Predicting success of direct endoscopic necrosectomy with lumen-apposing metal stents for pancreatic walled-off necrosis

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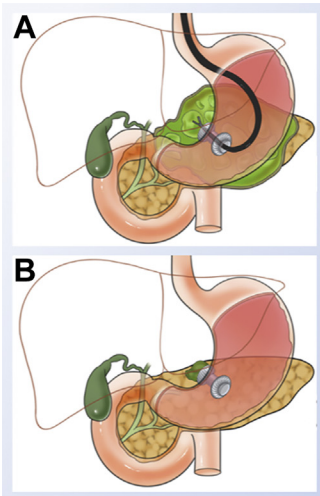
GRAPHICAL ABSTRACT



Predictors of DEN Failure for Pancreatic WON

Predictors	OR [95% CI]	*p* value
APACHE-II	0.70 [0.55, 0.90]	0.005
Percentage of necrosis (>50%)	0.16 [0.03, 0.77]	0.022
Paracolic gutter extension	0.08 [0.02, 0.42]	0.003

Background and Aims: Direct endoscopic necrosectomy (DEN) with lumen-apposing metal stents (LAMSs) is increasingly used in the management of pancreatic walled-off necrosis (WON). However, it still remains unknown which patients will fail to respond to DEN with LAMSs and require additional surgical intervention. Therefore, the aim of our study was to explore predictors of successful DEN with LAMSs for pancreatic WON.

Methods: This is a retrospective analysis of a prospectively collected database. All consecutive patients who underwent DEN with LAMSs for pancreatic WON were included. Collected data were demographics, disease severity, morphologic features, and procedure characteristics. Potential factors affecting DEN outcome were predefined and analyzed.

Results: One hundred one consecutive patients undergoing DEN with LAMSs for WON were identified, among whom 4 patients were excluded for technical failure (n = 1) and previous debridement without LAMSs (n = 3). In the 97 included patients, clinical success was achieved in 79 patients (81.4%). In logistic multivariable regression, 3 independent factors were negatively associated with success of DEN with LAMSs: increasing Acute Physiology and Chronic Health Evaluation II score (odds ratio [OR], .70; 95% confidence interval [CI], .55-.90; P = .005), >50% pancreatic necrosis (OR, .16; 95% CI, .03-.77; P = .022), and paracolic gutter extension (OR, .08; 95% CI, .02-.42; P = .003). A receiver-operating characteristic curve of the prediction model with these 3 factors demonstrated an area under the curve of .926.

Conclusions: Paracolic gutter extension, increasing Acute Physiology and Chronic Health Evaluation II score, and >50% gland necrosis are negative predictors for success of DEN with LAMSs in WON. This prediction model with nomogram may be helpful in clinical decision-making and prognostication. (Gastrointest Endosc 2022;96:522-9.)

(footnotes appear on last page of article)

Over the past decade, endoscopy has become the standard first-line treatment for symptomatic pancreatic walled-off necrosis (WON).[1-4] Multiple studies have promoted shifting the treatment strategy from surgical step-up to endoscopic approaches.[5-7] Unlike pancreatic pseudocysts, WON has a vastly different nature history and usually contains large amounts of solid components, leading to increased risk of stent occlusion and subsequent infection.[8,9] Therefore, endoscopic drainage alone is less effective for WON over pancreatic pseudocysts (63.2% vs 93.5%),[10] and direct endoscopic necrosectomy (DEN) is frequently required.

DEN refers to direct insertion of an endoscope for extensive irrigation and mechanical removal of necrotic tissues. With decreased risks of pancreatocutaneous fistula and major adverse events, DEN is preferable to surgical intervention when feasible.[5,6] Furthermore, immediate DEN at the time of initial stent placement does not increase risk of adverse events but facilitates earlier WON resolution with fewer necrosectomy sessions over delayed DEN.[11] Recently, a novel lumen-apposing metal stent (LAMS) has been introduced into the management of WON and has gained great popularity. Characterized by a biflanged design and larger diameters (10-20 mm), the LAMS not only allows better drainage and easier direct access for DEN but also minimizes the risk of stent migration or occlusion. With excellent outcomes, the LAMS has been recommended as standard management of WON by a multi-institutional consensus.[2] A randomized trial (MISER trial) further demonstrated the superiority of DEN with LAMSs over minimally invasive surgery.[12]

However, despite the high success rates reported for DEN using LAMSs, up to 10% of patients do not respond to DEN and ultimately require surgery.[11] Currently, it still remains unknown which patients are mostly likely to be successfully treated by DEN with LAMSs and which patients will require additional surgery. Therefore, the aim of this study was to explore predictors of success for DEN with LAMSs for pancreatic WON.

METHODS

Patients

In this retrospective study of a prospectively collected registry, which was approved by our hospital's Institutional Review Board, all consecutive patients who underwent DEN with LAMSs (AXIOS; Boston Scientific, Marlborough, Mass, USA) for WON between July 2014 and October 2018 were included. WON was defined per the 2012 revised Atlanta classification as a mature and encapsulated collection with both liquid and necrotic solid components (on CT, magnetic resonance imaging, and/or EUS), usually occurring >4 weeks after the onset of necrotizing pancreatitis.[13] Patients with technical failure (without another LAMS session), previous surgical or endoscopic debridement were excluded. According to a standardized method for DEN management,[14] a contrast-enhanced cross-sectional image (CT or magnetic resonance imaging) was routinely performed within 10 days before the intervention, and blood tests (including routine chemistries, blood counts, and coagulation parameters) were also obtained within 24 hours before DEN. Anesthesia was consulted to formally evaluate the patient, and surgical backup was arranged for all procedures. Written informed consent of the procedure was obtained by all patients or their legal representatives.

Patients were identified for the study and divided into 2 groups, success versus failure, according to treatment response. Medical data were collected and reviewed retrospectively, including basic demographics, etiology of pancreatitis, disease severity within 24 hours before DEN, WON morphologic features, procedure characteristics, microbiologic cultures, and clinical outcomes.

Procedures

All procedures were performed by 7 expert endoscopists with EUS experience of more than 10 years. All procedures were performed with the patient under general anesthesia with endotracheal intubation. CO_2 insufflation was used throughout. A linear EUS was used to first evaluate the lesion including WON size, location, presence of encapsulation and internal septations, and amount of necrosis. The optimal puncture site, avoiding vasculature, was confirmed under EUS and Doppler flow guidance. LAMS placement was performed with either a cold or electrocautery-enhanced (hot) system according to a previously published technique.[14,15] Then, immediate DEN was performed through the LAMS with a forward-viewing endoscope, including irrigation and fragmentation of necrotic material. Various accessories (Roth nets, large forceps, and cold snares) could be used for fragmentation, and a large amount of warmed normal saline solution, dilute hydrogen peroxide, or bacitracin solution was used for irrigation. The endpoint of DEN was exposure of pink granulation tissue lining the wall. Finally, debris after copious lavage was aspirated, and either double-pigtail plastic stents or a nasocystic tube was inserted at the discretion of endoscopists.

After DEN with LAMSs, all patients were scheduled for follow-up in a standardized fashion.[14] Clinical follow-up was scheduled within 6 weeks, and cross-sectional imaging was performed 4 weeks after the procedure and every 4 weeks thereafter until WON resolution. If cross-sectional imaging demonstrated resolution of the WON, LAMSs were removed at follow-up endoscopy. For persistent or recurrent symptoms or persistent collection on imaging, repeated DEN or percutaneous catheter drainage was performed. Patients who still did not achieve resolution were referred to surgery.

Definitions and potential predictors

Clinical success was defined as both resolution of symptoms and a decreased WON cavity size to $\leq$3 cm without

surgical intervention or death within a 6-month period.[9,16] Organ failure and systemic inflammatory response syndrome (SIRS) were assessed according to the modified Marshall scoring system used in the revised Atlanta classification.[13] Paracolic gutter extension was defined as an extension inferiorly along either retrocolic space to at least the lateroconal fascia.[17]

Several potential predictors were predefined for analysis. First, demographics were age, sex, body mass index, etiology, Charlson comorbidity index score,[14] history of antiplatelet or anticoagulation therapy, and American Society of Anesthesiology class. Second, disease severity (within 24 hours before DEN) included leukocyte count, hematocrit, serum albumin, serum calcium, Acute Physiology and Chronic Health Evaluation (APACHE) II score,[18] admission to intensive care unit, organ failure, and SIRS. Third, morphologic features on cross-sectional imaging (according to previous study[17]), included maximal length of WON, percentage of pancreatic necrosis (≤50%, >50%), CT severity index,[19] pattern of pancreatic necrosis (central, right-sided, left-sided, subtotal, scattered), paracolic gutter extension, heterogeneity of the collection, gas bubbles in WON, and hemorrhage into the collection. Fourth, procedure characteristics were previous drainage before DEN, LAMS type (cold or hot), technical aspects of necrosectomy (irrigation only and debridement), number of LAMSs, and size of the largest LAMS. Finally, infection of WON was defined by the comprehensive assessment of clinical manifestation, increased laboratory parameters, gas bubbles in WON, and positive microbiologic culture of the WON collection.[20]

Statistical analysis

Continuous data are summarized as mean ± standard deviation or median with interquartile range. Categorical data are summarized as frequencies with proportion. The association between potential predictive factors and the success of DEN with LAMSs was first evaluated by univariable analysis, including the Student t test and Wilcoxon rank-sum test for continuous data and the χ^2 and Fisher exact test for categorical data.

Potential predictors associated with the success of DEN with LAMSs in univariable analysis ($P < .05$) were included in the multivariable logistic regression analysis. The backward stepwise elimination method was used to exclude variables with $P > .05$ from the model. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated, and a 2-sided $P < .05$ was considered statistically significant. Receiver-operating characteristic curve and Hosmer-Lemeshow goodness of fit test were performed to evaluate discrimination and calibration of the prediction model. The K-fold cross-validation method was used for internal validation of the model. A nomogram was constructed on the basis of the outcome of the multivariable logistic regression analysis. Data analysis was performed by IBM SPSS statistics version 22.0 (IBM Corp, Armonk, NY, USA) and R statistics version 3.5.3 (Vienna, Austria).

RESULTS

Patients and procedures

Of 101 consecutive patients undergoing DEN with LAMSs for WON, 4 patients were excluded for previous DEN with double-pigtail plastic stents (n = 2), technical failure (n = 1), and previous video-assisted retroperitoneal debridement (n = 1) (Fig. 1). The final cohort of 97 patients (67 men, 30 women) had a mean age of 53.5 ± 16.6 years. The detailed characteristics of the 97 patients are shown in Table 1 and Supplementary Table 1 (available online at www.giejournal.org). Etiologies of acute pancreatitis were 26.8% for alcohol induced, 25.8% gallstone pancreatitis, 25.8% idiopathic, and 21.8% for other causes (drug, post-ERCP, hypercalcemia, hypertriglyceridemia, etc). Indications for DEN were abdominal pain in 63 patients (64.9%), infected WON in 25 (25.8%), and gastric outlet or biliary obstruction in 9 (9.3%).

Among the 97 patients included in the analysis, the mean APACHE-II score was 5.0 ± 3.7. Eighteen patients (18.6%) experienced SIRS, and 10 patients (10.3%) encountered organ failure within 24 hours before DEN. Eight patients (8.2%) were admitted to the intensive care unit before DEN. The maximum WON size on cross-sectional imaging was 12.0 ± 5.2 cm. Eighteen patients (18.6%) were found to have greater than 50% pancreatic necrosis, whereas paracolic gutter extension was seen in 14 patients (14.4%). The other WON characteristics are shown in Table 1.

Previous percutaneous catheter drainage had been performed in 13 patients (13.4%). The interval from onset of acute pancreatitis to DEN was 41.0 ± 11.0 days. One hundred seven LAMSs (74 hot, 33 cold) were deployed with 10 patients undergoing 2 LAMS insertions. Among the 10 patients, 8 underwent successful placement of 2 LAMSs at the index procedure to upsize, whereas 2 underwent subsequent stent exchange because of misplacement or occlusion of a previous LAMS. Most LAMSs were performed using a transgastric route (95.3%) followed by a transduodenal route (4.7%). The 15-mm LAMS was the most commonly used (90.6%), followed by 10-mm (4.7%) and 20-mm (4.7%) LAMSs (Supplementary Table 1).

Clinical success of DEN with LAMSs was achieved in 79 patients (81.4%), and the median duration from primary DEN to resolution was 31 days (interquartile range, 22-48). Slightly more than half of the patients (50.5%) required additional unplanned procedures excluding routine stent removal. The median number of unplanned procedures per patient was 1, ranging from 0 to 6 repeated procedures. Among the 18 patients who did not achieve clinical success with DEN, 11 patients underwent video-assisted retroperitoneal debridement, 5 patients died,

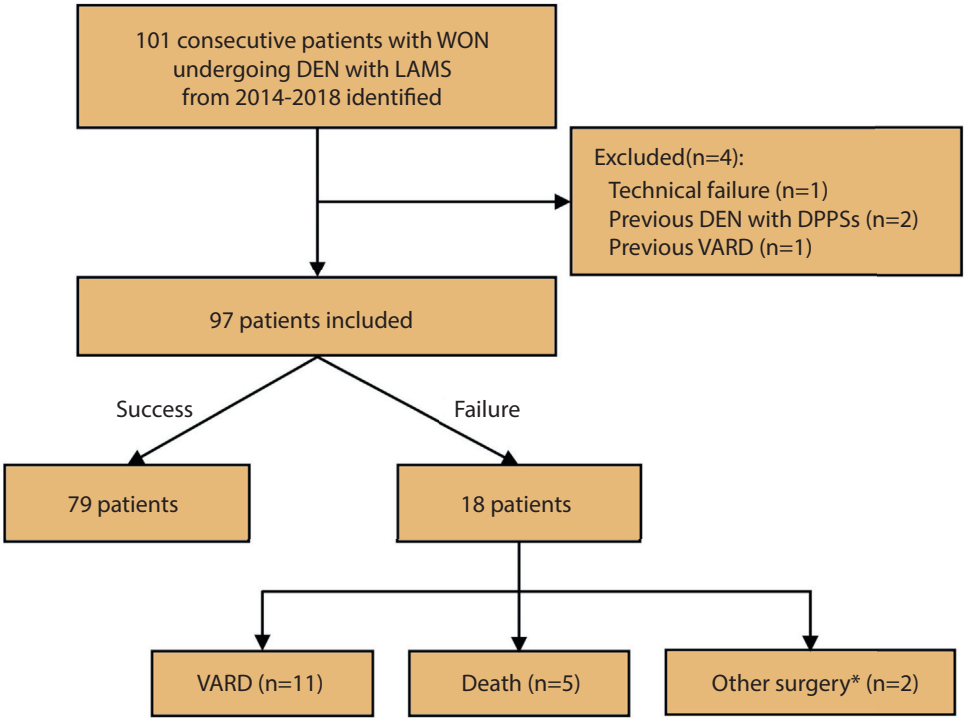


Figure 1. Flowchart of patients included in the study. *WON*, Walled-off necrosis; *LAMS*, lumen-apposing mental stent; *DEN*, direct endoscopic necrosectomy; *DPPSs*, double-pigtail plastic stents; *VARD*, video-assisted retroperitoneal debridement. *Surgery for adverse events (1 perforation and 1 stent migration).

and 2 patients were transferred to surgery for severe adverse events (1 perforation, 1 stent migration).

Success prediction of DEN with LAMSs

Twenty-nine potential predictors were predefined, and the results of the univariate analysis are summarized in Table 1. The following variables were associated with the clinical outcome of DEN in univariable analyses ($P < .05$): age, leukocyte count, albumin, APACHE-II score, SIRS, maximal length of the WON, percentage of necrosis, pattern of necrosis, CT severity index , paracolic gutter extension, heterogeneous WON, and infected WON. Multivariable analysis was subsequently performed, and the following variables remained negatively associated with success of DEN: increasing APACHE-II score (OR, .70; 95% CI, .55-.90; $P = .005$), percentage of necrosis >50% (OR, .16; 95% CI, .03-.77; $P = .022$), and paracolic gutter extension (OR, .08; 95% CI, .02-.42; $P = .003$) (Supplementary Table 2, available online at www.giejournal.org).

A receiver-operating characteristic curve of the model showed an area under the curve of .926 (Fig. 2). The Hosmer-Lemeshow goodness of fit test indicated reasonable calibration of the prediction model ($P = .457$), and a K-fold cross-validation (k = 7) showed good internal validation of the model with a mean accuracy and area under the curve of .877 and .923, respectively. A nomogram was designed with the 3 factors that were independently associated with clinical outcomes of DEN with LAMSs (Fig. 3). As per the algorithm, points were allotted to each of these 3 factors separately, with the probability for success with DEN increasing with total points. The most favorable score (ie, approximately 178 points) would be found in a patient with <50% pancreatic necrosis, no paracolic gutter extension, and an APACHE-II score of 0, resulting in a 99.3% chance of success for DEN with LAMSs. Conversely, if a patient had an APACHE-II score ≥10 points combined with >50% necrosis and paracolic gutter extension, total points would be less than 37.5, correlating to a ≤10% (9.4%) chance of successful DEN with LAMSs.

DISCUSSION

With the advent of LAMSs and evidence provided by the MISER trial, endoscopic necrosectomy for WON has gained great popularity.[9,12] Compared with the surgical step-up approach, DEN with LAMSs had the advantages of fewer adverse events, lower hospital stays and medical costs, and higher quality of life.[7,12] In this retrospective study, we demonstrated a clinical success rate of DEN with LAMSs for WON of 81.4%. An increasing APACHE-II score, >50% pancreatic necrosis, and paracolic gutter extension were independent negative predictors for success of DEN with LAMSs.

In our study, the clinical success rate was similar to that in previous studies, which was reported to be 80.4% to 94%.[9,21-26] The clinical success rates were fairly similar across studies with variance likely because of the lack of

TABLE 1. Univariable analysis of predictors for success of DEN with LAMSs in 97 patients with WON

Predictors	Total (n = 97)	Successful DEN		*P* value
		Yes (n = 79)	No (n = 18)	
Demographics				
Male sex	67 (69.1)	55 (69.6)	12 (66.7)	.81
Age, y	53.5 ± 16.6	51.7 ± 17.1	61.3 ± 11.2	<.01
Body mass index, kg/m^2	27.8 ± 7.2	27.5 ± 7.6	29.1 ± 5.2	.42
Charlson comorbidity score	2.9 ± 2.0	2.6 ± 2.5	3.9 ± 3.3	.07
American Society of Anesthesiology class (III-IV)*	42 (43.3)	32 (40.5)	10 (55.6)	.25
Etiology				.86
Gallstone	25 (25.8)	19 (24.1)	6 (33.3)	
Alcoholic	26 (26.8)	22 (27.8)	4 (22.2)	
Idiopathic	25 (25.8)	21 (26.6)	4 (22.2)	
Other	21 (21.8)	17 (21.5)	4 (22.2)	
Antiplatelet/anticoagulation therapy	24 (24.7)	17 (21.5)	7 (38.9)	.22
Disease severity*				
Leukocytes, 10^9/L	10.1 ± 7.0	9.0 ± 6.2	15.1 ± 8.3	<.01
Hematocrit, %	32.4 ± 6.3	32.9 ± 6.4	30.0 ± 5.0	.07
Albumin, g/dL	3.2 ± .7	3.3 ± .7	2.8 ± .6	<.01
Calcium, mg/dL	8.8 ± .7	8.8 ± .7	8.7 ± .7	.38
Acute Physiology and Chronic Health Evaluation II score	5.0 ± 3.7	4.1 ± 2.9	9.1 ± 4.0	<.01
Intensive care unit admission	8 (8.2)	4 (5.1)	4 (22.2)	.06
Organ failure	10 (10.3)	6 (7.6)	4 (22.2)	.16
Systemic inflammatory response syndrome	18 (18.6)	9 (11.4)	9 (50.0)	<.01
Morphologic features†				
Maximal length, cm	12.0 ± 5.2	11.2 ± 4.8	15.8 ± 5.3	<.01
Percentage of necrosis >50%	18 (18.6)	7 (8.9)	11 (61.1)	<.01
CT severity index	8.0 ± 1.7	7.7 ± 1.6	9.3 ± 1.2	<.01
Pattern of necrosis				<.01
Left-sided	31 (40.0)	30 (38.0)	1 (5.6)	
Central	29 (30.0)	24 (30.4)	5 (27.8)	
Right-sided	10 (10.3)	8 (10.1)	2 (11.1)	
Subtotal	19 (19.6)	9 (11.4)	10 (55.6)	
Scattered	8 (8.2)	8 (10.1)	0 (0)	
Paracolic gutter extension	14 (14.4)	5 (6.3)	9 (50.0)	<.01
Heterogeneous WON	64 (66.0)	47 (59.5)	17 (94.4)	.01
Gas bubbles in WON	21 (21.6)	15 (19.0)	6 (33.3)	.31
Hemorrhagic collection	6 (6.2)	3 (3.8)	3 (16.7)	.13
Procedure characteristics				
Previous drainage	13 (13.4)	9 (11.4)	4 (22.2)	.40
Days from onset to DEN	41.0 ± 11.0	40.2 ± 9.9	44.4 ± 14.6	.261
Techniques of necrosectomy (debridement vs irrigation only)	58 (60.0)	47 (59.5)	11 (61.1)	.90
Coexist multiple LAMSs	8 (8.2)	4 (5.1)	4 (22.2)	.06
Size of largest LAMS, mm	15.0 ± 1.6	14.9 ± 1.7	15.3 ± 1.2	.42
Infected WON	56 (57.7)	38 (48.1)	18 (100)	<.01

Values are n (%) or mean ± standard deviation.
DEN, Direct endoscopic necrosectomy; *LAMS*, lumen-apposing mental stents *WON*, walled-off necrosis.
*At least 24 hours before DEN.
†On cross-sectional image.

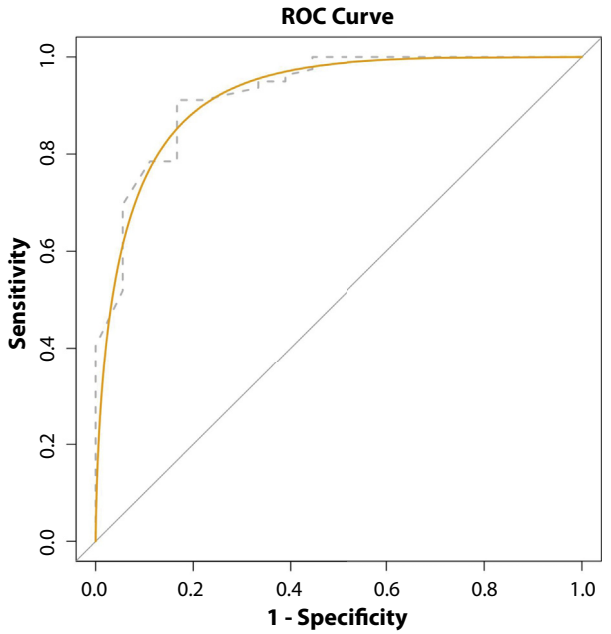


Figure 2. Receiver-operating characteristic curve of the multivariable regression model for predicting success of direct endoscopic necrosectomy with lumen-apposing mental stents for walled-off necrosis. Area under the curve, .926. *ROC*, Receiver-operating characteristic.

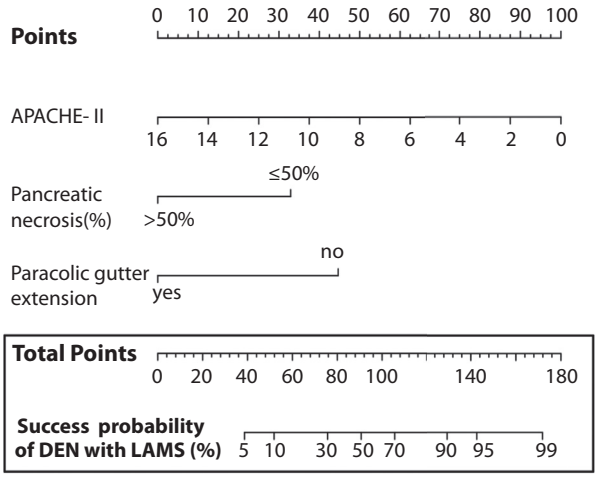


Figure 3. Nomogram for the prediction of success with DEN with LAMS for walled-off necrosis. *APACHE-II*, Acute Physiology and Chronic Health Evaluation II; *LAMS*, lumen-apposing mental stents; *DEN*, direct endoscopic necrosectomy.

a standardized definition. An Asian consensus determined that the rate of clinical success (ie, resolution of the WON cavity) for endoscopic necrosectomy was approximately 82% on review of 38 published articles.[26] In a subsequent U.S. multicenter center series of DEN with LAMSs for WON, clinical success was achieved in 87.5% of 271 patients with success defined as both WON cavity resolution and symptomatic improvement.[11]

To the best of our knowledge, this is the first study to rigorously investigate the prediction of success of DEN with LAMSs for WON. In the JENIPaN study[27] and a U.S. multicenter study,[28] obesity (body mass index >32 kg/m^2) and poor medical health (American Society of Anesthesiology class ≥III), respectively, were shown to be risk factors for failed traditional endoscopic necrosectomy with double-pigtail plastic stents. The EUS morphologic features of WON (extent of necrosis, increasing WON size, and amount of solid debris) were also believed to be associated with unsuccessful endoscopic transmural drainage necessitating more aggressive treatments.[29] In a multicenter retrospective study comparing LAMSs with double-pigtail plastic stents for WON, 189 patients were included (102 LAMS, 87 plastic stents), with DEN performed in 81.4% (83/102) of the LAMS group and 48.4% (42/87) of the plastic stent group.[9] LAMS placement and performance of ERCP <30 days after drainage were independent predictors of success for endoscopic WON treatment, with paracolic gutter extension a negative predictor.

Differing from previous studies, our study included patients undergoing primary DEN exclusively with LAMSs. Additionally, it incorporated an extensive list of predefined, clinically relevant, potential predictors. Another unique feature was that our study considered acuity of illness determined at the time of DEN rather than the highest severity of illness from disease onset. This is an important difference because most DENs were performed roughly 1 month after disease onset. Finally, the included variables were available before DEN and were not based on findings at the time of or after the procedure, allowing construction of a predictive model with a nomogram to estimate LAMS success rate.

In our prediction model, paracolic gutter extension was the strongest negative predictor of success of DEN with LAMSs. This is consistent with prior reports suggesting that distant extension of WON indicates a more severe form of necrotizing pancreatitis associated with increased mortality (from 22% to 46%).[30] Second, although usually continuous with central necrosis, WONs with paracolic gutter extension are remote and less accessible for DEN from a transgastric or transduodenal access site.[26,31] Consequently, adjunctive aggressive percutaneous catheter drainage or surgery is often required. Rische et al[20] reported that subsequent surgical intervention was necessary for 25% of patients with WON extending to the lower abdomen. Percentage of necrosis was another morphologic predictor, which was in line with previous relevant studies.[17,29] Patients with a large percentage of necrosis were more likely to develop multiple-organ failure, followed by an increased mortality.[32,33] In a post-hoc analysis from the Dutch Pancreatitis Study Group,[17] in 130 patients with catheter drainage, increased percentage of necrosis was negatively associated with success of catheter drainage (OR, .54; 95% CI, .30-.96; P = .03). The rationale for the negative impact of these morphologic predictors on clinical outcomes is not

entirely understood. However, remote recesses of WON may be less amenable to gastric access and the effects of gastric acid, and extensive necrotic debris may also be a source of infection and sepsis. Nevertheless, these findings should not be interpreted to mean that DEN with LAMSs is not advisable for these patients, and surgical necrosectomy should be directly applied as the initial step. In our study, if only 1 of 2 morphologic predictors were present and the APACHE-II score was <8, patients still had at least a 50% chance of successful resolution of WON by DEN with LAMSs.

The APACHE-II score was also associated with success of DEN with LAMSs, which is one of the most widely accepted methods for evaluating the severity of acute pancreatitis.[34] As a good reflection of current health status, the APACHE-II score can be administered on any day, unlike other disease severity assessment tools that only focus on the early admission period. In our study, we demonstrated that the APACHE-II score, at the time of DEN, was also useful for predicting success of DEN with LAMSs more than 4 weeks after the onset of acute pancreatitis. For patients with high APACHE-II scores, DEN with LAMSs alone tends to be inadequate, and more aggressive interventions will be needed. In our model, if a severely ill patient had a high APACHE-II score $\geq$12, even without complicated collections (>50% necrosis and paracolic gutter extension), the success rate of DEN with LAMSs was <66%. Conversely, if a patient is stable (APACHE-II score $\leq$3), even if combined with 1 of 2 morphologic risk factors, the success rate was more than 88%.

The final prediction model, consisting of 3 variables, was used to create a nomogram. This nomogram may be clinically useful for several reasons. First, the model may better inform clinical decision-making regarding initial treatment of WON. Second, it may allow early identification of patients at higher risk for clinical failure after DEN and allow closer monitoring of these patients with more expeditious surgical intervention. Third, this information regarding procedure outcomes and prognosis may facilitate communication with patients and the informed consent process. Finally, this model may provide a reference for risk stratification in future studies.

This nomogram would have the most clinical utility if applied to patients with increased concern for procedural failure. Worsening APACHE-II score, a high degree of necrosis, or extension of the WON to the paracolic gutters should raise concern for poor outcomes with DEN. In these cases, it may be helpful to refer to our nomogram for more specific prognostic information. If it is determined that DEN would carry a high risk of failure, additional measures should be taken beyond DEN with LAMSs alone. This may include placement of a nasocystic catheter for ongoing lavage of the WON cavity or external drainage. A step-up approach is preferred to direct surgical intervention in most cases, as demonstrated by the MISER trial.[12]

There are several limitations to our study. The main limitation of the study is the retrospective nature with its inherent bias. The timing and techniques of DEN and additional surgery were at the discretion of the doctors and were not protocolized. Some inflammatory markers, such as C-reactive protein and IL-6, are useful regarding assessment of disease severity,[5] yet they were not available for most included patients. Confirmed diagnosis of a disconnected pancreatic duct was absent in most patients because MRCP or ERCP was not routinely performed in our cohort. Although 97 patients represented a relatively large cohort, there could be concerns about model overfitting based on the rule of thumb. The concerned Type I error and relative bias were reported to be within acceptable levels despite fewer than 10 events per predictor variable, in particular for adequate control of confounding.[35] Given data availability and significant association, our model with 3 explanatory predictors seems to be reasonable, and subsequent research for external validation will provide greater stability. Finally, referral bias may be present, particularly for very large collections that may have gone directly to percutaneous drainage or surgery.

In conclusion, this prediction model with nomogram regarding response to DEN with LAMSs in the treatment of WON may be helpful in clinical decision-making and prognostication. Paracolic gutter extension, increasing APACHE-II score, and >50% gland necrosis are negative predictors for success in the endoscopic management of WON. A larger study with external validation is currently ongoing.

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Abbreviations: APACHE-II, Acute Physiology and Chronic Health Evaluation II; DEN, direct endoscopic necrosectomy; LAMS, lumen-apposing metal stent; SIRS, systemic inflammatory response syndrome; WON, walled-off necrosis.

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APPENDIX

SUPPLEMENTARY TABLE 1. Characteristics and outcomes of 97 patients undergoing DEN with LAMSs for walled-off necrosis

Characteristics	Values
Ethnicity	
White/black/Hispanic	86 (88.7)/3 (3.1)/8 (8.2)
Indications for DEN	
Pain/infection/obstruction	63 (64.9)/25 (25.8)/9 (9.3)
No. of LAMSs deployed	107
Hot LAMSs/cold LAMSs	74 (69.2)/33 (30.8)
LAMS access	107
Transgastric/transduodenal	102 (95.3)/5 (4.7)
Patients with multiple LAMSs to upsize	8 (8.2)
Clinical success	79 (81.4)
Days from DEN to resolution	31 (22-48)
Patients with unplanned procedures	49 (50.5)
Unplanned procedures	1 (0-6)
Additional surgery	13 (13.4)

Values are n (%) or median (interquartile range).
LAMS, Lumen-apposing mental stent; *DEN*, direct endoscopic necrosectomy.

SUPPLEMENTARY TABLE 2. Multivariable regression analysis of predictors for success of direct endoscopic necrosectomy with lumen-apposing mental stents for walled-off necrosis

Predictor	Odds ratio	95% Confidence interval	*P* value
Acute Physiology and Chronic Health Evaluation II*	.70	.55-.90	<.01
Percentage of necrosis† >50% vs ≤50%	.16	.03-.77	.02
Paracolic gutter extension	.08	.02-.42	<.01

*At least 24 hours before direct endoscopic necrosectomy.
†On cross-sectional image.