Radiologic Predictors of Increased Number of Necrosectomies During Endoscopic Management of Walled-off Pancreatic Necrosis

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Goals: No established methods exist to predict who will require a higher number of endoscopic necrosectomy sessions for walled-off necrosis (WON). We aim to identify radiologic predictors for requiring a greater number of necrosectomy sessions. This may help to identify patients who benefit from aggressive endoscopic management.

Materials and Methods: This is a multicenter retrospective study of patients with WON at 3 tertiary care centers. WON characteristics on preintervention computed tomography imaging were evaluated to determine if they were predictive of requiring more endoscopic necrosectomy.

Results: A total of 104 patients were included. Seventy patients (67.3%) underwent endoscopic necrosectomy, with median of 2 necrosectomies. WON largest transverse diameters ($P=0.02$), largest coronal diameters ($P=0.01$), necrosis pattern [likelihood ratio (LR) = 17.85, $P<0.001$], spread (LR = 11.02, $P=0.01$), hemorrhage (LR = 8.64, $P=0.003$), and presence of disconnected pancreatic duct (LR = 6.80, $P=0.01$) were associated with undergoing ≥ 2 necrosectomies. Patients with septations/loculations were significantly less likely to undergo ≥ 2 necrosectomies (LR = 4.86, $P=0.03$).

Conclusions: Several computed tomography radiologic features were significantly associated with undergoing ≥ 2 necrosectomies. These could help identify patients who will undergo a higher number of endoscopic necrosectomy sessions.

Key Words: pancreatic fluid collections, walled-off pancreatic necrosis, endoscopic necrosectomy, radiologic predictors

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Pancreatic fluid collections are fluid-filled cavities that develop and evolve in the setting of acute and chronic pancreatitis and pancreatic necrosis. Most fluid collections resolve spontaneously, however, many will mature over several weeks into organized collections. Organized collections that contain both solid and liquid debris and arise from necrotizing pancreatitis are referred to as walled-off pancreatic necrosis (WON).[1] Endoscopic approaches to managing WON include transmural drainage and mechanical debridement with necrosectomy.[2] Many patients with WON do not require endoscopic necrosectomy to achieve resolution of their WON,[3–5] however, some patients with more complex and difficult WON require multiple sessions of endoscopic necrosectomy to achieve resolution.[6]

Features on computed tomography (CT) performed before intervention in patients with WON have previously been studied as predictors for requiring endoscopic or surgical necrosectomy after percutaneous drainage and as predictors of the success of endoscopic management of WON management without the need for surgery.[7–9] A retrospective study of patients undergoing percutaneous catheter drainage of WON followed by surgical or endoscopic necrosectomy if clinically indicated demonstrated that CT radiologic variables of the percentage of pancreatic necrosis and WON heterogeneity were predictors for requiring either surgical or endoscopic necrosectomy following percutaneous drainage.[7] In another retrospective study of patients with pseudocysts and WON, reduced pancreatic perfusion <50% and solid components were predictors of an endoscopic diagnosis of WON and of requiring necrosectomy at any time during the treatment course.[8]

No CT characteristics to our knowledge have been evaluated as predictors for requiring a higher number of necrosectomy sessions during endoscopic management of WON. Predicting which patients will likely have more complex and difficult WON earlier on may help to identify patients who benefit from a more aggressive endoscopic management approach. The aim of our study was to identify WON CT characteristics predictive of requiring a greater number of endoscopic necrosectomy sessions during endoscopic management of WON, which was defined as requiring at least the median number of necrosectomy sessions.

MATERIALS AND METHODS

Study Design

This is a multicenter retrospective study of patients with WON who underwent primary endoscopic drainage between February 2007 to August 2017 at 3 tertiary care

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centers. Patients who underwent endoscopic management of WON and had preintervention contrast-enhanced CT imaging available were identified retrospectively using endoscopic databases. Pancreatic WON was defined as per revised Atlanta classification as a mature encapsulated collection of pancreatic or peripancreatic necrosis containing both liquid and solid debris, which was determined by cross-sectional imaging and/or endoscopic ultrasound (EUS).[1] Patients were excluded if they had percutaneous drainage or surgical intervention of their WON before the initiation of endoscopic intervention, did not have preendoscopic intervention CT imaging available, were lost to follow-up during endoscopic management of their WON, or had <30 days follow-up following endoscopic drainage. WON characteristics on preintervention CT imaging were evaluated to determine if they were predictive of requiring more endoscopic necrosectomy sessions during endoscopic management of WON, which was defined as requiring at least the median number of necrosectomy sessions. Institutional review board study approval was obtained by each center (#201707053) and the study was registered with ClinicalTrials.gov (#NCT03801070).

Data Collection

Patient data including demographics, endoscopic management, clinical course, clinical outcomes, and procedure-related complications was collected retrospectively from endoscopic databases and electronic medical records at each center. Radiologic data regarding WON imaging characteristics was collected using the most recent preendoscopic intervention CT imaging. Radiologic data was collected by an attending radiologist at each tertiary care center.

Endoscopic Management

Endoscopic transmural drainage and endoscopic necrosectomy were performed as clinically indicated at the discretion of the performing endoscopist at each center. Endoscopic necrosectomy consisted of mechanical debridement of necrotic tissue and WON cavity irrigation with normal saline. Various tools, including snares, forceps, and baskets, were used for mechanical debridement at the discretion of the performing endoscopist. Indications for endoscopic management of WON included infected WON, gastric outlet or biliary obstruction, refractory abdominal pain, ongoing systemic illness, anorexia, or persistent weight loss.[10] Endoscopic transmural drainage was performed under EUS guidance using standard technique.[11] The transmural tract was created with a plastic biliary stent, metal biliary or esophageal stents, or lumen-apposing metal stents (LAMS) as per endoscopist preference and availability. Periprocedural antibiotics were given and anesthesia was administered by an anesthesiologist or nurse anesthetist under medical direction. Endoscopic necrosectomy was initiated following endoscopic drainage on either a routinely planned (scheduled) basis or only if clinically indicated (step-up). Endoscopic necrosectomy could be performed immediately following endoscopic transmural drainage at the index procedure but was generally delayed and performed during a subsequent procedure to allow tract maturation. Repeat endoscopic necrosectomy sessions were performed at the discretion of the performing endoscopist. Supplemental endoscopic techniques, such as irrigation with hydrogen peroxide or irrigation via a nasocytic tube with the distal end placed in the WON cavity for catheter-directed irrigation with normal saline, were done as per endoscopist preference. Patients generally underwent repeat contrast-enhanced CT following 4 to 6 weeks after endoscopic drainage to assess for resolution of the WON, or sooner if their clinical status deteriorated. Transmural stent removal was performed following complete or near-complete WON resolution, which was determined on cross-sectional imaging; however, plastic transmural stents could be left in place indefinitely in cases of the suspected disconnected pancreatic duct. Escalation of therapy to percutaneous drainage or surgical necrosectomy was performed at the discretion of the treating physicians.

WON Radiologic Characteristics

The following WON radiologic parameters were analyzed from the contrasted preendoscopic intervention CT imaging by attending radiologists: collection density (homogenous or heterogenous), necrosis location (pancreatic, extrapancreatic, or both), percentage pancreatic necrosis (< 30%, 30% to 50%, > 50%), necrosis pattern (central, right sided, left sided, subtotal, scattered, or total), WON spread (central, right, left, bilateral), presence of gas bubbles (yes or no), presence of hemorrhage (yes or no), presence of septations or loculations (yes or no), presence of disconnected pancreatic duct (yes or no), largest transverse diameter (mm), largest coronal diameter (mm), and presence of multiple noncommunicating collections (yes or no) (Table 1). Definitions of WON radiologic characteristics were adapted from the 2012 revised Atlanta classifications and from a surgical study predicting the success of catheter drainage in WON.[1,7,12] All studies were reviewed by attending radiologists at the study centers (A.S., T.T., and K.A.) who were blinded to the details of subsequent treatment.

Statistical Analysis

Analyses were performed using SPSS. The median number of necrosectomies performed for patients who underwent endoscopic necrosectomy was determined. The association between each WON radiologic characteristic and requiring equal to or greater than the median number of necrosectomies was determined on univariate analysis. A logistic regression model was created, which included characteristics with a *P*-value <0.05 on univariate analysis to identify predictors of requiring ≥ 2 necrosectomy sessions. Multivariate backward deletion binary logistic regression analysis was then performed. Statistical significance was determined by a 2-tailed *P*-value <0.05.

RESULTS

Patient Demographics and Endoscopic Management

A total of 104 patients were included for analysis. The mean patient age was 53.8 years old (SD = 15.3 y) with 63% male. The underlying etiology of pancreatitis included gallstones (47.1%), alcohol (14.4%), hypertriglyceridemia (2.9%), idiopathic (28.8%), and other (pancreatic masses, medications, and mumps) (6.7%). All patients (100%) underwent successful endoscopic transmural drainage of their WON. Nearly half of patients underwent endoscopic transmural drainage with a LAMS (n = 51, 49.0%). Of those patients, 23 (45.1%) had double pigtail stents placed through the LAMS. Forty-three percent of patients underwent endoscopic transmural drainage with plastic stents alone, while 8 patients (7.7%) had non-LAMS metal stents used (biliary or esophageal). The majority of the transmural

TABLE 1. Classifications and Definitions of WON Radiologic Characteristics

Radiological Classification Term	Definition
Collection density	
Homogenous	Collection with single density
Heterogenous	Collection with multiple densities
Necrosis location	
Pancreatic	Focal area of nonenhancement in visualized pancreatic parenchyma or WON collection replacing any pancreatic parenchyma
Extrapancreatic	WON collection entirely separate from the pancreas, with completely normally enhancing and intact pancreatic parenchyma
Both	Pancreatic parenchyma with areas of nonenhancement or replacement with WON collection, in addition to the extension of the WON collection outside of the pancreas or separate WON collection outside of the pancreas
Percentage pancreatic necrosis	Approximate percentage of pancreatic parenchyma that is nonenhancing and/or replaced by WON. Not applicable if necrosis extrapancreatic only
<30%	
30%-50%	
>50%	
Pattern of necrosis	Distribution of area of pancreatic nonenhancement and/or replacement of pancreas by WON. Not applicable if necrosis extrapancreatic only
Central	Involvement of pancreatic neck and/or body with a viable pancreatic head and viable upstream tail of at least 3 cm
Right sided	Involvement primarily in the head without or with minimal necrosis of other parts of the pancreas
Left sided	Involvement primarily in the pancreatic tail with or without the involvement of the body and normal enhancement of the head and neck
Subtotal	Involvement of pancreatic neck, body, and the greater part of the pancreatic head and tail (near-complete necrosis but not total necrosis)
Scattered	Scattered areas throughout the pancreas without full-thickness or transparenchymal necrosis
Total	Involvement of the entire pancreas
Spread of WON collection	
Central	Central area (intraperitoneal in the lesser sac and/or subperitoneal in the mesenteries) and/or in the retroperitoneum without full extension to the lateroconal fascia
Right	Extension to right retrocolic space or retroperitoneum (ie, right anterior pararenal space, posterior pararenal space, perirenal space—may extend to the extraperitoneal spaces of the pelvis) and at least extending to the lateroconal fascia with or without concomitant involvement of the central area
Left	Extension to left retrocolic space or retroperitoneum (ie, left anterior pararenal space, posterior pararenal space, perirenal space—may extend to the extraperitoneal spaces of the pelvis) and at least extending to the lateroconal fascia with or without concomitant involvement of the central area
Bilateral	Extension to both retrocolic spaces or retroperitoneum at least extending to lateroconal fascias on both sides with or without concomitant involvement of the central area
Gas bubbles	Note if any present
Hemorrhage	Heterogenous area with attenuation above 40-50 HU that is not viable pancreatic tissue
Septations/loculations	Note if any present
Disconnected pancreatic duct	Full (or near full) width necrosis of the pancreatic parenchyma with viable upstream pancreas
Largest diameter in transverse plane	In millimeters
Largest diameter in coronal plane	In millimeters
Multiple collections that are not communicating	Note if >1 separate WON collection

WON indicates walled-off necrosis.

drainage was performed via the stomach (n = 93, 89.4%), while 8 patients (7.7%) underwent cystduodenostomy. Three patients (2.9%) underwent a multigateway approach with multiple transmural entry sites. Two patients had a multigateway approach performed as their initial endoscopic drainage management, while 1 patient had a second transmural entry site created during a subsequent procedure. Hydrogen peroxide irrigation was performed in 4 patients (3.8%), while a nasocystic tube was used in 23 patients (22.1%). Seventy patients (67.3%) underwent endoscopic necrosectomy as part of endoscopic management of their WON, undergoing median of 2 necrosectomies (range: 1 to 8). Fifty-eight patients (56%) underwent <2 necrosectomies, while 46 patients (44%) underwent 2 or more necrosectomy sessions. Of the patients who underwent necrosectomy, 19 (27%) had necrosectomy preformed immediately following endoscopic transmural drainage during the index procedure. Fifty-nine patients (56.7%) had undergone scheduled approach to necrosectomy, while 45 patients (43.3%) underwent a step-up approach, where necrosectomy was only initiated after clinical deterioration or lack of improvement following endoscopic drainage (Fig. 1). The median number of days in between repeat necrosectomy sessions was 14.5 days (range: 2 to 46 d).

As the median number of necrosectomies for patients who required necrosectomy after endoscopic drainage was 2, the patients who underwent <2 necrosectomy (<2 necrosectomy group) and patients who underwent 2 or more necrosectomy (≥2 necrosectomy group) were compared for analysis. There were no significant differences between the

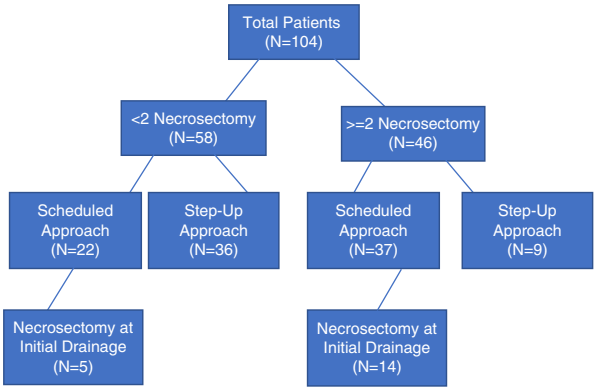

FIGURE 1. Breakdown of necrosectomy approaches for the <2 and ≥2 necrosectomy groups. full color online

patients who underwent <2 and ≥2 necrosectomies regarding age ($P=0.9$), gender ($P=0.7$), pancreatitis etiology ($P=0.5$), transmural stent type ($P=0.4$), or transmural drainage location ($P=0.7$) (Table 2). The ≥2 necrosectomy group was significantly more likely to have undergone irrigation with hydrogen peroxide at 8.7% versus 0% ($P=0.02$) and nasocystic tube irrigation at 32% versus 14% ($P=0.02$). The <2 necrosectomy group had a significantly higher percentage of patients who underwent step-up necrosectomy, while the ≥2 necrosectomy group was significantly more likely to undergo necrosectomy at the index procedure (Table 3).

WON Radiologic Features

Mean transverse and coronal plane WON collection diameters were 135.8 ± 45.1 and 114.1 ± 47.5 mm, respectively. Thirty-five percent of the collections appeared homogenous on CT, while 63.4% appeared heterogenous. The majority of the collections had both extrapancreatic and pancreatic necrosis (n = 96, 92.3%), while 1.9% had isolated pancreatic and 5.8% had extrapancreatic necrosis. The percentage of necrosis was <30% for 26.0% patients, 30% to 50% for 18.2% patients, and >50% for 55.8%.

TABLE 2. Comparison of Baseline Characteristics for <2 and ≥2 Necrosectomy Groups

Baseline Characteristic	<2 Necrosectomies (N = 58)	≥2 Necrosectomies (N = 46)	*P*
Mean patient age (y)	53.7	53.9	0.9
Patient gender (male)	36	30	0.7
Pancreatitis etiology			0.5
Biliary	23	26	
Alcohol	10	5	
Triglycerides	2	1	
Idiopathic	18	12	
Other	5	2	
Transmural stent type			0.4
Plastic	23	22	
Metal biliary	6	2	
Lumen-apposing metal stent	29	22	
Transmural drainage location			0.7
Stomach	52	41	
Duodenum	5	3	
Multigateway	1	2	

TABLE 3. Comparison of Necrosectomies for <2 and ≥2 Necrosectomy Groups

Necrosectomy Procedure Details	<2 Necrosectomies (N = 58)	≥2 Necrosectomies (N = 46)	*P*
Median number necrosectomy sessions	0	2	
Mean number necrosectomy sessions	0.41	2.8	<0.0001
Necrosectomy performed at index procedure [n (%)]	5 (8.6)	14 (30.4)	0.005
Necrosectomy performed as step-up [n (%)]	36 (62.1)	9 (19.6)	<0.0001
Days between repeat necrosectomy sessions [median (range)]	20 (6-40)	14 (2-46)	

Necrosis pattern varied from central (27.9%), right (7.7%), left (10.6%), subtotal (39.4%), scattered (6.7%), and total (3.8%). WON spread was central for 62.5% patients, right for 3.8% patients, left for 30.8% patients, and bilateral for 2.9% patients. Gas bubbles were noted in 16.3% WON collections, while hemorrhage and septations were noted in 8.7% and 49.0%, respectively. Disconnected pancreatic duct was noted in 57.7% cases. Separate noncommunicating WON collections were noted in 42.3% cases. In cases of separate collections, only the WON collection that was endoscopically intervened on was assessed.

Imaging characteristics associated with requiring ≥2 necrosectomy sessions were WON largest transverse and coronal diameters 147.3 ± 43.0 versus 126.6 ± 45.0 mm ($P=0.02$) and 127.2 ± 49.3 versus 103.7 ± 43.7 mm ($P=0.01$), respectively. Necrosis pattern [likelihood ratio (LR) = 17.85, $P<0.001$], spread (LR = 11.02, $P=0.01$), hemorrhage (LR = 8.64, $P=0.003$), and presence of disconnected pancreatic duct (LR = 6.80, $P=0.01$) were also associated with undergoing ≥2 necrosectomies (Table 4). Patients with septations/loculations were significantly less likely to undergo ≥2 necrosectomies (LR = 4.86, $P=0.03$). Neither necrosis location ($P=0.11$), necrosis percentage ($P=0.09$), presence of gas bubbles ($P=0.8$), nor the presence of multiple separate collections ($P=0.2$) were associated with undergoing ≥2 necrosectomies.

Clinical Outcomes

Two patients (1.9%) had ongoing endoscopic treatment at the time of data collection. Excluding patients with ongoing endoscopic treatment, complete resolution of WON was achieved in 94 (93%) patients after a mean of 91.4 days. WON resolution occurred in 94.7% and 93.1% of patients for the <2 and ≥2 necrosectomy groups, respectively ($P=1.0$). The mean follow-up time was 260.4 days following endoscopic drainage. The ≥2 necrosectomy group had significantly longer follow-up (mean: 311.82 vs. 177.7 d, $P=0.02$). Procedure-related complications occurring during the course of endoscopic management included bleeding (n = 2, 1.9%), perforation (n = 1, 0.9%), death (n = 1, 0.9%),

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TABLE 4. Significant Walled-off Necrosis Radiologic Characteristic Differences Between <2 and ≥2 Necrosectomy Groups

	n (%)			
Radiological Classification Term	**<2 Necrosectomies (N = 58)**	**≥2 Necrosectomies (N = 46)**	**Likelihood Ratio**	***P***
Necrosis pattern			17.85	0.00
Central	19 (32.8)	10 (21.7)		
Right	3 (5.1)	5 (10.9)		
Left	11 (19.0)	0 (0)		
Subtotal/total	25 (43.1)	31 (67.4)		
Spread			11.02	0.01
Central	41 (70.7)	24 (52.2)		
Right	4 (6.9)	0 (0)		
Left	12 (20.7)	20 (43.5)		
Bilateral	1 (1.7)	2 (4.3)		
Hemorrhage	1 (1.7)	8 (17.3)	8.64	0.003
Disconnected pancreatic duct	27 (46.6)	33 (71.7)	6.80	0.01
Septations/loculations	34 (58.6)	17 (37.0)	4.86	0.03

stent occlusion (n = 3, 2.9%), and premature stent migration (n = 3, 2.9%). Complication rates for the <2 and ≥2 necrosectomy groups were similar ($P = 0.2$). The death occurred in 1 alcoholic patient in the <2 groups who never required necrosectomy but developed symptoms of a gastric outlet obstruction 6 weeks after the placement of a cystduodenostomy, along with fungemia, septic shock, disseminated intravascular coagulation, and gastric necrosis. Upper endoscopy done shortly before death noted a patent lumen-apposing metal cystduodenostomy stent which was partially obstructing the duodenal lumen, which was removed. Bleeding occurred in 2 patients in the ≥2 necrosectomy group. In 1 patient, pulsatile bleeding occurred during the patient's second necrosectomy, which was stopped with a coagulation grasper. This was 31 days after his initial LAMS placement. While no active bleeding was noted on subsequent angiography, a gastroduodenal artery pseudoaneurysm was empirically coil embolized. Clinical data regarding the second patient's bleeding is unavailable.

Three patients (2.9%) required percutaneous drain placement following the initiation of endoscopic management of their WON. One patient (0.9%) required surgery. The proportion of patients requiring surgery or percutaneous drainage following endoscopic transmural drainage were similar for both groups at 3.4% versus 4.3% ($P = 0.8$). During their endoscopic treatment course, 33.7% of patients had WON-related hospital readmissions following initiation of endoscopic drainage, with a median of 1 (range: 1 to 4) readmissions and median of 7 (range: 2 to 35) total days of hospitalization. Patients who underwent ≥2 necrosectomies were significantly more likely to be readmitted for a WON-related issue following endoscopic transmural drainage (52% vs. 19%, $P = 0.001$).

On multivariate analysis, no variables were significantly associated with undergoing ≥2 necrosectomy sessions, while the presence of septations/locations (odds ratio = 4.0, confidence interval: 1.49-10.8) and use of a step-up approach (odds ratio = 5.28, confidence interval: 2.07-13.5) were significantly associated with undergoing <2 necrosectomies.

DISCUSSION

In this multicenter retrospective study of 104 patients, we identified CT radiologic predictors for undergoing a higher number of endoscopic necrosectomy sessions. We defined this as requiring at least the median number of necrosectomy sessions, which was 2 necrosectomy sessions for our study. In our study, just under half of the cohort patients (44%) required 2 or more necrosectomy sessions. Of the examined WON radiologic characteristics, WON largest transverse and coronal diameters, necrosis pattern, WON spread, hemorrhage, and presence of disconnected pancreatic duct were significantly associated with undergoing ≥2 necrosectomies.

The association of larger size of the WON cavity with undergoing an increased number of necrosectomies makes sense intuitively, as a larger collection will likely contain more solid debris that may prevent resolution with endoscopic drainage alone and necessitate mechanical removal with endoscopic necrosectomy. In a 2007 retrospective study of 53 patients undergoing endoscopic drainage/necrosectomy of WON which examined radiologic factors including size, location, contents, disconnected pancreatic duct, and extension into the paracolic gutters, WON size (>15 cm) was significantly associated with failure of endoscopic therapy and need for operative treatment.[9] The association of larger WON size and failed endoscopic therapy was attributed to more extensive underlying necrotic debris contained within larger WON collections. Increased size on EUS was similarly significantly associated with requiring an increased number of endoscopic procedures to achieve a successful outcome in a retrospective study of 43 patients undergoing endoscopic management of WON.[13]

The association of a disconnected pancreatic duct seen on CT and undergoing an increased number of necrosectomies is not surprising, as the presence of a disconnected pancreatic duct has previously been demonstrated to have a significant effect on the endoscopic management of WON. In a retrospective study of patients undergoing endoscopic drainage of pancreatic fluid collections, patients with a disconnected pancreatic duct were significantly more likely to undergo necrosectomy and underwent significantly more reinterventions.[14] According to the study authors, while disconnected pancreatic duct are often thought of as risk factors for collection recurrence after the resolution, they are also a marker of "difficult" collections that require a more aggressive management approach to achieve resolution. Likewise, the presence of blood in the setting of hemorrhagic WON also likely presents a more "difficult" collection. The presence of clotted blood debris in addition to necrotic debris contained in the WON cavity may act as a barrier to endoscopic drainage and also call for a more

aggressive endoscopic approach, however, caution should be taken with excluding pseudoaneurysms in this population.

In our study, the presence of septations or loculations was significantly associated with undergoing <2 necrosectomies and was the only radiologic variable to be a significant predictor on the multivariable analysis. On the surface, this finding seems out of place, as loculations would theoretically require mechanical debridement to break apart, thereby leading to a higher number of endoscopic necrosectomies. However, as septations/loculations span the entire width of the collection, they may make a WON collection appear more complex than it truly is, with large areas of the collection being made up of simple fluid rather than solid necrotic debris. Septations may also limit the portion of the WON cavity that is endoscopically accessible, thereby limiting the amount of debris available for mechanical debridement and decreasing the number of necrosectomy sessions. The presence of septations may also help to maintain transmural stent patency and thus decrease the amount of necrosectomy sessions required for WON resolution by restricting large solid debris in other WON segments from occluding transmural stents during rapid drainage following stent placement. As the WON resolution for patients with septations/loculations in our study was similar to that of patients without septations/resolutions (92%), enough drainage must still be occurring via the cystenterostomy to ultimately allow successful resolution without additional sessions of mechanical debridement. To our knowledge, no other studies have noted an association between the presence of loculations/septations and the management of WON. This should be examined further in future prospective studies.

One notable strength of our study was the use of blinded expert radiologists in grading the radiologic criteria. A recent international interobserver agreement study noted good interobserver agreement for describing peripancreatic fluid collections among both nonradiologist clinicians and radiologists, with significantly higher interobserver agreement seen for expert radiologists.[15] While expert radiologists were used in our study, the majority of the significant radiologic variables, notably WON size, presence of hemorrhage, septations/loculations, or disconnected pancreatic duct are commonly noted on radiology reports and therefore should be easily accessible information for nonradiologist clinicians.

Our study has several limitations. The most significant limitation is the retrospective nature of this study. The decision to perform necrosectomy and the specific necrosectomy techniques were not standardized, were subject to patient and interventionalist bias, and may have been influenced by additional unmeasured variables. In addition, retrospective chart review can limit the accuracy and completeness of data collection, notably with patient diagnosis, risk factors, and other clinical variables. Data collection was limited to our own institutions, so patient care in other hospital systems may not have included. While the radiologic data was collected prospectively by blinded radiologists, the management of WON was heterogenous as no standard approach to performing endoscopic necrosectomy exists, with patients undergoing endoscopic necrosectomy on either a scheduled basis after endoscopic drainage or only if clinically indicated, at varying intervals, and with varying types of stents used for endoscopic drainage.[5,14,16,17] While there were no significant differences between the <2 and ≥ 2 necrosectomy groups regarding potentially confounding variables, such as stent type and cystenterostomy location, other significant differences were noted between the 2 groups. The ≥ 2 necrosectomy group was significantly more likely to have undergone the use of nasocystic tube irrigation and cavity irrigation with hydrogen peroxide. Limited data exists to support a clinically significant effect of either therapy on the management of WON, with most data reported as case series.[18] This likely did not have a clinical impact on the number of necrosectomies and, if anything would have decreased the amount of necrosectomies required in the ≥ 2 group due to supplemental chemical or mechanical debridement. The <2 necrosectomy group was also significantly more likely to have undergone a step-up approach to endoscopic necrosectomy, meaning that necrosectomy was initiated only if clinically indicated. Collectively, this suggests that the ≥ 2 necrosectomy group patients were recognized as needing a more aggressive management approach, either based on CT appearance, endoscopic appearance of their WON cavity, or clinical course. This is supported by the fact that patients who underwent ≥ 2 necrosectomy sessions were significantly more likely to be readmitted to the hospital for a WON-related issue following endoscopic drainage and had significantly longer clinical follow-up.

Another limitation of our study is that the quantity of debris contained in the WON cavity was not directly assessed as a CT radiologic variable. Theoretically, an increased quantity of debris would require more necrosectomy for debridement and removal. This was demonstrated in a retrospective study of 43 patients undergoing endoscopic management of WON which determined that patients with $>40\%$ solid debris, as assessed via EUS based on visual judgment by the endoscopist, were more likely to undergo endoscopic or surgical necrosectomy.[13] However, this variable would be technically difficult to quantify on cross-sectional imaging.[12] CT has limited sensitivity for the detection of solid WON debris.[19] In a retrospective study evaluating preinterventional CTs of pseudocysts and WON using blinded radiologists, 24.6% of the study patients did not have solid WON debris seen on CT scan but later underwent endoscopic necrosectomy, while only 13.8% who had solid debris seen underwent necrosectomy.[8] Solid debris may also not be a reliable measurement radiographically. In a retrospective study, interobserver variability for solid debris was only fair.[20] In addition, assessing the quantity of debris would not distinguish between mobile debris that would likely drain spontaneously through a cystenterostomy tract and adherent debris which would likely require mechanical removal with necrosectomy.

In the current study, we evaluated radiologic features of CT images as these were the most readily available preintervention. However, magnetic resonance imaging (MRI) is superior to CT in identifying solid debris,[19] and in identifying the presence of a disconnected pancreatic duct with magnetic resonance cholangiopancreatography. MRI may also allow for an accurate determination of the percentage of solid debris.[21] Future studies of radiologic predictors of MRI should be done to determine if MRI variables are superior to CT in predicting if patients will require a greater number of endoscopic necrosectomy sessions.

Our study was conducted across several tertiary care centers, with expert and experienced endoscopists and radiologists in the diagnosis and management of WON. This may pose a limitation of the generalizability of our conclusions for nontertiary care centers, such as community

hospitals, where these patients are not typically frequently managed. As many of these complex patients ultimately require transfer to tertiary care centers for their care, this may be useful in aiding in the management of those patients by improving methods to identify patients who may benefit from referral to a tertiary care center for a more aggressive endoscopic approach. However, this would necessitate that nontertiary care center physicians and radiologists are able to assess the pertinent variables on CT imaging, which may be somewhat limited in a nontertiary care center setting.

CONCLUSIONS

While many patients with WON will not require endoscopic necrosectomy during their management course, other patients with more complex and difficult WON will require multiple sessions of endoscopic necrosectomy to achieve resolution. Predicting which patients will require a greater number of necrosectomy sessions is important for setting patient expectations upfront, as well as for identifying patients who may benefit from a more aggressive endoscopic management approach. To our knowledge, no radiologic predictors have been established to help predict which patients will require a greater number of necrosectomy during their endoscopic treatment course. In our study, CT radiologic features including WON largest transverse and coronal diameters, necrosis pattern, spread, hemorrhage, and presence of disconnected pancreatic duct were significantly associated with undergoing ≥ 2 necrosectomies. These factors should be used prognostically to help identify patients who will likely undergo a higher number of endoscopic necrosectomy sessions and may benefit from a lower threshold to initiate endoscopic necrosectomy after drainage, scheduled and/or more frequent endoscopic necrosectomy, and/or the addition of supplemental techniques including nasocystic tube drainage or hydrogen peroxide irrigation. Future prospective studies are needed to establish a definitive role of CT predictors in the management of WON.

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