0 (0.0)
Peritonitis	0 (0.0)	3 (1.7)
Stent migration	1 (2.5)	1 (0.6)
Other	2 (5.1)	4 (2.3)
Late adverse events [> 14 days] *n* (%)	9 (23.1)	55 (31.6); *P* value = 0.294
Bleed	2 (5.1)	9 (5.2)
Perforation	0 (0.0)	2 (1.1)
Infection	1 (2.5)	10 (5.7)
Stent/PD related, (migration, occlusion)	2 (5.1)	12 (6.9)
VTE (DVT/PE/SMV/PV)	0 (0.0)	10 (5.7)
Fistula	4 (10.2)	8 (4.6)
Other	0 (0.0)	6 (3.4)

DMD dual modality drainage, *PD* percutaneous drain, *VTE* venous thromboembolism, *DVT* deep vein thrombus, *PE* pulmonary embolism, *SMV* superior mesenteric vein, *PV* portal vein

with those patients who could wait for the procedure until 28 days.

Our results suggest that patients who underwent early DMD had similar technical and clinical success compared to patients who underwent the procedure later. Adverse events rates were similar in both groups. The earliest drainage was feasible at 10 days after the onset of AP with most patients undergoing drainage in the third week or later. Independent review of CECT by a radiologist determined that nearly 44% of the NFC in ED group was completely encapsulated, and nearly 39% of the patients in LD were incompletely encapsulated. Although the optimal imaging modality to evaluate degree of encapsulation is unclear, CECT is widely accepted, and MRI and EUS can be useful as well.

DMD approaches the NFC with percutaneous and endoscopic drainage simultaneously. The percutaneous drain allows for drainage of the collection along with an ability to flush/irrigate the collection which acts as means of partial debridement. The endoscopic transluminal stents help with the egress of fluid, necrotic material, and pancreatic secretions. The initial proof of concept published the experience of 15 patients at Virginia Mason Medical Center, Seattle

Table 5 Radiological findings and outcomes based on degree of encapsulation

Radiological findings	< 28 days, $n = 39$	≥ 28 days, $n = 174$	*P* value
Pancreatic necrosis score, median [range]	6 [2–6]	6 [2–6]	0.128
CTSI score, m ± SD	8.3 ± 1.6	8.7 ± 1.6	0.198
Contents of dominant collection	$n = 32$	$n = 158$	
Homogenous fluid, *n* (%)	12(37.5)	45 (28.5)	0.310
Non-homogenous fluids, *n* (%)	20 (62.5)	113 (71.5)	0.310
Gas, *n* (%)	4 (10.3)	20 (12.7)	0.980
Complete encapsulation of fluid collection, *n* (%)	14 (43.8)	96 (60.8)	0.080
Degree of encapsulation and outcomes	< 100% (Incomplete) Encapsulation	100% (Complete) Encapsulation	*P* value
	$n = 81$	$n = 110$	
Technical success, *n* (%)	80 (98.8)	109 (99.1)	0.827
Clinical success, *n* (%)	72 (88.9)	104 (94.5)	0.151
Procedural/post procedural adverse events ≤ 14 days, *n* (%)	18 (22.2)	32 (29.1)	0.286
Late complications > 14 days, *n* (%)	29 (35.8)	33 (30.0)	0.397

CTSI Computer tomography severity Index

with DMD [16]. A subsequent study by Ross et al. with 117 patients who underwent DMD for WON showed favorable long-term clinical outcomes—DMD has been shown to prevent the development of chronic pancreatico-cutaneous fistula (PCF), reduce the need for surgery, decrease the need for necrosectomies, and has shown significantly low mortality of under 10% [17]. Compared to percutaneous drainage alone, DMD demonstrated a shorter LOS, and reduced radiological and endoscopic procedural requirements in the treatment of WON [24]. Moreover, the advent of LAMS has introduced stents with larger lumens for endoscopic drainage and improved access for endoscopic necrosectomy, where required.

There have been a few studies comparing the outcomes of early vs late endoscopic drainage of NFC [11–13]. In all the studies performed to date, the most common indication for early drainage was infection. A small series by Chantarojanasiri and colleagues compared 12 ED patients to 23 LD. All patients in the early group had technical success, and adverse events were similar in both early and late groups [11]. A study by Oblizajek et al. compared 19 patients with ED to a matched group of LD [13]. The primary outcome of fluid resolution was achieved in all patients, and there was no significant difference in adverse events or mortality. The duration of treatment until resolution was higher in the early group compared to the late group (median = 103 vs 69 days). However, our study showed a similar duration of treatment until resolution among ED vs LD groups (median days = 64 vs 67, $P = 0.409$). The median interval from onset of AP to drainage in these studies was 23 days with the earliest drainage at 15 days. Another larger study by Trikudanathan et al. compared 76 ED patients to 117 LD and reported a significantly increased mortality rate and need for rescue open necrosectomy in the ED group [12]. No patients required surgical necrosectomy in our study. The need for endoscopic necrosectomy in the ED group ranged from 50 to 100% in these 3 studies. However, endoscopic necrosectomy was needed only in 7.7% of patients in our study. This is likely attributable to the dual modality approach which has shown to reduce, or even obviate, the need for surgical or endoscopic necrosectomy in our institution. LOS for the early group was higher in our study which is similar to 2 other studies [12, 13].

This being the first study to compare the outcomes of early vs late drainage of NFC using DMD has several strengths. A propensity score matching was performed to create a robust match for the study group. A detailed and predefined inclusion and exclusion criteria were included, and a detailed review of images independently by a radiologist to evaluate the degree of encapsulation, contents of NFCs, and degree of necrosis was performed. Some limitations of this study include its retrospective nature which has an inherent risk of bias. In addition, the sample size is small which is mainly due to very limited number of patients getting interventions at less than 28 days. Finally, this is a single center study from a center with significant expertise in managing patients with severe acute pancreatitis and NFC by DMD. As such the results of this study may be difficult to generalized.

Even though complete encapsulation of a pancreatic NFC has been thought to take 4 weeks, the reality is that the exact time period varies from patient to patient. CT scans are helpful in determining the degree of encapsulation, collection contents, and the positional vicinity of the NFC to the GI lumen. EUS can further define the wall of the collection and the distance to the stomach. A sinogram through a

percutaneous drain may also help assess complete encapsulation. Hence, a multidisciplinary approach on a case-to-case basis, with collaborative evaluation by radiologists and gastroenterologists, to determine if an NFC can be endoscopically drained seems apt rather than a preset timeline of 28 days determining the course of treatment.

In summary, early DMD of NFC within a period of 28 days, if necessary, is feasible and safe and can be performed when appropriate expertise in managing these complex patients exists. Larger prospective studies and randomized trials are required to validate our findings.

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