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Research Letter

Comparison of early and delayed intervention for symptomatic acute necrotizing pancreatitis: Need for Re-intervention and clinical outcomes

Pankaj Singh [a,*], Vikas Singla [a], Muzaffer Rashid Shawl [a], Akash Goel [a], Kaushal Madan [a], Pankaj Gupta [a], Pallavi Garg [a], Vivek Saxena [c], Amit Kumar [b]

[a] Centre for Gastroenterology, Hepatology & Endoscopy, Max Super Speciality Hospital, Saket, New Delhi, 110017, India
[b] Department of Radiology, Saket, New Delhi, 110017, India
[c] Department of Interventional Radiology, Saket, New Delhi, 110017, India

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Acute Necrotizing Pancreatitis (ANP) is associated with significant morbidity and mortality. Symptomatic ANP often requires interventional drainage. In general, delaying the drainage till 4 weeks from the onset of pancreatitis is recommended [1]. However, patients with clinical deterioration despite conservative treatment may need early drainage (<4 weeks). The aim of this study was to compare early drainage (<4 weeks) with delayed drainage (>4 weeks) for symptomatic ANP in terms of clinical outcome and need for re-intervention.

This is a retrospective study of prospectively maintained database of all consecutive patients with acute pancreatitis (AP) admitted in tertiary care center between February 2021 and August 2023. All patients were managed as per the standard treatment protocol as defined previously [2]. The indication for early drainage was deteriorating clinical condition despite optimum supportive treatment including antibiotics for suspected infected necrosis. Delayed drainage was performed for symptomatic walled off Necrosis (WON) [1]. Endoscopic ultrasound (EUS) guided transluminal drainage (ETD) was done for walled off peri-gastric or peri-duodenal collection by preferably placing a lumen apposing metal stent. Percutaneous drainage (PCD) was done for those who were not fit for endoscopic drainage, collections with ill-defined walls or peripherally located collections. For those with persistent infection despite adequate drainage, endoscopic necrosectomy was performed either by direct transluminal endoscopic necrosectomy (DEN) or percutaneous endoscopic necrosectomy (PEN) depending on the route of initial drainage (details of drainage and necrosectomy are available in the Supplementary appendix). Both early and delayed drainage groups were compared in terms of need for re-intervention (additional drains or endoscopic/surgical necrosectomy) and clinical outcomes. The primary outcome was a composite of control of infection, resolution of organ failure, survival and resolution of symptoms. Secondary outcomes were individual components of primary outcome, complications and duration of hospital stay. The complications were graded according to Clavien-Dindo classification [3]. The study was approved by Institutional Ethics Board (IEC REF.NO: BHR/RS/MSSH/DDF/SKT2/IEC/LGS/23-22).

Statistical analysis was done using SPSS version 22 (IBM Corp., Armonk, NY, USA). Continuous variables are expressed as either mean (± standard deviation) or median (interquartile range). Categorical variables are expressed as number of patients and percentage. The two groups were compared by using the two-tailed Student t-test or Mann–Whitney *U* test for continuous variables and $\chi 2$ test or Fisher exact test for categorical variables, respectively. A p value of ≤ 0.05 was considered statistically significant.

* Corresponding author. Gastroenterology Centre for Gastroenterology, Hepatology and Endoscopy Max Super Speciality Hospital, Saket 1, Press Enclave Road, Saket, New Delhi, 110017, India.
E-mail address: pankajdoc06@gmail.com (P. Singh).

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The baseline clinical details of all patients with acute pancreatitis are outlined in the Supplementary Table 1. Out of 160 patients with acute pancreatitis, 67 patients had ANP and 55 had infected pancreatic necrosis. Fifteen patients responded to non-interventional treatment. Fifty-two symptomatic patients with ANP, of whom 40 had IPN, required interventions.

Early drainage was done in 27 of 52 patients at a median of 22 days (range,7–33) from the onset of pancreatitis. Twelve patients (44.44 %) had complete encapsulation and 15 patients (55.55 %) had partial encapsulation of acute necrotic collections. Nine patients underwent ETD, PCD was done in 16 patients with peripheral collections, and 2 patients underwent both ETD and PCD. 90 % of the patients who underwent ETD required DEN and 83.3 % of the patients with initial PCD required PEN. Delayed drainage was done in 25 symptomatic patients with WON, who initially got stabilized with conservative treatment; 19 patients (76 %) underwent ETD, 5 patients (20 %) underwent PCD and 1 patient underwent both. Of these, 10/20 patients with initial ETD required DEN and 4/6 patients with initial PCD required PEN.

Table 1
Baseline demographic details, interventions and clinical outcomes of early and delayed drainage in symptomatic pancreatic necrosis.

Characteristics	Early (<4 Weeks), (n = 27)	Delayed (>4 Weeks), (n = 25)	P value
Median age (Range), Years	33 (16–65)	35 (12–71)	0.45
Sex (Male: Female)	2.85:1	4:1	
Etiology, n (%)			0.20
Biliary	6 (22.22)	8 (32)	
Alcohol	11 (40.74)	4 (16)	
Idiopathic	8 (29.62)	12 (48)	
Post ERCP	2 (7.4)	1 (4)	
Necrotic Collection, n %			0.14
Sterile	4 (14.81)	8 (32)	
Infected	23 (85.52)	17 (68)	
Size of Necrosis, cm, Median (Range)	15 (8.2–28.51)	10.50 (6.50–21.93)	0.02
Extent of Necrosis			0.08
<30 %	2 (7.40)	5 (20)	
30–50 %	6 (22.22)	11 (44)	
50–70 %	12 (44.45)	7 (28)	
>70 %	7 (25.93)	2 (8)	
Location of Necrosis, n (%)			0.003
Central (peri-gastric/lesser sac)	9 (33.33)	19 (76)	
Peripheral (para-colic gutters/pelvis)	6 (22.22)	4 (16)	
Central with deep extension	12 (44.45)	2 (8)	
Encapsulation at intervention, n (%)			0.0012
Complete	12 (44.44)	23 (92)	
Partial	15 (55.56)	2 (8)	
Indications for Initial Interventions, n (%)			0.35
Infected Necrosis failed to conservative treatment	14 (51.85)	9 (36)	
Infected Necrosis with New onset organ failure	7 (25.93)	2 (8)	
Persistent mechanical symptoms	6 (22.22)	14 (56)	
Median no. days from onset of AP to Interventions, (Range)	22 (7–27)	46 (30–90)	<0.00001
Initial interventions, n (%)			0.03
Endoscopic transluminal drainage (ETD)	9 (33.33)	19 (76)	
Percutaneous drainage (PCD)	16 (59.26)	5 (20)	
Both ETD & PCD	2 (7.40)	1 (4)	
Subsequent Re-Interventions, n (%)	25 (92.59)	15 (60)	0.01
Direct Endoscopic Necrosectomy (DEN)	8 (29.62)	9 (36)	
Additional PCD	10 (37.03)	3 (12)	
Percutaneous Endoscopic Necrosectomy (PEN)	13 (48.14)	3 (12)	
Both DEN & PEN	2 (7.40)	1 (4)	
VARD	1 (3.70)	0	
Surgical Necrosectomy	1 (3.70)	2 (8)	
Surgery due to other cause	1 (3.70)	2 (8)	
Primary composite outcome, n (%)	20 (74.04)	23 (92)	0.08
Resolution of organ failure, n (%)	5/8 (62.6)	2/2 (100)	0.15
Control of Infection, n (%)	12/14 (85.71)	8/9 (88.88)	0.41
Mortality, n (%)	7 (25.92)	1 (4)	0.02
Resolution of mechanical symptoms, n(%)	8/8 (100)	13/14 (92.85)	0.21
Necrosis resolution,			0.63
Complete, n (%)	18 (66.66)	17 (68)	
Partial, n (%)	6 (22.22)	4 (16)	
Complications, n (%)			0.22
Stent occlusion infection	3 (11.11)	4 (16)	
Bleeding	8 (29.62)	6 (24)	
Minor bleeding (subsided spontaneously)	3 (11.11)	1 (4)	
Major bleeding requiring angioembolization	5 (18)	5 (20)	
Bowel Perforation	1 (3.70)	2 (8)	
Infection post necrosectomy	5 (18.51)	2 (8)	
Internal bowel fistula (Cysto-enteric)	5 (18.51)	1 (4)	
External pancreatic fistula	3 (11.11)	1 (4)	
None	8 (29.62)	15 (6)	
Clavien–Dindo ≥ III complication, n (%)	9 (33.33)	5 (20)	0.27
Median length of ICU stays, days (IQR)	10 (0–154)	0 (0–60)	0.33
Median length of hospital stays, days (IQR)	35 (2–180)	15 (4–120)	0.0007

Comparison of early and delayed drainage for clinical outcomes

Baseline characteristics of both the groups are outlined in Table 1. The need for re-intervention with placement of additional drains and/or need for endoscopic necrosectomy was significantly higher in the early drainage group vis-a vis delayed drainage (92.59 % vs 60 %, p = 0.01): in terms of additional drains (37 % vs 12 %), and endoscopic necrosectomy (85.1 % vs 52 %). No significant difference was noted in terms of the primary composite outcome (74.04 % vs 92 %, P = 0.08) and complication rate (33.3 % vs 20 %, P = 0.27). Among the secondary outcomes, mortality (25.92 % vs 4 %, P = 0.02) and median length of hospital stay (35 days vs 15 days, P < 0.05) were significantly higher in the early drainage group (additional details are available in Supplementary Table 2).

A recent multicenter trial 'the POINTER trial' compared immediate versus postponed drainage, and found no benefit of immediate drainage, with lesser number of interventions in delayed drainage. However, 37 patients had died, and 51 patients underwent drainage prior to randomization, suggesting that sick patients who might have benefited from early intervention were excluded from randomization in that study [4]. Three recent retrospective studies reported early endoscopic drainage to be safe and effective with outcomes similar to those with delayed drainage [5–7]. These studies may not truly represent the entire cohort of acute pancreatitis requiring early drainage as those with deep extension that cannot be drained endoscopically were mostly excluded. The strength of our study is inclusion of all patients with acute pancreatitis irrespective of the severity and the route of drainage utilized. This is likely to represent the real-life situations. The limitations of this study are the retrospective nature, smaller sample size and a single center data.

The causes of mortality in our patients with early drainage were persistent multi-organ failure and infection. The mortality of 25.9 % in this group of sick patients compares well with the reported mortality of 29 % in those with organ failure and infected necrosis in the Dutch study [8].

With the availability of lumen apposing metal stents (LAMS), 91 % of the endoscopic transluminal drainage in our series was done with LAMS. This could be another possible reason for the comparable risk of complications and ease of subsequent necrosectomy in the early drainage group. In this study, complete encapsulation was seen in 44 % of patients who underwent early drainage. This supports the notion, as also highlighted by Trikudanathan et al. [5], that a 4-week waiting period before intervention is an arbitrary time frame, and early step-up intervention may be feasible and helpful in patients with at least partially encapsulated collections and clinical worsening despite optimum medical treatment.

Authors contributions

Pankaj Singh: data acquisition and analysis, wrote the manuscript draft. Muzaffer Rashid Shawl, Pallavi Garg, Pankaj Gupta and Akash Goel: treated and enrolled the patients in the study, critically reviewed the manuscript. Amit Kumar: radiologic assessment and intellectual inputs prior the intervention, and participated in writing the manuscript. Vivek Saxena did the radiologic interventions and participated in manuscript writing. Kaushal Madan and Vikas Singla: study conception and design, critically revised the manuscript with intellectual inputs and final approval of the version to be published

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.pan.2025.07.004.

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