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Predicting need for intervention in acute necrotizing pancreatitis following discharge- A single center experience in 525 patients

Guru Trikudanathan [a,*], Ahmed Dirweesh [a], Nauroze Faizi [b], Robben Schat [b], Gaurav Suryavwanshi [a], Scott Lunos [c], David Jonason [a], Nabeel Azeem [a], Stuart K. Amateau [a], Shawn Mallery [a], Anil Chauhan [b], Martin L. Freeman [a]

[a] Division of Gastroenterology, Hepatology and Nutrition, University of Minnesota, USA
[b] Department of Radiology, University of Minnesota, USA
[c] Clinical and Translational Science Institute, Biostatistical Design and Analysis Center, University of Minnesota, USA

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ABSTRACT

Background and aims: The clinical course of necrotizing pancreatitis (NP) is variable and unpredictable, with some patients managed conservatively, but a significant proportion become symptomatic and needing intervention for drainage and/or necrosectomy. The aim of this study was to identify patients based on baseline clinical and imaging metrics who will likely need intervention and therefore closer follow-up.

Methods: All NP patients managed in our institution between 2010 and 2019 were identified from a prospective database and those who did not undergo intervention during initial hospitalization were followed longitudinally post discharge until clinical and imaging resolution of necrosis. Patients were categorized into a conservative arm or intervention arm (endoscopic/percutaneous/surgical drainage and/or necrosectomy) for criteria defined according to IAP/APA guidelines. Clinical and imaging characteristics during initial presentation were analyzed between the two groups to identify independent predictors for eventual intervention using multivariable logistic regression. A nomogram was designed based on factors that were significant as defined by P value < 0.05.

Results: Among 525 patients, 340 who did not meet criteria for intervention during initial admission were included for study and followed for an average 7.4 ± 11.3 months. 140 were managed conservatively and 200 needed intervention (168 within 6 months and 32 after 6 months). Independent predictors of need for eventual intervention were white race [OR 3.43 (1.11–10.62)], transferred status [OR 3.37 (1.81–6.27)], and need for TPN [OR 6.86 (1.63–28.9)], necrotic collection greater than 6 cm [OR 8.66 (4.10–18.32)] and necrotic collection with greater than 75% encapsulation [OR 41.3 (8.29–205.5)]. A prediction model incorporating these factors demonstrated an area under the curve of 0.88.

Conclusions: Majority of NP patients do not need intervention during initial admission but may require drainage/necrosectomy mostly in the first 6 months following discharge. Need for subsequent intervention can be accurately predicted by a combination of clinical and imaging features on index admission.

1. Background and Aims

Pancreatic parenchymal and/or peripancreatic tissue necrosis [necrotizing pancreatitis (NP)] occurs in approximately 15–20% of patients with acute pancreatitis (AP) [1,2]. The natural history and clinical course of NP is variable and unpredictable with some collections warranting intervention. The primary indications for intervention (endoscopic, percutaneous or surgical) include infected necrotic collections, or symptomatic walled off necrosis including ongoing gastric, intestinal or biliary tract obstruction, "persistent unwellness", disconnected pancreatic duct syndrome with symptomatic and persistent collections [2,3]. With aggressive medical management including nutritional and intensive care support, some necrotic collections may spontaneously resolve with

* Corresponding author.
E-mail address: triku001@umn.edu (G. Trikudanathan).

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conservative expectant management without need for endoscopic, percutaneous or surgical intervention. Previous longitudinal studies evaluating the natural history of NP have shown that 23–70% of patients will eventually develop complications or symptoms which will warrant intervention (drainage and/or necrosectomy) [4–8]. Currently it is unclear which subset of hospitalized NP patients who are discharged without intervention can be managed conservatively, but ultimately need intervention. It would be desirable to identify patients on admission, who will develop late symptoms and complications, as they could benefit from closer surveillance [4].

We hypothesized that clinical metrics and imaging characteristics identified during initial hospitalization could be used to predict the likelihood of eventual drainage or intervention. The aim of this study was to evaluate possible predictors to identify patients likely to need eventual intervention after discharge and therefore closer follow up.

2. Methods

2.1. Patients

Consecutive patients with collections resulting from NP managed at University of Minnesota Medical Center between 2010 and 2019 were identified from our prospectively maintained database. Whenever interventions were indicated, management decisions were made in a multidisciplinary manner involving pancreatologists/therapeutic endoscopists, interventional radiologists, intensivists and surgeons using our previously described algorithm [9]. Patients needing interventions were managed using an endoscopically centered step-up approach with endoscopic or percutaneous drainage as the first line management depending on the location of the collection. Subsequently endoscopic necrosectomy were performed as needed with video-assisted retroperitoneal debridement (VARD) or open necrosectomy reserved for clinical failure of step-up approach or severe complications such as peritonitis. Adjuvant percutaneous drainage was performed in addition to endoscopic drainage in the setting of large necrotic collection with deep retroperitoneal extension, peritoneal involvement and for scattered multifocal collection with subsequent sinus tract endoscopy as needed. Early advancement to oral diet was encouraged with enteral nutrition via nasojejunal tube (NJ) feeds or percutaneous gastrostomy tube with jejunal extension (PEG/J) reserved for patients who do not tolerate oral diet or when daily requirement could not be met by oral nutrition alone. Dieticians were routinely consulted to evaluate nutritional status, to follow and manage NP patients who were not tolerating oral nutrition. Nutritional status was individually assessed by anthropometric measurements, nutrition labs, and other markers for malnutrition including muscle wasting, loss of subcutaneous fat, edema performed every week. Energy requirement of 25 kcal/kg/day was generally considered the initial goal but individual calorie requirements were reassessed twice a week, and personalized recommendations based on ESPEN guidelines were made [10]. Total parenteral nutrition (TPN) was considered last resort for patients who could not tolerate enteral nutrition. TPN was indicated in patients with NP who do not tolerate EN or who are unable to tolerate targeted requirements, or if there exists contraindication such as bowel obstruction or prolonged paralytic ileus [10].

Patients were discharged if they were clinically stable (no new fevers of 101.5 F for 48 h, no worsening organ dysfunction, pain reasonably managed on oral pain medications) and met our hospital discharge criteria. They were followed in 1–2 weeks following discharge, with interval cross-sectional imaging to evaluate the evolution or determine resolution of necrotic collection in the pancreas clinic. Patients were followed longitudinally until clinical and imaging resolution of necrosis.

2.2. Study design

NP patients who did not undergo drainage/intervention during initial hospitalization were included in this study. Based on whether patients underwent eventual intervention or not, they were categorized to "conservative" and "intervention" groups.

Data with regards to demographics (age, sex, race), body mass index (BMI), Charlson comorbidity index, etiology of pancreatitis, clinical metrics to quantify disease severity [transfer status, organ failure (as defined on supplemental table), need for ICU admission, length of stay, inability to tolerate oral nutrition and need for enteral nutrition or total parenteral nutrition (TPN)] were collected for both the groups. Contrast enhanced computed tomography (CECT) performed on initial admission or transfer were reviewed for study purposes by a group of two expert body-imaging radiologists (NF and AC; or NF and RS). Any disagreements were resolved in consultation with a third body-imaging radiologist (RS in case of disagreements between NF and AC, and AC in case of disagreements between NF and RS). All three radiologists were blinded to patient's clinical history and outcome. Imaging characteristics including size of the largest collection, degree of encapsulation, presence of gas bubbles within collection, presence of ascites, spread of peripancreatic collections and other characteristics of collections on CT were assessed as per definitions listed in supplemental table.

2.3. Predictive factors

The following predefined parameters on initial hospitalization were analyzed for successful prediction of eventual intervention:

Demographic criteria: [1] age [2], sex [3], race [4], BMI [5], etiology [6], Charlson comorbidity index.

Disease severity criteria including [7] transfer status [8] organ failure -acute kidney injury (AKI), respiratory failure, circulatory failure [9], multiorgan failure [10] persistent organ failure [11], admission to intensive care unit (ICU) [12], length of hospital stay (LOS) [13], need for nutritional support -enteral feeding (NJ/PEG/J) or (TPN).

Morphological characteristics of necrotic collections on CT [14]: site of collection-pancreatic necrosis or peripancreatic necrosis or both [15], number of collection-single vs. multiple [16], size of the collection (<6 cm or >6 cm) [17], characteristic of collection (homogenous vs. heterogenous) [18], degree of encapsulation of the collection [19], presence of gas bubbles within the collection, (20) presence of ascites and (21) spread pattern of peri-pancreatic collections.

2.4. Statistical analysis

Baseline demographics, clinical characteristics detailing the severity of pancreatitis and imaging characteristics were summarized between those managed conservatively and those who needed intervention eventually. Means and standard deviations (SD) were reported for continuous variables and counts and percentages for categorical variables. Simple and multiple logistic regression models were used to assess associations between covariates and eventual intervention. Variables included in the final multivariable model were determined by using a stepwise selection procedure using significance levels ($p < 0.10$ for entry into model, $p < 0.05$ to stay in model). Results are presented as odds ratios (ORs) and 95% confidence intervals (CI). P-values less than 0.05

were considered statistically significant. Predictive accuracy was assessed by area under the ROC curve (AUC). The final model was internally validated using cross-validation and a nomogram was created. SAS V9.4 (SAS Institute Inc., Cary, NC) was used for the analysis. R v4.0.3 was used to construct the nomogram.

3. Results

3.1. Baseline characteristics of study cohort

525 patients with NP were managed at our institution during the study period. Among these 44 (8%) were lost to follow up or were <18 years and were excluded. Among the 481 patients, 141 (29%) underwent interventions within 4 weeks were excluded. 340 patients were discharged and were longitudinally followed for an average 7.4 ± 11.3 months and formed the final study cohort as shown in Table 1. Among the 340 patients, 140 (41%) were managed conservatively, while 200 (59%) underwent one or more forms of intervention. Indications for these interventions included infected necrosis in 91 (45.5%), gastric outlet obstruction 49 (24.5%), abdominal pain and persistent unwellness 57 (28.5%) and biliary obstruction 3 (1.5%). Among those 200 patients, 168 (84% underwent intervention within the first 6 months following onset of acute pancreatitis, whereas [n = 32 (16%)] beyond 6 months. More than three fourths of patients (n = 152) were definitively managed by single interventions either endoscopic transluminal drainage/necrosectomy (n = 135) or percutaneous drainage (n = 17). One fourth of the patients (n = 48) needed multimodality management with 15 (7.5%) needing rescue open necrosectomy after failure of minimally invasive interventions as shown in Fig. 1.

3.2. Successful prediction of eventual intervention

The results of the univariable logistic regression are summarized in Table 2. The following predictors were associated with eventual intervention in univariable analysis: white race[OR 2.88(1.19–6.99), $P = 0.02$], biliary etiology [OR 2.93 (1.41–6.08), $P = 0.004$], patients transferred to our center from outside facilities [OR 2.99 (1.9–4.7), $P < 0.0001$], acute kidney injury on admission [OR 3.29 (2.08–5.20), $P < 0.0001$], circulatory failure on admission [OR 2.34 (1.17–4.68), $P = 0.02$], multi-organ failure on admission [OR 1.93 (1.17–3.19), $P = 0.01$], persistent organ failure [OR 1.83 (1.07–3.14), $P = 0.03$], need for enteral nutrition [OR 1.95 (1.22–3.11), $P = 0.0002$], need for TPN [OR 10.71(3.24–35.46), $P = 0.0001$] or imaging characteristics including [necrotic collection> 6 cm {OR 8.45 (4.58–15.56), $P < 0.0001$}, degree of encapsulation->75% {OR 42.26(9.5–187.74), $P < 0.0001$}, presence of gas bubbles with necrotic collection- 3.79 {OR (1.53–9.39), $P = 0.004$}]. In multiple logistic regression analysis, the following variables remained significantly associated with successful prediction of need for eventual intervention: white patients [adjusted OR 3.43 (1.11–10.62), $P = 0.03$], transferred status [adjusted OR 3.37 (1.81–6.27, $P = 0.0001$)], and need for TPN [adjusted OR 6.86 (1.63–28.9), $P = 0.009$], necrotic collection greater than 6 cm [adjusted OR 8.66 (4.10–18.32, $P < 0.0001$)], necrotic collection with greater than 75% encapsulation [adjusted OR 41.28 (8.29–205.5), $P < 0.0001$] as shown in Table 3 In order to exclude referral bias, we performed a subgroup analysis including patient primarily admitted to our center for management. Multivariable analysis showed that white patients [adjusted OR 4.78 (1.09–21.01, $P = 0.03$)], necrotic collection greater than 6 cm [adjusted OR 4.91 (1.44–16.7, $P = 0.011$)], necrotic collection with greater than 75% encapsulation [adjusted OR 42.7 (8.13-NC, $P < 0.0001$)]. Need for TPN was not a significant predictor in non-transferred patients [adjusted OR 2.16 (0.31–15.04. $P = 0.44$].

3.3. Final prediction model

A receiver operating characteristic curve of the model demonstrated an area under the curve of 0.88 as shown in Fig. 2.

4. Discussion

This present single center study identified clinical and imaging characteristics on initial hospitalization for NP which can predict the likelihood of future drainage or intervention after initial

Table 1
Baseline demographic and disease severity characteristics on initial hospitalization.

Characteristic	All patients (N = 340)	Conservative (N = 140)	Intervention (N = 200)	*P* value
Age (years), mean (SD)	52.1 (15.9)	51.0 (16.8)	52.9 (15.3)	0.28
Male [n (%)]	238 (70%)	100 (71.4%)	138 (69%)	0.56
Race [Whites, n (%)]	317 (93.2%)	125 (89.3%)	192 (96.0%)	**0.02**
BMI (in kg/m^2), mean (SD)	29.0 (6.5)	29.2 (6.3)	28.8 (6.6)	0.62
Etiology, n (%)				**0.03**
Idiopathic	40 (11.8%)	21 (15%)	19 (9.5%)	
Alcohol	125 (36.8%)	60 (42.9%)	65 (32.5%)	
Biliary	120 (35.3%)	34 (24.3%)	86 (43%)	
Drug induced	11 (3.2%)	6 (4.3%)	5 (2.5%)	
Hypertriglyceridemia	21 (6.2%)	9 (6.4%)	12 (6%)	
Post ERCP induced	17 (5%)	8 (5.7%)	9 (4.5%)	
Trauma	6 (1.8%)	2 (1.4%)	4 (2%)	
Charlson CI, mean (SD)	2 (2.1)	2.1 (2.3)	1.9 (1.9)	0.37
Transferred from outside hospital, n (%)	205 (60.3%)	63 (45%)	142 (71%)	< **0.0001**
Multi-organ failure, n (%)	96 (28.2%)	29 (20.7%)	67 (33.5%)	**0.01**
Persistent organ failure, n (%)	79 (23.2%)	24 (17.1%)	55 (27.5%)	**0.03**
BISAP score, mean (SD)	1.9 (1.1)	1.7 (1.0)	2.1 (1.1)	**0.0008**
Need for ICU admission, n (%)	119 (35%)	45 (32.1%)	74 (37%)	0.36
Length of stay (in days) [median (IQR)]	10 (4–22)	12 (6.5–20)	8 (3–23)	0.11
Nutrition				< **0.0001**
Oral nutrition	182 (53.5%)	93 (66.4%)	89(44.5%)	
Enteral nutrition (NG/NJ/PEG-J)	126 (37.1%)	44 (31.4%)	82 (41.0%)	
Total parenteral nutrition	32 (9.4%)	3 (2.1%)	29 (14.5%)	

BMI- Body mass index, Charlson CI- Charlson comorbidity index, IQR-interquartile range.

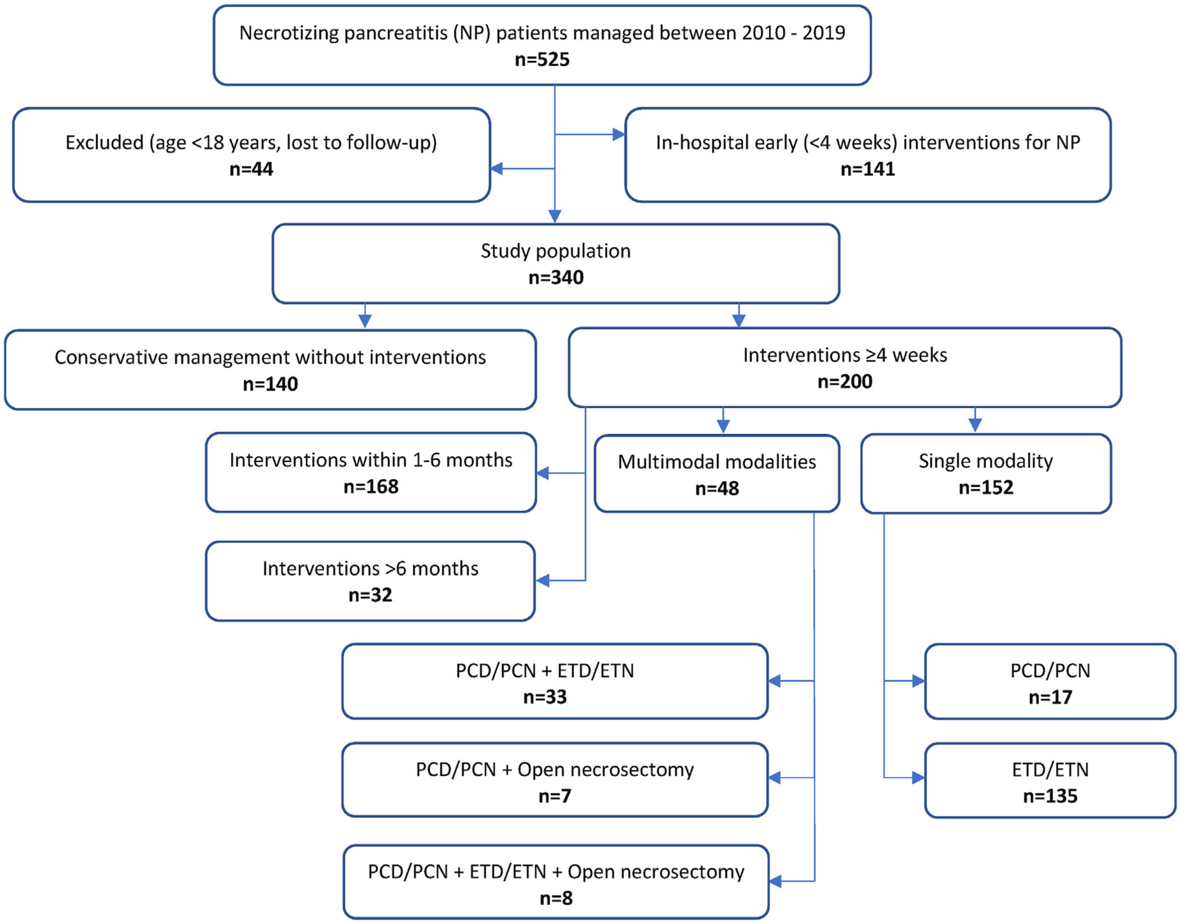

Fig. 1. Inclusion flowchart
PCD, Percutaneous drainage; PCN, Percutaneous necrosectomy; ETD, Endoscopic transluminal drainage; ETN, Endoscopic transluminal necrosectomy.

hospitalization and discharge. Transferred patients, white race, patients requiring TPN for nutrition, necrotic collections larger than 6 cm and necrotic collections which are fully encapsulated (75% or more) were more likely to undergo drainage or intervention after discharge. The constructed nomogram (Fig. 3) can guide prognostication at the time of initial discharge and aid in triaging patients who will need closer follow up. Conversely, a predictive strategy also enables in identifying patients who will likely be managed conservatively and avoid unnecessary repeated cross-sectional imaging such as CT.

Current guidelines recommend conservative, non-interventional management of asymptomatic necrotic collections regardless of the size, duration and extent of the collection [2,3,11]. Majority of studies suggest that nearly 50% of NP patients have spontaneous resolution of necrotic collections [4,6,7,12]. In this study, among the 525 NP patients managed at our institution, 140 patients (27%) were managed conservatively without need for any intervention. Interestingly 21% of patients had multiorgan failure on admission and 17% of patients had persistent organ failure, and therefore a predicted severe disease course on admission with 32% ultimately needing ICU admission. This was similar to an earlier multicenter prospective study by the Dutch Pancreatitis group wherein they showed that among the 397 patients managed conservatively, 16% had organ failure on admission and nearly half had a predicted severe course of disease with APACHE II > 8 on admission [12]. Despite predicted severity of disease course on admission, patients were managed conservatively without any intervention. In the recently published POINTER trial, among the infected necrosis patients randomized to the postponed drainage strategy, 39% of the patients were managed conservatively on antibiotics without need for intervention [13]. These studies all suggest that even in patients with predicted severe course of disease on admission, who ultimately develop infected necrosis, the best initial strategy is conservative management with antibiotics and close monitoring.

Our findings were also consistent with another study which reported that 70% needed intervention within 3 months [5]. Similar to that study, reasons for increased need for intervention was likely because 60% of were transferred from other hospitals with moderately severe or severe acute pancreatitis, with a high proportion of patients with single or multi-organ failure with more extensive necrosis [5]. One of the most ominous complications of expectant management is direct erosion of arteries by necrosis and development of arterial pseudoaneurysms which could rupture resulting in life threatening bleeds [4]. Fortunately none of the patients who were managed conservatively developed vascular complications such as arterial pseudoaneurysms with gastrointestinal bleeding consistent with prior observations [4–7]. In our study, a majority (84%) of patients underwent interventions in the first 6 months following onset of acute pancreatitis, in concordance with other studies showing no complications after 6–7 months after onset of acute pancreatitis [4,7]. These observations underscore the need for assiduous follow up during the first six months following hospitalization.

Table 2
Univariable analysis of factors predicting any intervention in necrotizing pancreatitis.

Predictor	OR (95% CI)	P value
Demographics		
Age	1.01 (0.99–1.02)	0.28
Male sex	0.87(0.54–1.4)	0.56
White race	2.88 (1.19–6.99)	0.02
BMI	0.99(0.96–1.03)	0.62
Charlson comorbidity index	0.95(0.86–1.06)	0.37
Etiology		**0.0320**
Idiopathic	Ref	**-**
Alcohol	1.28 (0.63–2.59)	0.5002
Biliary	2.93 (1.41–6.08)	0.0040
Drug induced	0.97 (0.25–3.67)	0.9582
Hypertriglyceridemia	1.54 (0.54–4.46)	0.4220
Post ERCP	1.30 (0.42–4.05)	0.6474
Trauma	2.32 (0.38–14.08)	0.3618
Disease severity		
Transfer	2.99 (1.9–4.7)	< **0.0001**
Acute kidney injury on admission	3.29 (2.08–5.20)	< **0.0001**
Respiratory failure on admission	0.77(0.49–1.19)	0.24
Circulatory failure on admission	2.34 (1.17–4.68)	**0.02**
Multi-organ failure on admission	1.93 (1.17–3.19)	**0.01**
Persistent organ failure	1.83(1.07–3.14)	**0.03**
Need for ICU admission	1.24(0.79–1.96)	0.36
Length of stay	1.01(0.998–1.02)	0.11
Need for enteral or total parenteral nutrition (TPN)		< **0.0001**
Oral	Ref	**-**
Enteral	1.95 (1.22–3.11)	**0.0002**
TPN	10.10 (2.97–34.3)	**0.0052**
Imaging characteristics on index CT		
Site of necrosis		0.83
Pancreatic	Ref	
Peri-pancreatic	0.86 (0.47–1.58)	0.63
Both	1.02 (0.62–1.69)	0.94
Characteristic of necrosis		
Homogenous	Ref	
Heterogenous	1.33 (0.68–2.61)	0.41
Number of necrotic collections		0.92
Single	0.98(0.63–1.51)	
Multiple	Ref	
Degree of encapsulation		< **.0001**
None	Ref	–
(<75%)	4.92 (1.10–22.08)	0.0377
(>75%)	42.26 (9.5–187.74)	< **0.0001**
Size of necrotic collection		< **0.0001**
(<6 cm)	Ref	
(>6 cm)	8.45(4.58–15.56)	
Spread of peri-pancreatic collection[a]		
None	0.76 (0.30–1.94)	0.57
Anterior pararenal	0.69 (0.37–1.29)	0.25
Retromesentric plane	1.33 (0.79–2.23)	0.28
Lateral conal plane	1.53 (0.67–3.50)	0.31
Perinephric	1.13 (0.70–1.82)	0.63
Retorenal	1.41 (0.35–5.75)	0.63
Posterior pararenal	1.53 (0.67–3.50)	0.31
Illio-psoas	1.17 (0.58–2.37)	0.66
Paracolic gutter	1.00 (0.60–1.65)	0.99
Peritoneal space	0.69 (0.14–3.49)	0.66
(Perihepatic, subphrenic, hepatorenal, perisplenic)		
Presence of gas bubbles within necrotic collection	3.79 (1.53–9.39)	**0.004**
Presence of ascites	1.26(0.77–2.07)	0.36

[a] Data missing in 24 patients.

Most clinical predictors of severity such as transferred status, single organ failure (acute kidney injury and circulatory failure), multi-organ failure, persistent organ failure, increased BISAP scores, failure to tolerate oral nutrition and need for enteral nutrition or TPN were associated with need for intervention on univariable analysis. However, among this only hospital transfer status and need for TPN emerged as independent predictors for need for intervention on multivariable analysis. Hospital transferred status is a well-established surrogate for disease severity in AP [14,15]. In our study cohort, the transferred patients had greater initial disease severity with significantly more persistent organ failure (27.8% vs. 16.3%, $P = 0.02$), were more likely to need ICU admission (40.5% vs. 26.7%, $P = 0.01$) and increased rates of infected necrosis (38.1% vs. 11.9%, $P < 0.0001$) in comparison with primary admissions. Patients with NP often develop severe ileus and gastric outlet obstruction from edema and/or evolving necrotic or fluid collections often necessitating need for enteral nutrition or TPN. Inability to tolerate oral nutrition and need for enteral nutrition or

Table 3
Multivariable logistic regression analysis.

Predictor	Adjusted OR (95% CI)	P-value
Race (White)	3.43 (1.11–10.62)	0.0321
Transfer	3.37 (1.81–6.27)	0.0001
Degree of Encapsulation		<.0001
(None)	Ref	–
(<75%)	4.07 (0.82–20.34)	0.0871
(>75%)	41.28 (8.29–205.5)	<.0001
Size		
(≥6 cm)	8.66 (4.10–18.32)	<.0001
2 (<6 cm)	Ref	
Nutrition		0.0123
Oral	Ref	-
Enteral	1.79 (0.96–3.32)	0.0672
TPN	6.86 (1.63–28.90)	0.0087

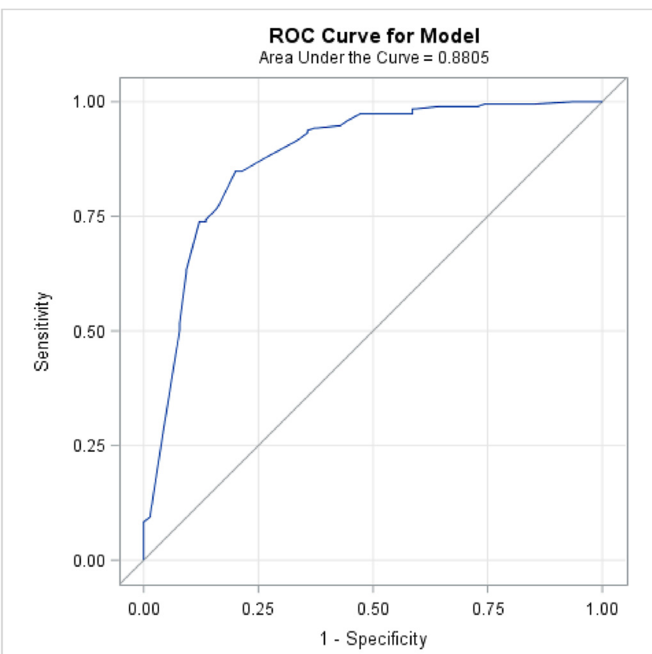

Fig. 2. Receiver operating characteristic curve of the multivariable regression model for predicting need for eventual intervention for necrotizing pancreatitis. It includes predictors white race, transfer status, size of collection >6 cm, degree of encapsulation (>75%), inability to tolerate PO and need for TPN.

TPN has been recognized as an important qualitative metric and an integral component in the recently proposed pancreatitis activity scoring system (PASS) score to quantitatively gauge disease activity in patients with acute pancreatitis [16]. PASS score >60 on discharge was associated with early readmission for pancreatitis symptoms and complications within 30 days of discharge [16]. In our study, TPN [OR 6.86 (1.63–28.9), $P = 0.009$] were associated with need for subsequent drainage or intervention. Among the 29 patients on TPN who underwent intervention, two thirds (19/29) were for infected necrosis. Patients on TPN are presumably vulnerable to infection of necrotic collections by alteration in gut mucosal permeability and subsequent bacterial translocation, thus greater likelihood of infection and perhaps need for intervention. Interestingly both length of index hospitalization and need for ICU admission were not significant predictors which suggests that patient can be managed conservatively despite prolonged hospital or ICU stay.

Since the pancreas is a retroperitoneal organ, extra-pancreatic inflammation and resultant necrotic collection usually involves retroperitoneal and retrocolic spaces including the anterior and posterior para-renal space, peri-renal space, and deep pelvis. Occasionally necrotic collection spill into sub-peritoneal and peritoneal spaces including the perihepatic, peri-splenic and hepatorenal space [17]. Our study suggests that the number of collection (single vs. multiple), the sites of necrosis (pancreatic or peripancreatic or both) or spread into deep retroperitoneum or peritoneal spaces did not impact the need for intervention. These findings are consistent with a recent study which concluded no association between unusual sites of collection and clinical outcomes [17].

The size of the necrotic collection was an independent predictor for need for eventual intervention. In our study, 6 cm or larger collections were at 8 times higher risk for needing drainage or necrosectomy, suggesting that large collections are unlikely to resolve spontaneously. Interestingly, this finding has been refuted by few smaller studies which showed no significant difference in size of walled off necrosis at presentation between patients who remained asymptomatic versus patients who developed symptoms or complications related to intervention [4,7]. Other studies have shown that size of the necrotic collections over 6 cm are an independent predictor of persistence or requirement for drainage, while size <6 cm was one of two independent predictor of spontaneous resolution [6,8]. A very recent study from Mayo clinic concluded that pancreatic fluid collections ≥10 cm in size, paracolic extension, or ≥ 30% solid necrosis were predictive of need for additional step-up therapies following the index drainage procedure including endoscopic necrosectomy, additional drainage or surgical intervention [18]. This study suggests that while larger asymptomatic collections are not alone an indication for drainage, a higher risk for eventual symptoms warrants close observation [18].

Multiplanar coronal and sagittal reconstructions were evaluated to quantify the degree of encapsulation. Necrotic collection was considered encapsulated when there was a discrete smooth enhancing wall between the collection and the adjacent tissue and was rated for its completeness with (>75%) considered complete and (<75%) as partial. Collections which appeared ill-defined with no discernible wall were categorized as having "none". In our study, full encapsulation of collections (>75%) was the strongest predictor of ultimate need for intervention. The pathophysiology of encapsulation of necrotic collection is poorly understood, but it is believed that the release of activated proteolytic enzymes and resultant acinar cell injury incites an extensive local and systemic inflammation [19] With time, the body attempts to contain the area of inflammation to further mitigate the spread of toxic enzymes and wall off the necrotic collections [19]. While the rate of encapsulation is likely influenced by the magnitude of inflammatory response along with immune-mediated and patient factors, it is also possible that patients with fully encapsulated collections are followed more closely, with a lower threshold for intervention by providers as soon as they are indicated as seen in our study. Presence of gas within necrotic collection caused by gas forming organisms or loss of integrity of the gastrointestinal tract is considered pathognomonic of infected necrosis. Surprisingly in our study, while gas in the collection was significant on univariate analysis [OR 3.79 (1.53–9.39), $P = 0.04$], it did not emerge as an independent predictor on multivariate analysis.

The current study has some strengths and number of potential limitations which deserve to be acknowledged. A potential strength is that it is based on a prospectively maintained database of all consecutive patients admitted to the hospital with NP of any extent, with patients managed by the entire spectrum of interventions available for NP, baseline assessment of severity by means of validated scores and defined radiological follow-up. Our cohort was

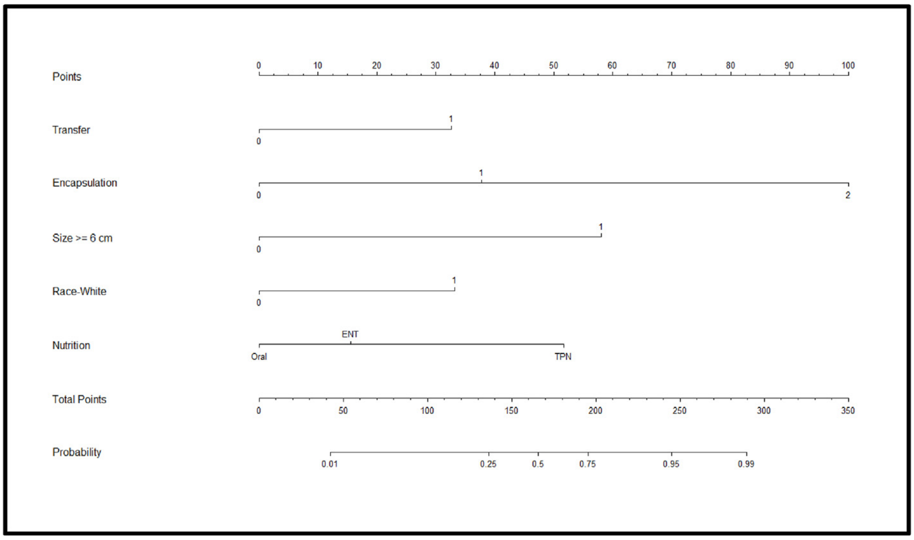

Fig. 3. Nomogram for the prediction of need for eventual intervention.
For each predictor, a value can be mapped to the points axis. The total of the points can be found in the total points axis and the associated probability of intervention can be obtained. For encapsulation 0 = none, 1 = <75%, 2 = >75%, for yes/no variables 1 = yes.

large, and all images were reviewed by two radiologists with body imaging expertise blinded to patient information and clinical outcomes.

The current study is a retrospective analysis of a prospective database and predefined variables were limited by availability. Although we included detailed clinical predictors which encompassed known indicators for severity of disease, it is possible that other factors not available from our prospective database are of predictive value. Further this study was conducted in a single tertiary center mostly after referral from a wide range of outside hospitals, and by a highly specialized multi-disciplinary team with extensive expertise in the entire spectrum of interventions for NP and results may not be readily generalizable. To eliminate referral bias, we performed a subgroup analysis in patients primarily admitted to our institution. Except need for TPN, we were able to draw the same conclusions (white patients, necrotic collection size >6 cm and >75% encapsulated collections remained significant predictors). Finally, although internally validated by cross validation, our model lacks external validation. Further multicenter prospective studies are warranted to validate the conclusions of our study.

In conclusion, nearly three fifth of patients who were discharged needed eventual intervention for drainage and necrosectomy, with majority during the first 6 months. A prediction model was developed based on readily available baseline clinical and imaging parameters that can help stratify NP patient who are likely to need intervention at an early stage of the disease. The information provided by the nomogram can guide triaging of patients who will need more rigorous outpatient follow up, however external validation will be required to improve the reliability of the estimates and their applicability to a more general population.

Guarantor of article

Guru Trikudanathan MD, FASGE, Associate Professor of Medicine Division of Gastroenterology 406 Harvard St SE, MMC36, Minneapolis, MN 55455, USA.

Disclosures and COI

GT, SKA, SM are consultants for Boston Scientific.

All other authors have no conflict of interest relevant to this manuscript.

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