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ORIGINAL ARTICLE

Safety and Efficacy of Early (<4 Weeks of Illness) Endoscopic Transmural Drainage of Post-acute Pancreatic Necrosis Predominantly Located in the Body of the Pancreas

Surinder Singh Rana[1] · Ravi Sharma[1] · Kamal Kishore[2] · Lovneet Dhalaria[1] · Rajesh Gupta[3]

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Abstract

Background Endoscopic transmural drainage is usually not performed for pancreatic necrotic collection (PNC) < 4 weeks after onset of acute necrotizing pancreatitis (ANP) because of lack of encapsulating wall and increased risk of complications.

Objective Study safety and efficacy of early (<4 weeks) endoscopic transluminal drainage in patients with symptomatic PNC.

Methods Retrospective analysis of data base of patients with PNC treated with endoscopic transmural drainage within 4 weeks of onset of ANP (early drainage) was done. The outcomes and complications were compared with patients with PNC who underwent delayed endoscopic drainage (≥4 weeks of onset of ANP).

Results Thirty-four patients (26 males; mean age: 35.9 ± 8.6 years) underwent early and 136 patients (115 males; mean age: 37.9 ± 9.4 years) underwent delayed endoscopic drainage. The PNC was significantly larger (12.3 ± 2.1 cm vs 10.5 ± 2.7 cm, p <0.001) with increased solid component (47.7 ± 8.9% vs 28.3 ± 11.7%, p <0.001) in the early group. Clinical success was achieved in 94% patients in the early group and all patients in the delayed group. Direct endoscopic necrosectomy was performed more frequently in the early group (50% vs 7.4%; p<0.001). There was increased mortality (5.7% vs 0%), need for rescue surgical necrosectomy (5.7% vs 0%), and clinically significant bleeding (20% vs 1.5%, p<0.001) in the early group as compared to the delayed group.

Conclusion Early endoscopic drainage of PNC is feasible and seems to be safe as well as effective but is associated with increased risk of complications as compared to delayed drainage.

Keywords Endosonography · Pancreatic necrosis · Stent · Acute pancreatitis · Computed tomography

Introduction

Pancreatic necrotic collections (PNC) are an important local complication of acute necrotizing pancreatitis (ANP) with infected necrotic collections being responsible for significant morbidity and mortality.[1–3] Patients with infected necrotic collections usually need an interventional procedure for resolution and these patients were traditionally treated surgically.[4] The traditional surgical intervention of "open necrosectomy" was associated with significant morbidity and mortality because of associated surgical stress of laparotomy.[5–7] Minimally invasive management options including step-up percutaneous drainage (PCD), endoscopic drainage, laparoscopic transgastric necrosectomy, and video-assisted retroperitoneal debridement (VARD) have been shown to be associated with improved outcomes in patients with pancreatic necrotic collections.[2, 4, 8, 9]

Endoscopic or minimally invasive surgical drainage/necrosectomy techniques are the effective treatment options currently available for treatment of PNC. Because of increased risk of development of external pancreatic fistula (EPF) as well as poor efficacy in removing solid necrotic debris, PCD alone is not used for treatment of pancreatic necrosis. However, PCD forms an important component of step-up

✉ Surinder Singh Rana
drsurinderrana@gmail.com

[1] Department of Gastroenterology, Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh 160012, India

[2] Department of Biostatistics, Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh 160012, India

[3] Department of Surgical Gastroenterology, Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh 160012, India

treatment of PNC.[9] Recent high-quality studies including randomized controlled studies have shown that endoscopic drainage is associated with lower mortality and adverse effects in comparison to minimally invasive surgical techniques and therefore is the preferred intervention technique for management of patients with pancreatic necrosis.[10–13]

However, all PNC cannot be drained endoscopically and endoscopic transluminal drainage is possible in those collections that are adjacent to the stomach or duodenum and are encapsulated with a well-formed circumscribed wall.[8, 14] The necrotic collections with a well-formed wall are known as walled-off necrosis (WON) and the process of encapsulation usually takes 4 weeks or more from the onset of ANP.[1] The pancreatic necrotic collections developing within the first 4 weeks of illness are known as acute necrotic collections (ANC) and do not have a well-formed wall. Patients with ANC are usually not treated with endoscopic drainage because of concern of increased risk of complications due to lack of well-formed wall as well as concern with draining a predominantly solid necrotic collection with poor demarcation between viable and necrotic tissue.[4, 7, 15] Therefore, symptomatic ANC without a well-formed wall have been treated with either a step-up approach or an initial PCD followed by endoscopic transluminal drainage.[16, 17]

However, the cutoff of 4 weeks for endoscopic drainage is arbitrary and necrotic collections may get walled off completely or partially within 4 weeks of onset of illness.[17] Few studies have assessed the safety and efficacy of endoscopic transluminal drainage of PNC within 4 weeks of onset of illness and have reported encouraging results.[18–22] However, the experience with endoscopic drainage in the early phase is limited and there are concerns about increased frequency of adverse effects, need for surgical intervention, as well as mortality. In this retrospective study, we report the safety and efficacy of early endoscopic transluminal drainage (<4 weeks after onset of ANP) in patients with symptomatic PNC and compare them with the results of endoscopic transluminal drainage done in patients with symptomatic WON after 4 weeks of onset of illness.

Patients and Methods

A retrospective analysis of data base of patients with PNC treated with endoscopic transmural drainage at a tertiary care center in North India over last 9 years from 2011 to 2020 was done. The diagnosis of ANP as well as the classification of PNC into ANC and WON was based on the revised Atlanta classification.[1] All the enrolled patients with PNC had been earlier diagnosed with acute necrotizing pancreatitis (ANP) based on cross-sectional imaging findings done at days 3 to 7 of illness. Informed consent was obtained from all the patients prior to the procedures and the study was approved by the Institute Ethics Committee (IEC). All patients who underwent endoscopic drainage for symptomatic PNC during the study period were included in the study. Patients with underlying chronic pancreatitis, prior intervention, gastrointestinal fistulation of PNC, severe coagulopathy, or cardiorespiratory illness precluding safe endoscopic drainage as well as unclear date of onset of symptoms of acute pancreatitis were excluded from the study. The collections were drained if the patient had persistent sepsis (persistent, worsening or new-onset organ failure, fever, leukocytosis), persistent abdominal pain, or persistent symptoms due to biliary or gastric outlet obstruction. Endoscopic transmural drainage was categorized as early or delayed based on timing of endoscopic intervention from the onset of symptoms of acute pancreatitis (< 4 weeks or ≥4 weeks after onset of symptoms respectively).

Patient demographics, etiology of ANP, size of PNC, details of endoscopic transmural drainage procedure, its outcome details, and complications were retrieved from the data base. All patients in the standard intervention arm underwent endoscopic ultrasound (EUS)–guided transmural drainage whereas patients in the early phase of illness (< 4 weeks) underwent an endoscopic or percutaneous drainage of the PNC after a multi-disciplinary discussion involving an endoscopist, interventional radiologists, and surgeons. The contrast-enhanced computed tomography (CT) images were reviewed for the formation of an encapsulating wall. Up to 2018, all patients with symptomatic PNC in the early phase of illness were treated with a step-up approach involving an initial PCD followed by surgical necrosectomy in non-responders. After 2018, all symptomatic PNC adjacent to the stomach or duodenum were treated with an initial endoscopic transmural drainage after an inter-disciplinary consultation involving an endoscopist, interventional radiologists, and surgeons. Initial PCD was done in patients who were too sick for an endoscopic drainage or had PNC not amenable to endoscopic drainage because of being located away from the stomach or duodenum like in the root of the mesentery, retroperitoneum, or in para-colic location.

Indications for Endoscopic Transluminal Drainage

The indications for endoscopic drainage were as follows:

- CT- and EUS-confirmed pancreatic necrotic collection located adjacent to the stomach or duodenum.
- Symptomatic pancreatic necrotic collection in the form of either ongoing infection as evident by abdominal pain and fever despite administration of intravenous antibiotics or gastric outlet or biliary obstruction by the collection or new-onset organ failure
- Patients deemed stable enough to undergo endoscopic drainage by the treating team. PCD was done in patients who were too sick for an endoscopic drainage or had PNC

not amenable to endoscopic drainage because of being located away from the stomach or duodenum

Endoscopic Transmural Drainage (Figs. 1 and 2)

All endoscopic procedures were performed by a single experienced endoscopist under conscious sedation and after a detailed informed consent. A detailed EUS examination using a linear scanning echoendoscope (EG-3870 UTK linear echoendoscope, Pentax Inc, Tokyo, Japan, or UCT180 linear echoendoscope, Olympus Optical Co. Ltd., Tokyo, Japan) was conducted before embarking upon endoscopic drainage. A careful evaluation of the morphology of the PNC including presence or absence of an encapsulating wall as well as percentage of solid necrotic debris was done. The echogenic material present in the PNC on EUS was suggestive of necrotic debris. Using an approximate visual judgment of the endoscopist, the amount of solid necrotic debris was judged as a percentage of total size of the necrotic collection. Thereafter, endoscopic transmural drainage was performed under EUS guidance using a standard technique described previously.[14, 17] Either multiple plastic stents (2–5 in number, 7 or 10 Fr; 5 cm in length) or lumen-apposing metal stents (LAMS) (Nagi stent (14 or 16 mm), Taewoong Medical Co., Ltd., Seoul, Korea, or Plumber Stent (16-mm diameter), MI Tech Gyeonggi-Do, 17706, Korea, or Hot Axios stent (15-mm diameter), Boston Scientific, Natick, MA, USA) were used as per the endoscopist discretion, percentage of solid necrotic debris, and patient's preference depending upon affordability due to economic considerations and availability of health insurance. Patients who were drained with multiple plastic stents also underwent placement of additional nasocystic drain for irrigation and aspiration. After successful initial drainage, the patients were re-assessed clinically as well as with a contrast-enhanced computed tomography (CT) after 3 days. No further intervention was done in patients who responded clinically along with >50% reduction in the size of the PNC. Patients who did not have symptomatic improvement or had new-onset organ failure or fever along with < 50% reduction in size of collection underwent additional procedures as mentioned below. Patients with clinical improvement but < 50% reduction in size of collection were closely followed up and further intervention was done depending upon onset of new symptoms or clinical deterioration.

Patients with Multiple Plastic Stents

The nasocystic drain was removed in patients who responded clinically with reduction in the size of collection by >50% and multiple plastic stents were left in situ until resolution. Patients with < 50% reduction in size of collection with new-onset or persistent fever or organ failure underwent additional procedures with exchange of multiple plastic stents or direct endoscopic necrosectomy (DEN) at the endoscopist's discretion. Upon completion of DEN, multiple plastic stents were replaced. Additional sessions of DEN were performed, if needed, after assessing the clinical response as well as imaging findings at intervals of 72–120 h. Patients with persisting symptoms, significant remaining solid necrotic debris, requiring >2 sessions of DEN, and willing for metallic stent placement underwent LAMS placement to facilitate DEN. The decision for surgery was taken in non-responders after reviewing the clinical condition and radiological findings, in consultation with patient and pancreatic surgeons.

Patients with Fully Covered Self-Expanding Metallic Stents

No further intervention was done in patients who responded clinically with reduction in the size of collection by >50%. However, in non-responders, DEN was performed using a combination of accessories like grasping forceps, snare, Dormia basket, and Roth basket by introducing a gastroscope directly into the necrotic cavity via the metallic stent. If the LAMS was clogged with necrotic material, the stent was declogged and a 7-Fr nasocystic catheter (NCC) was inserted through the LAMS into the necrotic cavity for irrigation. The decision for surgery was taken in non-responders after reviewing the clinical condition and radiological findings, in consultation with patients and pancreatic surgeons.

Definitions

Early drainage was defined as drainage performed within 4 weeks of onset of symptoms and delayed drainage was defined as drainage performed ≥4 weeks after onset of symptoms of ANP. Technical success was defined as successful placement of EUS-guided stent (plastic or LAMS) in an initial attempt. Clinical success was defined as symptomatic improvement accompanied with radiological resolution of PNC and avoidance of surgery. The patients were hospitalized until clinical and radiological resolution. The complications were diagnosed according to the American Society for Gastrointestinal Endoscopy lexicon.[23]

Outcome Parameters

Patients in both the groups (early and delayed) were followed until the final outcome of either recovery or mortality. The groups were compared for the demographic features, baseline clinical characteristics, indications of interventions, number and types of interventions performed, need for DEN, complications encountered, need for surgery, and final outcome.

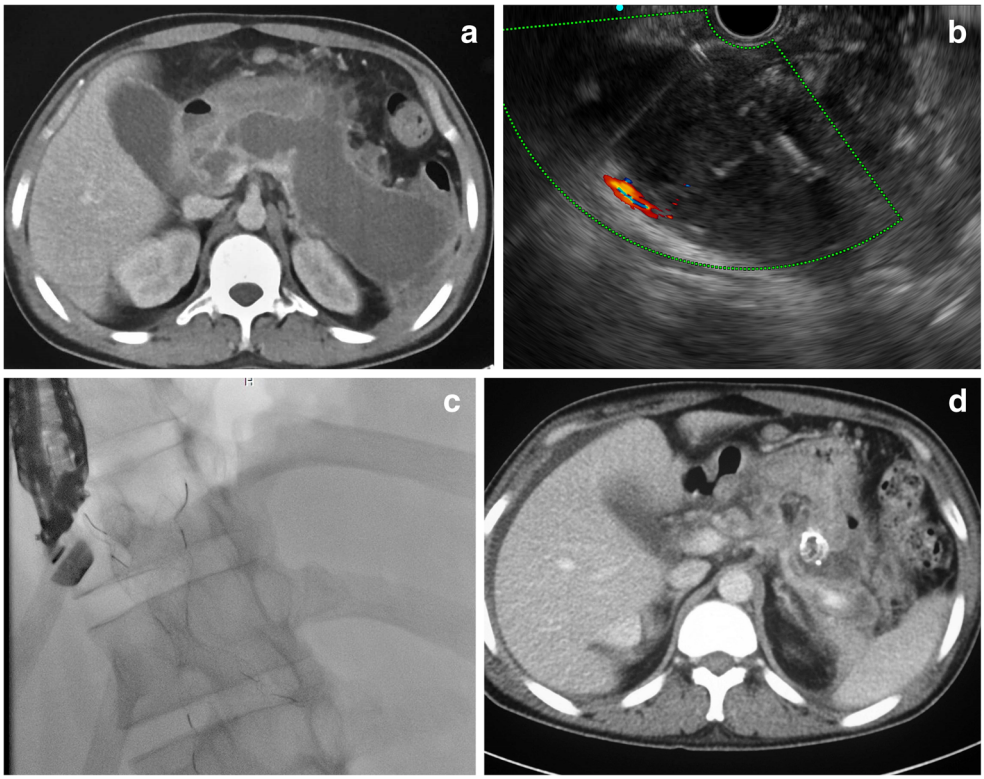

Fig. 1 **a** CT abdomen: a large acute necrotic collection. **b** EUS-guided drainage at day 21 of illness. **c** EUS-guided LAMS placement. **d** CT day 25 of intervention: resolved necrotic collection with LAMS in situ

Statistical Analysis

Initially collected data was entered into an appropriate spreadsheet, and the same was used as a reference for further data processing. Subsequently, initial data was replicated and saved as a master sheet for data cleaning, coding, and statistical analysis. The qualitative and quantitative data were presented as frequency (percentages) and mean ± standard deviation, respectively. The mid-p exact and Pearson's chi-square tests were used to calculate the p value and confidence intervals (CI) for 2 × 2 and 2 × 3 contingency tables, respectively. The Shapiro-Wilk test, along with boxplots and pp-plots, was used to ascertain the normality of the continuous data. Levene's test for homogeneity was used to determine heteroscedasticity in the data. Subsequently, p value and CI are reported using Student's t-test for the appropriate scenario of equal or unequal variance for different continuous measures. The continuous and categorical data was analyzed using SPSS 22 (IBM, New York, USA) and OpenEpi version 3.1 (citation: Dean AG, Sullivan KM, Soe MM. OpenEpi: Open Source Epidemiologic Statistics for Public Health, version. www.OpenEpi.com, updated 2013/04/06, accessed 20/08/2020), respectively. A Bonferroni adjustment to overall two-tailed $p<0.05$ gave $p < 0.003$ to declare the statistical significance for all the analysis.

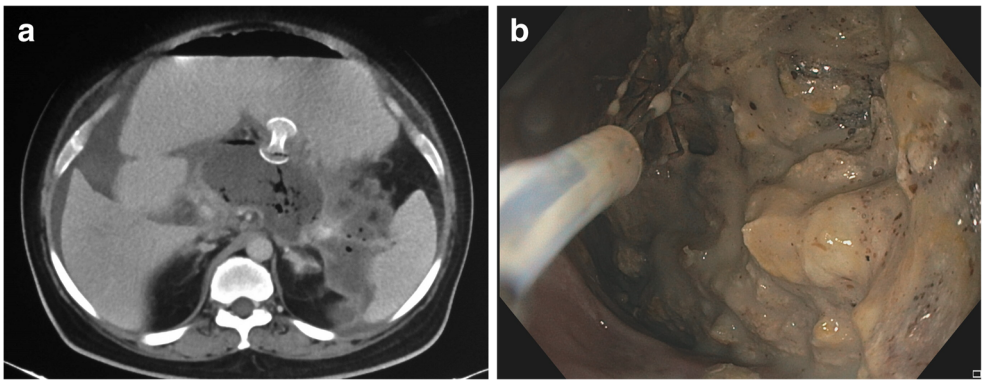

Fig. 2 **a** CT abdomen: persistent necrotic collection after LAMS placament. Air present inside the collection as well as in the retroperitoneum. **b** DEN being performed through the LAMS

Results

Demographic Profile

During the study period, 170 patients (141 males) with symptomatic PNC were treated with an endoscopic transmural drainage. Out of these 170 patients, 34 patients (26 males; mean age: 35.9 ± 8.6 years) underwent early and 136 patients (115 males; mean age: 37.9 ± 9.4 years) underwent delayed endoscopic transmural drainage. Early endoscopic drainage is being performed at our unit since 2018 and during this period, 34 patients underwent endoscopic transmural drainage and 62 patients underwent percutaneous drainage (22 patients too sick to undergo endoscopic drainage and 40 patients having PNC located away from the stomach or duodenum). Alcohol (64.7% in early and 65.1% in the delayed group) was the most common etiology of ANP followed by gallstone (23.5% in early and 20.6% in the delayed group) in both the groups. The baseline demographic profile of both the groups was comparable (Table 1).

The mean size of necrotic collection prior to drainage was significantly more in the early group as compared to the delayed group (12.3 ± 2.1 cm vs 10.5 ± 2.7 cm, p <0.001). Also, collection drained earlier had significantly higher amount of solid necrotic content as compared to collections drained later (47.7 ± 8.9% vs 28.3 ± 11.7%, p <0.001). The sites of PNC were also comparable between both the groups with pancreatic body being the most common site (93.9% vs 89.7% respectively, p value 0.75) (Table 1). All patients in the delayed group had a well-formed wall encapsulating the ANC whereas 26 patients (74.2%) in the early group had a well-formed wall. The mean time of intervention since the onset of disease was significantly earlier in the early group as compared to the delayed group (23.7 days ± 2.6 days in the early group and 74.6 ± 19.7 days in the delayed group, p value <0.001). Infection remained the most common indication of endoscopic drainage procedure in the early group (79.4%) as compared to the delayed group (32.9%), with the difference being statistically significant (p value <0.001) (Table 1). The other indications for drainage in the early group were persistent abdominal pain in 3 (8.8%), gastric outlet obstruction in 3 (8.8%), and biliary obstruction in 1 (2.9%) patient respectively. In the delayed group, the other indications for drainage were persistent abdominal pain, gastric outlet obstruction, and biliary obstruction in 83 (61%), 8 (5.8%), and 3 (2.2%) patients respectively. At the time of drainage, organ failure was present in 15 patients (44%) in the early group (acute lung injury in 12 patients and acute kidney injury in 5 patients) whereas none of the patients in the delayed group had organ failure. Leukocytosis at the time of drainage was observed in 25 patients (73.5%) in the early group and 37 patients (27.2%) in the delayed group (<0.001).

Technical success was achieved in all the patients in both the early and delayed drainage groups. Clinical success was achieved in 94% patients in the early drainage group and all patients (100%) in the delayed drainage group, and the difference was not clinically significant. LAMS was more frequently inserted in patients with PNC drained earlier as compared to patients in the delayed group (11 (32.4%) vs 12 (8.8%); p <0.001). Also, DEN was done more frequently in patients in the early drainage group as compared to patients in the delayed group (17 (50%) vs 10 (7.4%); p<0.0001). Additional percutaneous drainage for peripheral collection was done in 5 (14.7%) and 9 (6.6%) patients in the early and delayed drainage groups respectively (p=0.15). The patients in the early drainage group required significantly more number of endoscopic sessions for complete resolution compared to patients in the delayed drainage group (6.0 ± 1.7 vs 3.1 ± 1.1 sessions; p<0.001). However, the time taken for resolution was comparable between the two groups (31.6 ± 6.0 days vs 29.5 ± 8.5 days; p=0.20). There was increased mortality (5.7% vs 0%), need for rescue surgical necrosectomy (5.7% vs 0%), as well as post-procedure bleeding (20% vs 1.5%, p<0.001) in the early drainage group as compared to the delayed drainage group. In the early drainage group, bleeding occurred in seven (20%) patients with four patients having peri-procedural bleeding and three patients having post-procedural bleeding. Peri-procedural bleeding occurred during dilatation of the transmural tract in one patient and during DEN in three patients. Patient having bleeding following dilatation of the transmural tract had a bleeder identified at the site of dilatation and could be successfully managed with endoscopic clip application. One patient had massive bleed during DEN leading to hemodynamic collapse and could not be salvaged despite emergency laparotomy. Two patients had self-limiting peri-procedural bleed and no pseudoaneurysm was identified on CT angiography. However, both these patients had splenic vein thrombosis with peri-gastric collaterals but did not have either esophageal or gastric varices. Post-procedural bleeding occurred in three patients at 1, 3, and 7 days of the DEN. Two patients had hemodynamic collapse and underwent emergency surgery. One patient had massive bleed from ~1-cm rent in the anterior wall of the splenic vein near the spleno-mesenteric junction and the hemostasis was achieved by suturing the rent in by using 4-0 polypropylene. In the other patient, no definite bleeder was identified and diffuse oozing was encountered. The cavity was packed with sponges and the bleeding subsided. However, patients succumbed to ongoing sepsis and organ failure. One patient had bleeding from splenic artery pseudoaneurysm and was successfully treated with angioembolization. In the delayed drainage group, bleeding occurred in two patients (1.5%) and both patients had delayed post-procedural bleeding. Bleeding was self-limiting in one

Table 1 Demographic profile, procedural details, and outcome of endoscopic drainage of pancreatic necrotic collection in the early and delayed drainage groups

Parameter	Early (*N*=34)	Late (*N*=136)	*p* value	95% CI
Mean age (year) ± SD	35.9 (8.6)	37.9 (9.4)	0.25	−5.5–1.5
Males, *n* (%)	26 (76.5)	115(84.6)	0.26	0.2–1.6
Etiology, *n* (%)				
Alcohol	22 (64.7)	94 (65.1)	0.89	
Gall stones	8 (23.5)	28 (20.6)		
Others	4 (11.8)	14 (10.3)		
Infected PNC, *n* (%)	27 (79.4)	42 (32.9)	<0.001	3.5–22.6
Location of PNC, *n* (%)				
Body	31 (93.9)	122 (89.7)	0.75	
Head	1 (3.0)	8 (5.5)		
Tail	1 (3.0)	6 (4.4)		
WON size (cm) mean (SD)	12.3 (2.1)	10.5 (2.7)	<0.001	0.9–2.8
Solid debris (%) mean (SD)	47.7 (8.9)	28.3 (11.7)	<0.001	15.1–23.6
Time of intervention after onset of ANP (days)* mean (SD)	23.7 (2.6)	74.6 (19.7)	< 0.001	−[54.4 to 47.5]
Number of endoscopic sessions* mean (SD)	6 (1.7)	3.1 (1.1)	<0.001	2.3–3.6
Plastic stents, *n* (%)	23 (67.6)	124 (91.2)	<0.001	0.1–0.5
LAMS, *n* (%)	11 (32.4)	12 (8.8)	<0.001	1.9–12.6
DEN, *n* (%)	17 (50.0)	10 (7.4)	<0.001	4.9–32.4
Time to resolution (days) ± SD	31.6 (6.0)	29.5 (8.5)	0.20	−1.1 to 5.3
Salvage surgery, *n* (%)	2 (5.7)	0 (0)		
Bleeding, *n* (%)	7 (20.0)	2 (1.5)	< 0.001	3.4–120
Mortality[§], *n* (%)	2 (5.7)	0 (0)		
Follow-up (months)* mean (SD)	8.6 (4.4)	51.4 (34.8)	< 0.001	−[48.9 to 36.7]

*p value and CI reported for unequal variance. [§] Not calculated as cell value is zero

CI confidence intervals, *SD* standard deviation, *PNC* pancreatic necrotic collection, *ANP* acute necrotizing pancreatitis, *WON* walled-off necrosis, *LAMS* lumen-apposing metal stents, *DEN* direct endoscopic necrosectomy

patient and due to bleeding gastro-duodenal artery pseudoaneurysm in the other patient. The pseudoaneurysmal bleeding was successfully treated with angioembolization.

None of the patients was re-hospitalized within 90 days after discharge for re-intervention for the drained necrotic collections or occurrence of any local pancreatic complication.

Discussion

Endoscopic transmural drainage with plastic or metal stents is a safe and effective therapeutic modality for treatment of symptomatic WON.[24] An important pre-requisite for endoscopic transmural drainage for WON is that the collection should be encapsulated and located adjacent to the stomach or duodenum. As per revised Atlanta classification, it usually takes >4 weeks for the pancreatic necrotic collection to get encapsulated, and therefore endoscopic transmural drainage is usually performed >4 weeks of onset of ANP.[1] Along with getting encapsulated, the necrotic collection also tends to get liquefied with time with clearer demarcation of necrotic tissue from the viable tissue, and therefore delayed (>4 weeks) endoscopic drainage of PNC is recommended.[25] Early (< 4 weeks) endoscopic drainage of PNC is usually not advocated because of fear of increased risk of complications and poor outcomes and this inference has been drawn from the results of early surgical necrosectomy in comparison to delayed surgical necrosectomy. However, recently, few studies have reported encouraging results with early (<4 weeks) endoscopic transmural drainage of PNC.[17, 18, 20, 21] In the current study, we also have observed that early (<4 weeks) endoscopic drainage of PNC is feasible and seems to be safe and effective.

Oblizajek et al. studied 19 patients with early endoscopic drainage of PNC.[20] Similar to our study, the most common indication for early intervention was infection of the collection and the intervention was performed after a median of 23 days after the onset of ANP. Completely encapsulating wall was observed in 42% patients and both clinical success and technical success were observed in all the studied patients. None of the patients died and the authors did not find any significant difference in the adverse events between early and delayed endoscopic drainage of PNC. Chantarojanasiri et al. studied

35 patients with PNC who underwent EUS-guided transmural drainage (12 early and 23 delayed) using 19 metallic stents and 16 plastic stents.[21] The endoscopic intervention was performed after a median time of 23 and 85 days after onset of ANP in the early and delayed drainage groups respectively. All the collections drained were encapsulated and the technical success was 100% in both the groups. The complications, mortality, and clinical success were comparable between the two groups.

Trikudanathan et al. compared the results of early (<4 weeks) endoscopic intervention in 76 patients with results of standard (>4 weeks) endoscopic intervention in 117 patients with pancreatic necrotic collections.[18] Similar to our and previously discussed studies, infection was a more common indication for drainage in the early group as compared to the standard group. Completely encapsulating wall around the PNC was observed in only 6.8% patients in the early group. They reported that patients in the early drainage group had significantly increased in mortality (13% vs 4%, $p = 0.02$), need for rescue open necrosectomy (7% vs 1%, $p = 0.03$), as well as median hospital (37 days vs 26 days, $p = 0.01$) and ICU stay (median 2.5 days vs 0 days, $p = 0.001$) compared to the standard drainage group. However, there was no significant difference in the frequency of complications between the two groups. In our study, 74% patients in the early drainage group had a well-encapsulated wall and had significantly more solid necrotic debris as compared to the delayed drainage group. The patients in the early drainage group required significantly more number of endoscopic sessions as well as increased need for DEN for complete resolution compared to patients in the delayed drainage group. Similar to the study by Trikudanathan et al., we also observed increased mortality and need for rescue surgical necrosectomy in the early drainage group. However, in contrast to their study, we also observed increased frequency of clinically significant bleeding in the early drainage group.

Surgery in the early phase (within days of onset of illness) of ANP is associated with increased mortality rates of up to 65% as well as increased risk of complications.[26] Hungness et al. reported that patients with ANP who underwent early (<2 weeks) surgical debridement had a trend toward higher mortality (29% vs 18%) and increased frequency of major complications ($p < 0.05$) compared to patients who underwent late (>2 weeks) debridement.[27]

Therefore, the current consensus is to perform surgical necrosectomy after week 2 of the illness when the necrotic and viable tissue can be differentiated.[28] However, as surgical debridement is associated with increased mortality and morbidity, there have been numerous attempts to develop minimally invasive interventions to improve the outcome of patients with infected pancreatic necrosis. PNC after 4 weeks of illness tend to get walled off and therefore can be safely and effectively treated with endoscopic transmural drainage. However, non-encapsulated PNC in weeks 3–4 of illness are considered unsuitable for endoscopic drainage and are currently best treated with a percutaneous step-up treatment approach.[9, 16, 17] The results of the abovementioned studies including ours suggest that endoscopic transmural drainage of PNC is feasible in patients earlier than 4 weeks of onset of ANP and it seems to be safe and efficacious.

However, endoscopic transmural drainage in the early phase of illness is more challenging due to poorly formed encapsulating wall as well as increased proportion of solid necrotic debris compared to a well-formed WON in the delayed phase that has predominantly liquid content. Consequently, these patients need multiple endoscopic interventions including DEN and have higher post-procedure morbidity as well as mortality. Therefore, these procedures in the early phase should best be performed by a skilled interventional gastroenterologist in a carefully selected group of patients at select centers with extensive expertise in these procedures and surgical as well as interventional radiological support. Moreover, all PNC in the early phase cannot be drained endoscopically and a significant number of collections would need a percutaneous step-up approach for effective management. PNC in hemodynamically unstable patients are difficult to drain and these patients may be best managed with percutaneous drainage. Also, the PNC should be centrally located so that it can be drained through the transgastric or transduodenal route. The PNC located in the root of the mesentery or peripherally located (para-colic, pelvic, perirenal, deep retroperitoneal) collections are best managed with percutaneous drainage. Also, the cost-effectiveness of endoscopic and percutaneous drainage approaches needs to be evaluated by prospective studies. The use of LAMS and multiple endoscopic sessions would probably lead to increased cost of endoscopic approach compared to the percutaneous route but this increased cost could be possibly offset by quicker resolution and thus decreased overall duration of illness.

There are limitations associated with our study. First and foremost, it is a retrospective study from a tertiary hospital and thus suffers from the inherent drawbacks of a retrospective study, including the selection bias. It is a single-center study with a small sample size and data of few patients have been used in the previous publications on pancreatic endotherapy from our unit.[14, 17, 24, 29] Also, the data on initial severity of disease including severity scores, C-reactive protein, serum creatinine at presentation, number of organ failure at the onset of disease, days of intensive care unit treatment, and presence or absence of retroperitoneal fat necrosis on day 5 of imaging is missing from the retrospective analysis of an endoscopic data base. Also, patients in both groups underwent variable interventions as well as varying numbers and types of stents, and these could have induced bias in the results. The study was conducted in the unit with extensive experience in interventional EUS and pancreatic endotherapy, and therefore the results may not be generalizable.

In conclusion, early (<4 weeks) endoscopic transmural drainage of PNC is feasible and seems to be safe as well as effective but requires multiple endoscopic sessions as well as increased requirement of DEN and is associated with increased risk of complications as compared to delayed (>4 weeks) endoscopic drainage. Prospective comparative studies are required to confirm these results as well as define the exact role of endoscopic drainage in management of pancreatic necrosis within 4 weeks of onset of ANP.

Author Contribution Surinder Singh Rana: collection and interpretation of data, drafting of manuscript, design of study; Ravi Sharma: collection and interpretation of data; Kamal Kishore: interpretation and analysis of data; Lovneet Dhalaria: collection and interpretation of data; Rajesh Gupta: collection and interpretation of data

Declarations

Conflict of Interest The authors declare no competing interests.

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