

Association Between the Morphological Features of Necrotizing Pancreatitis on Endoscopic Ultrasound and the Outcome of Endoscopic Transmural Step-Up Approach

Ling Ding

First Affiliated Hospital of Nanchang University

Xue-Yang Li

First Affiliated Hospital of Nanchang University

Ji-Xue Tan

Nanchang University

Liang Xia

First Affiliated Hospital of Nanchang University

Wen-Hua He

First Affiliated Hospital of Nanchang University

Hui-Fang Xiong

First Affiliated Hospital of Nanchang University

Yong Zhu

First Affiliated Hospital of Nanchang University

Pi Liu

First Affiliated Hospital of Nanchang University

Xu Shu

First Affiliated Hospital of Nanchang University

Zhi-Jian Liu

First Affiliated Hospital of Nanchang University

Yin Zhu (✉ zhuyin27@sina.com)

First Affiliated Hospital of Nanchang University

You-Xiang Chen

First Affiliated Hospital of Nanchang University

Nong-Hua Lu

First Affiliated Hospital of Nanchang University

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Abstract

Background

To investigate the association between features of necrotic collections on endoscopic ultrasound (EUS) and outcomes of the endoscopic transmural step-up approach.

Methods

This was a retrospective cohort study analyzing patients with necrotic collections underwent endoscopic transmural step-up approach. According to the amount of solid necrotic debris quantified as a percentage of the total collection size, participants were divided into three groups: <30% (group 1), 30%-50% (group 2), and >50% (group 3).

Results

Out of a total of 134 patients, the mean necrotic collection size was 8.5 (7.0, 10.0) cm, with <30% (group 1), 30%-50% (group 2) and >50% (group 3) solid debris present in 52, 59, and 23 patients, respectively. Patients with more solid necrotic debris needed more sessions of necrosectomy (group 1, 1 (0, 1) time vs. group 2, 1 (1, 2) time vs. group 3, 2 (2, 3) times, $P<0.001$), more likely experienced stent occlusion (group 1, 9.6% vs. group 2, 16.9% vs. group 3, 34.8%; $P<0.05$), and had a longer hospital stay (group 1, 25.5 (17.3, 44.0) days vs. group 2, 28.0 (19.0, 41.0) days vs. group 3, 40.0 (30.0, 58.0) days; $P<0.05$). Procalcitonin (OR, 6.14; 95% CI, 1.40-26.94; $P<0.05$) and any organ failure (OR, 11.51; 95% CI, 2.42-54.78; $P<0.01$) were independently associated with clinical failure of the endoscopic transmural step-up approach.

Conclusions

More solid debris on EUS predicted more sessions of necrosectomy, stent occlusion, and hospital stay. Procalcitonin and organ failure are risk factors for clinical failure of the endoscopic transmural step-up approach.

Background

Acute pancreatitis (AP) is a common and potentially lethal disease. Approximately 10%-20% of patients develop necrotizing pancreatitis (NP). This subset of patients may face a complex, prolonged clinical course, with an associated mortality rate of up to 20–30% if infected pancreatic necrosis (IPN) develops.¹ Over the last decade, approaches to managing NP have evolved from open surgery to endoscopic or percutaneous step-up approaches due to the efficacy and lower morbidity and mortality rates of minimally invasive interventions.^{2,3} The endoscopic transmural approach is an effective treatment with acceptable mortality (6%) and complication rates (36%) but is technically demanding.⁴ However, factors of the endoscopic approach associated with poor prognosis are rarely studied.

The extent of necrosis assessed by contrast-enhanced computed tomography (CECT) is associated with the prognosis of the endoscopic transmural approach.^{5,6} However, since acute necrotic collection (ANC) and walled-off necrosis (WON) contain a mixture of both fluid and solid necrotic debris, CECT may not readily distinguish solid from liquid content. Endoscopic ultrasound (EUS) can be used for this distinction by detecting the echogenic material present in necrotic collection suggestive of solid debris.⁷ However, the value of EUS in predicting the clinical outcomes of endoscopic approaches for ANC or WON has rarely been studied. Previously, Surinder et al⁸ investigated the association between morphological features of WON on EUS and the outcome of endoscopic transmural drainage (ETD), and they identified that EUS has important therapeutic implications; collections with a large size and more solid debris require more aggressive therapy to achieve successful outcomes. This was a promising finding. However, this study had a relatively small sample size of 43 patients, no multivariate analysis was performed, and the results may have been affected by confounding factors. Thus, the value of EUS in predicting clinical outcomes of the endoscopic transmural approach for ANC or WON still needs further research.

Herein, we aimed to retrospectively analyze patients with ANC or WON who underwent ETD as the initial intervention and to investigate the relationship between morphological features of necrotic collection on EUS and clinical outcomes of the endoscopic transmural step-up approach. Furthermore, we identified risk factors for predicting clinical failure of the endoscopic transmural step-up approach in the management of NP.

Methods

Study design and participants

This was a single-center, retrospective cohort study. Adult NP patients who underwent ETD and/or endoscopic transmural necrosectomy (ETN) in the Department of Gastroenterology at the First Affiliated Hospital of Nanchang University, a tertiary care referral center in China, from April 2015 to April 2020 were analyzed. Patients who underwent ETD without EUS guidance were excluded due to the lack of images. Patients whose primary collection was drained by both endoscopic and percutaneous approaches were excluded due to the confounding effect on the evaluation of the research results. All patients were followed for at least six months after discharge, and patients who were lost to follow-up were excluded. The study was in accordance with the Declaration of Helsinki. The clinical data was achieved from a prospectively maintained database in our center, which was approved by the Ethics Committee of the First Affiliated Hospital of Nanchang University (No.: 2011001). Written informed consent was waived due to the retrospective nature of the study.

EUS image and data collection

EUS images continuously collected at the time of initial ETD were retrieved from the endoscope system, all of which included more than 30 images or a video for a very thorough evaluation of a collection from different angles. EUS images or videos were reviewed again by two experienced endoscopists who were

blinded to the clinical outcomes of all patients. They reviewed the EUS images respectively, and there were no difference between the judgment of the two reviews. The detailed morphological features of necrotic collection on EUS, which included the collection location and size, were reviewed with special emphasis on the amount of solid necrotic debris. Echogenic material present in the necrotic collection was suggestive of solid debris. Quantification of the amount of solid debris present in the collection as a percentage of the total size of the collection was attempted. The section of EUS image where necrotic debris was most was chose. According to the amount of solid necrotic debris, participants were divided into three groups: <30% (group 1), 30%-50% (group 2), and >50% (group 3). The cut-offs were chose according to the Balthazar CT severity index. The sample graphs are shown in Figure 1.

Data, including the baseline characteristics, interventions, and clinical outcomes, were obtained from a prospectively maintained database; this database is a data repository for the clinical data of all AP patients admitted to our department recorded by a special research assistant. The baseline characteristics included sex, age, body mass index (BMI), AP etiology, smoking status, drinking status, and disease severity. Disease severity was evaluated by the temperature, C-reactive protein and procalcitonin level, systemic inflammatory response syndrome (SIRS) score, and presence of organ failure, all of which were assessed one week before initial ETD. Organ failure included respiratory failure, circulatory failure and renal failure and was defined as a score of 2 or higher using the modified Marshall scoring system.^{7,9} Intervention details, including the primary indication, timing, stent type, and intervention type and session, were also recorded. Clinical outcomes included the rates of clinical success, disease- or stent-related complications and mortality as well as the length of hospital stay. Clinical success was defined as no related symptoms and near-complete resolution assessed by imaging, without additional open surgery, death, or collection recurrence at the three-month follow-up.^{10,11} Clinical failure was determined when clinical success was not achieved.

Interventions

All management decisions regarding interventions were made by a multidisciplinary team that included endoscopists, pancreatologists, surgeons, interventional radiologists, radiologists, and intensivists using our previously described algorithm.^{10,11} In this study, enrolled patients were managed using a strategy based on an endoscopically centered step-up approach. All primary necrotic collections adherent to the stomach or duodenum were drained by ETD and/or subsequent ETN only. For necrotic collections not in communication with the primary collection, percutaneous drainage (PCD) and/or sinus tract endoscopy was used adjunctively. Open surgery was reserved for patients in whom failure of the step-up approach or severe complications such as severe abdominal bleeding occurred.

All of the interventions were performed by experienced gastroenterologists in our center. A linear echoendoscope (Olympus GIF-H290, Tokyo, Japan) was used to examine and assess the necrotic collections. The puncture path was oriented in a way that avoided blood vessels. Under EUS guidance, a COOK 19-G needle was used to puncture the necrotic collections, and then the fluid was aspirated for examination. A 0.035-inch guidewire (Boston Scientific, Marlborough, MA, USA) was inserted through the

puncture needle into the capsule. Through the guidewire, a wire-guided needle knife (Cook Medical, Limerick, Ireland) was inserted and used to excise the wall of the stomach or duodenum using an endotherm knife. Then, the needle knife was withdrawn. A fully covered self-expandable metal stent (FCSEMS) (18mm*40mm or 18mm*50mm, Boston Scientific, Marlborough, MA, USA) or lumen-apposing metal stent (LAMS) (16mm*40mm, custom produced by Micro-Tech, Nanjing, China for clinical study) stent was placed through the guidewire.^{10,11} If a patient did not show clinical improvement or resolution of the necrotic fluid, ETN was performed as needed after initial ETD. All ETNs in our cohort were delayed up to 4 weeks after AP onset to allow for the development of a wall around the necrotic collections, consistent with the recommendations of the newest guidelines.¹ ETN was repeated as needed based on the clinical course and until there was complete resolution of the necrotic collections.

Statistical analysis

Quantitative variables are presented as medians (interquartile ranges (IQRs)), and categorical variables are reported as absolute numbers and proportions. Linear-by-Linear Association (Chi-square test) was conducted to test the trend in categorical variables. Spearman correlation was used in continuous variables. Logistic regression analysis was performed to determine the independent risk factors for clinical failure of the endoscopic transmural step-up approach. Factors in the unadjusted models ($P < 0.1$) were included in the multivariable models. The correlation between the amount of solid necrotic debris and the number of ETNs in patients with clinical success was assessed by using the Pearson correlation coefficient. $P < 0.05$ was considered statistically significant. Data were analyzed using SPSS software (v17.0; SPSS Inc., Chicago, IL, USA).

Results

Baseline characteristics

A total of 140 patients with NP were managed by ETD and/or ETN at our center during the study period. Four patients were excluded because they lacked EUS images ($n=2$), or were lost to follow-up ($n=2$). Two patients whose primary collection was drained by both endoscopic and percutaneous approaches were also excluded. Finally, 134 patients were included in our cohort. The study flow chart is shown in Figure 2. Most necrotic collections (79.9%) were located in the body and/or tail of the pancreas, with 6.0% located in the head and 14.2% in the whole pancreas. The median necrotic collection size was 8.5 (7.0, 10.0) cm, with the extent of solid necrotic debris ranging from 10% to 90% and a median of 30% (20%, 50%). The proportion of solid necrotic components was $<30\%$ (group 1), 30%-50% (group 2), and $>50\%$ (group 3) in 52, 59, and 23 of these patients, respectively. There were no significant differences among the three groups in terms of sex, age, BMI, AP etiology, smoking status, drinking status, or disease severity, which were assessed with the temperature, C-reactive protein and procalcitonin level, SIRS score, and presence of organ failure one week before initial ETD. The details of baseline characteristics are shown in Table 1.

Interventions

In the cohort, infection was the primary indication for intervention in nearly half of the patients, with a significantly higher proportion in patients with larger amounts of solid necrotic debris (group 1, 46.2% vs. group 2, 55.9% vs. group 3, 78.3%; $P<0.05$). ETD was the initial intervention in all patients and was performed >4 weeks after AP onset in 85.1% of patients, with no difference among the three groups. An LAMS was placed in the majority of patients in all groups, with 82.7% in group 1, 93.2% in group 2, and 87.0% in group 3. An FCSEMS was placed in the other participants in the cohort. 111 (82.8%) patients needed ETN for no clinical improvement or resolution of the necrotic fluid after ETD. All ETNs in our cohort were delayed up to 4 weeks after AP onset. A significantly larger number of ETNs was required in patients with more necrotic debris (group 1, 1 (0, 1) time vs. group 2, 1 (1, 2) time vs. group 3, 2 (2, 3) times, $P<0.001$). The amount of solid debris was significantly correlated ($r=0.556$, $P<0.001$) with the number of ETN sessions. Nearly a quarter of patients were managed in combination with adjunctive PCD for additional collections not suitable for endoscopic therapy, and there were no significant differences among all groups. Among the patients, only 9 (6.7%) required subsequent sinus tract endoscopy. Only 5 (3.7%) patients required open surgery due to failure of the minimally invasive step-up approach.

Clinical outcomes

Most of the patients in our cohort achieved clinical success, and there was no significant difference (group 1, 80.8% vs. group 2, 89.8% vs. group 3, 82.6%). No significant differences in disease-related complications were observed, including new-onset organ failure, transient fever, new-onset infection, abdominal bleeding, gastrointestinal bleeding, and gastrointestinal fistula. Patients with a larger amount of necrotic debris were more likely to experience stent occlusion (group 1, 9.6% vs. group 2, 16.9% vs. group 3, 34.8%; $P<0.05$). The incidence of stent migration and dislodgment were not significantly different among the three groups. There was no significant difference in the mortality rate among all groups (group 1, 11.5% vs. group 2, 8.5% vs. group 3, 13.0%). The length of hospital stay (group 1, 25.5 (17.3, 44.0) days vs. group 2, 28.0 (19.0, 41.0) days vs. group 3, 40.0 (30.0, 58.0) days; $P<0.05$) was significantly longer in patients with more necrotic debris. The details of the interventions and clinical outcomes are outlined in Table 2.

Multivariate logistic regression analysis for clinical failure

Twenty (14.9%) patients achieved clinical failure. Among them, 14 patients died, 3 patients transferred to open surgery, and 3 patients occurred collection recurrence. The results of univariate analysis for predictors of clinical failure in the endoscopic transmural step-up approach for ANC or WON are shown in Table 3. Factors associated with clinical failure in the unadjusted models ($P<0.1$) were included in the multivariable models. Procalcitonin (adjusted odds ratio (AdjOR), 6.14; 95% CI, 1.40-26.94; $P<0.05$) and any organ failure (AdjOR, 11.51; 95% CI, 2.42-54.78; $P<0.01$) were independently associated with clinical failure. (Table 4)

Discussion

The association between EUS and the clinical outcomes of endoscopic transmural approaches for ANC or WON has rarely been studied. In this retrospective cohort study, we analyzed data of 134 patients with necrotic collection who underwent ETD and/or ETN, and we found that patients with more solid necrotic debris quantified as a percentage of the total collection size on EUS required a larger number of ETNs to achieve clinical success. The incidence rate of stent occlusion was higher, and the length of hospital stay was longer in patients with more necrosis. Whereas, procalcitonin and any organ failure were independently associated with clinical failure of the endoscopic transmural step-up approach.

Compared to CECT, EUS has the advantages of distinguishing solid from liquid content by detecting the echogenic material present in necrotic collections.⁷ Surinder et al⁸ first investigated the association between morphological features of WON on EUS and outcomes of ETD and found that with increasing collection size ($r = 0.320$, $P = 0.047$) and amount of solid debris ($r = 0.800$, $P < 0.001$), there was a significant increase in the number of endoscopic procedures required for a successful outcome. Although this was a promising finding, the study included a relatively small sample and the results may have been affected by confounding factors. Thus, we conducted this study and found that patients with more solid necrotic debris quantified as a percentage of the total collection size required a larger number of ETNs to achieve clinical success. However, the correlation coefficient was low ($r = 0.556$), and the extent of necrosis was not significant in the logistic regression analysis. This showed that the value of EUS for prediction was limited, for which there may be several reasons. First, although EUS can be used to distinguish solid from fluid content, quantifying the amount of necrosis is difficult. We tried to quantify the amount of solid debris present in the necrotic collection as a percentage of the total collection size, which may still not represent the actual amount of necrosis. Second, the efficiency of drainage and/or necrosectomy is also affected by other factors, including the viscosity of fluid collection, systemic inflammation and the organ function of patients. Although this, we found that more necrotic debris was associated with more incidence of stent occlusion. If there were extensive solid necrotic material based on EUS, stent occlusion might be avoided by changing the algorithm to scheduled endoscopic necrosectomy every 4 to 5 days rather than doing it on an “as needed” basis.

Procalcitonin and any organ failure were independent risk factors for predicting clinical failure in the endoscopic transmural approach. Procalcitonin is an early quick-response marker of SIRS, and its serum levels correlate well with the incidence of infected necrosis, organ failure, and death in patients with NP.¹² Our results therefore suggested that serum procalcitonin ≥ 0.5 ng/ml (vs. <0.5 ng/ml) one week before initial ETD could be used as a risk factor to assess a patient’s response to the endoscopic transmural approach. The OR of any organ failure one week before initial ETD approached 12, which indicated the high value of any organ failure for predicting clinical failure. The relatively higher mortality risk and severe illness might account for the higher risk of clinical failure in patients who develop complications of organ failure.¹³ Similarly, Hollemans et al⁶ reported a post hoc analysis revealing that male sex, multiple organ failure, an increasing percentage of pancreatic necrosis and collection heterogeneity are negative predictors for the success of catheter drainage in INP. However, the study included only 17

patients treated under endoscopy, and the features of necrosis were assessed on CECT, in which it is difficult to distinguish solid from fluid content.¹⁴

It is important to highlight the wide variability in the use of ETD and/or ETN. We adopted a strategy based on the endoscopically centered step-up approach. First, ETD was optimal for primary necrotic collections adjacent to the stomach or duodenum, with subsequent use of ETN as required. Although we did not adopt different methods such as multiple stent placement, aggressive irrigation, or multiple transluminal gateway techniques to improve drainage efficiency, the prognosis was quite good. The all-cause mortality rate was 10.4%, which was somewhat lower than the 15–39% mortality rate suggested in the overall literature and was similar to that reported in recent randomized trials on the endoscopic step-up approach.^{2,3,15–17} We believe our low mortality rate may be related to the following reasons: 1) our emphasis on a multidisciplinary team and our use of a minimally invasive intervention strategy as the first choice; 2) our choice of metal stents, providing a larger tract for drainage; and 3) the delay in endoscopic necrosectomy of at least 4 weeks.^{10,11}

A potential strength of our study was that the study was a cohort study based on a prospectively maintained database that included all patients with NP undergoing ETD during the study period. Thus, the study represented the entire spectrum of patients rather than a preselected group of patients and thus reduced selection bias. However, there are some limitations of the current study. First, although two experienced endoscopists reassessed the EUS images and quantification of the solid debris was performed, one section of EUS image may not represent the total amount of necrotic debris. More approaches to measure the volume of necrosis objectively should be explored in future study. secondly, this was a single-center study, and all procedures were performed at a highly specialized tertiary care center with extensive experience in pancreatic endotherapy, which may not be available in smaller institutions. Thus, the representativeness of the conclusions may be affected.

Conclusions

In conclusion, more solid debris on EUS predicted more sessions of necrosectomy, stent occlusion, and hospital stay. Procalcitonin and organ failure are risk factors for clinical failure of the endoscopic transmural step-up approach. Precise and early predictions regarding the outcomes of ETD and/or ETN are important for determining subgroups of patients who might experience complications and have an eventful course, and for facilitating patient counseling and guiding clinical decision making.

List Of Abbreviations

EUS, endoscopic ultrasound;

AP, Acute pancreatitis;

NP, necrotizing pancreatitis;

IPN, infected pancreatic necrosis;

CECT, contrast-enhanced computed tomography;

ANC, acute necrotic collection;

WON, walled-off necrosis;

ETD, endoscopic transmural drainage;

ETN, endoscopic transmural necrosectomy;

BMI, body mass index;

SIRS, systemic inflammatory response syndrome;

PCD, percutaneous drainage;

FCSEMS, fully covered self-expandable metal stent;

LAMS, lumen-apposing metal stent;

IQR, interquartile range;

OR, odds ratio;

CI, confidence interval;

Declarations

Ethics approval and consent to participate: the AP database was approved by the Ethics Committee of the First Affiliated Hospital of Nanchang University (NO: 2011001). The ethics approval and written informed consent for using the data were waived by the Ethics Committee of the First Affiliated Hospital of Nanchang University due to the retrospective nature of the study.

Consent for publication: not applicable.

Availability of data and materials: the datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests: the authors declare that they have no competing interests.

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Authors' contributions: Ling Ding conceived the idea, designed the study, and wrote the manuscript. Xue-Yang Li and Ji-Xue Tan collected and analyzed the data. They contributed equally to the work, and shared co-first authorship. Liang Xia, Wen-Hua He, and Hui-Fang Xiong revised the study design. Yong Zhu, Pi Liu, Xu Shu, Zhi-Jian Liu, and Yin Zhu performed the procedure in our center. Yin Zhu reviewed all EUS image, and analyzed the data. You-Xiang Chen, and Nong-Hua Lu revised the manuscript. All authors read and approved the final manuscript.

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Tables

Table 1

Baseline characteristics of NP patients underwent ETD compared between different groups divided by solid necrotic debris on the EUS*

	All (n = 134)	Group 1 (n = 52)	Group 2 (n = 59)	Group 3 (n = 23)	P
Sex					0.131
Male	68 (50.7%)	29 (55.8%)	31 (52.5%)	8 (34.8%)	
Female	66 (49.3%)	23 (44.2%)	28 (47.5%)	15 (65.2%)	
Age, yr	49.0 (39.0, 61.0)	49.5 (38.3, 61.8)	50.0 (39.0, 59.0)	47.0 (42.0, 62.0)	0.635
BMI, kg/m ²	22.9 (20.3, 25.1)	22.7 (19.6, 24.5)	22.9 (21.0, 25.0)	24.2 (20.5, 28.9)	0.084
Etiology					0.516
Biliary	63 (47.0%)	23 (44.2%)	28 (47.5%)	12 (52.2%)	
Alcoholic	7 (5.2%)	5 (9.6%)	1 (1.7%)	1 (4.3%)	
Hyperlipidemia	28 (20.9%)	9 (17.3%)	12 (20.3%)	7 (30.4%)	
Others	36 (26.9%)	15 (28.8%)	18 (30.5%)	3 (13.0%)	
Smoker	31 (23.1%)	11 (21.2%)	17 (28.8%)	3 (13.0%)	0.713
Drinker	32 (23.9%)	11 (21.2%)	13 (22.0%)	8 (34.8%)	0.425
Location of collection*					0.082
Head	8 (6.0%)	6 (11.5%)	2 (3.4%)	0 (0.0%)	
Body-tail	107 (79.9%)	41 (78.8%)	46 (78.0%)	20 (87.0%)	
Whole pancreas	19 (14.2%)	5 (9.6%)	11 (18.6%)	3 (13.0%)	
Size of collection*	8.5 (7.0, 10.0)	8.3 (7.4, 10.0)	8.0 (7.0, 11.0)	10.0 (7.3, 11.5)	0.319
Temperature > 38 °C†	52 (38.8%)	17 (32.7%)	22 (37.3%)	13 (56.5%)	0.074
C-reactive protein, mg/L †	42.1 (7.2, 109.5)	26.1 (5.0, 107.3)	39.0 (6.4, 105.8)	74.8 (15.1, 131.5)	0.148

Data are n (%), or median (IQR). NP, necrotizing pancreatitis; ETD, endoscopic transmural drainage; EUS, endoscopy ultrasound; BMI, body mass index; SIRS score, systemic inflammatory response syndrome score; IQR, interquartile range. *The amount of solid necrotic debris in the PFC was quantified as a percentage of the total size of the collection assessed by the EUS during the initial ETD, as well as location and size of collection. †The indicators were assessed one week before initial endoscopic transmural drainage. ‡Patients with one or more organ failure including respiratory failure, circulatory failure or renal failure assessed according to Modified Marshall score.

	All (n = 134)	Group 1 (n = 52)	Group 2 (n = 59)	Group 3 (n = 23)	P
Procalcitonin, ng/ml †	0.0 (0.0, 1.1)	0.0 (0.0, 1.0)	0.1 (0.0, 1.0)	0.3 (0.0, 1.2)	0.592
SIRS score, points †	1.0 (0.0, 3.0)	0.0 (0.0, 2.8)	1.0 (0.0, 3.0)	2.0 (0.0, 3.0)	0.161
Any organ failure †‡	15 (11.2%)	7 (13.5%)	5 (8.5%)	3 (13.0%)	0.774
<p>Data are n (%), or median (IQR). NP, necrotizing pancreatitis; ETD, endoscopic transmural drainage; EUS, endoscopy ultrasound; BMI, body mass index; SIRS score, systemic inflammatory response syndrome score; IQR, interquartile range. *The amount of solid necrotic debris in the PFC was quantified as a percentage of the total size of the collection assessed by the EUS during the initial ETD, as well as location and size of collection. †The indicators were assessed one week before initial endoscopic transmural drainage. ‡Patients with one or more organ failure including respiratory failure, circulatory failure or renal failure assessed according to Modified Marshall score.</p>					

Table 2

Interventions and clinical outcomes of NP patients underwent ETD compared between different groups

	All (n = 134)	Group 1 (n = 52)	Group 2 (n = 59)	Group 3 (n = 23)	P
Primary indication for intervention					0.013
Infection	75 (56.0%)	24 (46.2%)	33 (55.9%)	18 (78.3%)	
Other indications*	59 (44.0%)	28 (53.8%)	26 (44.1%)	5 (21.7%)	
Time from AP onset to initial ETD					0.912
<4 weeks	20 (14.9%)	8 (15.4%)	8 (13.6%)	4 (17.4%)	
≥4 weeks	114 (85.1%)	44 (84.6%)	51 (86.4%)	19 (82.6%)	
Stent type for initial ETD					0.347
LAMS	118 (88.1%)	43 (82.7%)	55 (93.2%)	20 (87.0%)	
FCSEMS	16 (11.9%)	9 (17.3%)	4 (6.8%)	3 (13.0%)	
Total number of ETN, times	1.0 (1.0, 2.0)	1.0 (0.0, 1.0)	1.0 (1.0, 2.0)	2.0 (2.0, 3.0)	< 0.001
PCD	32 (23.9%)	13 (25.0%)	14 (23.7%)	5 (21.7%)	0.762
Sinus tract endoscopy	9 (6.7%)	4 (7.7%)	4 (6.8%)	1 (4.3%)	0.613
Open surgery	5 (3.7%)	2 (3.8%)	2 (3.4%)	1 (4.3%)	0.958
Clinical success	114 (85.1%)	42 (80.8%)	53 (89.8%)	19 (82.6%)	0.573
Disease-related complications					
New-onset organ failure	20 (14.9%)	8 (15.4%)	8 (13.6%)	4 (17.4%)	0.912
Transient fever	16 (11.9%)	8 (15.4%)	7 (11.9%)	1 (4.3%)	0.190
New-onset infection	6 (4.5%)	1 (1.9%)	2 (3.4%)	3 (13.0%)	0.055
Abdominal bleeding	11 (8.2%)	4 (7.7%)	5 (8.5%)	2 (8.7%)	0.868
Gastrointestinal bleeding	10 (7.5%)	5 (9.6%)	2 (3.4%)	3 (13.0%)	0.940
Gastrointestinal fistula	6 (4.5%)	2 (3.8%)	2 (3.4%)	2 (8.7%)	0.451

Data are n (%), or median (IQR). LAMS, lumen-apposing mental stent; FCSEMS, fully-covered self-expanding mental stent; ETN, endoscopic transmural necrosectomy; PCD, percutaneous drainage. *Other indications included gastric outlet obstruction, biliary tract obstruction, and abdominal symptoms. †Other complications included pulmonary embolism, digestive tract obstruction, atrial fibrillation, and chest tightness. P < 0.05 were bolded.

	All (n = 134)	Group 1 (n = 52)	Group 2 (n = 59)	Group 3 (n = 23)	P
Other complications†	4 (3.0%)	3 (5.8%)	1 (1.7%)	0 (0.0%)	0.132
Stent-related complications					
Stent occlusion	23 (17.2%)	5 (9.6%)	10 (16.9%)	8 (34.8%)	0.011
Stent migration	2 (1.5%)	0 (0.0%)	1 (1.7%)	1 (4.3%)	0.156
Stent dislodgment	13 (9.7%)	7 (13.5%)	6 (10.2%)	0 (0.0%)	0.089
Death	14 (10.4%)	6 (11.5%)	5 (8.5%)	3 (13.0%)	0.991
Length of hospital stay, days	31.0 (19.8, 46.0)	25.5 (17.3, 44.0)	28.0 (19.0, 41.0)	40.0 (30.0, 58.0)	0.015
<p>Data are n (%), or median (IQR). LAMS, lumen-apposing mental stent; FCSEMS, fully-covered self-expanding mental stent; ETN, endoscopic transmural necrosectomy; PCD, percutaneous drainage. *Other indications included gastric outlet obstruction, biliary tract obstruction, and abdominal symptoms. †Other complications included pulmonary embolism, digestive tract obstruction, atrial fibrillation, and chest tightness. P < 0.05 were bolded.</p>					

Table 3
Univariate Logistic regression analysis of predictors for failure of endoscopic transmural drainage and necrosectomy in NP patients

	OR (95%CI)	P
Male (Ref: female)	0.76 (0.29, 1.98)	0.578
Age, yr (Ref: <45)		
45–55	0.69 (0.19, 2.54)	0.572
55–65	1.30 (0.37, 4.58)	0.678
≥65	1.71 (0.44, 6.74)	0.440
BMI, kg/m ² (Ref: <24)		
24–28	0.87 (0.25, 3.02)	0.826
≥ 28	0.33 (0.04, 2.79)	0.311
Etiology (Ref: biliary)		
Alcoholic	0.45 (0.05, 4.03)	0.476
Hyperlipidemia	0.10 (0.01, 0.80)	0.030
Others	0.08 (0.01, 0.61)	0.015
Smoker (Ref: no smoker)	0.54 (0.15, 1.99)	0.356
Drinker (Ref: no drinker)	0.77 (0.24, 2.48)	0.660
Location of collection (Ref: head)		
Body-tail	0.42 (0.08, 2.28)	0.311
Whole pancreas	1.07 (0.16, 7.15)	0.943
Size of collection, cm (Ref: <10)		
≥ 10	3.29 (1.02, 10.61)	0.047
Solid necrotic debris, % (Ref: <30)		
30–50	0.48 (0.16, 1.41)	0.181
≥ 50	0.88 (0.25, 3.18)	0.851
Temperature, °C (Ref: <38)		
≥38	6.24 (2.11, 18.48)	0.001
C-reactive protein, mg/L (Ref: <100)		

OR: odds ratio; CI: confidence interval. P < 0.05 were bolded.

	OR (95%CI)	P
≥ 100	2.73 (1.01, 7.43)	0.049
Procalcitonin, ng/ml (Ref: <0.5)		
≥0.5	6.26 (2.11, 18.60)	0.001
SIRS score, points (Ref: <2)		
2	0.97 (0.11, 8.77)	0.982
3	5.85 (1.63, 20.93)	0.007
4	7.39 (2.12, 25.76)	0.002
Organ failure (Ref: no any organ failure)	10.19 (3.14, 33.06)	<0.001
Any‡		
Indication for intervention (Ref: non-infection)		
Infection	9.00 (2.00, 40.59)	0.004
Time from AP onset to initial ETD, weeks (Ref: <4)		
≥4	0.46 (0.14, 1.43)	0.178
Stent type for initial ETD (Ref: FCSEMS)		
LAMS	1.26 (0.26, 6.02)	0.772
OR: odds ratio; CI: confidence interval. P < 0.05 were bolded.		

Table 4

Multivariate Logistic regression analysis of predictors for failure of endoscopic transmural drainage and necrosectomy in NP patients

	OR (95%CI)	P
Procalcitonin, ng/ml (Ref: <0.5)		
≥0.5	6.14 (1.40, 26.94)	0.016
Organ failure (Ref: no any organ failure)		
Any	11.51 (2.42, 54.78)	0.002
Factors in unadjusted models (P < 0.1) were included in the multivariable models. Multivariate model adjusted for etiology, size of collection, temperature, C-reactive protein, procalcitonin, SIRS score, organ failure, indication for intervention. P < 0.05 were bolded.		

Figures

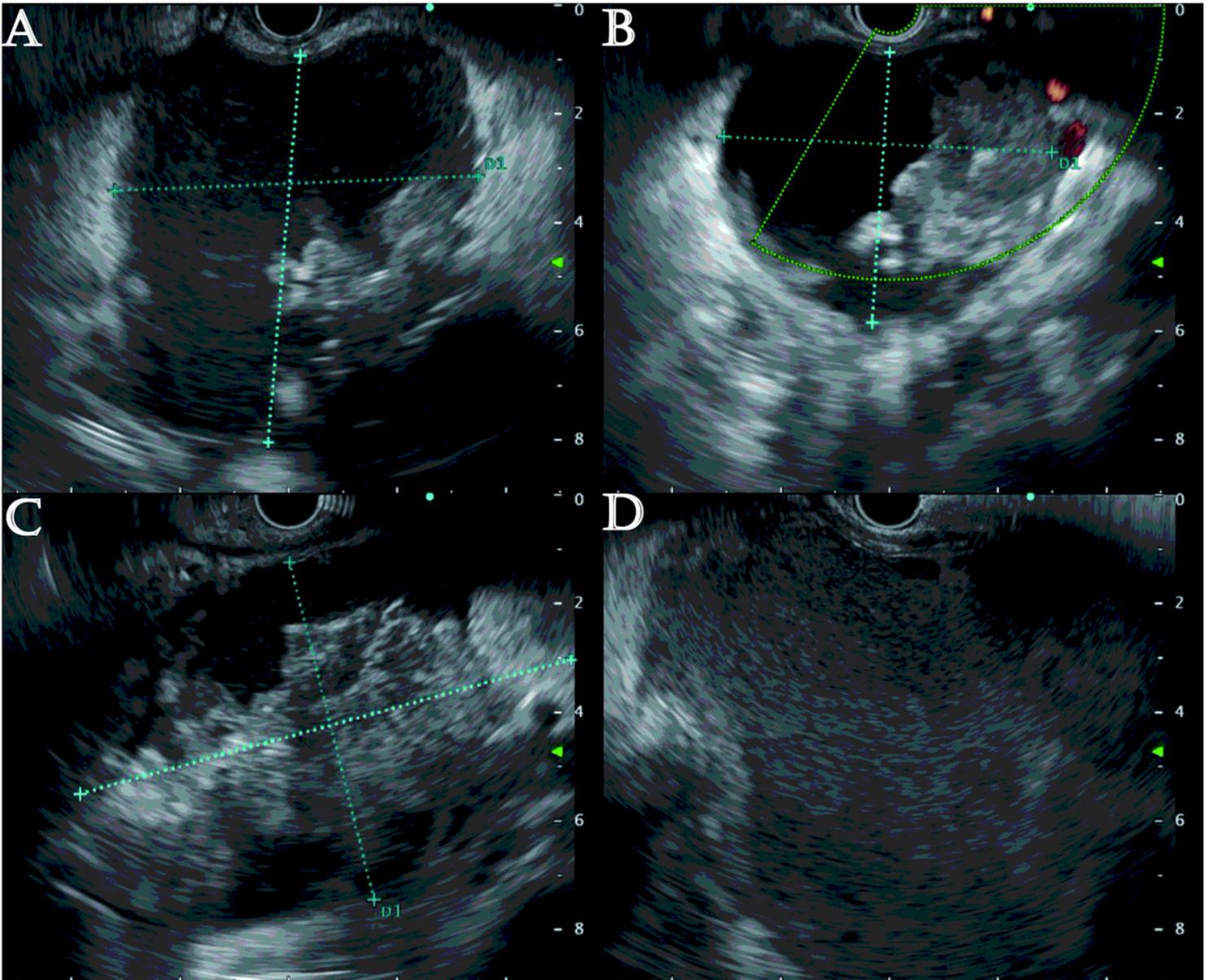


Figure 1

The association between the morphological features of necrotic collection on EUS and ETN sessions. (A) Necrotic collection with predominantly liquid content and <30% solid necrotic debris was successfully treated with a single session of ETN. Necrotic collection with 30%-50% (B) and >50% (C) solid necrotic debris needed two sessions of ETN. (D) Necrotic collection with predominantly purulent liquid content and minimal necrosis also needed a single session of ETN. ETN, endoscopic transmural necrosectomy.

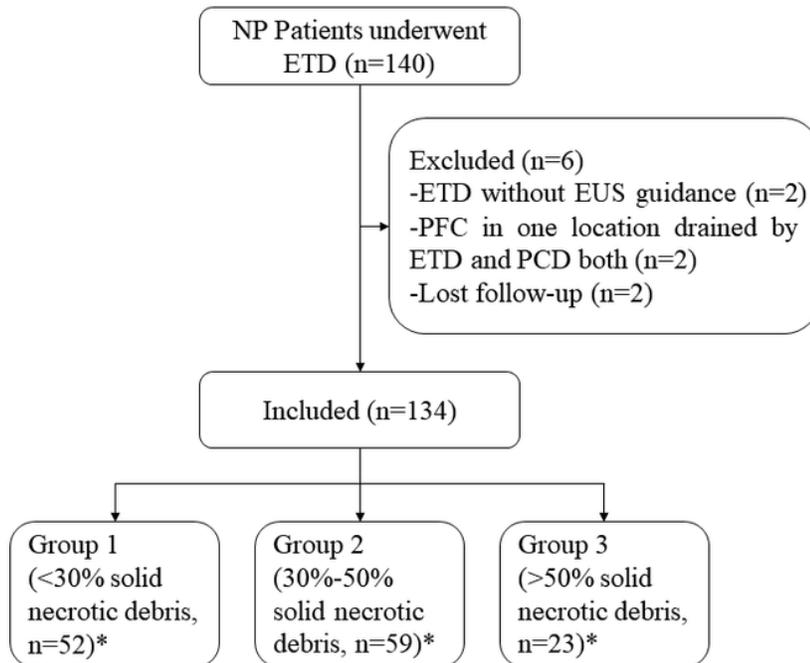


Figure 2

Flow chart of patients included and exclusion. NP, necrotizing pancreatitis; ETD, endoscopic transmural drainage; EUS, endoscopy ultrasound; PFC, pancreatic fluid collection; PCD, percutaneous drainage. *The amount of solid necrotic debris in the PFC was quantified as a percentage of the total size of the collection assessed by the EUS during the initial ETD.