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CLINICAL TRIAL

Nonsuperiority of Simultaneous Compared With Sequential Interventions in Infected Necrotic Collections at Multiple Sites in Acute Necrotizing Pancreatitis: A Randomized Trial

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ABSTRACT

Background: Patients with infected pancreatic necrosis (IPN) may need multiple interventions when the necrotic collection is multifocal. However, the efficacy of simultaneous interventions has not been compared with sequential interventions in this group of patients.

Methods: We performed a single-center, open-label, superiority, randomized trial at a tertiary-level hospital to compare simultaneous versus sequential intervention of infected necrotic collections involving at least two anatomical sites. In the simultaneous group (Group A), all sites were drained simultaneously. In the sequential group (Group B), only the largest site or the site with gas foci was drained initially. Additional interventions in either group were done based on predefined clinical criteria. The primary outcome was the Comprehensive Complication Index (CCI) until clinical success or death. Secondary outcomes were the number of interventions, major disease-related complications, and mortality. An intention-to-treat analysis was performed.

Results: We assessed 253 patients for eligibility, and 60 patients were enrolled (29 in Group A and 31 in Group B). The mean age was 36.9 ± 13.4 years. The mean CCI was similar among both groups (72.5 ± 28.3 vs. 64.4 ± 34.9; 95% CI, −24.59 to 8.39). The number of interventions in Group B was significantly lower (4.17 ± 2.00 vs. 2.97 ± 1.94; 95% CI, −0.18 to −2.22). Development of new-onset organ failure (34.5% vs. 38.7%), need for surgical intervention (27.5% vs. 22.5%), and mortality (41.3% vs. 38.7%) were not significantly different between the groups.

Conclusion: A simultaneous intervention approach aimed at draining multiple sites is not superior to a sequential intervention approach guided by clinical outcomes in patients with IPN involving multiple sites.

Trial Registration: CTRI identifier: CTRI/2022/07/04387

Bikkina Venkat Siddharda and Jimil Shah are co–first authors and contributed equally to this work.

1 | Introduction

Acute pancreatitis is one of the common gastrointestinal emergencies requiring hospitalization with increasing incidence across the globe. Though the majority of patients have interstitial pancreatitis, around 20%–25% of the patients develop acute necrotizing pancreatitis (ANP) [1–4]. Infection develops in around one-third of patients with necrotizing pancreatitis with mortality in this subset of patients reaching up to 35% [1–4]. Though around 30% of patients with infected pancreatic necrosis (IPN) improve by conservative management, the majority of patients require multiple interventions in the form of percutaneous, endoscopic, or surgical drainage [2, 5, 6]. Since the introduction of the "step-up approach" using minimally invasive techniques, it has become a standard of care for the management of IPN [7–10].

The minimally invasive "step-up approach" can be done either using an endoscopic route or a percutaneous route, depending on the characteristics and location of the collection as well as the availability of expertise [5, 7]. Despite the widespread adoption of the "step-up approach," the timing and frequency of the interventions are still evolving. Regarding the timing of interventions, current guidelines recommend waiting till the late phase of pancreatitis (at least 4 weeks) to ensure encapsulation and liquefaction of collection [11–13]. However, in a recent multicentric trial comparing immediate versus postponed intervention in patients with infected necrotizing pancreatitis, immediate intervention using minimally invasive techniques were not associated with an increased risk of complications [5]. Recently a multicentric trial showed that upfront necrosectomy at the time of endoscopic ultrasound (EUS)–guided drainage of the IPN with significant necrosum (> 33%) is associated with a lower number of reinterventions as compared with the endoscopic step-up approach [14].

As ANP is a dynamic disease, many patients have ongoing inflammation in the retroperitoneal space, which can spread along the interfacial planes in the paracolic space, pararenal space, pelvis, or even in the mediastinum [15, 16]. Though most of the published studies on interventions in patients with IPN have included patients with collections localized to one anatomical site, around 30%–40% of patients have collections involving multiple anatomical sites [5, 17, 18]. Management of such IPN involving multiple sites is challenging as anatomical communication does not correlate with physiological communication due to the presence of solid necrotic debris, interfacial plane, septations within the collection, fluid viscosity, and gravity factors. In this scenario, placing endoscopic stents or percutaneous catheters at one site may not drain the entire collection due to the factors described above. Whether upfront drainage of collection at multiple sites (simultaneous drainage) has better clinical outcomes compared with sequential drainage as per clinical response has not been investigated previously. At present, the sequential approach of drainage of different sites gradually in a 'step-up' manner is most commonly performed in clinical practice [7]. We hypothesized that simultaneous interventions should expedite clinical improvement by draining all the collections upfront. In the absence of evidence to guide the management in this group of patients, we performed a randomized trial comparing simultaneous versus sequential intervention (control group) in patients with IPN involving multiple sites.

2 | Methods

2.1 | Study Design and Participants

The study was a prospective, open-label, single-center, superiority, randomized controlled trial conducted at a tertiary care hospital in North India from July 11, 2022, to September 5, 2023. The trial was approved by the Institute Ethics Committee (No: INT/IEC/2022/SPL-612) and registered at the clinical trial registry of India at ctri.nic.in (CTRI/2022/07/043878). Written informed consent was obtained from all the patients or their legal representatives before the enrollment. All authors had access to study data and reviewed and approved the final manuscript.

All patients admitted with a diagnosis of moderately severe or severe ANP were screened for inclusion [19]. We included patients who had (1) ANP of more than 1-week duration and (2) the necrotic collection should be at least at two different anatomical sites with > 5 cm in size at each site, and (3) a proven or clinically suspected infected collection [5, 7]. Details of the inclusion criteria have been provided in Appendix S1. We excluded patients with (1) age < 12 years, (2) having asymptomatic collections, (3) requiring drainage of collection due to only pressure symptoms like abdominal pain, biliary obstruction, or gastric outlet obstruction, (4) who had previous intervention in any of the necrotic collections, (5) pregnant and lactating females, and (6) who did not give consent for the enrollment in the study.

2.2 | Procedures

All patients of moderately severe and severe ANP were managed conservatively in the initial first week of illness as per standard guidelines [11–13]. If the patient continued to have SIRS or organ failure, they underwent a cross-sectional imaging, preferably contrast-enhanced CT (CECT) abdomen. If the patient had drainable collections at two different anatomical sites as previously defined (size > 5 cm at each site), they were screened for the inclusion criteria along with the trial of antibiotic therapy and other conservative therapy. The patients who failed to respond to the antibiotic therapy for 72 h or continued to worsen on the conservative management were considered for enrollment after obtaining the informed consent. The enrollment was decided after reviewing the patient's clinical status and imaging profile by a multidisciplinary team consisting of an interventional gastroenterologist, interventional radiologist, and surgical gastroenterologist. Apart from the intervention, other supportive therapies, including antibiotics, nutrition, and organ support systems, were equal across both arms.

The initial interventions in both arms were via minimally invasive routes. The method of minimally invasive intervention (endoscopic or percutaneous) was decided based on the collection location, its characteristics, and the patient's clinical status. Surgical interventions were to be reserved in case of failure of minimally invasive interventions or complications due to the previous interventions, like bleeding, perforation, or enterocutaneous fistula. Interventions in the initial 3 weeks of the disease course were performed only in the presence of persistent or

worsening organ failure, which failed to respond to the conservative therapy, including a trial of antibiotic therapy. Moreover, absent or partial encapsulation was not a contraindication for the intervention in either group (Figure 1 and Appendix S1).

Group A (simultaneous interventions group): In this arm, drainage procedures at multiple sites were done simultaneously (within 24 h of randomization). The intervention route (endoscopic or percutaneous) was individualized for each collection based on feasibility and multidisciplinary discussion. Patients were reassessed after 72 h for clinical response. Patients who responded to the initial intervention as per the criteria were continued with supportive management. In nonresponders, repeat imaging (CECT-abdomen) was done after 72 h. If the size of collections was reduced by < 25%, percutaneous catheter drainage (PCD) upgradation or endoscopic necrosectomy was performed depending upon the initial intervention. In the case of a more than 25% reduction in the collection size, conservative treatment was continued, and the patient was reassessed again at 72 h for the clinical response. The above steps were continued until the complete resolution of SIRS and organ failure [5, 7].

Group B (sequential intervention group): In this arm, initial drainage was performed at the largest collection site or site with gas foci. The route of intervention (endoscopic or percutaneous) was again individualized for each collection as per feasibility and by the multidisciplinary team as described above. Patients were reassessed after 72 h of initial intervention for the clinical response. In responders, supportive treatment was continued. In nonresponders, the size of the collection in which the initial intervention was done was assessed by cross-sectional imaging (CECT abdomen). In case of a < 25% decrease in the size of the collection, a PCD upgradation or endoscopic necrosectomy was done as per the initial method of drainage. In case of a more than a 25% reduction in the size of the collection, the next largest collection was drained [5, 7]. The above steps were continued in both arms till the complete resolution of SIRS and organ failure (Figures S3 and S4).

Nonresponse to treatment was defined as below in either group: (1) increasing or less than 10% decrease in leucocyte counts, C-reactive protein; (2) any worsening organ failure; (3) new onset organ failure. These criteria were assessed at 72 h after the initial intervention [5, 7].

2.3 | Study Outcomes

The primary endpoint was the Comprehensive Complications Index (CCI), which included all complications occurring after randomization till clinical success or death and graded according to the Clavien–Dindo classification [5]. CCI is a validated tool to incorporate various complications after an intervention. All complications are graded into five types according to their severity. CCI is the sum of all complications weighted for their severity. The score ranges from 0 to 100, with a higher score representing more severe complications [5, 20, 21]. Clinical success was defined as a reduction of the intervened pancreatic collection size to less than 2 cm along with the removal of percutaneously placed drains and/or transmurally placed metal stent after resolution of SIRS and organ failure, if any.

Secondary outcomes included new-onset organ failure, mean number of interventions per patient (endoscopic and/or radiological), significant bleeding (a drop of > 2 g/dL and/or requiring intervention), perforation of a visceral organ,

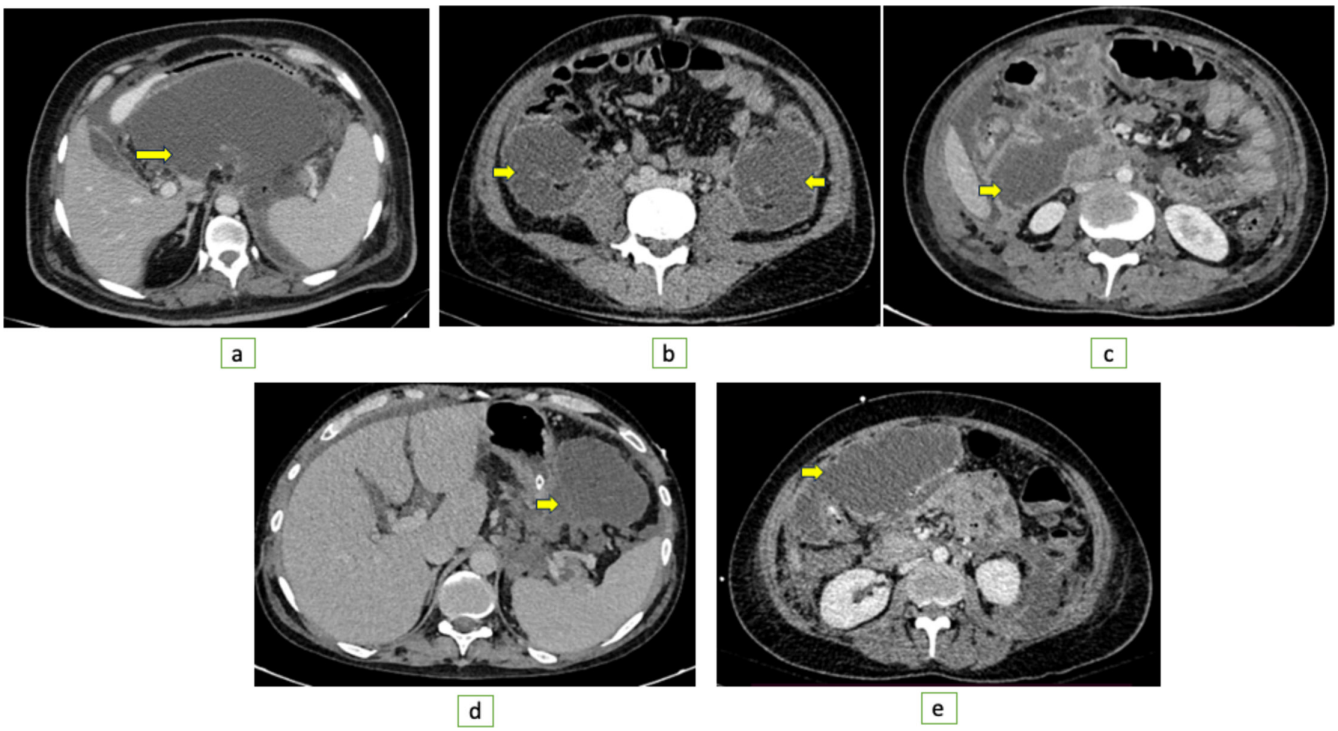

FIGURE 1 | Contrast-enhanced CT showing various sites of pancreatic necrotic collections (arrow): (a) lesser sac; (b) right and left paracolic gutter; (c) right anterior pararenal space; (d) gastrosplenic location; (e) in the omentum.

enterocutaneous fistula, external pancreatic fistula, requirement of surgical intervention, length of hospital stay after randomization, and mortality. The secondary end-points were also measured till clinical success. The primary and secondary outcomes were noted by the gastroenterologist involved in the patient care (BVS, JS). All the team members involved in patient care had access to the complete data, and any discrepancies involving the study outcomes of a particular patient were resolved after discussion with the team members every week (Appendix S1).

2.4 | Randomization and Masking

Randomization was done using a computer-generated sequence of random numbers with variable block randomization (block sizes 4 and 6). Allocation was concealed by the use of serially numbered opaque sealed envelopes. After the decision to include the patient was made and informed written consent was obtained, the envelope was opened, and patients were randomly assigned (1:1) into either simultaneous or sequential intervention groups. An appropriate intervention, according to the group, was performed within 24 h of the randomization. Given the nature of interventions, neither participants nor physicians involved in the study were masked for the procedure.

2.5 | Statistical Analysis

The sample size was calculated based on the primary endpoint. A mean CCI score of 60 (with a standard deviation of 20) for the sequential drainage is based on the previous studies [5]. We hypothesized that the simultaneous drainage group would reduce the mean CCI by 15 points compared with the sequential group due to the rapidity of drainage of all infected collections [5]. Using the online calculator OpenEpi Version 3, we calculated a sample size of 28 in each arm with 80% power and an alpha error of 0.05 to detect the assumed difference. Assuming a 5% dropout rate, we calculated a final sample size of 60.

The statistical analysis was carried out using IBM SPSS v23.0 (USA) statistics software. Mean with standard deviation (SD) was calculated for normally distributed continuous data; otherwise, median and interquartile range (IQR) were reported. Categorical variables are presented as frequency and percentages. An unpaired *t* test was used to compare quantitative variables between the two study groups. The chi-square test or Fisher exact test was used to compare the categorical variables. An intention-to-treat analysis on all randomly assigned patients was performed for the primary and secondary endpoints. The results were presented as relative risk or mean difference with 95% confidence intervals (CI).

3 | Results

3.1 | Baseline Characteristics

A total of 253 patients were screened for inclusion criteria between July 2022 and September 2023, and 60 were included in the study (29 in simultaneous interventions and 31 in the sequential intervention group) (Figure 2). The mean age of the study population was 36.9 ± 13.4 years, and 41 patients were male (68.3%). The majority of patients ($n = 43$; 71.7%) had severe disease, and 40 patients (66.7%) had persistent organ failure at the time of randomization (Table 1). Regarding necrotic

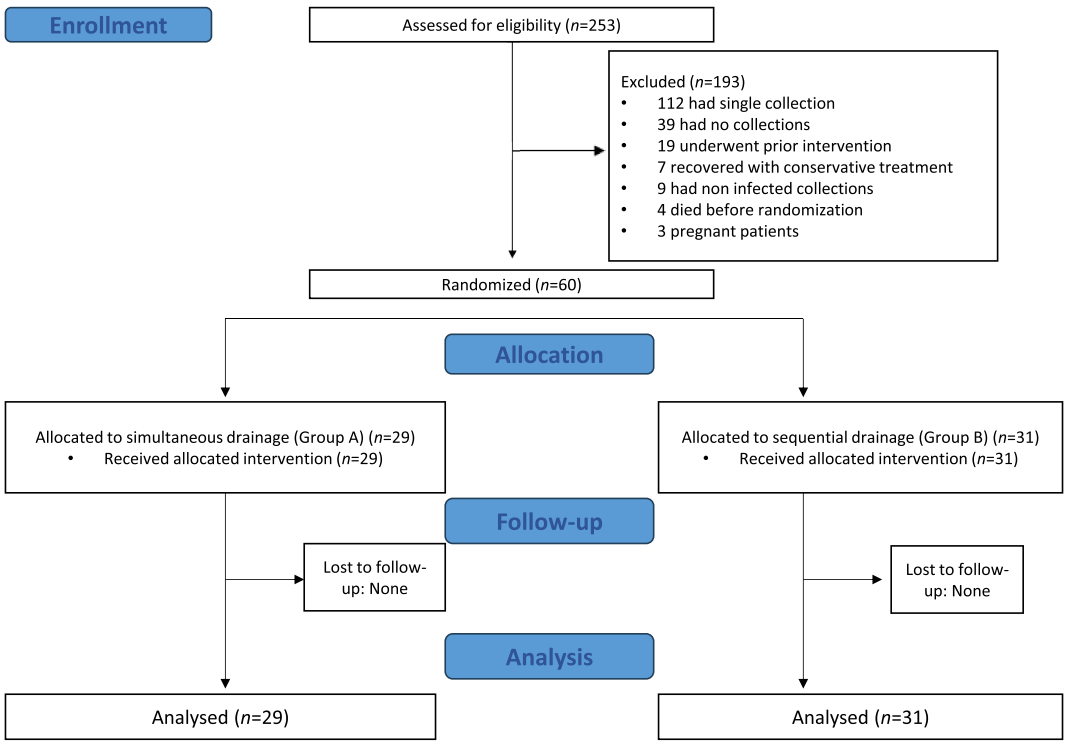

FIGURE 2 | Consort diagram of the study cohort.

TABLE 1 | Baseline characteristics of the study cohort.

Parameter	Simultaneous intervention group ($n=29$) (%)	Sequential intervention group ($n=31$) (%)	p value
Age (median (IQR)) (years)	35 (27–45)	35 (28–46)	0.69
Gender (male)	17 (58.6)	24 (77.4)	0.12
Etiology of pancreatitis			
Gallstones	8 (27.6)	13 (41.9)	
Alcohol	10 (34.5)	14 (45.1)	0.09
Hypercalcemia	3 (10.3)	0 (0)	
Idiopathic	8 (27.6)	4 (12.9)	
Moderately severe disease	7 (24.1)	10 (32.3)	
Severe disease	22 (75.9)	21 (67.7)	0.49
Presence of SIRS	29 (100)	31 (100)	0.43
Persistent Organ failure	20 (68.9)	20 (64.5)	0.71
Acute lung injury	20 (33.3)	19 (31.6)	0.53
Acute kidney injury	1 (1.6)	2 (3.3)	0.59
Cardiovascular failure	2 (3.3)	2 (3.3)	0.94
mCTSI score (10/10)	24 (82.8)	28 (90.3)	0.39
Total leukocyte count (10^3/dL)			
Median (IQR)	14.2 (11.3–20.3)	15 (10.9–20)	0.79
Mean ± SD	16.0 ± 7.0	15.4 ± 6.5	
CRP (mg/dL)			
Median (IQR)	196 (122–258)	172.5 (133.3–222.5)	
Mean ± SD	202.8 ± 92.1	180.4 ± 72.6	0.30
Procalcitonin (ng/mL)			
Median (IQR)	0.7 (0.353–2.45)	0.82 (0.35–2.60)	0.56
Mean ± SD	4.28 ± 14.09	6.834 ± 20.13	
Days of illness at time of randomization			
Median (IQR)	26 (20–45)	31 (21.5–51.5)	0.60
Mean ± SD	35.1 ± 20.0	38.4 ± 24.4	

Abbreviations: CRP—C-reactive protein; mCTSI—modified CT severity index; SIRS—systemic inflammatory response syndrome.

collections, 53 patients (88.3%) had collections involving two sites, whereas seven patients (11.7%) had collections involving three sites according to the predefined criteria. Regarding the inclusion criteria, 36 patients (60%) had culture positivity, 9 patients (15%) had culture positivity along with gas configuration in the collection, and one patient (1.7%) had only gas configuration in the preprocedural CT scan. Fourteen patients (23.3%) had clinically suspected infected pancreatic necrosis (Table S1). Baseline characteristics were comparable across both arms (Tables 1 and 2).

Patients in both groups underwent the intended interventions. In the simultaneous group (Group A), 65.5% of patients ($n=19$) had multiple percutaneous catheter placements, whereas 34.5% of patients ($n=10$) had drainage by both EUS-TMD (endoscopic ultrasound-guided transmural drainage) and percutaneous catheters. In the sequential group (Group B), 74.2% of patients ($n=23$) had PCD as the first intervention, whereas 25.8% of patients ($n=8$) had EUS-TMD as the first intervention (Table 3, Figures S1 and S2).

3.2 | Study Outcomes

The mean CCI score in Group A was 72.5 ± 28.3 and 64.4 ± 34.9 in Group B, which was not statistically significant (mean difference −8.1; 95% CI, −24.59 to 8.39; $p=0.332$) (Tables 4 and S2).

TABLE 2 | Details of pancreatic collections of the study cohort.

Parameter	Simultaneous intervention group ($n = 29$) (%)	Sequential intervention group ($n = 31$) (%)	p value
Collection sites			
Peripancreatic	23	29	
Left PCG	6	14	
Left PRS	15	11	
Right PCG	5	5	
Right PRS	1	1	0.23
Peri-hepatic	7	2	
Others	4	4	
The largest diameter of the collection (mean ± SD) (cm)			
First site	15.3 ± 5.1	14.6 ± 4.3	0.15
Second site	8.8 ± 2.7	8.5 ± 2.5	0.55
Third site	9.0 ± 4.35	7.75 ± 1.7	0.62
Presence of gas configuration	3 (5)	7 (11.6)	0.20
> 30% of pancreatic necrosis	21 (72.4)	24 (77.4)	0.65
Extent of wall formation (of the collection at largest site)			
< 20% (absence of wall)	6 (20.7)	4 (12.9)	0.72
20%–80% (partial wall)	10 (34.5)	12 (38.7)	
> 80% wall (complete wall)	13 (44.8)	15 (48.4)	

Abbreviations: PCG—paracolic gutter; PRS—pararenal space.

TABLE 3 | Details of the first intervention of the study cohort.

Parameter	Simultaneous intervention group ($n = 29$) (%)	Sequential intervention group ($n = 31$) (%)	p value
1st intervention			
Single percutaneous intervention		23 (74.2)	
EUS-TMD		8 (25.8)	
Multiple percutaneous interventions	19 (65.5)		0.46
EUS-TMD with percutaneous intervention	10 (34.5)		
Sites of 1st interventions			
Peripancreatic	23	19	
Left PCG	6	7	
Left PRS	14	3	
Right PCG	5	0	NA
Right PRS	1	0	
Perihepatic	6	1	
Others	4	1	
Mean time for clinical success after randomization (days)	43.7 ± 35.7	33.6 ± 25.8	0.21

Abbreviations: EUS-TMD—endoscopic ultrasound guided transmural drainage; NA—not applicable; PCG—paracolic gutter; PRS—pararenal space.

TABLE 4 | Primary and secondary outcomes of the study cohort.

Parameter	Simultaneous intervention group ($n=29$) (%)	Sequential intervention group ($n=31$) (%)	p value	Relative risk or mean difference (95% CI)
Primary outcome				
CCI (mean ± SD)	72.5 ± 28.3	64.4 ± 34.9	0.332	−8.1 (−24.59 to 8.39)
Secondary outcomes				
New onset organ failure	10 (34.5)	12 (38.7)	0.734	0.89 (0.46–1.74)
Bleeding	6 (20.7)	2 (6.4)	0.172	3.2 (0.70–14.64)
Enterocutaneous fistula	5 (17.2)	3 (9.7)	0.417	1.78 (0.47–6.79)
External pancreatic fistula	4 (13.7)	3 (9.7)	0.552	1.42 (0.35–5.83)
Need for surgical intervention	8 (27.5)	7 (22.5)	0.654	1.22 (0.51–2.94)
Total interventions (endoscopic and/or radiological) (mean ± SD)	4.17 ± 2.00	2.97 ± 1.94	0.021	−1.20 (−0.18 to −2.22)
Hospitalization days (mean ±SD)	28.9 ± 23.6	22.1 ± 18.2	0.213	−6.80 (−17.65 to 4.04)
Mortality	12 (41.3)	12 (38.7)	0.832	1.07 (0.58–1.99)

Abbreviation: CCI—comprehensive complication index.

New onset organ failure was seen in 10 patients of Group A and 12 patients of Group B (relative risk 0.89; 95% CI, 0.46–1.74; $p=0.734$). Eight patients had significant bleeding in the study cohort (six in Group A and two in Group B; relative risk 3.2; 95% CI, 0.70–14.64; $p=0.172$) (Table S3). Eight patients developed enterocutaneous fistulization in the study population (five in Group A and three in Group B; relative risk 1.78; 95% CI, 0.47–6.79; $p=0.417$). Six patients had post-PCD fistulization, one patient had post-VARD (video-assisted retroperitoneal dissection) fistulization, and one patient had spontaneous fistulization (five colonic and three small intestinal in location). Six patients needed surgery, and the other two were managed conservatively. Six of them eventually succumbed to the illness (Table S4); 25% ($n=15$) of the patients needed surgical intervention due to persistent SIRS after initial drainage ($n=9$) or GI fistulization ($n=6$). Nine patients eventually succumbed to illness post-surgery (relative risk 1.22; 95% CI, 0.51–2.94). Patients enrolled in Group B had a significantly lower mean number of interventions (endoscopic and/or, radiological) compared with Group A (4.17 ± 2.00 vs. 2.97 ± 1.94; mean difference −1.20; 95% CI, −0.18 to −2.22; $p=0.021$). In Group B, 19 patients achieved clinical success, and in 68.4% of patients (13/19), drainage of the second collection was not needed after the initial drainage of the larger collection. Moreover, when we excluded the initial interventions, both groups required similar numbers of reinterventions (2.17 ± 2.02 in Group A vs. 1.97 ± 1.94 in Group B; mean difference −0.2; 95% CI, −0.82 to 1.23). The mean hospitalization days were 28.9 ± 23.6 in Group A and 22.1 ± 18.2 (mean difference −6.80; 95% CI, −17.65 to 4.04; $p=0.213$). A total of 24 (40%) patients succumbed to the disease in the study cohort (12 in each group; relative risk 1.07; 95% CI, 0.58–1.99; $p=0.832$) (Tables 3 and S2–S4).

4 | Discussion

In this randomized trial, simultaneous interventions at all sites in patients with IPN did not improve the clinical outcomes or mortality compared with sequential interventions tailored according to the clinical response. In the sequential group, two-thirds of patients did not require additional intervention at the second site after draining the largest site. These results suggest that in patients undergoing intervention for extensive infected necrotic collections involving multiple sites, draining the largest component or the component with the gas configuration should be a preferred approach.

In our study, we found that the overall CCI and mortality were higher compared with previously published prospective studies [5, 7]. In a recently published POINTER trial, the mean CCI was 57 and mortality was 11.5%, compared with our study where the mean CCI was 68.3 with an overall 40% mortality. In the POINTER trial, only 20% of patients had a severe disease, while in the present study, around three-fourths of patients had severe disease, with two-thirds of patients having persistent organ failure at the time of randomization [5]. Initial radiological studies have also shown that a higher volume of extra-pancreatic necrosis is associated with a stormy clinical course with an increased need for intervention, lengthy hospitalization time, and higher mortality [22, 23]. Similarly, Baroud et al., in a recent retrospective study, showed that patients with diffuse collection (extending in > 2 abdominal quadrants) and/or higher (> 30%) solid debris were associated with more complicated courses requiring necrosectomies and prolonged hospital admission [24]. In the present study, all patients had collections at multiple sites with a higher necrosis

burden, which could also contribute to an overall higher CCI score in the study cohort.

The present study re-emphasizes the clinical outcomes shown in the POINTER trial, even in sicker patients with a higher burden of necrotic content. In the POINTER trial, around 35% of patients did not require any intervention in the postponed intervention arm, and they improved with conservative management [5]. In our study, around two-thirds of patients improved after drainage of the largest collection and continuation of conservative treatment in the sequential intervention arm, which was the reason for the lower mean interventions in the sequential drainage arm.

As ANP is a dynamic and heterogeneous disease that evolves over a period of time, the management/intervention protocol needs to be individualized. Modes of intervention in the IPN depend on various factors, including the location of the collection, wall character of the same, availability of expertise for percutaneous or endoscopic drainage, and overall clinical condition of the patient. Over the last two decades, EUS-TMD has become a modality of choice for centrally placed collections, with generalized adoption of the technique [9, 10]. In our study, however, 57% of centrally placed collections (24 out of 42) were intervened using the percutaneous route. Out of that 24 patients, 3 patients were intervened during the early phase of illness (< 3 weeks) with an ill-defined encapsulating wall, 9 patients had respiratory failure with significant respiratory distress making them unsuitable for repeated endoscopic procedures, and 10 patients had both the early phase of disease along with respiratory failure. The absence of availability of bedside EUS-guided drainage of the collection at our center was also an important limitation that made percutaneous interventions a procedural choice in patients with respiratory distress during the current study, as per current recommendations [12]. However, we do acknowledge this important limitation of the present study.

Our study has a few limitations. As the main objective of our trial was to check for clinical success rates between the two groups, we did not include long-term follow-up of the included patients. Due to the nature and complexities of the interventions, the current study was an open-label study; hence, bias in reporting cannot be ruled out. There was also heterogeneity among the intervention modalities in the study cohort. As acute pancreatitis is a complex and dynamic disease that evolves, such heterogeneity is expected in a real-life clinical scenario, which we wanted to replicate for wider adaptability. Considering that having multiple infected necrotic collections at different sites is rare, we find our sample size modest.

To conclude, in patients with infected necrotic collections involving multiple sites, simultaneous drainage of all sites is not superior to sequential drainage guided by the clinical outcomes. The sequential approach is associated with fewer interventions during the disease course, yet achieves similar clinical outcomes.

Acknowledgments

The authors have nothing to report.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Deidentified data are available on a reasonable request from the corresponding author.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.