Dual-modality drainage of infected and symptomatic walled-off pancreatic necrosis: long-term clinical outcomes

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Background: Management options for symptomatic and infected walled-off pancreatic necrosis (WOPN) have evolved over the past decade from open surgical necrosectomy to more minimally invasive approaches. We reported the use of a combined percutaneous and endoscopic approach (dual modality drainage [DMD]) for the treatment of symptomatic and infected WOPN, with good short-term outcomes in a small cohort of patients.

Objective: To describe the long-term outcomes of 117 patients with symptomatic and infected WOPN treated by DMD.

Design: Review of a prospective, internal review board–approved database.


Patients: All patients with symptomatic and infected WOPN treated by DMD at our institution between 2007 and 2012.

Intervention: DMD of symptomatic and infected WOPN.

Main Outcome Measurements: Disease-related mortality, pancreaticocutaneous fistula formation, need for early and late surgical intervention, procedure-related adverse events.

Results: A total of 117 patients underwent DMD for symptomatic and infected WOPN. A total of 103 have completed treatment, with all percutaneous drains removed. Ten patients are still undergoing treatment, and 4 patients died with percutaneous drains in place (3.4% disease-related mortality). For the patients completing therapy, the median duration of follow-up was 749.5 days. No patients required surgical necrosectomy or surgical treatment of DMD-related adverse events; 3 patients required late surgery for pain (n = 2) and gastric outlet obstruction (n = 1). There were no procedure-related deaths. In patients who have completed treatment, percutaneous drains have been removed in 100%; no patients have developed pancreaticocutaneous fistulas.

Limitations: Single-center design, lack of a comparison group.

Conclusion: DMD for symptomatic and infected WOPN results in favorable clinical outcomes; complete avoidance of pancreaticocutaneous fistulae, surgical necrosectomy, and major procedure-related adverse events, while maintaining single-digit disease-related mortality. (Gastrointest Endosc 2014;79:929-35.)
The past decade has witnessed the emergence of several new options for the management of infected or symptomatic walled-off pancreatic necrosis (WOPN). Whereas open surgical necrosectomy has been the historical criterion standard,1,3 newer, less-invasive techniques have been developed and implemented in clinical practice, with equivalent, and in some cases, superior, clinical outcomes.4-8 New data from a randomized clinical trial comparing initial surgical necrosectomy to a “step-up” approach of percutaneous drainage followed by, if clinically necessary, video-assisted retroperitoneal debridement, suggested superior clinical outcomes with the latter approach.9

Our institution has been performing percutaneous drainage of symptomatic WOPN for > 20 years.10 Although surgical necrosectomy could be avoided in most cases and single-digit mortality achieved, there was an associated 20% rate of chronic pancreaticocutaneous fistula (PCF) formation because of the presence of disconnected pancreatic duct syndrome.11-12 Building on this experience, we developed a combined endoscopic and percutaneous approach to symptomatic WOPN—the dual-modality drainage (DMD)—in which transenteric stents were placed endoscopically into the necrosum immediately after percutaneous drainage.13 This allowed redirection of pancreatic juice into the GI tract, thus decreasing the risk of PCF formation in patients with disconnected glands. Although the initial experience describing this technique in 15 patients appeared promising, longer-term outcomes in a larger patient cohort have remained an open question.

The aim of this study was to describe the short-term and long-term clinical outcomes in a large cohort of patients who have undergone DMD for symptomatic WOPN at our institution.

METHODS

Patients
All patients undergoing primary DMD for symptomatic or infected WOPN at our institution between October 2007 and June 2013 were included in this analysis. An internal review board–approved, prospective database was reviewed. Patients who had undergone “rescue” DMD (those who had percutaneous drains placed outside our institution and subsequently had transenteric drains placed on transfer to our hospital in an attempt to avoid PCF formation) were excluded from this analysis.

Indications for drainage
Indications for DMD of WOPN were as follows: (1) evidence of infected necrosis. The diagnosis of infected necrosis was based on initial clinical suspicion, supported by relevant imaging findings and confirmed at the time of percutaneous drainage by Gram stain and culture of an aspirate of the necrosum; (2) clinical deterioration and/or patient failure to improve clinically despite maximal medical management; and (3) symptomatic gastric outlet obstruction secondary to extrinsic compression from the necrosum.

The decision to proceed with DMD in any patient was made in a multidisciplinary fashion involving a team of gastroenterologists, hospitalists, interventional radiologists, intensive-care specialists, and, where needed, pancreaticobiliary surgeons.

DMD
This technique has been previously described in detail.13 Briefly, patients were initially brought to the interventional radiology suite, where the necrosum was accessed under US and/or CT guidance. The insertion site for percutaneous drainage of pancreatic fluid collections (PFCs) was primarily dependent on the location of the collection. However, there were many additional factors that were considered in choosing the insertion site. The trajectory of the catheter needed to avoid the vasculature, the bowel space, and the pleural space. The path of the catheter needed to be relatively straight to avoid kinks with patient motion. The entry of the catheter into the collection was directed toward the dependent portion of the collection so that gravity could assist in drainage. Finally, accessibility of the insertion site for wound care and flushing was considered. Once accessed, a sample of the necrosum was obtained and sent for Gram stain and culture. The tract was then dilated, and an initial smaller-caliber drain was placed.

The patient was then taken immediately to the endoscopy suite, and general anesthesia was administered. The necrosum was accessed either endoscopically (if a visible bulge was present intraluminally) with a needle-knife sphincterotome (Cook Endoscopy, Winston-Salem, NC) or under EUS control by using a 19-gauge needle or EUS-directed transenteric drainage system (Navix; Xlumena, Mountain View, CA). After wire-guide access was achieved, the tract was dilated by using either a bougie 4F to 6F dilating catheter (Cook), needle-knife sphincterotome (Cook), or Navix device, subsequent to which further dilation was performed by using a 6 to 8-mm CRE balloon dilator (Boston Scientific, Natick, Mass) (or 8-mm balloon on the Navix catheter). Two 7F (varying lengths) double pigtail stents (Cook) were placed across the gastric or duodenal wall to maintain the tract. In the case of multiple areas of WOPN, multiple percutaneous drainage catheters

Take-home Message
- Dual-modality drainage for symptomatic and infected walled-off pancreatic necrosis results in favorable clinical outcomes, complete avoidance of pancreaticocutaneous fistulae, surgical necrosectomy, and major procedure-related adverse events while maintaining single-digit disease-related mortality.
were placed; however, transenteric stents were placed into the necrosum, which was in closest proximity to the GI tract. Once placed, transenteric stents were not intentionally manipulated throughout the course of treatment.

A nasoenteric feeding tube may have been placed at the time of the drainage procedure, based on the patient’s nutritional status. Culture-directed antibiotics were prescribed postoperatively.

Follow-up drain manipulations and CT scans were not performed per protocol but rather they were dictated by the patient’s clinical course. Repeated intervention in the form of progressive up-sizing of the percutaneous drains was typically performed to allow for adequate drainage of necrotic debris, with maximum size reaching 24F. Patients in whom the necrosum was extremely viscous typically required the largest-caliber drains. Additional percutaneous drains may have been placed if clinically warranted. Drains were flushed with 10 to 20 mL of saline solution 3 times daily until the necrosum had completely resolved by CT scan. At this point, the drain was capped, and a repeat CT was performed 2 weeks later. If there was no evidence of a residual fluid collection, the percutaneous drains were removed (Fig. 1).

Pancreatography obtained by magnetic resonance imaging or endoscopically was used to determine the duration of transenteric drain placement. In patients with disconnected pancreatic duct syndrome, transenteric stents were left in place indefinitely; in those patients whose stents migrated spontaneously, replacement was not performed unless clinically indicated. In those with intact glands, transenteric stents were removed endoscopically (unless spontaneous migration had occurred). Patients undergoing endoscopic pancreatography had a pancreatic duct stent placed at the discretion of the endoscopist.

Results

A total of 180 patients with symptomatic WOPN were treated at our center during the study period, and 117 (65%; 74 men; mean age 55.2 years) underwent DMD. A total of 55 patients underwent DMD for infected necrosis; the remainder (n = 62) were treated for failure to clinically progress or gastric outlet obstructive symptoms. Of the entire cohort, 105 (88%) completed treatment, with all percutaneous drains removed, 10 (8.5%) are still undergoing treatment, and 4 patients (3.4%) died with percutaneous drains in place (disease-related mortality). The mean CT severity index as defined by Balthazar was 7.8 (1.6); 70 patients (60%) were hospitalized in the intensive care unit. A total of 75 patients (64.1%) were found to have disconnected pancreatic duct syndrome. Patients underwent an average of 1.4 (1.0) ERCPs during the observation period; pancreatic duct stents were placed in 53 patients (45.2%). For patients completing treatment, the median duration of follow-up was 749.5 days. Additional demographics are presented in Table 1.

The mean time interval from onset of severe acute pancreatitis to initiation of DMD was 75.5 (82.2) days (Fig. 2). In the first 20 patients, the mean time to intervention was 46.7 (52.1) days, whereas, in the next 97 patients, the mean time to intervention was 82.2 (86.7) days; this difference was statistically significant (P < .05). An average of 1.3 (0.7) percutaneous drainage catheters were placed in the cohort. In patients who completed DMD, the median duration of percutaneous drainage was 63 days. This group underwent a mean of 7 (3.3) CT scans and 6.1 (3.0) interventional radiology–directed percutaneous drainage catheter investigations and/or manipulations during the course of treatment. Of the patients completing therapy, none developed a pancreaticocutaneous fistula (Table 2).

DMD-related early adverse events included self-limited bleeding in 4 patients, asymptomatic pneumoretroperitoneum (n = 1), and infection of the pancreatic bed.
secondary to premature removal of the percutaneous drainage catheter \((n=1)\). Zero patients required surgical necrosectomy or surgery for the management of a procedure-related adverse event. Late adverse events included 1 patient in whom spontaneous migration of the transgastric stents resulted in a localized, contained colon perforation necessitating percutaneous removal of the stent by interventional radiology. Three patients underwent surgery after completion of DMD: 2 patients underwent distal pancreatectomy for ongoing pain, 1 patient underwent a gastrojejunostomy for gastric outlet obstruction. Four patients \((3.4\%)\) died from adverse events related to severe acute pancreatitis, 1 patient died of multiple-system organ failure \(\text{found to have occult pancreatic cancer at autopsy}\), 2 patients died from persistent hemorrhage from the pancreatic bed, and 1 patient died from a mucous plug while in a rehabilitation facility after discharge \(\text{(Table 3)}\).

Recurrent PFCs were seen during the follow-up period in 8 of the 103 patients \((7.8\%)\) completing DMD. Four PFCs were seen in patients with disconnected duct syndrome, and 4 were seen in patients with an intact pancreas. All 4 recurrent PFCs seen in patients with disconnected duct syndrome were secondary to migration of the transenteric stents. Three of the patients were managed expectantly for asymptomatic fluid collections, and cystoduodenostomy with resolution of symptoms was performed in the fourth patient. A small subgroup of patients with disconnected duct syndrome were noted to have spontaneous migration of the transenteric stents without subsequent formation of a PFC. Once could surmise that, in this group, either the orphaned tail ceased to produce pancreatic juice, or, more likely, a small fistula between the tail of the pancreas and the GI tract persisted, despite the absence of stents.

In patients with an intact pancreas, 2 of the 4 recurrent PFCs were related to high-grade stenosis of the pancreatic duct. These were initially managed with endoscopic retrograde pancreatography and pancreatic duct stent placement; however, both recurred after stent removal. Both patients remained asymptomatic and were managed expectantly. The other 2 patients developed peripancreatic abscesses that were successfully managed with percutaneous drainage. Finally, 2 patients returned several months after the completion of DMD with episodes of relapsing acute pancreatitis. Both of these patients had disconnected duct syndrome and had spontaneous migration of their transgastric stents. CT scans revealed a dilated pancreatic duct in the orphaned tail; both were treated conservatively.

**DISCUSSION**

Over the past several years, it has become increasingly evident that a minimally invasive, step-up approach to the management of patients with symptomatic and infected WOPN leads to improved clinical outcomes over early aggressive management. Although many techniques now exist for the management of severe acute pancreatitis complicated by WOPN \(\text{(percutaneous, endoscopic, surgical, and combined)}\), 1 must consider the ultimate goal of any of these therapeutic options in assessing these procedures, both alone and in comparison. Single-digit mortality, avoidance of open surgery and PCFs as well as minimal procedure-related morbidity and mortality should, at a minimum, be the standards to which any nonsurgical approach to drainage of infected WOPN should be held. The data reported herein would suggest that DMD meets each of these criteria.

Our institution has been performing percutaneous drainage as part of the management of infected WOPN for over 2 decades. The DMD concept represents a small modification of this known technique that grew out of an effort to reduce the 20% observed incidence of PCF seen with percutaneous drainage alone. In almost all cases, PCFs in the setting of WOPN result from the surgical or
percutaneous drainage of the viable tail of the pancreas in patients with disconnected pancreatic duct syndrome. Endoscopic, transgastric or transduodenal drains placed immediately after percutaneous drain placement act merely to redirect the flow of pancreatic juice back into the GI tract in patients in whom the normal, transpapillary flow has been disrupted by severe pancreatic inflammation. This allows for the eventual removal of large-caliber percutaneous drains that, in comparison to the transenteric drains, perform all of the work of debridement and drainage of devitalized tissue and debris from the pancreatic bed. Without transgastric or transduodenal drains, the path of least resistance for pancreatic juice from the disconnected tail of the gland would be through the percutaneous drainage catheter, thus guaranteeing the development of PCF. The elimination of PCF by DMD likely accounts, in large part, for the reduction in radiology resource use and hospital stay that we have previously demonstrated over percutaneous drainage alone.16-17

Several large series have emerged over the past few years from both the United States and Europe describing the experience with other forms of endoscopic intervention for infected WOPN, the most common being direct endoscopic necrosectomy.18-19 Each of these series describes procedure-related adverse events in up to 26% of patients, with procedure-related mortality in smaller, but still significant, numbers. In the multicenter European trial, the GEPARD study,19 a 26% procedure-related adverse-event rate was observed, with a 2.1% procedure-related mortality. Free abdominal perforation was noted in 5 patients (5.3%), with 1 resulting in death and 2 requiring surgical repair. Fourteen percent of patients experienced bleeding, resulting in 1 death and 2 open surgeries; 2 patients had air emboli resulting in death (n = 1) and a stroke (n = 1). The U.S. Multi-center Trial18 reported 2 cases of retrogastric perforation that were successfully treated by conservative means, 1 case of massive hemorrhage after balloon dilation that required open surgical repair, and 1 procedure-related death secondary to hypotension.

Although this was not a comparison trial between DMD and direct endoscopic necrosectomy, it is clear that the procedure-related adverse events associated with DMD in our series were less than those reported in every series on direct endoscopic necrosectomy. This most likely is related to several factors, including the smaller caliber of balloon dilation performed during DMD likely accounts, in large part, for the reduction in radiology resource use and hospital stay that we have previously demonstrated over percutaneous drainage alone.16-17

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### TABLE 2. Additional procedure-related data for patients treated with DMD for infected and symptomatic WOPN

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of percutaneous drainage, median, d</td>
<td>63</td>
</tr>
<tr>
<td>No. percutaneous drains, mean (SD)</td>
<td>1.3 (0.7)</td>
</tr>
<tr>
<td>No. CT scans, mean (SD)</td>
<td>7 (3.3)</td>
</tr>
<tr>
<td>No. tube checks, mean (SD)</td>
<td>6.1 (3.0)</td>
</tr>
<tr>
<td>No. ERCPs, mean (SD)</td>
<td>1.4 (1.0)</td>
</tr>
<tr>
<td>% of patients with pancreatic duct stents placed at some point in treatment</td>
<td>45.2</td>
</tr>
<tr>
<td>Immediate procedure-related adverse events</td>
<td></td>
</tr>
<tr>
<td>Self-limited bleeding</td>
<td>N = 4</td>
</tr>
<tr>
<td>Asymptomatic pneumoperitoneum</td>
<td>N = 1</td>
</tr>
<tr>
<td>Infection</td>
<td></td>
</tr>
</tbody>
</table>

DMD, Dual-modality drainage; WOPN, walled-off pancreatic necrosis; SD, standard deviation.

### TABLE 3. Clinical outcomes for patients treated with DMD for infected and symptomatic WOPN

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease-related mortality</td>
<td>3.4%</td>
</tr>
<tr>
<td>Persistent hemorrhage</td>
<td>N = 2</td>
</tr>
<tr>
<td>Mucous plug</td>
<td>N = 1</td>
</tr>
<tr>
<td>Multiple-system organ failure</td>
<td>N = 1</td>
</tr>
<tr>
<td>Procedure-related mortality</td>
<td>0%</td>
</tr>
<tr>
<td>Chronic pancreaticocutaneous fistula</td>
<td>N = 0</td>
</tr>
<tr>
<td>Absence of external drains (living patients only)</td>
<td>100%</td>
</tr>
<tr>
<td>Need for early surgery</td>
<td>N = 0</td>
</tr>
<tr>
<td>Necrosectomy</td>
<td>N = 0</td>
</tr>
<tr>
<td>Procedure-related adverse events</td>
<td></td>
</tr>
<tr>
<td>Need for late surgery</td>
<td>N = 2</td>
</tr>
<tr>
<td>Pain</td>
<td>N = 1</td>
</tr>
<tr>
<td>Gastric outlet obstruction</td>
<td></td>
</tr>
</tbody>
</table>

DMD, Dual-modality drainage; WOPN, walled-off pancreatic necrosis.
can occur only with the passage of time. Most series report improved clinical outcomes when intervention is delayed as long as possible.\(^{15}\) Our data suggest a change in practice pattern over time, with a statistically significant increase in time to intervention over the course of the study period.

Our study is not without limitations. First, the results reported herein represent a single-center experience with a long history of expertise in the percutaneous management of infected WOPN. Without question, the availability of interventional radiologists with dedication to and expertise in this area has impacted our clinical outcomes in a favorable manner. It is unclear, or even doubtful, whether the results of this study can be generalized to institutions without such expertise. Second, there is clearly selection bias in our results because only patients with WOPN located adjacent to the gastric wall or duodenum are eligible for DMD. As such, the results of our analysis cannot be generalized to patients with WOPN located at some distance from the wall of the GI tract, where internal fistulization would not be technically feasible. In our experience, this is rarely an issue because most patients presented with WOPN that was within close proximity to the stomach or duodenum.

Third, many of our patients had symptomatic WOPN as opposed to infection as an indication for drainage. There are existing data to suggest that some patients with infected necrosis may not need intervention at all.\(^{20-22}\) Patients with symptomatic WOPN are typically those who fail to progress clinically, have gastric outlet obstruction secondary to the necrosum, or have a deteriorating clinical condition despite maximal medical therapy without overt infection on Gram stain of the necrosum. Whether these patients would have improved without intervention remains a significant question; however, the clinical outcomes reported herein would suggest that DMD has a beneficial effect in such individuals. Finally, a major limitation is the need for a percutaneous drainage catheter for a median duration of 60 days. Although this is clearly a drawback to DMD, our data suggest that this is a small price to pay in exchange for an extremely low (3\%) disease-related mortality rate. In addition, unlike any of the other major, multicenter reports on direct endoscopic necrosectomy (which requires no long-term percutaneous drain), we have demonstrated a 0\% procedure-related mortality with DMD.

Pancreatography—either endoscopic or by magnetic resonance—is imperative to help determine the duration of transenteric stent placement. In patients with an intact pancreatic duct, transenteric stents were removed at the completion of therapy. Patients in whom pancreatography confirmed the presence of a disconnected gland had transenteric stents left in place indefinitely. In the follow-up period, there were no adverse events related to long-term transenteric stent placement per se. On the other hand, there were 8 cases of recurrent pancreatic fluid collections, 50\% of which occurred in patients with a disconnected pancreatic duct in whom transenteric stents had migrated.

One could argue the clinical benefit of performing DMD in patients with an intact pancreatic duct. Although there is likely some truth to this argument, the reality is that in a significant percentage of patients with severe acute pancreatitis and resultant WOPN, determining whether or not the pancreas is intact can be extremely difficult with non-invasive imaging. Moreover, we limited early endoscopic pancreatography (ie, at the time of transenteric drain placement) to patients who, based on imaging, had a high risk of an ongoing main pancreatic duct leak, which would be amendable to stenting. As such, there was a significant percentage (35.1\%) of patients without disconnected duct syndrome who underwent DMD; whether or not there was clinical benefit to this approach over percutaneous drainage alone in this subgroup remains an open question. We operated under the assumption that, in the absence of convincing evidence to the contrary, every patient had a disconnected gland, because the risk of not performing DMD in a patient with an undiagnosed disconnected gland—namely PCF formation—was higher than the small procedure-related risk associated with transenteric stent placement. Patients with symptomatic or infected WOPN and an intact gland in which a main pancreatic duct leak can be identified and likely can be treated with transpapillary pancreatic duct stent placement and percutaneous drainage without the need for transenteric stent placement, or DMD.

Clearly, infected and symptomatic WOPN remains an important clinical problem that requires a multidisciplinary approach to management—regardless of the treatment applied. Each treatment modality described for this application is a variation on a common theme—drainage of liquefied necrosis and debridement of necrotic tissue, either mechanically or by flushing and the passage of time. Morbidity and mortality related to severe acute pancreatitis should be related to the disease process itself, not the treatment. The data presented herein clearly demonstrate single digit mortality, complete absence of PCF, minimal procedure-related morbidity, zero procedure-related mortality, and no need for surgical debridement (and associated incisional hernias) or fistula repair. Although these data are not without limitations, they clearly support a minimally invasive, “less is more” approach to treatment of infected and symptomatic WOPN.

REFERENCES


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