

Safety and Efficacy of Video-Assisted Retroperitoneal Debridement for Infected Pancreatic Collections

A Multicenter, Prospective, Single-Arm Phase 2 Study

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Background: The feasibility of video-assisted retroperitoneal debridement (VARD) for infected pancreatic walled-off necrosis is established. We provide prospective data on the safety and efficacy of VARD.

Design: Multicenter, prospective, single-arm phase 2 study.

Setting: Six academic medical centers.

Patients: We evaluated 40 patients with pancreatic necrosis who had infection determined using Gram stain or culture.

Interventions: Percutaneous drains were placed at enrollment, and computed tomographic scans were repeated at 10 days. Patients who had more than a 75% reduction in collection size were treated with drains. Other patients were treated with VARD. Crossover to open surgery was performed for technical reasons and/or according to surgeon judgment.

Main Outcome Measures: Efficacy (ie, successful VARD treatment without crossover to open surgery or death) and safety (based on mortality and complication rates). Patients received follow-up care for 6 months.

Results: We enrolled 40 patients (24 men and 16 women) during a 51-month period. Median age was 53 years (range, 32-82 years). Mean (SD) Acute Physiology and Chronic Health Evaluation II score at enrollment was 8.0 (5.1), and median computed tomography severity index score was 8. Of the 40 patients, 24 (60%) were treated with minimally invasive intervention (drains with or without VARD). Nine patients (23%) did not require surgery (drains only). For 31 surgical patients, VARD was possible in 60% of patients. Most patients (81%) required 1 operation. In-hospital 30-day mortality was 2.5% (intent-to-treat). Bleeding complications occurred in 7.5% of patients; enteric fistulas occurred in 17.5%.

Conclusions: This prospective cohort study supports the safety and efficacy of VARD for infected pancreatic walled-off necrosis. Of the patients, 85% were eligible for a minimally invasive approach. We were able to use VARD in 60% of surgical patients. The low mortality and complication rates compare favorably with open debridement. An unexpected finding was that a reduction in collection size of 75% according to the results of computed tomographic scans at 10 to 14 days predicted the success of percutaneous drainage alone.

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ACUTE PANCREATITIS AFFECTS 210 000 people each year in the United States, reflecting a 50% increased incidence during the past 20 years. Twenty percent of patients develop severe pancreatitis with pancreatic necrosis and infected collections.^{1,2} Patients with infected pancreatic walled-off necrosis (WON) require timely and effective drainage. Open necrosectomy is effective, but it is associated with significant morbidity due to risks of incisional hernia (25%-50%), hemorrhage (10%), enteric fistula (17%-20%), and mortality (6%-34%).³⁻⁶

Percutaneous drainage often requires repeated interventions. Effectiveness is limited because of loculations and the presence of solid necrotic tissue, which cannot

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easily be drained via small catheters. Moreover, patients can develop malnutrition, immunodeficiency, and systemic sepsis while waiting for the necrotic tissue to become liquefied and drainable. Historically, percutaneous treatment failures required crossover to open necrosectomy to effectively debride the necrotic tissue.

Minimally invasive endoscopic⁷ and laparoscopic⁸⁻¹⁰ techniques combine the benefits of open necrosectomy and percutaneous drainage while avoiding the problems associated with each. Video-assisted retroperitoneal debridement (VARD) is one such technique. Although VARD feasibility is established, limited evidence exists regarding its safety and efficacy.¹¹⁻¹⁴

The purpose of this study is to describe the safety and efficacy of VARD for infected WON and to better define the populations most likely to benefit from it. We hypothesized that VARD is safe and effective and is associated with improved outcomes when compared with open necrosectomy. This article reports the safety and efficacy results of a prospective, multicenter study of VARD.

METHODS

Six tertiary centers served as study sites: (1) University of Washington Medical Center (Seattle), (2) Harborview Medical Center (Seattle), (3) Veterans Administration Puget Sound (Seattle), (4) University of Toronto (Toronto, Ontario, Canada), (5) Portland Veterans Administration (Portland, Oregon), and (6) Oregon Health and Science University (Portland). Sites 5 and 6 began the study, but only sites 1 through 4 recruited patients. Site 4 was added later in the study. Institutional review board and National Institutes of Health human subjects regulations were followed.

PATIENTS

Between May 2003 and August 2007, all patients admitted with a diagnosis of acute pancreatitis or necrotizing pancreatitis were screened for enrollment. Inclusion criteria were an infected acute postnecrotic collection or known infected WON on computed tomographic (CT) scan. Infection was determined using fine-needle aspiration Gram stain or culture. Exclusion criteria were an inability to obtain informed consent, age younger than 18 years, prior necrosectomy, pancreatic pseudocyst (sterile or infected) according to the International Symposium on Acute Pancreatitis,¹⁵ pregnancy, absolute neutrophil count of less than 500/mL, or the primary team or family not being committed to surgery in a moribund patient.

ANTIBIOTICS AND NUTRITION

Prophylactic antibiotics for pancreatitis were not used.¹⁶ Antibiotics were used for targeted therapy when clinically appropriate but stopped when the patient was afebrile with a normal white blood cell count for 24 hours. Perioperative antibiotics were given for 24 hours. Nasojejunal feeding was preferred when tolerated¹⁷⁻¹⁹; otherwise, parenteral nutrition was given.

TREATMENT ALGORITHM

When patients with percutaneous drains were transferred to a study hospital, intraoperative or drain cultures confirmed infection. All patients underwent abdominal ultrasonography to exclude gallstones.²⁰ Patients with gallstones underwent cholecystectomy within 6 months of hospital discharge.²¹ After enrollment, a percutaneous retroperitoneal drain was placed within 48 hours and upsized every 3 to 4 days until a 20F catheter size was reached. When we developed our treatment algorithm (**Figure**), we acknowledged that some study patients might undergo successful percutaneous drainage and therefore be subjected to unneces-

sary surgery. Because there were no reliable criteria to define this group, we created a priori a study pathway: patients with at least a 75% reduction in collection size on 10- to 14-day postenrollment CT scan measurements would be treated with drains alone. All other patients underwent VARD. An attempt was made to wait 4 weeks from the onset of pancreatitis before operative intervention. The principal investigator (K.H.) was present for the first 2 VARD procedures performed at each site to help orient the site investigators to protocol details and ensure consistency of operative techniques. The VARD technique is described elsewhere.^{11,12,22}

Crossover from VARD to open necrosectomy occurred because of the technical inability to complete the VARD procedure or surgeon judgment. Open laparotomy was performed when patients did not respond to 24 to 48 hours of resuscitation, remained hemodynamically unstable despite percutaneous drainage, or had a known intra-abdominal complication (eg, perforated viscus).²³⁻²⁵ Open necrosectomies were performed through a chevron or midline incision following a local lavage method.^{23,26} Postoperative lavage with sodium chloride solution was continued for 5 days or until the effluent was clear for 24 hours.

DATA MANAGEMENT

We used a secure database. Date of symptom onset was the initial visit to a health care professional. Total treatment time was the time from the initial visit to removal of the last drain.

All enrollment CT scans were contrast-enhanced, helical scans and were classified posttreatment by 1 radiologist (P.F.) in a masked fashion using CT scan classification per the International Symposium on Acute Pancreatitis,¹⁵ computed tomography severity index score,²⁷ Balthazar score,²⁸ and PANCOD classification.²⁹ A secondary aim was to predict the suitability of VARD for collections in different areas, so the anatomical location of collections was recorded.³⁰

Acute Physiology and Chronic Health Evaluation II and Multiple Organ Dysfunction scores^{31,32} were determined at enrollment. Multiple Organ Dysfunction scores were obtained daily for patients in the intensive care unit and before each operation. We did not collect C-reactive protein.

PRIMARY AIM

Our primary aim was to assess the efficacy (a) and safety (b, c, and d) of VARD for infected pancreatic collections. Primary outcome measures were as follows:

a. VARD efficacy: the ability of VARD to treat the patient without a need for crossover to open necrosectomy or death. Clinical success was defined as complete resolution of the collection according to the results of a CT scan.

b. Primary complication rate: incidence of intraoperative or postoperative bleeding resulting in a blood transfusion and postoperative enteric fistulas confirmed by the results of a fistulogram.

c. Mortality.

d. Incidence of other postoperative secondary complications, including pneumonia, pulmonary embolus, incisional hernia, pseudocyst, pseudoaneurysm, deep vein thrombosis, renal failure, myocardial infarction, bowel ischemia, central line infection, septic thrombophlebitis, and pancreatic fistula.

Primary outcomes were analyzed as in-hospital or within 30 days from the last operative intervention (whichever period was longer) to enable comparisons with the open-surgery literature. Given the long treatment times with this disease, patients received follow-up for 6 months.

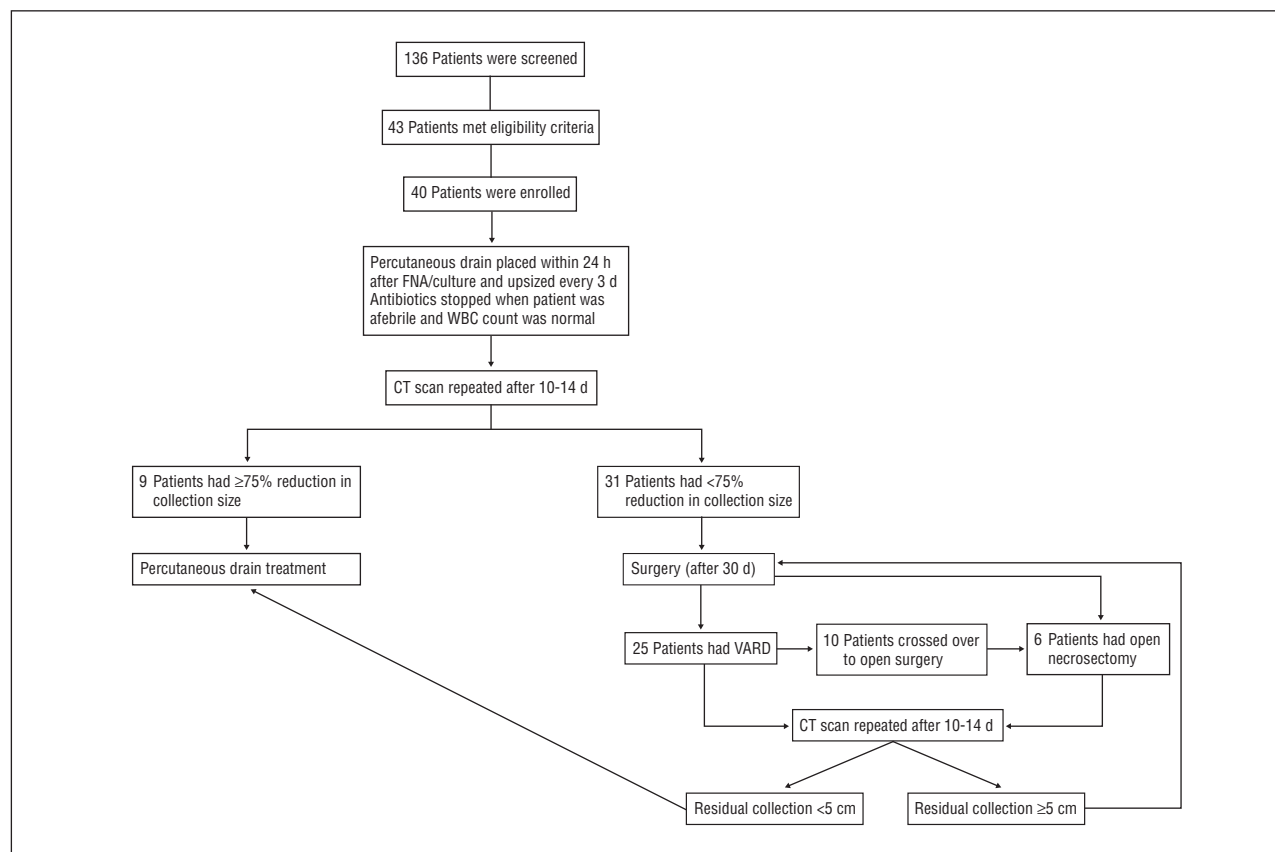


Figure. Study treatment algorithm. We screened 136 patients admitted with a diagnosis of acute pancreatitis or necrotizing pancreatitis. Of these, 43 patients met the eligibility criteria: infected acute postnecrotic collection or walled-off necrosis on a computed tomographic (CT) scan using fine-needle aspiration (FNA) Gram stain or culture. Three eligible patients refused study participation; hence, 40 patients were enrolled. VARD indicates video-assisted retroperitoneal debridement; WBC, white blood cell.

SECONDARY AIM

The secondary aim was to identify variables that could predict which patients could undergo drainage successfully with a minimally invasive approach (drains with or without VARD). Data analyzed included prepancreatitis body mass index (calculated as weight in kilograms divided by height in meters squared), time from pancreatitis onset to enrollment, drain sizes, axial CT scan measurements from the skin surface to the lateral edge of the collection at the midaxillary line under the 10th rib, and CT scan morphologic variables.

SAFETY MONITORING AND STATISTICS

A data safety and monitoring board reviewed serious adverse events (death and complications) and performed an interim evaluation after 20 patients were enrolled and each patient had received follow-up for more than 30 days. The study would have been stopped if more than 25% of patients who underwent VARD had experienced complications.³³⁻³⁶ Baseline characteristics were summarized using means (standard deviations) or medians (quartiles) for continuous measurements; frequencies and percentages were reported for categorical variables. The primary outcome measure was successful treatment with VARD without crossover to open surgery or death. Forty patients were included because we aimed to define efficacy with a precision of plus or minus 12% based on an expected 20% rate of mortality or crossover to open surgery. We thought that plus or minus 12% was a necessary goal so that with a success rate of 80% or

greater, the 95% confidence intervals would not contain success rates lower than 55%. A 1-sided lower confidence limit for the success rate was computed using an exact binomial test. The rate of intraoperative and secondary complications was computed as the ratio of patients experiencing hemorrhagic complications and/or enteric fistulas divided by the total number of patients. We reported the combination of complications according to the treatment received and considered each complication separately. Baseline covariates were evaluated as predictors of successful VARD treatment (successful VARD vs crossover to open surgery or death) using *t* tests for means, Kruskal-Wallis tests for medians, and the Fisher exact test for categorical variables.

RESULTS

STUDY OVERVIEW AND POPULATION CHARACTERISTICS

Study population characteristics appear in **Table 1**. Of the patients, 30 (75%) were overweight or obese. Enrollment CT scan characteristics are given in **Table 2**. Twenty-eight patients (70%) had a computed tomography severity index score higher than 6. Thirty patients (75%) had involvement of the right or left paracolic gutter. Almost all patients (92%) had the study treatment more than 4 weeks from the onset of pancreatitis (me-

Table 1. Characteristics of the 40 Patients in the Study Population

Characteristic	Value
Sex, No. (%)	
Male	24 (60)
Female	16 (40)
Age, median (range), y	53 (32-82)
BMI before pancreatitis, median (range)	30 (18-53)
Etiologic features of pancreatitis, No. (%)	
Biliary	18 (45)
Alcohol	13 (33)
Postoperative	1 (2)
Traumatic	1 (2)
Hypertriglyceridemia	1 (2)
Other	6 (16)
Referral from outside of facility	29 (73)
Duration of treatment at outside facility before transfer, median (range), d	20 (0-59)
Prognostic and severity-of-illness indexes	
Ranson score (n = 39)	
≤3	35
4-6	3
7	1
APACHE II score at enrollment, mean (SD)	8 (5.1)
MOD score	
At enrollment (n = 39)	
0	24
1	6
2	4
≥3	5
Highest No. reported while patient was in ICU (n = 22)	
0	14
1	2
2	2
≥3	4

Abbreviations: APACHE II, Acute Physiology and Chronic Health Evaluation II; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); ICU, intensive care unit; MOD, Multiple Organ Dysfunction.

dian, 57 days; range, 4-444 days). Using the new Working Group Classification under way (<http://www.pancreasclub.com/resources/AtlantaClassification.pdf>, unpublished data, 2009), 37 patients (92%) had infected WON. The Figure describes the flow of patients. Almost two-thirds (60%) of the study patients were successfully treated with minimally invasive techniques (percutaneous drains with or without VARD; **Table 3**).

PERCUTANEOUS DRAINAGE ONLY

Although we predicted that less than 3% of patients would be successfully treated with percutaneous drainage alone,³ we found that 9 patients (23%) were in this group. This subgroup had a reduction in collection size of at least 75% during the 10- to 14-day period following enrollment. No one in this group required surgery. One of these 9 patients had resolution of his collection but died of bleeding in the upper gastrointestinal tract. The cause of death was erosive esophagitis and gastric varices secondary to sinistral portal hypertension from splenic vein thrombosis. No blood was present in the drains. This was the only patient with in-hospital 30-day mortality.

Table 2. Enrollment CT Characteristics of the 40 Patients in the Study Population

Characteristic	Value ^a
Balthazar score	
D	5
E	35
CTSI score, median (range)	8 (3-10)
Location of collection	
Head	1
Head/body/tail	6
Body/tail	3
Head/body/tail/left gutter ^b	7
Body/tail/left gutter ^b	7
Head/body/tail/left gutter/right gutter ^b	8
Body/tail/left gutter/right gutter ^b	2
Head/body/tail/left gutter/right gutter/pelvis ^b	6
Extension into small-bowel mesenteric root and/or central collection inferior to uncinate process	12
PANCODE descriptors ²⁹	
Extent of pancreatic nonenhancement, %	
0	10
<30	10
30-50	9
>50	11
Relationship with pancreas	
Intrapancreatic only	3
Intrapancreatic and adjacent	27
Adjacent only to pancreas	10
Separate	0
Encapsulation	
Complete	21
Partial	13
None	6
Content	
Homogeneous	5
Heterogeneous	35
Mass effect on adjacent organs/structures	29
Shape	
Round/oval	20
Irregular	20
Loculated gas bubbles	24
Air fluid level	21

Abbreviations: CT, computed tomographic; CTSI, computed tomography severity index.

^aData are presented as number of patients unless otherwise indicated.

^bThese 5 locations comprise 75% of the study population.

VARD EFFICACY

Of the 31 surgical patients, 25 underwent VARD. The VARD procedure was possible 60% of the time (1-sided 95% confidence limit, >42%). Most patients (81%) required only 1 VARD procedure, and no patient required more than 2. The mean (SD) operative time for VARD cases was 135 (40) minutes. Ten patients who underwent VARD crossed over to open surgery. Four patients had 1 or 2 VARD procedures with successful resolution of the lateral component of their collection, but also a persistent central collection extending into the mesenteric root that required subsequent open surgery. Six patients had an attempted VARD procedure but crossed over to open surgery when the lateral wall of the collection could not be reached from the flank.

Six patients underwent a planned open necrosectomy: 5 patients required 1 operation and 1 patient re-

Table 3. VARD Safety, Efficacy, and Treatment Times^a

Measure	Study Population (N = 40)	Percutaneous Drains Alone (n = 9)	VARD (n = 25)	Planned Open Surgery (n = 6)
Primary efficacy and safety end points, No. (%)				
Successful drainage without open surgery	24 (60)	9 (100)	15 (60)	0
Crossover to open surgery	16 (40)	NA	10 (40)	6 (100)
Primary complications				
Bleeding, intraoperative	1 (2.5)	NA	1 (4)	0
Bleeding, postoperative	2 (5)	1 (11)	1 (4)	0
Enteric fistula	7 (17.5)	4 (44)	2 (8)	1 (17)
Mortality	1 (2.5)	1 (11)	0	0
Secondary safety end points, No. (%)				
Other complications				
Pneumonia	1 (2.5)	0	1 (4)	0
DVT	1 (2.5)	0	1 (4)	0
Renal failure	1 (2.5)	0	1 (4)	0
Central line infection	2 (5)	0	2 (8)	0
Pseudocyst	3 (7.5)	0	2 (8)	1 (17)
Pancreatic fistula	4 (10)	0	2 (8)	2 (33)
Follow-up 3 mo after discharge (n = 38)				
Pseudocyst	2 (5)	0	1 (4)	1 (17)
Pancreatic fistula	11 (29)	3 (33)	5 (20)	3 (50)
Mortality, cumulative	2 (5)	1 (11)	1 (4)	0
Follow-up 6 mo after discharge (n = 38)				
Pancreatic fistula	8 (21)	1 (11)	5 (20)	2 (33)
Mortality, cumulative	2 (5)	1 (11)	1 (4)	0
Treatment times, d				
Total hospital days, median (interquartile range)	57 (40-80)	48 (25-50)	64 (48-84)	54 (19-71)
Total treatment time, median (interquartile range)	182 (155-211)	179 (129-224)	182 (152-215)	184 (155-208)
Total time in ICU, mean (SD)	10 (16)	6 (11)	9 (15)	19 (22)

Abbreviations: DVT, deep vein thrombosis; ICU, intensive care unit; NA, not applicable; VARD, video-assisted retroperitoneal debridement.

^aMortality and complications were defined as in-hospital or within 30 days from the last operative intervention, whichever involved the longer period. Three- and 6-month follow-up visits were used to assess complications and vital status. Hospital days refers to days at both an outside hospital and the study hospital; total treatment time indicates symptom onset to drain removal.

quired 2. The most common reason for a planned open necrosectomy was persistent hemodynamic instability after 24 to 48 hours of resuscitation (n=4). Ischemic bowel and gangrenous cholecystitis were the 2 findings. Of the remaining 2 patients, 1 had successful percutaneous drainage of a lateral collection with a remaining central collection, and the surgeon believed that a VARD was not feasible. In the second patient, VARD was stopped because of an operating room equipment problem. The most common reason for crossover from VARD to open surgery (planned or unplanned), which occurred in 11 of the 16 patients (69%) in this group, was a centromedial collection with extension into the mesenteric root not accessible from the flank.

SAFETY END POINTS

The primary safety end points appear in Table 3. There were 3 bleeding complications. The first patient is described in the "Percutaneous Drainage Only" subsection of this section. The other 2 bleeding complications occurred in patients who underwent VARD. One was an intraoperative laceration of the splenic inferior pole controlled with packing. The other occurred 1 week after VARD from a ruptured pseudoaneurysm of the gastroduodenal artery that was successfully embolized. There was a 17.5% incidence of enteric fistulas (n=7) in the study group: 4 enteric fistulas in the percutaneous drain group (2 small-bowel, 1

colocutaneous, and 1 colon/stomach/duodenum), 2 enteric fistulas in the patients who had VARD first and planned open operations second (small-bowel and colocutaneous), and 1 gastric fistula in the patient who underwent an open procedure and had ischemic bowel. All enteric fistulas resolved with nonoperative treatment.

Secondary complications are indicated in Table 3. One patient died between 3 and 6 months after discharge. His enormous collections had been treated for more than 1 year with drains and antibiotics. A VARD procedure and an open necrosectomy were attempted, but his abdomen was inoperable.

PREDICTORS OF MINIMALLY INVASIVE TREATMENT SUCCESS

Our secondary aim was to identify factors that would predict success of a minimally invasive approach (drains ± VARD). The finding of a 75% reduction in collection size on the CT scan 10 to 14 days after enrollment predicted with 100% accuracy the success of catheter drainage alone. The presence on CT scan of a central collection extending inferiorly into the mesenteric root was a significant negative predictor for VARD ($P=.02$). No other predictors were found (**Table 4**). The data analyzed were as follows:

1. Prepancreatitis body mass index. Patients who crossed over from VARD to an open procedure had a body

Table 4. Predictors for Minimally Invasive Treatment Success

Predictor	Minimally Invasive Success			P Value ^a
	Percutaneous Drains (n = 9)	VARD (n = 15)	Crossover to Open Surgery (n = 10)	
BMI, mean (SD)	30.7 (2.4)	28.8 (6.0)	33.5 (10.8)	.24
Time from onset of pancreatitis to enrollment, median (range)	26 (0-154)	49 (0-209)	31 (0-322)	.64
Size of first percutaneous drain, median (range)	10F (8F-12F)	10F (8F-14F)	10F (8F-12F)	.99
Size of largest percutaneous drain, median (range)	20F (16F-20F)	16F (0-26F)	20F (14F-24F)	.24
Distance from skin at 10th rib to lateral tip of collection, mean (SD), cm	10.0 (5.8)	8.2 (3.1)	9.3 (5.0)	.55
Location of collection in the head, body, or tail, No. (%) ^b	2 (22)	2 (13)	3 (30)	.36
Extent of pancreatic nonenhancement $\geq 30\%$, No. (%)	5 (56)	8 (53)	5 (50)	.99
Adjacent to pancreas, No. (%)	8 (89)	15 (100)	10 (100)	.99
Encapsulation, No. (%) ^c	7 (78)	14 (93)	9 (90)	.95
Content homogeneous, No. (%)	1 (11)	0	1 (10)	.40
Loculated gas bubbles, No. (%)	5 (56)	10 (67)	7 (70)	.99
Air fluid level, No. (%)	4 (44)	9 (60)	6 (60)	.99
Extension into small-bowel mesenteric root and/or central collection inferior to uncinate process, No. (%)	2 (22)	3 (20)	7 (70)	.02

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); VARD, video-assisted retroperitoneal debridement.

^aComparisons were made using *t* tests for means, Kruskal-Wallis tests for medians, and the Fisher exact test for categorical variables.

^bRefers to the head/body/tail group (n = 10) vs the 75% group, described in Table 2.

^cIndicates complete + partial vs none.

mass index about 4.7 points higher than those who successfully underwent VARD ($P = .24$).

2. Time from pancreatitis onset to study enrollment. We postulated that the necrotic debris would undergo liquefaction necrosis and that the degree of liquefaction would parallel disease duration. Therefore, we expected that with increasing time more liquefaction would lead to higher rates of successful percutaneous drainage. Surprisingly, the time from symptom onset to treatment end for the 9 patients in the drain-only group was shorter than in the VARD and open surgery groups.

3. Drain sizes (Table 4). Once a patient was enrolled and the first drain was placed, most patients had 2 up-sizings before the second CT scan. The mean size of the first drain placed was 10F (range, 8F-14F), which was sequentially upsized to 20F (range, 14F-26F) during the next 10 to 14 days before the follow-up CT scan. Drain sizes were not different for the drain-only group compared with patients requiring surgery. We could not predict success based on initial drain size or the largest drain used.

4. Axial CT scan measurements from the skin surface to the lateral edge of the collection at the midaxillary line under the 10th rib.³⁷ Because of variability in adipose tissue, muscle tissue, and anasarca, we looked at axial CT scan measurements from the skin surface to the collection. We hypothesized that a long distance would pose a technical challenge for accessing the lateral wall of the collection during VARD. There were no differences between groups.

5. CT scan characteristics (Table 2). The only CT scan morphologic criteria able to predict minimally invasive success was the presence of a central collection with inferior extension. Drain plugging with necrotic debris is thought to be the main reason for drain failure, so we

postulated that patients with parenchymal necrosis (vs peripancreatic tissue necrosis) would have a lower chance of successful percutaneous drainage. This was not supported with our data. In fact, 7 of 9 patients who successfully underwent drainage had parenchymal necrosis.

COMMENT

Sixty percent of patients with infected pancreatic collections caused by necrotizing pancreatitis were safely and effectively treated with a minimally invasive procedure (drains with or without VARD). The Dutch Acute Pancreatitis Study Group has named this sequential treatment strategy the “step-up approach.”¹⁰ Applying this concept to our cohort, 85% of patients with infected WON were eligible for a step-up approach. Successful VARD was possible in patients having the full spectrum of collections, ranging from isolated peripancreatic collections to those extending into the pelvis. For patients requiring surgery, VARD was possible in almost two-thirds of patients. The most common reason for crossover to open surgery was the presence of a centromedial collection with inferior extension into the mesenteric root—a significant negative predictor for successful VARD. It is possible that an endoscopic transgastric approach might be better in these cases.^{7,38} Of the 6 patients who had a planned open necrosectomy, most required a laparotomy to exclude an intra-abdominal catastrophe. It is unlikely that the numbers in this group could be reduced further in any other study.

Our low complication and mortality rates compare favorably with open necrosectomy, establishing the safety of VARD. When deciding on primary safety end points, we focused on bleeding, enteric fistulas, and mortality.

Pooled data on studies of open necrosectomy report a 10% hemorrhage rate, an 11% enteric fistula rate, and 6% to 30% in-hospital 30-day mortality.^{23,33-36,39-42} These numbers are in contrast with our surgical complication rates of 6% hemorrhage, 10% enteric fistulas, and no mortality. With intent-to-treat, the safety profile is still favorable with 7.5% hemorrhage, 17.5% enteric fistulas, and a 2.5% in-hospital 30-day mortality. The enteric fistula rate was high in the percutaneous drain group, but all patients healed without surgery. At 6 months, mortality was 5%, which is still very favorable.

The repeated operation rate was low. Regardless of approach, most patients (81%) required only 1 trip to the operating room. The remainder required 2. This contrasts with a repeated operation rate of 27% for open necrosectomy, with some patients needing as many as 5 procedures.³³ A local lavage technique was used because it was the founding principle for VARD development and our open necrosectomy method. Compared with other minimally invasive procedures, transgastric endoscopic debridement involves a median of 3 (range, 1-12) repeated debridements, and sinus tract endoscopy has a median of 3 secondary procedures.^{7,8,43} We believe that our low repeated operation rate can be attributed to the combination of aggressive percutaneous drainage and delaying surgery for more than 30 days.^{34,35,44,45} The use of aggressive percutaneous drainage has 2 advantages. The frequent catheter upsizing avoids surgery in some patients and enables a delay of operative therapy in others by stabilizing clinical sepsis. As the infection is decompressed, antibiotics may even be discontinued. During this time, the collection wall matures and the necrotic tissue demarcates, thereby increasing surgical safety and the possibility for a single operation.

An important study result was the unexpected finding that 23% of patients (9 of 40) did not require surgery and were treated successfully with drains alone. A 75% reduction in collection size on the CT scan 10 to 14 days after enrollment predicted with 100% accuracy the success of percutaneous drainage. This raises the probability that a higher percentage of patients may have been effectively treated with percutaneous drainage using a lower cutoff (eg, 60% reduction in collection size). Given the small patient numbers in this group, generalizations should be made with caution owing to potential selection bias. We continue to use this criterion successfully and are currently investigating the predictability of successful drainage using a lower cutoff. It is noteworthy that 1 death in this series was attributed to misuse of prolonged percutaneous drainage and antibiotics. Much progress has been made demonstrating improved outcomes with delaying surgery to the 30-day point.^{34,35,44,45} However, little data are available regarding the dangers of waiting too long. A common error is placing a small drain, with serial CT scans demonstrating minimal "interval decrease in size" of the collection relative to the remaining collection. The error is perpetuated when patients are provided inadequate nutrition to meet the high metabolic demands of their chronic sepsis and given "suppressive" antibiotics for months at a time. Patients often become immunocompromised and debilitated. The chronic catabolic state and slow path to death can be reversed only with surgical drainage. We hope that our treat-

ment algorithm may provide some objective guidelines for deciding when percutaneous drainage has failed and a patient needs surgery.

Because we have performed VARD for more than 10 years, we believe that our results are attributed to experience; however, several confounders exist and invite comment on study limitations. First, our low mortality rate must be viewed against the selection bias inherent in this study. Although all patients admitted with a diagnosis of acute pancreatitis were screened for enrollment, most patients were transferred from outside facilities weeks into their illness. Our mortality rate included only patients reaching our centers. Thus, our study may underestimate the mortality rate compared with those with earlier referral and complete evaluation of all patients in a region. Second, this was not a randomized trial, so time bias is relevant. Improvements in outcome compared with historical controls need to be considered against a backdrop of simultaneous advances in critical care, benefits to delayed surgical intervention, and the temporizing effect of drains. Delaying surgery beyond the 30-day point reduces mortality by 50% in contrast to operating between days 1 through 14 and days 15 through 29, and almost all patients in this study fell into the post-30-day group.^{34,35,44,45}

The myriad of open, percutaneous, laparoscopic, and endoscopic methods for necrosectomy call for continued equipoise until data confirm that one is better than another. We cannot determine from our data that drains with or without VARD are superior to open surgery—only that the safety and efficacy profile is good. Future studies should address issues such as cost, hospital discharge status, and radiation doses from the multiple CT scans required with minimally invasive approaches. The most popular methods are variations of retroperitoneal debridement using endoscopic assistance^{8-10,14} and transgastric endoscopy.^{7,38} The VARD procedure are an early version of single-incision laparoscopic surgery and may advance as this technology develops.⁴⁶ Transgastric endoscopy is preferred for centromedial collections in the head and neck that abut the stomach and duodenal walls, the location most problematic for VARD. However, the transgastric route cannot access collections in the paracolic gutter and pelvis, which comprised 75% of the patients in our study who benefited from VARD. Although minimally invasive techniques should be successful in most patients, we anticipate that in the future a hybrid approach will be adopted by a multidisciplinary team, ending with a tailored treatment for each patient.

CONCLUSIONS

This prospective, multicenter study supports the safety and efficacy of VARD for infected WON. Of our patients, 85% were eligible for a minimally invasive approach. For patients needing surgery, VARD was possible in almost two-thirds of them, with most patients requiring just 1 operation. The most common reason for crossover from VARD to an open procedure was a centromedial collection with extension into the mesenteric root that could not be accessed via the flank. The safety profile was excellent with low mortality and complica-

tion rates that compare favorably with the literature on open surgery. An unexpected finding was that a reduction in collection size of 75% at 10 to 14 days after the institution of an aggressive drainage protocol predicted the success of percutaneous drains with 100% accuracy.

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INVITED CRITIQUE

Minimally Invasive Approaches to Infected Pancreatic Collections

In this article, Dr Horvath and her colleagues from 3 separate facilities describe their experience with VARD for infected pancreatic "collections." Congratulations to this group for completing a prospective evaluation of a novel surgical approach. Minimally invasive approaches for pancreatic debridement have been reported by several groups and include percutaneous, laparoscopic, retroperitoneal, and transgastric methods. Our group at the University of California, Los Angeles School of Medicine has had some success with laparoscopic debridement. The efficacy for most of these methods has yet to be universally accepted, but in the future pancreatic surgeons will need expertise with a combination of these techniques so that we can effectively treat all patients without open surgery. This article has shown that in a highly select group of patients VARD is feasible, safe, and effective, and perhaps less morbid than open surgery. In addition, the data suggest that percutaneous drainage alone may be all that is needed for some patients.

The group of patients included in this study appear to have relatively mild disease and are, therefore, not comparable to patients with severe acute pancreatitis who require open debridement. Analysis of these patients reveals that 88% had a Ranson score of 3 or less, an average Acute Physiology and Chronic Health Evaluation II score of 8, and a multiorgan dysfunction score of 0. Although these patients all had percutaneously proven evidence of infection, the severity of the disease appears to be less than many reports. Video-assisted retroperitoneal debridement may be best applied to those patients in which an interval of time has passed from the initial episode and who continue to linger with infection.

Understanding exactly what conditions were being addressed with VARD in this study is not clear. These different collections can represent pancreatic necrosis, acute peripancreatic fluid collections, infected pancreatic ne-

crosis, or pancreatic abscess. Each has a different natural history and management. Bradley and Dexter¹ review this in a recent publication describing the nomenclature of peripancreatic and pancreatic conditions in the face of pancreatitis. This study design was developed to include 40 patients with infected pancreatic necrosis. Of the patients who were enrolled, 25% exhibited no pancreatic necrosis on computed tomographic scans, and another 25% had less than 30% necrosis. More than half the patients had a collection characterized as "encapsulated," more than half had a collection with an air fluid level, and half of the collections were either oval or round. Because of these descriptions, it may be that several collections in this series were actually pancreatic abscesses. If this were the case, the finding that nearly 25% of the patients were effectively treated with just percutaneous drainage would make sense.

Video-assisted retroperitoneal debridement appears to be a viable alternative to open debridement for some patients with infected pancreatic collections. The timing of VARD and the exact conditions that VARD should be used may become apparent in time. This approach may well be incorporated into practice as our techniques for addressing infected pancreatic necrosis evolve.

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