

Multiple transluminal gateway technique for EUS-guided drainage of symptomatic walled-off pancreatic necrosis

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Background: Walled-off pancreatic necrosis often leads to severe clinical deterioration necessitating open debridement or endoscopic necrosectomy. A new EUS-based approach was devised to manage this condition by creating multiple transluminal gateways to facilitate effective drainage of the necrotic contents.

Objective: To compare treatment outcomes between patients with walled-off pancreatic necrosis managed endoscopically by a multiple transluminal gateway technique (MTGT) or a conventional drainage technique (CDT).

Design: Retrospective study.

Setting: Tertiary-care referral center.

Patients: This study involved patients with severe acute pancreatitis complicated by walled-off pancreatic necrosis managed endoscopically.

Intervention: In MTGT, 2 or 3 transmural tracts were created by using EUS guidance between the necrotic cavity and the GI lumen. While one tract was used to flush normal saline solution via a nasocystic catheter, multiple stents were deployed in others to facilitate drainage of necrotic contents. In the CDT, two stents with a nasocystic catheter were deployed via 1 transmural tract.

Main Outcome Measurements: Resolution of symptoms, radiological findings on follow-up CT, and the need for subsequent surgery or endoscopic necrosectomy.

Results: Of 60 patients with symptomatic walled-off pancreatic necrosis, 12 (3 women, mean age 55.1 years) were managed by MTGT and 48 (12 women, mean age 55.2 years) by CDT. Treatment was successful in 11 of 12 (91.7%) patients managed by MTGT versus 25 of 48 (52.1%) managed by CDT ($P = .01$). Although 1 patient in the MTGT cohort required endoscopic necrosectomy, in the CDT cohort, 17 required surgery, 3 underwent endoscopic necrosectomy, and 3 died of multiple-organ failure. Treatment success was more likely for patients treated by MTGT than by CDT (adjusted odds ratio = 9.24; 95% confidence interval, 1.08-79.02; $P = .04$) when we adjusted for the size of the walled-off pancreatic necrosis and pancreatic duct stent placement.

Limitations: Selective patient population.

Conclusion: The EUS-guided MTGT is an effective treatment option for the management of symptomatic walled-off pancreatic necrosis because it obviates the need for surgery and endoscopic necrosectomy and its attendant procedure-related morbidity. Prospective studies are required to confirm these preliminary but promising data. (Gastrointest Endosc 2011;xx:xxx.)

Abbreviations: CDT, conventional drainage technique; CTD, conventional transmural drainage; MTGT, multiple transluminal gateway technique.

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Walled-off pancreatic necrosis is a term used to describe a well-circumscribed area of sterile or infected necrosis.¹ Although infection is an absolute indication for intervention in this condition, other indications for intervention include a rapid increase in size of the necrotic cavity, worsening pain, and gastric outlet or biliary obstruction.^{2,3} Traditionally, walled-off pancreatic necrosis is managed by surgical debridement and drainage that, even at expert centers, is associated with morbidity and mortality of 55% and 14%, respectively.^{4,5} Although the treatment outcomes of endoscopic transmural drainage are excellent and comparable with those of surgery for the management of uncomplicated pancreatic pseudocysts,⁶ the success rate is significantly less for the management of walled-off pancreatic necrosis.⁷ Therefore, several other minimally invasive techniques have been developed with the objective of facilitating better drainage of necrotic contents. This can be accomplished purely by endoscopic means (necrosectomy) or by a hybrid approach that combines endoscopy and percutaneous instrumentation or a combination of laparoscopy and endoscopy.⁸⁻¹⁰ The main objective of these techniques is to reduce the invasiveness, morbidity, and mortality associated with open surgery. In this report, we present our experience with a new EUS-based approach that was devised to manage walled-off pancreatic necrosis by creating multiple transluminal gateways to facilitate effective drainage of necrotic contents.

PATIENTS AND METHODS

Patients

The study cohort comprised all patients with symptomatic walled-off pancreatic necrosis who underwent endoscopic transmural drainage over a 6-year period from 2004 to 2010. Indications for endoscopic drainage were the following: (1) CT-confirmed walled-off pancreatic necrosis measuring >6 cm in size and located adjacent to the stomach or duodenum, (2) evidence of ongoing infection (abdominal pain and fever) despite administration of intravenous antibiotics, (3) continued clinical deterioration despite ongoing supportive measures, and (4) gastric outlet or biliary obstruction secondary to a mass effect by walled-off pancreatic necrosis. Excluded from the study were patients in whom the walled-off pancreatic necrosis was located more than 1.5 cm from the GI lumen and those with coagulopathy. All patients undergoing endoscopic drainage of peripancreatic fluid collections were prospectively enrolled in an institutional review board-approved database. This study was executed by review of these data. The study was approved by the University of Alabama at Birmingham Institutional Review Board.

Procedural technique

Patients with walled-off pancreatic necrosis underwent transmural drainage by one of two methods: multiple transluminal gateway technique (MTGT) or conventional

Take-home Message

- The multiple transluminal gateway technique (MTGT) entails the creation of multiple transmural tracts under EUS guidance for effective drainage of necrotic contents.
- Patients treated by MTGT had better clinical outcomes and less need for surgery compared with patients managed by conventional drainage techniques.

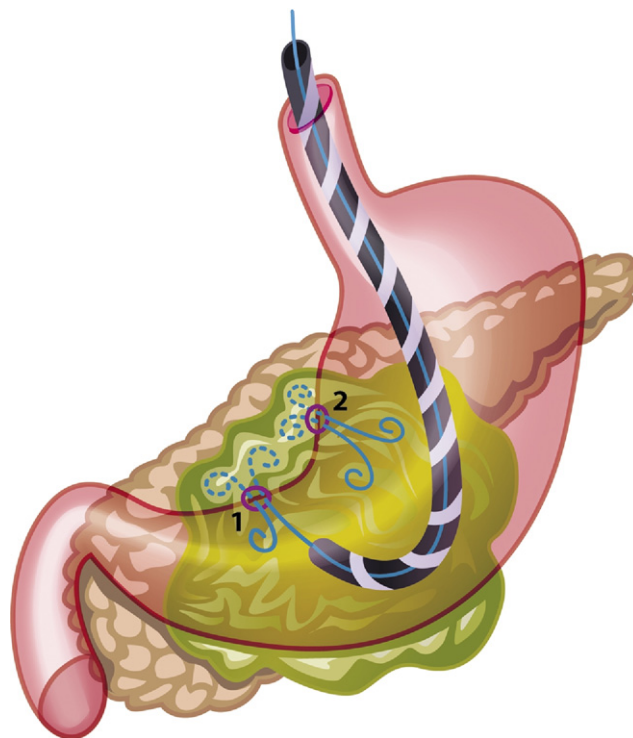


Figure 1. Illustration of MTGT for performing drainage of walled-off pancreatic necrosis.

transmural drainage (CTD). In MTGT, under EUS guidance (GF-UCT 140; Olympus America, Center Valley, Pa), the walled-off pancreatic necrosis (site 1) was accessed with a 19-gauge needle (EUSN-19-T; Wilson-Cook Endoscopy, Winston-Salem, NC), and a 0.035-inch guidewire (Jagwire, Boston Scientific, Natick, Mass) was coiled within it (Fig. 1). The transmural tract was sequentially dilated by using a 4.5F ERCP cannula (Proforma Cannula/Apollo 3^{AC}; CONMED Industries, Billerica, Mass) and then an 8-mm balloon dilator (CRE balloon; Boston Scientific). Initially, one 7F, 4-cm, double pigtail stent (Wilson-Cook Endoscopy) was deployed within the necrotic cavity. Then another area (site 2) in the same necrotic lesion that was distant from site 1 was identified for drainage by using EUS guidance (with the aid of fluoroscopy), and the same process was repeated (Fig. 2) but with dilation of the transmural tract to 15 mm and placement of multiple (2-4), 7F, double pigtail stents. Site 2 was identified by tracing



Figure 2. Fluoroscopic image revealing passage of a guidewire into a different site (site 2) in the walled-off pancreatic necrosis after initial placement of a transmurial stent (site 1).



Figure 3. Fluoroscopic image revealing creation of the 3 transmurial tracts in a patient with walled-off pancreatic necrosis measuring more than 150 mm in diameter.

the margins of the walled-off pancreatic necrosis that were most distant from site 1 but within reach of the EUS transducer. The procedure was completed with placement of an additional 7F, nasocystic catheter (Nasal Biliary Drainage Set; Wilson-Cook Endoscopy) adjacent to the previously placed transmurial stent at site 1. This was done by coiling a guidewire within the necrotic lesion by using an ERCP cannula and then passing the nasocystic catheter over the guidewire under fluoroscopic guidance. The rationale for dilating only up to 8 mm and placing a single stent at site 1 was to facilitate localization of another site for transmurial drainage because rapid evacuation of necrotic fluid (after multiple stent placements) may have precluded such localization. Also, this site was reserved for deployment of a nasocystic catheter before completion of the procedure. In select patients with very large walled-off pancreatic necrosis (>150 mm in diameter), 3 transmurial tracts were created for drainage (Fig. 3). In conventional drainage technique (CDT), only one site was drained either under EUS guidance or by endoscopic puncture of an area that had maximal luminal compression. One nasocystic catheter and up to 2 to 4 double pigtail stents were deployed at this site. Although there was no established criteria to select patients for treatment by either modality (MTGT vs CDT), in general, the MTGT approach was used when there was minimal drainage of necrotic fluid after initial puncture of the necrotic lesion. When feasible, an ERCP was undertaken before EUS to assess the presence of a main pancreatic duct leak. If a leak was demonstrated, transpapillary pancreatic stent placement was attempted to bridge the leak. Patients in whom ERCP was unsuccessful underwent MRCP for evaluation of the main pancreatic duct. An aspirate from the walled-off pancreatic necrosis was routinely sent for Gram staining and

culture in all patients, and appropriate culture-directed antibiotics were administered.

Postprocedure care

The nasocystic catheters were flushed and aspirated with 200 mL of normal saline solution every 4 hours. The nursing staff was instructed to shift the patient position in between the flushes so as to facilitate adequate drainage of necrotic contents. A nasojejunal or gastrojejunostomy feeding tube was placed by interventional radiology for enteral nutrition in all patients. At 72 to 96 hours, a repeat CT of the abdomen was obtained in all patients (Fig. 4A and B). If there was a decrease in size of the walled-off pancreatic necrosis by >50% in association with improvement in patient symptoms, and there was no necrotic fluid on aspiration of the drainage catheter, the nasocystic drain was removed. If symptoms were persistent, after interdisciplinary consultation with pancreatic surgeons, additional transmurial drainage by placement of stents, endoscopic necrosectomy, or surgery was undertaken. The interval between endoscopy sessions and follow-up CT scans was not standardized and was dependent on the patient's clinical progress. For patients managed endoscopically, a follow-up CT was obtained 6 to 8 weeks after patient discharge from the hospital. If the walled-off pancreatic necrosis had resolved, and the patients were symptomatically better, the transmurial stents were retrieved by endoscopy. For patients with a disconnected duct syndrome on ERCP or MRCP, the stents were left in place indefinitely.

Definition of complications

Perforation was defined as pneumoperitoneum on imaging studies in association with peritoneal signs. Multiple-organ failure was defined as failure of more than one organ

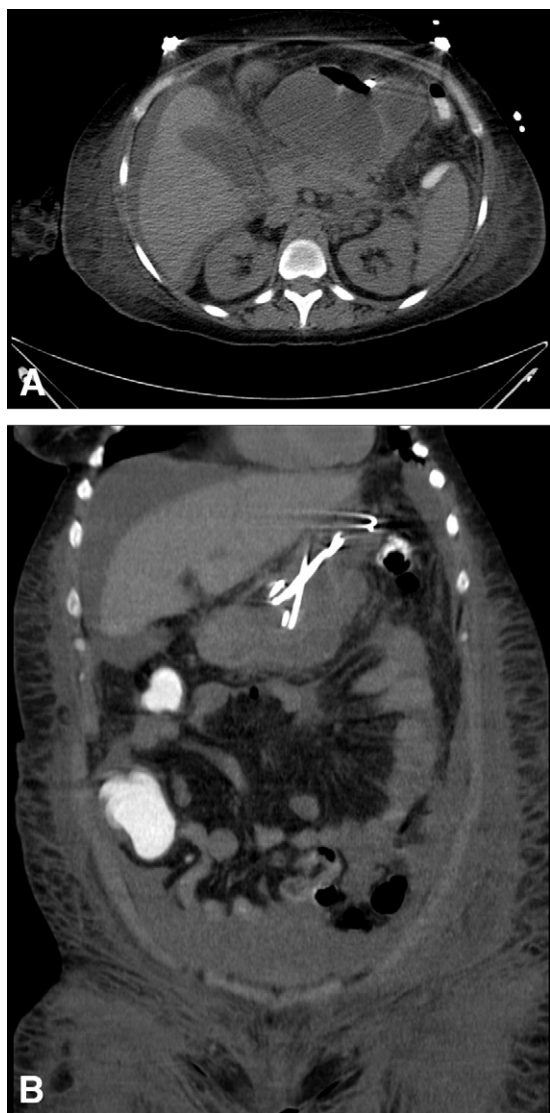


Figure 4. **A,** A CT of the abdomen revealing a large walled-off pancreatic necrosis. **B,** After drainage by the multiple transluminal gateway technique, a CT of the abdomen at 72 hours reveals marked resolution in size of the walled-off pancreatic necrosis. The multiple stents are better visualized on a coronal view.

after the initial endoscopic intervention that required supportive measures for sustenance of life. Bleeding was defined as any hemorrhagic event that required endotherapy, radiological interventions, blood product transfusion, or inpatient observation. Stent migration was defined as the need to retrieve a stent from within the walled-off pancreatic necrosis or enteral lumen.

Main outcome measures

Treatment success was compared between MTGT and CDT. Treatment success was defined as resolution of symptoms with improvement in radiological findings at follow-up CT and no need for subsequent surgery or endoscopic necrosectomy.

Statistical analysis

SAS (version 9.1, SAS, Cary, NC) statistical software was used to conduct data analysis. Continuous variables representing the patient characteristics such as age, serum albumin level, white cell count, and computed tomogram severity index were reported by using their means (standard deviation) and their medians (interquartile range). Categorical variables such as sex, etiology, and prior therapy were reported in terms of their frequency counts and proportions. Similar measures were adopted for reporting characteristics of walled-off pancreatic necrosis and its endoscopic management. A 2-sample *t* test was used for the means of the continuous variables, whereas a chi-square test was used to compare the frequencies. A 2-sample Wilcoxon rank-sum test was used to compare duration of stay for MTGT versus CDT. In case of a small sample size, Fisher's exact test was used for comparing the proportions. Treatment success and other outcome measures comparing MTGT versus CDT were conducted by using a 2-sided Fisher's exact test. Multiple logistic regression was used to evaluate the predictors of treatment success, and the results are reported by using adjusted odds ratios (OR) and their corresponding 95% confidence intervals (CI).

RESULTS

Of the 60 patients who underwent endoscopic drainage of walled-off pancreatic necrosis over a 6-year period, 48 were treated by CDT and 12 by MTGT. There was no difference in patient demographics, laboratory indices, and CT severity index between both cohorts (Table 1). With the exception of lesions in 8 patients (16.6%) in the CDT cohort, all other walled-off pancreatic necrosis lesions in both groups measured more than 80 mm in diameter, a majority of which were drained via the transgastric route (Table 2). Of the 12 patients who underwent drainage of the walled-off pancreatic necrosis by MTGT, 8 patients underwent drainage by creation of 2 transmural tracts and 4 patients by 3 transmural tracts. The median procedure duration for MTGT was significantly longer by 15 minutes than for CDT. There was no difference in the rate of pancreatic duct stent placements between both groups. Four of 12 patients in the MTGT cohort had successful pancreatic duct stent placements at ERCP; failure in 8 patients was caused by a disconnected duct syndrome that was evident on ERCP in 6 and on MRCP in 2. Seven of 48 patients in the CDT cohort had successful pancreatic duct stent placements. Reasons for not placing a pancreatic duct stent in the remaining 41 patients were disconnected duct syndrome in 25 patients, gastric outlet obstruction in 6, failed cannulation caused by pancreas divisum or ansa loop in 4, normal pancreatogram in 4, and pancreatic duct strictures that precluded stent placement in 2. When compared with that of CDT (Table 3), the rate of treatment success was significantly higher for patients

TABLE 1. Characteristics of patients with walled-off pancreatic necrosis managed by conventional drainage and a multiple transluminal gateway technique

Variable	Conventional drainage N = 48	MTGT N = 12	P value
Age, y			
Mean (SD)	52.44 (13.97)	51.75 (18.85)	.888
Median (IQR)	53.5 (42-62.5)	52 (40-67.5)	
Range	22-84	11-79	
Sex, male, no. (%)	34 (70.8)	8 (66.7)	.740
Previous therapy, no. (%)			
Endoscopy	1 (2.1)	0 (0)	
Surgery	3 (6.3)	1 (8.3)	
Radiology	6 (12.5)	0 (0)	
Etiology, no. (%)			
Alcohol	18 (37.5)	4 (33.3)	
Gallstones	9 (18.8)	2 (16.7)	
Idiopathic	13 (27)	5 (41.7)	
Other	8 (16.7)	1 (8.3)	
Serum albumin, mean (SD), mg/dL	2.25 (0.68)	2.17 (0.55)	.710
White cell count, mean (SD), mm ³	15.64 (7.03)	15.12 (6.17)	.815
CTSI, mean (SD)	7.83 (1.71)	8.67 (1.23)	.118

MTGT, Multiple transluminal gateway technique; SD, standard deviation; IQR, interquartile range; CTSI, computed tomogram severity index.

TABLE 2. Characteristics of walled-off pancreatic necrosis and its endoscopic management

Characteristic	Conventional drainage	MTGT	P value
Lesion diameter, (long axis), mm			
Mean (SD)	110.48 (39.09)	104.33 (21.25)	.466
Median (IQR)	110 (85-120)	110 (80-120)	
Range	45-220	80-133	
Lesion location			
Head, no. (%)	9 (18.7)	2 (16.7)	.999*
Body/tail, no. (%)	39 (81.3)	10 (83.3)	
Access route			
Duodenal, no. (%)	7 (14.6)	2 (16.7)	.999*
Gastric, no. (%)	41 (85.4)	10 (83.3)	
Pancreatic duct stent, no. (%)	7 (14.6)	4 (33.3)	.206*
Procedure duration, median (IQR), min	22 (15.5-41)	37 (33.5-42.5)	.017

MTGT, Multiple transluminal gateway technique; SD, standard deviation; IQR, interquartile range.

*Fisher's exact test was used.

TABLE 3. Clinical outcomes of patients with walled-off pancreatic necrosis

Predictor	Conventional drainage N = 48	MTGT N = 12	P value
Treatment success, no. (%)	25 (52.1)	11 (91.7)	.018*
Complications, no. (%)	5 (10.4)	0 (0)	.573*
Reintervention, no. (%)	12 (25)	6 (50)	.156*
Hospital stay, median (IQR), d	4.5 (2-16.5)	16.5 (4-45)	.079
Follow-up time, median (IQR), d	169 (60-228)	159.5 (112-228)	.539

MTGT, Multiple transluminal gateway technique; IQR, interquartile range.

*Fisher's exact test was used.

treated by MTGT (91.7% vs 52.1%; $P = .01$). One patient in the MTGT cohort, despite two sessions of transmural drainage that involved placement of additional transmural stents, had persistence of symptoms and walled-off pancreatic necrosis on follow-up imaging that required endoscopic necrosectomy. Of the 23 patients (47.9%) in the CDT cohort who had treatment failure, 17 underwent surgery for persistent walled-off pancreatic necrosis, 3 underwent endoscopic necrosectomy, and 3 died of sepsis. Although there were no procedural complications in the MTGT cohort, 5 complications were encountered in the CDT cohort that included new-onset multiple-organ failure in 3, bleeding in 1, and perforation in 1. Although 2 of 3 patients with multiple-organ failure died, 1 underwent surgical debridement and recovered completely. The patient who encountered perforation required surgery for repair of the perforation, and bleeding in another patient was managed by coil embolization by interventional radi-

ology. There was no significant difference in the rate of endoscopic reinterventions between the MTGT (median, 1.5 sessions) and CDT (median, 1.3 session) cohorts (Table 3). At reintervention, the transmural tracts were further dilated to 15 mm by using radial expansion balloons, and two or more 7F stents were deployed to facilitate better

TABLE 4. Predictors of treatment success in patients with walled-off pancreatic necrosis

Predictor	Adjusted OR	95% CI	P value
MTGT vs conventional drainage	9.24	1.08-79.02	.042
Pancreatic duct stent	3.14	0.56-17.71	.194
Lesion diameter	1.00	0.99-1.02	.647

OR, Odds ratio; CI, confidence interval; MTGT, multiple transluminal gateway technique; Variables included in analysis are the presence or absence of pancreatic duct stent placement and diameter of the walled-off pancreatic necrosis.

drainage. At a median follow-up of 159 days, all 11 patients who had successful outcomes in the MTGT cohort were doing well and were without symptom recurrence. Of the 25 patients with successful clinical outcomes in the CDT cohort, at a median follow-up of 169 days, 21 patients were doing well, 2 experienced recurrent pancreatitis, and 2 were lost to follow-up. The transmural stents were retrieved in all patients with an intact main pancreatic duct after resolution of walled-off pancreatic necrosis; the stents were left indefinitely in place in patients with disconnected duct syndrome. On multivariable analysis (Table 4), treatment success was more likely for patients treated by MTGT than by CDT (adjusted OR 9.24; 95% CI, 1.08-79.02; $P = .04$) when we adjusted for the size of the walled-off pancreatic necrosis and pancreatic duct stent placement.

DISCUSSION

This study describes a new EUS-based approach to the management of symptomatic walled-off pancreatic necrosis. In a select group of patients, the MTGT is a minimally invasive treatment option that precludes the need for surgery or endoscopic necrosectomy. Despite several recent developments, the management of walled-off pancreatic necrosis remains a challenge. To offset the morbidity and mortality associated with surgical debridement,^{4,5} other minimally invasive approaches such as percutaneous retroperitoneal necrosectomy, endoscopic necrosectomy, and combined endoscopic and percutaneous drainage techniques have been developed, each with its own set of limitations. Compared with surgical or percutaneous drainage, endoscopic necrosectomy is associated with a lower risk of pancreatic-cutaneous fistula, but the procedure-related morbidity is reported at 26% and mortality at 7%.¹¹ The MTGT described in this study has several inherent advantages. First, when compared with CTD, this technique permits increased drainage of the necrotic fluid, thereby diminishing the possibility of infection. With the use of 2 to 3 tracts, one serves as a channel for irrigation and the others act as

conduits for rapid drainage of the necrotic contents. This decompresses the cavity rapidly, facilitates better drainage, and minimizes the possibility of superimposed infection. Second, when compared with endoscopic necrosectomy, the procedure is less invasive and less resource consuming. When compared with a recent study on endoscopic necrosectomy that reported an average of 6 endoscopic sessions per patient, the average number of sessions in this report was only 1.5.¹¹ Also, the need to pass an endoscope into the retroperitoneum can be avoided, thereby decreasing the risk of pneumoperitoneum, hemorrhage, and air embolism.

In a recent, randomized trial that compared surgery and step-up approach, 35% of patients who underwent percutaneous drainage did not require subsequent necrosectomy.⁸ This emphasizes our study findings that better drainage of the necrotic cavity alone may preclude the need for more invasive interventions. Third, the chances of developing a percutaneous fistula after percutaneous drainage can be avoided, particularly in patients with disconnected duct syndrome. The creation of multiple tracts with placement of permanent transmural stents serves as a conduit for the disconnected portion of the gland.

This study has some limitations. The study cohort comprised a highly select group of patients: large walled-off pancreatic necrosis measuring >80 mm in diameter and in close approximation to the GI lumen. It may not be possible to create multiple tracts in patients with smaller-sized walled-off pancreatic necrosis. Also, patients with walled-off pancreatic necrosis located at distant sites are not amenable for endoscopic drainage. The long-term risks posed by multiple, permanent, indwelling stents in patients with disconnected duct syndrome is unclear. Also, this was a nonrandomized, retrospective study in which assessment of treatment response was subjective, and the potential for treatment bias cannot be excluded. Finally, the sample size is small, and these findings have to be validated in prospective studies involving a larger cohort of patients. The MTGT appears to be an effective endoscopic treatment option for patients with large, symptomatic, walled-off pancreatic necrosis. Although the cohort of patients who are likely to benefit is only modest, the procedure's minimally invasive nature, safety profile, and good clinical outcomes suggest that it can be a useful addition to the armamentarium of evolving techniques for the management of walled-off pancreatic necrosis. More studies are required to confirm these preliminary but promising data.

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