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Original Research Article

A Comparative Study between Endoscopic Transmural Drainage and Direct Endoscopic Necrosectomy in Acute Necrotizing Pancreatitis

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Abstract

Background: Acute necrotizing pancreatitis occurs in 10%–20% of patients with acute pancreatitis which is one of the most important acute abdominal diseases that require hospital admission. In the past 20 years, the treatment of pancreatic necrosis has shifted from open necrosectomy to minimally invasive techniques, such as endoscopic interventions. With the development of endoscopic techniques, the safety and effectiveness of endoscopic interventions have improved, but there exist several unresolved problems. Endoscopic transmural drainage (ETD) and Direct endoscopic necrosectomy (DEN)—often performed via Endoscopic Ultrasound-guided (EUS-guided) techniques—have emerged as the preferred, less-invasive, first-line, or "step-up" approach for managing walled-off pancreatic necrosis (WON) and infected necrotizing pancreatitis (INP), significantly reducing morbidity compared to traditional surgical necrosectomy.

Aim: It was aimed to compare the outcomes of minimally invasive surgery vs endoscopic approaches for patients with infected necrotizing pancreatitis.

Methods: A total of 90 patients, aged 18-70, both sexes with confirmed or suspected infected necrotizing pancreatitis, randomly divided into two groups. Patients were randomly assigned to groups that received minimally invasive surgery (Direct Endoscopic Necrosectomy, DEN, N=44) or Endoscopic Transmural Drainage ETD, N=46). The primary endpoint was a composite of major complications (new-onset multiple organ failure, new-onset systemic dysfunction, enteral or pancreatic-cutaneous fistula, bleeding and perforation of a visceral organ) or death during 6 months of follow-up.

Results: None of the patients assigned to the ETD approach developed enteral or pancreatic-cutaneous fistulae compared with 12/27.27% of the patients who underwent DEN (P=0.01). The mean number of major complications per patient was significantly higher in the DEN group (0.69 ± 1.03) compared with the endoscopy group (0.15 ± 0.44) (P=0.05). The physical health scores for quality of life at 3 months was better with the ETD approach (P =0.39) and mean total cost was lower as compared to DEN (P =0.03).

Conclusion: In a randomized trial of 90 patients, an endoscopic transluminal (ETD) approach for infected necrotizing pancreatitis, compared with minimally invasive surgery (DEN), significantly reduced major complications, lowered costs, and increased quality of life.

Keywords: Necrosectomy, acute necrotizing pancreatitis, direct endoscopic necrosectomy.

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Introduction

Acute pancreatitis (AP) is a disorder characterized by an acute inflammatory insult to the pancreatic–peripancreatic tissue resulting in its necrosis in few patients along with systemic injury and organ failures.[1,2] Organ failure and presence of PN especially infected necrosis have been shown to be important determinants of prognosis in AP.[2,3] Despite all efforts, morbidity and mortality associated with acute necrotizing pancreatitis (ANP), especially infected PN, remains high [4-6].

A cute pancreatitis is the third most common gastrointestinal disorder in the United States, requiring more than 275,000 hospitalizations annually [7]. Necrotizing pancreatitis occurs in 20% of patients who have acute pancreatitis and is associated with mortality rate of 8% to 39% [8]. Secondary infection of necrotic tissue is a dreaded complication that may result in sepsis and organ failure [9]. Although the traditional treatment approach to infected necrotizing pancreatitis has historically been open surgical necrosectomy, the technique is associated with high rates of adverse events (34%–95%) and death (11%–39%) [10-13].

Development of a mature encapsulating wall differentiates an acute necrotic collection (ANC) from a walled-off necrosis (WON), a process that usually takes around 4 weeks [13]. These infected necrotic collections have been traditionally treated with surgical necrosectomy. However, open surgical procedures in these patients were associated with increased morbidity and mortality.

Recent evidence suggests that minimally invasive techniques that incorporate a step-up approach of percutaneous catheter placement with subsequent minimally invasive surgical necrosectomy is superior to open surgical necrosectomy with lower rates of postoperative adverse events (40%) and long-term morbidity [14].

As an alternative to surgery, endoscopic approaches have gained increasing acceptance for the treatment of necrotic collections, with an adverse event rate between 10.4% and 24.5%, and a mortality rate less than 10% [15–18].

Endoscopic techniques have undergone iterative improvements over the past 2 decades to include endoscopic ultrasound (EUS)-guided transluminal drainage by creation of single or multiple tracts with placement of plastic or metal stents, concomitant placement of percutaneous drainage catheters, and mechanical debridement of the necrotic tissue via transluminal and/or percutaneous tracts using an endoscope [17–21. These techniques, when structured to the size and extent of the necrotic collection, appear to yield better treatment outcomes [21]. The positive outcomes can be attributed to reduced surgical anxiety and associated challenges, such as pancreatic fistulas, as well as the elimination of general anaesthesia and exploratory surgical procedures. If endoscopic transluminal drainage fails to significantly improve the patient's clinical condition, an endoscopic necrosectomy can be considered as an alternative. Alternatively, a step-up technique can be employed, where drainage is performed initially.

Therefore, it is unclear which minimally invasive approach, Direct Endoscopic Necrosectomy (DEN) or Endoscopic Transmural Drainage (ETD), is better for the treatment of necrotizing pancreatitis in terms of clinical outcomes, efficacy, safety, quality of life, and costs.

Hence, this study was carried out to evaluate the Minimally Invasive Surgery, DEN vs ETD, endoscopy randomized surgery in patients with necrotizing pancreatitis.

Materials and Methods

Materials

Study site: This prospective study was conducted at a tertiary care center in Northern India, (Department of Surgery, Varun Arjun Medical College and Rohilkhand Hospital, Shajahanpur, UP, India) over a period of two years.

Study Design: Prospective, randomized analytical study

Sample Size: 90 patients, aged 20 -70 years, both sexes, with confirmed acute necrotizing pancreatitis (ANP).

Study Group: Two groups, Group -A: Endoscopic Transmural Drainage (ETD), with 46 patients. Group-B: Direct Endoscopic Necrosectomy, (DEN), with 44 patients.

Inclusion criteria:

- Patients provided written informed consent before randomization.
- The study was approved by the Institutional Human Ethical Committee.

Exclusion criteria:

- Patients of ≤ 20 years
- Pregnant women
- Cancer Patients

Methods

All the patients who underwent an early drainage (within 4 weeks of the disease onset) for the management of APN, either via DEN or ETD, were identified or included in the final analysis. The diagnosis of ANP was based on revised Atlanta classification [7]. Patients underwent ETD only if there was some semblance of a wall in PN on EUS or cross-sectional imaging. During the same period, patients who underwent DEN in the early phase of illness and had partially or completely encapsulating wall were included for comparative analysis. Informed consent was obtained from all the patients prior to the procedures. Patients were subjected to a drainage procedure (DEN or ETD) in the presence of a symptomatic pancreatic fluid collection that failed to respond to conservative management. The indications for drainage included persistent sepsis (persistent, worsening or new onset organ failure, fever, and leukocytosis) or persistent symptoms due to pain, biliary obstruction, and gastric outlet obstruction. During the initial study period, all the pancreatic fluid collections in the first 4 weeks of illness were treated with DEN. Subsequently, it was discovered that few fluid collections were getting walled off before 4 weeks cutoff and these necrotic collections were preferably treated with ETD.

Drainage procedures

Endoscopic transluminal drainage. All ETD procedures were performed by a single experienced endoscopist under conscious sedation. The EUS examination was conducted with a linear scanning

echoendoscope (EG-3870 UTK linear echoendoscope, Pentax Inc, Tokyo, Japan or UCT180 linear echoendoscope, Olympus Optical Co. Ltd., Tokyo, Japan). Only the patients in whom semblance of an encapsulating wall, as assessed by the endoscopist on EUS, were considered for further treatment with ETD. On EUS, the size of the PN and percentage of solid debris were noted prior to puncture. The echogenic material present in the PN was suggestive of necrotic debris. Using an approximate visual judgment of the endoscopist, the amount of solid necrotic debris was done as a percentage of total size of collection. Using EUS, color Doppler, and fluoroscopy guidance, the optimal site of transluminal puncture was identified. Transgastric or transduodenal route was selected based on the proximity of the necrotic collection, ensuring minimal distance between pancreatic necrotic collection (PNC) and lumen and no intervening blood vessels. The collection was punctured with a 19 G EUS-fine needle aspiration needle (Echotip; Cook Endoscopy, Winston-Salem, NC, USA). After ensuring an optimal puncture, stylet was removed and necrotic material was aspirated for culture. Subsequently, a 0.035/0.025-inch guidewire was coiled into the cavity under EUS and fluoroscopic guidance. The tract was then dilated using a 4 mm biliary dilatation balloon catheter or a 6F electrocautery dilator. Subsequently, the drainage was achieved using multiple plastic stents or a biflanged fully covered self-expanding metallic stent (BFMS) as per the endoscopist discretion, percentage of necrotic debris, and patient's preference.

Among the recipients of plastic stents, the tract was further dilated up to 12–15 mm using wire-guided hydrostatic dilatation balloon (CRE-balloon dilators; Boston Scientific, Natick, MA, USA) and multiple, 7 Fr or 10 Fr, 5 cm, double-pigtail plastic stents were deployed. A 7 Fr nasocystic drain catheter was additionally deployed in patients who were drained using plastic stents during the initial procedure for the purpose of irrigation and active aspiration. Patients clinical condition was monitored and a repeat contrast-enhanced computed tomography (CT) abdomen was performed after 72 h of the ETD to look for residual collection. If the patient responded to therapy with reduction in collection size by >50%, nasocystic drain was removed.

Direct Endoscopic necrosectomy: Endoscopic necrosectomy was performed at the index session only if there was no drainage of liquid debris after transluminal stent placement. Necrosectomy was undertaken using a cap-fitted, single channel therapeutic gastroscope (outer diameter 11 mm; Olympus America Inc.). The technique of necrosectomy was tailored to the size of the necrotic cavity and the degree of adherence of debris and involved the following 3 steps: debridement, extraction of necrotic debris, and irrigation.

Debridement: 20–30-mm polypectomy snares were used if the necrotic collection was larger than 80 mm, and smaller (<20 mm) snares were used if the necrotic collection was smaller than 80 mm. If the debris was nonadherent, 15- to 30-mm oval snares (Acusnare; Cook Endoscopy) were used. If the necrotic debris was adherent, removal was accomplished using 15- to 25-mm round, braided-wire snares (Captivator II; Boston Scientific Corp.). Only the cold snare technique was adopted for debridement unless the necrotic debris was adherent to the cavity. In such instances, electrocautery assisted debridement (ERBE USA Inc, Marietta, GA) was performed using the following settings: Endo Cut Q, Effect 3, Cutting duration 1, Cutting interval 6. The polypectomy snare was placed around the base of the necrotic debris, closed tightly, and then lifted gently to ensure absence of entangled vasculature. Electrocautery was administered and the necrotic material was peeled away from the walls of the necrotic cavity. In patients with extensive collateral vasculature within the necrotic cavity, to minimize the risk of snaring a vessel, debridement was performed using a 19.5-mm wide-jaw, rattooth forceps (Rat-Tooth Alligator Jaw Grasping Forceps; Olympus America Inc.). Intraprocedural bleeding was managed using hemostatic forceps (Coagrasper Hemostatic Forceps; Olympus America Inc.). Extraction of debris: After necrosectomy, liquefied debris was suctioned using the gastroscope. Solid debris was extracted by suctioning chunks into the cap with the aid of wide-jaw, rattooth forceps or polypectomy snares. Smaller (≤ 14.9 mm) rattooth forceps were used for extraction of debris in patients with LAMS to prevent entanglement of the distal flange and accidental dislodgement of the stent. As the final step, a retrieval net was used to remove any residual debris.

Irrigation: Normal saline was used intermittently for irrigation of the necrotic cavity during the procedure; 250 to 300 mL of half-strength hydrogen peroxide mixed in equal volume of normal saline was used for irrigation toward the completion of each necrosectomy session with the intent of sterilizing the necrotic area. Hydrogen peroxide was used only toward the end of the procedure because the emanating effervescence precluded adequate visualization of the necrotic cavity.

Post-necrosectomy treatment: Two 7-Fr, 4-cm double-pigtail plastic stents were left in situ in patients undergoing transgastric necrosectomy to maintain patency of the tract. An 18- to 24-Fr nasocystic catheter was placed to facilitate lavage

of the necrotic cavity by flushing 250 mL of normal saline every 4 to 6 hours, with frequent repositioning of the patient to facilitate irrigation and drainage of the necrotic contents.

Post discharge Follow-up

Patients were discharged following clinical resolution of symptoms. An abdominopelvic CT and outpatient follow-up were scheduled at 6 weeks. The enteral feeding tube and percutaneous catheters were removed if patients were clinically well, CT scan demonstrated resolution of the necrotic collection, and the output was less than 10 mL per day. For the endoscopic cohort, as in routine clinical practice, a magnetic resonance cholangiopancreatography (MRCP) was performed at the initial outpatient clinic visit to assess the status of the main pancreatic duct. An endoscopic retrograde cholangiopancreatography was undertaken in lieu of an MRCP when the latter was contraindicated. If the main pancreatic duct was found to be intact, then the transmural stents were removed. In patients originally treated with LAMS but diagnosed with DPDS at follow-up, the LAMS were exchanged for double-pigtail plastic stents. The plastic stents were left in situ in patients with DPDS to minimize the risk of recurrent collections [28]. If a pancreatic duct leak was identified on pancreatography, a transpapillary stent was placed to bridge the leak. Patients with persistent symptoms and necrotic collection on follow-up CT scan underwent further interventions as determined by the interdisciplinary panel.

Endpoints

The primary endpoint was a composite of major complications comprising new-onset multiple organ failure or systemic dysfunction, enteral or pancreatic-cutaneous fistula, intra-abdominal bleeding, visceral perforation, or death during admission and until 6 months after discharge. In addition to analyzing the individual primary endpoint components as secondary endpoints, other analyzed variables included mean number of major complications per patient, presence of systemic inflammatory response syndrome (SIRS) at 72 hours after index intervention, surgical site infection, incisional hernia, pancreatic exocrine and endocrine status, procedure and disease-related adverse events, post procedure length of intensive care unit (ICU) and hospital stay, HRQoL, and total cost.

Moreover, the patients who developed new onset or persistent fever or organ failure, along with persistent residual collection, underwent additional procedures with one or multiple sessions of direct endoscopic necrosectomy (DEN). Among the patients who received plastic stents, the tract was first dilated up to 15 mm after removal of previously placed stents. Subsequently, a standard gastroscope was introduced into the cavity and necrosectomy was performed. Upon completion, multiple plastic stents were replaced. Among the patients in whom a BFMS was placed, the gastroscope was directly introduced into the cavity via the metallic stent and necrosectomy was performed. Additional sessions were performed if needed in a similar fashion after assessing the clinical response at intervals of 72 h. The decision for surgical necrosectomy (open or laparoscopic) was taken for patients who failed to improve after reviewing the clinical condition and radiological findings, in consultation with patient and pancreatic surgeons.

Statistical analysis:

The qualitative data were presented as percentages and the quantitative data were expressed as mean and standard deviation or median and range as applicable. Student's t-test and Mann–Whitney U-test were used to analyze quantitative data. The qualitative data were analyzed using Pearson's Chi-square test and Fisher's exact test. Normality of the data was assessed using Shapiro–Wilk test. A two-tailed $P \leq 0.05$ was considered statistically significant.

Results

A total of 90 patients, aged 20-70 years, both sexes, 57 / 63.33% females and 33/36.66% males were included in this study. All patients with APN were randomly divided into two groups according to surgical procedures. Group-A, with 46/51.11% patients (17/18.88% males and 29/32.22% females) who underwent Endoscopic Transluminal Drainage (ETD) management (within 4 weeks of the disease onset). Group-B, with 44/ 48.88% patients (16/17.77% males and 28/31.11% females) were included for DEN management.

Among 46 patients who were managed with ETD, mean age were 33.50 ± 8.68 years. While 44 patients were managed with DEN, mean age: 32.40 ± 9.00 years. Gallstone (61/67.77%), was the most common etiology of ANP followed by alcohol (26/28.88%) idiopathic (2/2.22%), and whereas 1 patient was caused by abdominal trauma and hyper-triglyceridemia. Demographic profile of both the groups was comparable [Table 1].

Table 1: Demographic profiles of both groups.

Parameters	Gr. A: ETD, n=46	Gr.B: DEN, n=44	P Value
Age-(Years) Mean (SD)	33.50 ± 8.68	32.40 ± 9.00	
Median (IQR)	49 (31–66)	47.5 (31–65.5)	0.456
Gender, n (%)			
Female, n=57	29/32.22%	28/31.11%	0.838
Male, n=33	17/18.88%	16/17.77%	
Cause of pancreatitis, n (%) (n=90) Gallstones, n=61	32 (35.55)	29 (32.22)	0.751
Alcohol,n=26	14 (15.55)	12 (13.33)	
Idiopathic,n=2	0 (0.00)	2 (2.22)	
Other, n=1	0	1 (1.11)	
Coexisting conditions, n (%)			
Cardiovascular disease	10 (11.11)	9 (10.00)	0.632
Pulmonary disease	6 (6.66)	4 (4.44)	0.577
Renal disease	4 (4.44)	5 (5.55)	0.657
Diabetes mellitus	8 (8.88)	11 (12.12)	0.229
ASA class, n (%) (n=90) II	4 (4.44)	3 (3.33)	0.558
Ill	33 (36.66)	31 (34.44)	
IV	9 (10.00)	10 (11.11)	
CT severity index, n (%) 0–2 (n=90)	0	0	0.442
4–6	1 (1.11)	3 (3.33)	
8–10 Type of necrotic collection, n (%) (n=90)	45 (50.00)	41 (45.55)	
Walled-off necrosis	31 (34.44)	33 (36.66)	.484
Acute necrotic collection	15 (16.66)	11 (12.22)	
Size of necrotic collection-AP axis (cm)			
Mean (SD)	10.0 (4.5)	10.0 (3.3)	
Median (IQR)	8.7 (6.3–12.8)	9.2 (7.7–12.1)	0.476
Size of necrotic collection-transverse axis (cm)			
Mean (SD)	11.7 (4.1)	11.8 (3.7)	
Median (IQR)	11.0 (8.6–14.1)	11.2 (9.0–15.5)	0.874
Percentage of necrosis (%)			
Mean (SD)	44.2 (18.1)	41.8 (15.8)	
Median (IQR)	43 (25–60)	44 (30–55)	0.746
Collection extending to lower abdomen/pelvis: n (%)	14 (15.55)	12 (13.33)	0.663
Infected necrosis: n (%)[c]	32 (35.55)	32 (35.55)	0.794
Disease severity: n (%)			
SIRS	15 (16.66)	16 (17.77)	0.811
ICU/high acuity care	28 (31.11)	23 (25.55)	0.665
Single-organ failure	2 (2.22)	3 (3.33)	0.668
Multiple organ failure	1 (1.11)	2 (2.22)	0.898
Acute physiology score (APS)			
Mean (SD)	26.8 (25.2)	25.6 (18.8)	
Median (IQR)	19 (10–37)	21 (13.5–37.5)	0.638
APACHE II score			
Mean (SD)	32.7 (13.5)	29.1 (21.3)	
Median (IQR)	30 (26–35)	22 (16–23)	0.071
Time to intervention from onset of pancreatitis (wk)			
<4	9 (26.5)	8 (21.9)	0.592
4–6	29 (55.9)	26 (50.0)	
>6	8(17.6)	10 (28.1)	
Nutritional support: n (%) Enteral feeding	12 (13.33)	18 (20.00)	0.176
Parenteral feeding	5 (5.55)	4 (4.44)	
Oral diet	26 (28.88)	22 (24.44)	
Nil per os	3 (3.33)	0	
Percutaneous catheter in situ prior to intervention: n (%)	11(12.22)	9 (10.00)	0.409

AP, anteroposterior; APACHE II; Acute Physiology And Chronic Health Evaluation II; IQR, interquartile range; SD, standard deviation; SIRS, systemic inflammatory response syndrome

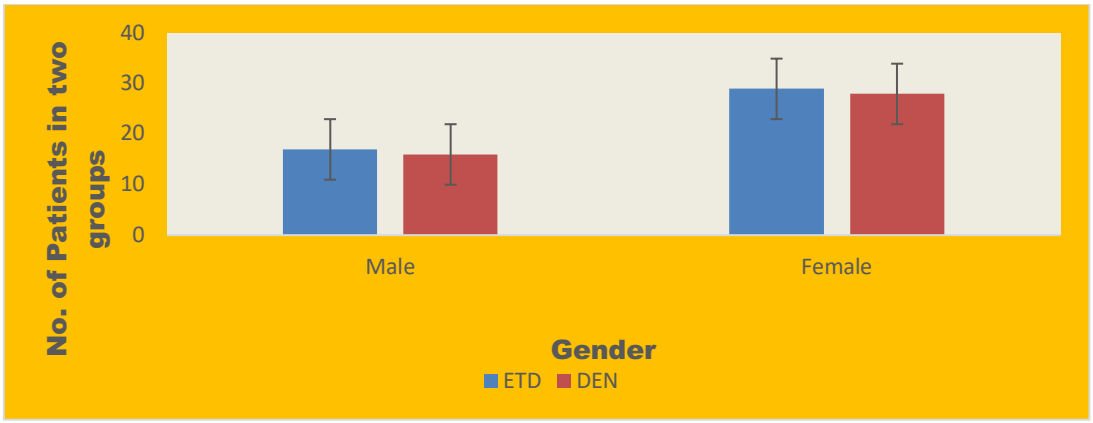

Figure 1: Gender wise distribution of patients in two groups. *Found not significant, p=0.838, $\chi^2 \approx 0.003$, **p > 0.05.**

There was no statistically significant difference in sex distribution between the ETD and DEN groups, indicating that both groups were well matched with respect to gender. Baseline demographic characteristics including age and sex were comparable between the ETD and DEN groups, with no statistically significant differences observed ($p > 0.05$), indicating adequate group matching for comparative analysis.

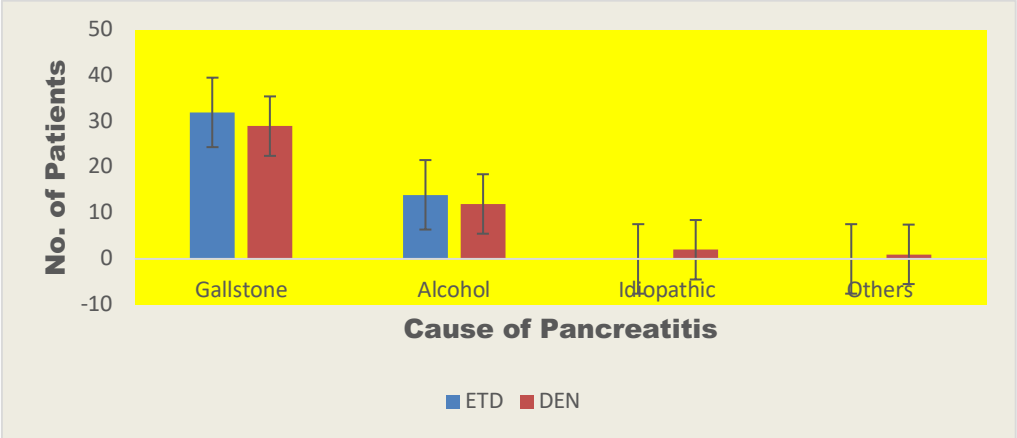

Figure-1A: Cause of pancreatitis in two groups. *Found not significant, p=0.751

Gallstones were the predominant etiology of acute necrotizing pancreatitis in both the ETD and DEN groups.

The distribution of etiological factors, including gallstones, alcohol, idiopathic, and other causes, was comparable between the two groups, with no statistically significant difference observed ($\chi^2 = 2.36$, df = 3, $p > 0.05$)." OR = 0.85 ,95% CI: 0.36 – 2.01, $p > 0.05$, RR = 0.91. Gallstone etiology did not significantly influence the likelihood of receiving DEN compared to ETD. Moreover, On univariate analysis, gallstone and alcohol-related pancreatitis were not significantly associated with the choice of endoscopic intervention. Multivariable logistic regression analysis demonstrated that etiology, age, and sex were not independent predictors of undergoing DEN versus ETD ($p > 0.05$ for all variables).Logistic Regression Results are delineated below.

Table 1(A): Variable

Variable	Adjusted OR	95% CI	p-value
Gallstones	0.89	0.38 – 2.09	>0.05
Alcohol	0.87	0.35 – 2.21	>0.05
Age	1.01	0.98 – 1.04	>0.05
Male sex	1.03	0.44 – 2.41	>0.05

Moreover, it was observed that the univariate and multivariable logistic regression analysis, cardiovascular, pulmonary, renal disease, and diabetes mellitus were not independently associated with the choice of endoscopic intervention. Baseline comorbidities were comparable between ETD and DEN groups ($p > 0.05$ for all variables). Regression Results are delineated below.

Table 1(B): Variable

Variable	Adjusted OR	95% CI	p-value
Cardiovascular disease	0.95	0.34 – 2.61	>0.05
Pulmonary disease	0.71	0.18 – 2.73	>0.05
Renal disease	1.41	0.36 – 5.48	>0.05
Diabetes mellitus	1.62	0.59 – 4.45	>0.05
Age	1.01	0.98 – 1.04	>0.05
Male sex	1.04	0.45 – 2.42	>0.05

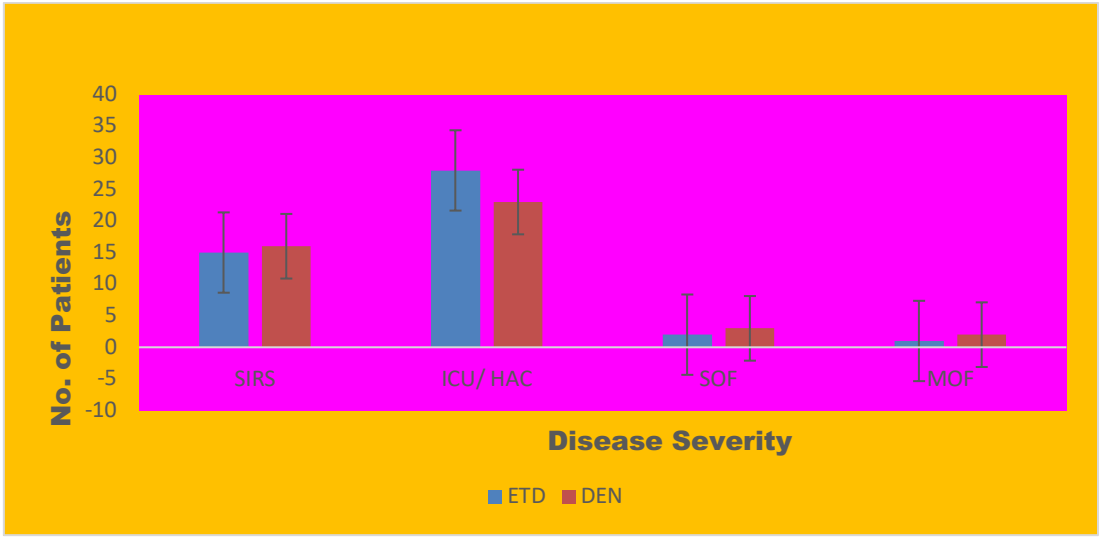

Figure-1B: Disease severity in two groups. *Found not significant,

There were no statistically significant differences in disease severity parameters, including SIRS, ICU requirement, and organ failure, between the ETD and DEN groups. Multivariable logistic regression confirmed that baseline severity was not an independent predictor of undergoing DEN versus ETD ($p > 0.05$ for all variables).Logistic Regression Results are delineated bellow.

Table 1(C): Variable

Variable	Adjusted OR	95% CI	p-value
SIRS	1.15	0.47 – 2.83	>0.05
ICU / High-acuity care	0.73	0.32 – 1.68	>0.05
Organ failure (any)	1.74	0.38 – 7.91	>0.05
Age	1.01	0.98 – 1.04	>0.05
Male sex	1.02	0.44 – 2.38	>0.05

It was also observed that the timing of endoscopic intervention from the onset of pancreatitis was comparable between the ETD and DEN groups. On univariate and multivariable logistic regression analyses, early or late intervention did not independently influence the likelihood of undergoing DEN versus ETD ($p > 0.05$ for all comparisons).

Table 1(D): Variable

Variable	Adjusted OR	95% CI	p-value
Intervention >6 weeks	1.38	0.49 – 3.86	>0.05
Intervention <4 weeks	0.92	0.32 – 2.64	>0.05
Age	1.01	0.98 – 1.04	>0.05
Male sex	1.03	0.45 – 2.41	>0.05
Severe disease*	1.21	0.53 – 2.79	>0.05

***Severe disease defined as ICU requirement and/or organ failure.**

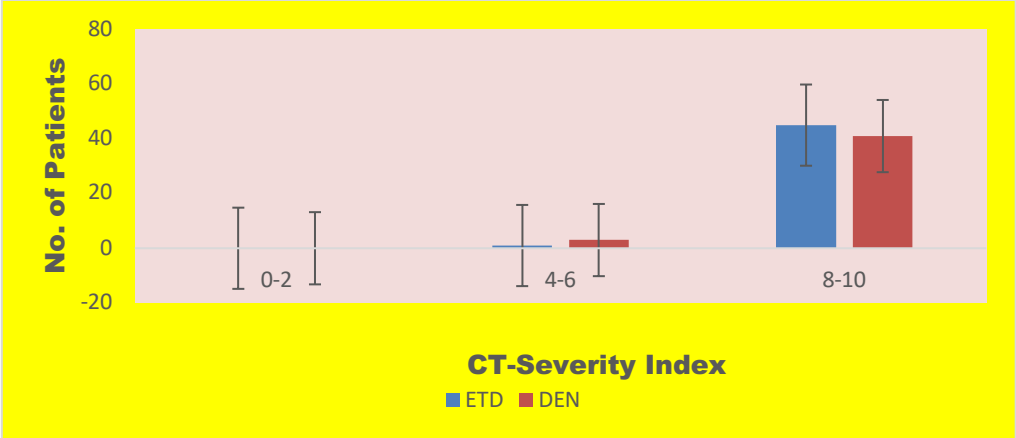

Figure 1C: CT severity index in two groups. *Found significant, p=0.442

Most patients in both groups had severe pancreatitis with a CT severity index of 8–10. There were no statistically significant differences in CT severity index or type of necrotic collection between the ETD and DEN groups. On multivariable logistic regression, radiological severity was not an independent predictor of treatment modality ($p > 0.05$). Adjusted Logistic Regression Results are delineated below.

Table 1 (E): Variable

Variable	Adjusted OR	95% CI	p-value
CTSI 8–10	0.88	0.21 – 3.69	>0.05
Walled-off necrosis	0.92	0.22 – 3.82	>0.05
Age	1.01	0.98 – 1.04	>0.05
Male sex	1.03	0.44 – 2.39	>0.05
Severe disease*	1.19	0.52 – 2.71	>0.05

The mean size of necrotic collection measured prior to drainage was also comparable between the DEN and ETD groups (12.56 ± 2.25 cm vs. 12.52 ± 2.31 cm, respectively, P = 0.812).

The sites of PNC were also comparable between both the groups, with pancreatic body being the most common site (body, head, and tail − 75.61%, 14.63%, and 4.88% and 91.3%, 4.35%, and 4.35% in the PCD and ETD groups, respectively, P = 0.391) [Table 1].

The anatomical distribution of pancreatic necrotic collections was comparable between the two groups, with the pancreatic body being the most commonly involved site. No statistically significant difference was observed in the site of necrosis between the DEN and ETD groups (p = 0.391)

Table 2: Major Clinical Outcomes Comparing ETD and DEN

Outcome	ETD (n = 46) n (%)	DEN (n = 44) n (%)	Risk Ratio (95% CI)	P value
Primary composite endpoint	4 (8.69)	13 (29.54)	0.29 (0.11–0.80)	**0.007**
Death	1 (2.17)	1 (2.27)	1.41 (0.25–7.91)	0.999
New-onset multiple organ failure	1 (2.17)	2 (4.45)	0.63 (0.11–3.51)	0.668
New-onset systemic dysfunction	0 (0.00)	1 (2.17)	—	0.485
Enteral–pancreatic cutaneous fistula	1 (2.17)	7 (15.90)	—	**0.001**
Reintervention for lack of improvement	11 (23.91)	14 (31.81)	1.18 (0.65–2.11)	0.585

Table 2, illustrating that the ETD significantly reduced major adverse outcomes, mainly driven by fewer fistulas.

Table 3: Procedural Burden and Resource Utilization

Variable	ETD (n = 46)	DEN (n = 44)	P value
Necrosectomy performed, n (%)	1 (2.17)	10 (22.72)	<0.001
Median interventions per patient (IQR)	1 (1–2)	1 (1–2)	0.475
Total interventions (study group)	28	36	—
Median hospital stay, days (IQR)	14 (6–22)	18.5 (11.5–29.5)	0.057
Median ICU stay, days (IQR)	0 (0–0)	0 (0–6.5)	0.044

Table 4: Long-term Pancreatic Function, Costs, and Quality of Life

Outcome	ETD	DEN	P value
New-onset diabetes, n (%)	6 (13.04)	9 (20.45)	0.522
Pancreatic insufficiency, n (%)	29 (63.04)	28 (63.63)	0.999
Median fecal elastase (mg/g)	62	56.5	0.472
Mean total cost (Rs)	75,830	117,492	0.039
Physical QoL score (PCS)	+5.29		0.039
Mental QoL score (MCS)	−0.22		0.962

The incidence of the primary composite endpoint was significantly lower in the ETD group compared with the DEN group (8.69% vs. 29.54%; RR 0.29, 95% CI 0.11–0.80; P = 0.007), indicating a 71% relative reduction in major adverse outcomes with ETD. This demonstrates a clear clinical advantage of a drainage-first strategy.

It was also demonstrated, significant differences in procedural intensity and healthcare resource utilization between the ETD and DEN groups. Patients undergoing Direct Endoscopic Necrosectomy (DEN) required necrosectomy significantly more often than those treated with Endoscopic Transmural Drainage (ETD) (22.72% vs. 2.17%, P < 0.001), indicating a substantially higher procedural burden associated with DEN.

Despite this difference, the median number of interventions per patient was similar in both groups, suggesting that most patients achieved clinical resolution with a limited number of procedures regardless of treatment strategy. However, at the study-group level, the total number of interventions was higher in the DEN group, reflecting increased cumulative procedural demand.

In terms of resource utilization, patients in the DEN group had a longer median hospital stay, although this did not reach statistical significance. In contrast, ICU stay was significantly longer in the DEN group (P = 0.044), highlighting increased post-procedural acuity and monitoring requirements following necrosectomy.

Overall, these findings indicate that ETD is associated with a lower procedural burden and reduced ICU utilization compared with DEN, supporting ETD as a less invasive and more resource-efficient initial treatment approach for acute necrotizing pancreatitis.

Discussion

This study provided a comprehensive comparative evaluation of Endoscopic Transmural Drainage (ETD) and Direct Endoscopic Necrosectomy (DEN) in the management of acute necrotizing pancreatitis. The principal finding is that ETD was associated with significantly fewer major adverse events, lower procedural burden, reduced ICU utilization, and lower healthcare costs compared with DEN, while achieving comparable survival and long-term pancreatic functional outcomes. These results strongly support a drainage-first, step-up endoscopic strategy in appropriately selected patients.

Primary Clinical Outcomes: The incidence of the primary composite endpoint was significantly lower in the ETD group than in the DEN group, reflecting a substantial relative reduction in major adverse outcomes. Importantly, mortality and new-onset organ failure were low and comparable between groups, indicating that the superiority of ETD was not related to differences in baseline disease severity or systemic progression, but rather to procedure-related morbidity.

These findings are consistent with prior randomized and observational studies demonstrating that aggressive early necrosectomy does not confer a survival advantage and may increase complications compared with minimally invasive step-up approaches [11–15]. The landmark PANTER trial and subsequent studies from the Dutch Pancreatitis Study Group have shown that limiting necrosectomy and escalating intervention only when necessary leads to improved outcomes in necrotizing pancreatitis [40,41].

Procedure-Related Morbidity: A key contributor to adverse outcomes in the DEN group was the significantly higher incidence of enteral–pancreatic cutaneous fistula formation. Mechanical debridement during DEN can disrupt fragile granulation tissue and adjacent bowel walls, predisposing to fistula formation. In contrast, ETD allows gradual drainage and liquefaction of necrotic contents, minimizing mechanical trauma.

Similar complication profiles have been reported in earlier endoscopic necrosectomy series, where fistula, bleeding, and perforation were more frequent with aggressive debridement strategies [36,37]. The low complication rates observed in the ETD group reinforce the safety of transmural drainage as an initial intervention.

Procedural Burden and Intervention Strategy: Although necrosectomy was required significantly more often in the DEN group, the median number of interventions per patient was similar between groups. This suggests that most patients can achieve clinical resolution with drainage alone, without the need for necrosectomy. The higher total number of procedures in the DEN group reflects

greater cumulative procedural demand at the population level.

These findings align with prior studies reporting that 60–80% of patients with walled-off necrosis improve with transmural drainage alone, reserving DEN for those with persistent infection or solid-dominant collections [38–40]. Our data further supported selective rather than routine use of necrosectomy.

Resource Utilization and Economic Impact: Patients treated with DEN experienced significantly longer ICU stays and incurred substantially higher total treatment costs. Increased ICU utilization likely reflects greater post-procedural acuity and the management of complications associated with necrosectomy. The observed cost difference is clinically and economically meaningful, particularly in resource-limited healthcare settings.

Previous cost-effectiveness analyses have demonstrated that minimally invasive step-up approaches reduce overall healthcare expenditure compared with more aggressive surgical or endoscopic necrosectomy strategies [41,42]. Our findings extend this evidence to contemporary endoscopic practice.

Long-Term Pancreatic Function: Rates of new-onset diabetes mellitus and pancreatic exocrine insufficiency were high but comparable between groups. This suggests that long-term pancreatic dysfunction is primarily determined by the extent of parenchymal necrosis rather than the type of intervention, a conclusion supported by multiple longitudinal studies [33–35]. Similar fecal elastase levels further confirm equivalent exocrine outcomes.

Quality of Life: An important and novel finding of this study is the significantly better physical component score (PCS) at 3-month follow-up in the ETD group, while mental health scores were similar. Improved physical quality of life likely reflects fewer complications, reduced ICU exposure, and faster functional recovery. Few studies have systematically evaluated patient-reported outcomes in this context, and our results support the incorporation of quality-of-life metrics into future pancreatitis trials [39].

Clinical Implications: Collectively, these findings provide strong evidence in favor of an ETD-first, step-up treatment paradigm, reserving DEN for patients with inadequate response to drainage or extensive solid necrosis. This approach is consistent with current international guidelines and expert consensus, which emphasize delaying and minimizing necrosectomy to reduce morbidity [27,38].

Strengths and Limitations: Strengths of this study include well-matched baseline characteristics, comprehensive assessment of clinical, economic, and patient-reported outcomes, and real-world applicability. Limitations include the non-randomized design and moderate sample size, which may limit the detection of differences in rare outcomes such as mortality. Nevertheless, the consistency of our findings with existing high-quality evidence supports their validity.

Conclusion

In patients with acute necrotizing pancreatitis, Endoscopic Transmural Drainage is associated with fewer major adverse events, reduced procedural burden, lower ICU utilization, decreased healthcare costs, and improved short-term physical quality of life compared with Direct Endoscopic Necrosectomy, without compromising survival or long-term pancreatic function. These results strongly support ETD as the preferred initial endoscopic strategy, with DEN reserved for selected cases within a step-up framework.

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