Abdominal Paracentesis Drainage Ahead of Percutaneous Catheter Drainage Benefits Patients Attacked by Acute Pancreatitis With Fluid Collections: A Retrospective Clinical Cohort Study*

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Objective: The efficacy and safety of ultrasound-guided abdominal paracentesis drainage ahead of percutaneous catheter drainage as the new second step of a step-up approach are evaluated.

Design: The observed parameters were compared between groups including mortality, infection, organ failure, inflammatory factor levels, indexes of further interventions, and drainage-related complications.

Patients: This retrospective study included 102 consecutive patients with acute pancreatitis from June 2009 to June 2011.

Interventions: In this step-up approach, all patients subsequently received medical management, percutaneous catheter drainage (with or without previous abdominal paracentesis drainage), and necrosectomy if necessary according to indications. The patients were divided into two groups: 53 cases underwent abdominal paracentesis drainage followed by percutaneous catheter drainage (abdominal paracentesis drainage + percutaneous catheter drainage group) and 49 cases were managed only with percutaneous catheter drainage (percutaneous catheter drainage-alone group).

Measurements and Main Results: The demographic data and severity scores of the two groups were comparable. The mortality rate was lower in the abdominal paracentesis drainage + percutaneous catheter drainage group (0%) than the percutaneous catheter drainage–alone group (8.2%) ($p = 0.050$). Compared with the percutaneous catheter drainage–alone group, the laboratory variables of the abdominal paracentesis drainage + percutaneous catheter drainage group decreased more rapidly, the mean number of failed organs was lower, and the interval from the onset of disease to further interventions was much longer. However, there was no significant difference in the prevalence and duration of infections between the two groups.

Conclusion: Application of abdominal paracentesis drainage ahead of percutaneous catheter drainage is safe and beneficial to patients by reducing inflammatory factors, postponing further interventions, and delaying or avoiding multiple organ failure. (*Crit Care Med* 2015; 43:109–119)

Key Words: abdominal paracentesis drainage; acute pancreatitis; minimally invasive treatment; percutaneous catheter drainage; the step-up approach

***See also p. 244.**

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Acute pancreatitis (AP) is a very serious, life-threatening disease with a very high mortality rate. Treatment of AP has developed as a zigzag process over a long history. Since the study by Freeny et al (1) first reported percutaneous catheter drainage (PCD) for treating patients with AP in 1998, increasing studies have concentrated on PCD-based integrative strategies to improve the effects of AP treatment. Recent reports have shown that a subset of patients with severe acute pancreatitis (SAP) who develop infected fluid collection, pancreatic necrosis, or pancreatic abscess can be managed by PCD alone (2). In 2010, a well-known study, Minimally Invasive Step-up

Approach versus Maximal Necrosectomy in Patients with Acute Necrotizing Pancreatitis, established a comprehensive treatment system for patients with AP, called a step-up approach (3), setting a milestone in the development of AP treatment. After that, the step-up approach, which consists of conservative therapy, PCD, and minimally invasive retroperitoneal necrosectomy, gradually replaced various kinds of traditional treatments and dominated the main trends in AP therapy (2). However, this approach may not be optimal and needs further improvement.

When the revised Atlanta classification of AP was released, it enabled standardized reporting of research and aided communication among clinicians (4). This current global consensus classification of AP offers a comprehensive understanding of AP severity and (peri)pancreatic collections (4). In particular, this classification differentiates among acute peripancreatic fluid collection (APFC), pancreatic pseudocyst, acute necrotic collection (ANC), and walled-off necrosis. Although this revision is not intended to be a management guideline (4), it enables us to evaluate the current treatments and find more appropriate therapies. That is to say, it is time for us to reconsider the situation of treating AP.

Based on the optional existed treatments, inspired by the revised Atlanta classification of AP, we are trying a novel step-up approach in which PCD is carried out after abdominal paracentesis drainage (APD) and necrosectomy is performed using a minimally invasive approach (endoscopic necrosectomy). The supporting reasons for concept of APD are as following. On one hand, similar in other kinds of diseases (such as liver cirrhosis), here abdominal paracentesis is also used for treating seroperitoneum in AP. On the other hand, a tube should be placed as drainage to persistently extract fluid, which is similar to PCD. APD is totally different from PCD in various aspects (2). First, different puncturation sites are used: APD is performed from the right paracolic sulci or left paracolic sulci into the abdominal cavity or pelvic cavity, whereas PCD is mainly performed in the (peri)pancreatic region, left pararenal region, or right pararenal region. Second, the puncturations have distinct purposes: in APD, puncturation is used to remove seroperitoneum; in contrast, PCD is used to eliminate (peri)pancreatic collections. Third, the timing of the puncturation varies: APD is carried out as early as possible (within 4 wk from the onset of AP), and PCD is started later (after 4 wk). In general, APD serves as a preparation step for further PCD. We use two or more catheters depending on the need. At least one catheter is used for the ingress of fluid from the abdominal or pelvic cavity, and the others are used for drainage of collections from the (peri)pancreas or egress of debris (**Fig. 1**). This policy was adopted to achieve more effective goals than those of the traditional step-up approach.

In this study, we aimed to determine whether it was necessary to perform APD ahead of PCD when treating AP patients with fluid collections. We collected the data of our patients who underwent PCD therapy from June 2009 to June 2011 and separated them into two groups: one group was given PCD-only treatment (without previous APD) and the other was treated with APD ahead of PCD. The results indicate that it is advisable to conduct APD before PCD, as doing so could reduce the mortality rate of patients with AP and reduce expenses, mainly by eliminating inflammatory materials (cytokines), postponing further intervention, shortening the reversal time of organ failure, and decreasing the prevalence of new onset of organ failure.

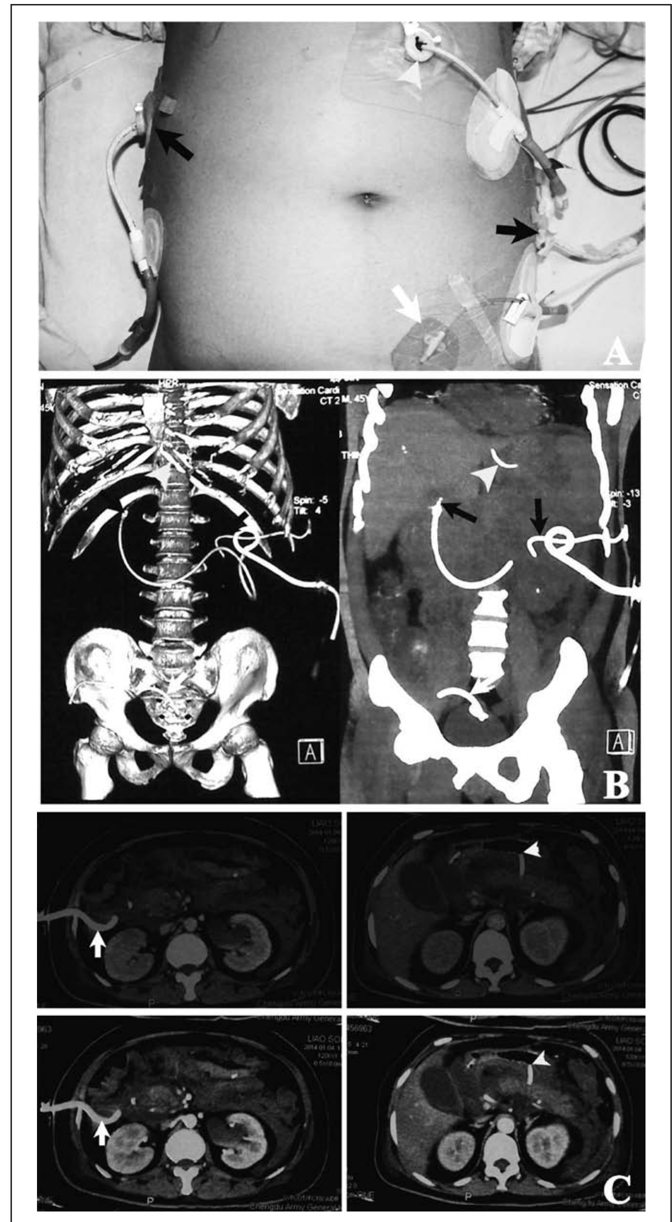

Figure 1. The placement of catheters under abdominal paracentesis drainage (APD) and percutaneous catheter drainage (PCD). In a patient with severe acute pancreatitis, both APD and PCD were used. **A** and **B**, Three APDs were as follows: two catheters, respectively, in the left paracolic sulci and right paracolic sulci (RPCS) (for ingress), as shown by *black arrows*; one catheter in the cavitas pelvis (for egress of fluid), displayed by *white arrows*. Meanwhile one PCD was in the (peri)pancreatic region (for egress of fluid), as presented by *white arrows*. **C**, In CT images, the *white arrows* show catheter in the RPCS by APD insertion done on day 18 of the disease; the *white arrows* show the end of catheter locating in the (peri) pancreatic region with residual collection by PCD intervention performed on day 85 after the onset of pancreatitis.

METHODS

Participants

Patient Selection. Included in this retrospective study were all patients with SAP and moderately severe acute pancreatitis

(MSAP) admitted to the General Surgery Center, Postdoctoral Working Station, China, from June 2009 to June 2011. Diagnoses of AP were based on clinical findings, biochemical variables, and computed tomography severity index (CTSI) per the revised Atlanta Classification (4). This study was performed according to the principles of the Declaration of Helsinki (modified 2000) and was approved by the Ethics Committee of Chengdu Military General Hospital (No. 2013032).

Inclusion Criteria. Adults (> 18 yr old) with a first episode of MSAP or SAP who underwent PCD were included in this study.

Exclusion Criteria. The exclusion criteria included the following:

1. AP subsequent to a second disease, endoscopic retrograde cholangiopancreatography, and suspected malignancy of the pancreas or biliary tree.
2. Patients with a medical history of immune deficiency, previous abdominal operation (exploratory laparotomy), or intraoperative diagnosis of AP.

Group Division. The patients were separated into two groups according to whether or not they had APD before PCD. The patients in the APD + PCD group underwent APD treatment in preparation of PCD intervention, and the patients in the PCD-alone group did not undergo APD before PCD.

Indications for Intervention

Indications for APD. When two vital conditions were simultaneously fulfilled, the patients underwent APD management: enough volume of fluid collections (> 50 mL) and a feasible pathway under imaging examination. In our approach, APD mainly aimed at fluid collection in the abdominal or pelvic cavity, whereas PCD mainly targeted necrotic collections presenting in the retroperitoneum. As to the timing, APD should be operated as early as possible if it was available (within 4 wk of disease onset).

Indications for PCD. Indications for PCD included patients who did not improve with previous management (2, 5), as evidenced by persistent fever, persistently raised leukocyte count/increasing trend of leukocyte count, worsening or new-onset organ failure, or presence of gas in the pancreatic bed. In addition, PCD should be done as late as possible to make enough qualiquation of necrosis. In this study, most PCDs were carried out after 4 weeks of disease onset.

Indications for Necrosectomy. Necrosectomy was carried out in the following circumstances: persistent/worsening sepsis after PCD, ongoing or tendentious leukocytosis, persistent/worsening or new-onset organ failure, inadequate drainage of collection and necrosis, failure to thrive, and presence of ongoing necrosis with bowel complications (e.g., necrosis, uncontrolled fistula, and obstruction).

Management Protocols

General Management. The following tests were conducted on all patients within 48 hours of admission: complete hemogram, coagulogram, serum calcium levels, renal and liver function tests, and blood gas analysis (**Fig. 2**). When a fever was present, blood cultures were taken. Initial contrast-enhanced CT was performed within the first week of the onset of disease and repeated depending on the indication. The images obtained were double-checked by two experienced radiologists to determine the CTSI value. A transabdominal ultrasound was performed occasionally if necessary. Acute Physiology and Chronic Health Evaluation (APACHE) II score and CTSI were calculated for each patient at the time of admission and serially calculated before and after each type of intervention.

The Novel Step-Up Approach. At the outset (first step), all patients were treated in a conservative manner, with fluid resuscitation and antibiotics, as described in the literature (2, 6–8). The second step included APD according to indication. If the catheter drainage was not competent, placement of additional catheters or repositioning, replacing, or upsizing of catheters was conducted by a professional intervention radiologist

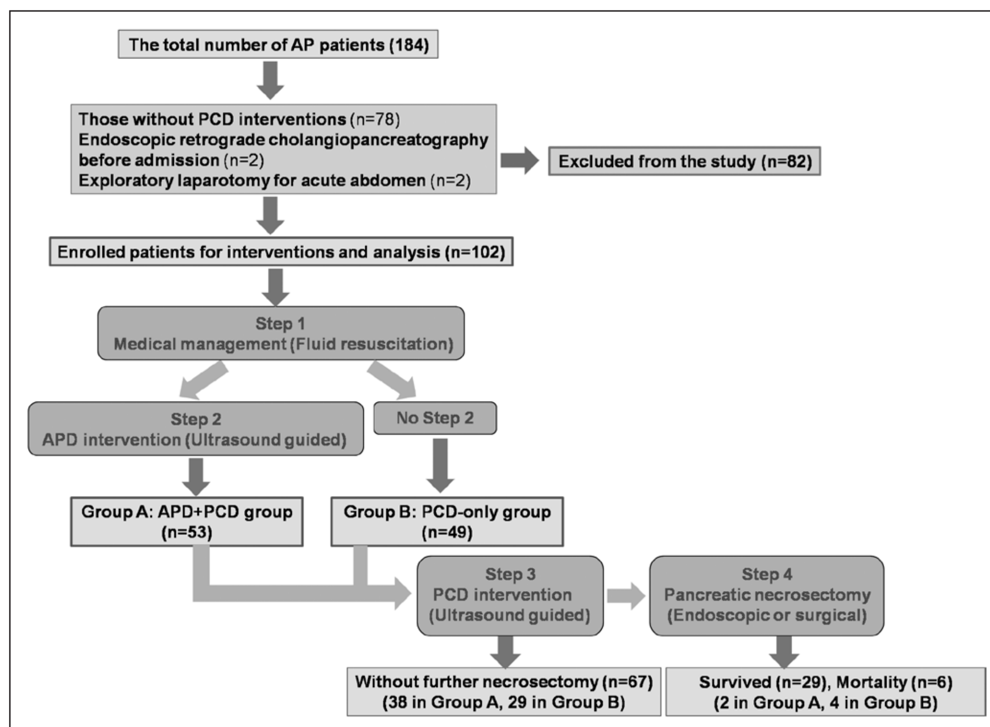

Figure 2. Study flow chart. This flow chart shows the process of patient's selection and therapeutic managements of acute pancreatitis (AP). APD = abdominal paracentesis drainage, PCD = percutaneous catheter drainage.

(**Supplemental Video 1**, Supplemental Digital Content 1, http://links.lww.com/CCM/B62). The number and size of the initial catheters were determined by the size, viscosity, and location of the collections. The third step was image-guided fine-needle aspiration and PCD to eliminate the debris and collections in the (peri)pancreas, similar to other reports (9–11). In accordance with widely accepted consensus (3, 7, 12, 13), if there was no clinical improvement or if ongoing necrosis with bowel complications was present, endoscopic or open necrosectomy with closed lesser-sac drainage and postoperative lavage was performed (fourth step).

APD Details. APD can be described simply as ultrasound-guided percutaneous puncture and catheterization, which is the standard treatment of seroperitoneum in many types of diseases, such as liver cirrhosis. In the present study, an initial 8F drainage catheter was used to drain fluid in the abdominal cavity for 3–5 days. The sinus tract of the drainage catheter was expanded gradually with a skin expander, and the 8F drainage catheter was gradually replaced with larger drainage tubes (up to 22F) over the next 5–10 days. Patients who recovered clinically and continued to have drainage were discharged from the hospital with the catheters in situ. Prior to discharge, the patients were taught about home catheter care and irrigation. The patients went to outpatient clinics in our department for follow-up. The drainage catheters were removed in the following situations: 1) catheter output of less than 10 mL/d of nonpurulent fluid for two consecutive days, with normal amylase levels; 2) no residual fluid found on a serial CT scan/ultrasonography; 3) signs of clinical recovery, such as absence of fever, accepting a normal diet, gaining weight, and able to carry out routine activities.

Data Collection

Primary Endpoints. The primary endpoint was mortality rate.

Secondary Endpoints. The secondary endpoints were as follows:

1. Rate of intervention-related complications, including bleeding, fistula, and discomfort
2. Severity scores (APACHE II and CTSI) of patients before and after APD
3. Differences in levels of inflammatory cytokines—C-reactive protein (CRP), interleukin (IL)-6, IL-10, tumor necrosis factor (TNF)-α—before and after APD
4. Prevalence of pneumonia, bacteremia, or sepsis before APD and reversal of sepsis after APD
5. Difference in leukocyte counts before and after APD
6. Prevalence of organ failure before and after APD (transient or persistent)
7. Details of PCD (interval from onset of AP to initial PCD, number of PCD interventions, initial catheter size of PCD, and complications with PCD)
8. Necrosectomy indexes (proportion of patients requiring necrosectomy after initial PCD, time from initial PCD to first necrosectomy, and number of necrosectomies)

Other Observational Variables. Other observational variables included the following:

1. Days in hospital and ICU
2. Cost
3. General information, including sex, age, and etiology

Statistical Analysis

The statistical analysis was carried out using SPSS version 16.0 for Windows (SPSS, Chicago, IL). Normality of data was determined by Kolmogorov-Smirnov tests of normality. Data were expressed as mean ± SD for normally distributed data and median and interquartile range for nonnormally distributed data. For normally distributed data, variables were compared using Student *t* test for two groups. For skewed data, the Mann-Whitney test was used. Qualitative or categorical variables were described as frequencies and proportions. Proportional variables were compared using the chi-test or Fisher exact test. All statistical tests were two-tailed and performed at a significance level of p value of less than 0.05.

RESULTS

General Information

According to the revised Atlanta severity classification (4), of 106 patients with AP admitted to our department who underwent PCD treatment between June 2009 and June 2011, 42 had MSAP and 64 had SAP (Fig. 2). Four patients were excluded from the study—two accepted endoscopic retrograde cholangiopancreatography before admission, and two underwent a laparotomy for acute abdomen and were intraoperatively detected as having AP. Of the 102 patients enrolled in the study, 53 were managed with the combination of APD and PCD (APD + PCD group) and 49 were managed without APD before PCD (PCD-alone group). In addition, 67 patients were cured without needing necrosectomy (38 in the APD + PCD group and 29 in the PCD-alone group), whereas the remaining 35 patients required necrosectomy after the initial PCD.

Baseline Data

The demographic data (age, sex, and etiology) of the PCD-alone group and the APD + PCD group were comparable (**Table 1**). The etiology of AP was mainly from bile duct problems (45.3% in APD + PCD group and 46.9% in PCD-alone group) and hyperlipidemia (18.9% in APD + PCD group and 18.4% in PCD-alone group). Apart from the demographic data, the severity scores of the APD + PCD group were similar to those of the PCD-alone group (15.5 ± 3.55 vs 14.7 ± 3.25 APACHE II, respectively; $p > 0.05$). The mean number of days from the onset of symptoms to discharge was a little higher in the PCD-alone group than in the APD + PCD group ($p > 0.05$) (Table 1); however, there was no difference in days in ICU ($p > 0.05$). The average total cost during hospitalization was significantly higher in the PCD-alone group compared with the APD + PCD group ($p < 0.05$) (Table 1).

Characteristics of APD

The total number of catheters used in 53 patients was 96. The median duration of APD was 15.6 days. Overall, the total

TABLE 1. Characteristics of 102 Patients Enrolled in This Study

Characteristic	APD + PCD Group	PCD-Alone Group	*p*
Number of patients	53	49	
Demographic data			
Age (mean ± SD)	59 ± 13.5	57 ± 12.7	0.065
Male:female	28:25	26:23	0.820
Referral after onset of symptoms (d) (mean ± SD)	12 ± 9.8	11 ± 8.5	0.541
Etiology (%)			0.750
Gallstone	24 (45.3)	23 (46.9)	
Alcohol abuse	16 (30.2)	14 (28.6)	
Hyperlipemia	10 (18.9)	9 (18.4)	
Other	3 (5.7)	3 (6.1)	
Classification			0.523
Moderately severe acute pancreatitis (42)	22	20	
Severe acute pancreatitis (60)	31	29	
Laboratory variables			
C-reactive protein (mg/L)	146.5 ± 20.53	142.5 ± 23.51	0.102
IL-6 (pg/L)	376.4 ± 63.21	354.6 ± 53.17	0.205
IL-10 (pg/L)	148.7 ± 47.57	136.2 ± 50.32	0.316
Tumor necrosis factor-α (pg/L)	18.3 ± 5.21	17.3 ± 5.93	0.345
Hypocalcemia (%)	12 (22.6)	11 (22.4)	0.587
Acidosis at admission pH < 7.2 (%)	7 (13.2)	5 (10.2)	0.137
Basic deficit at admission > 5 mEq/L (%)	11 (20.8)	10 (20.4)	0.726
Severity scores			
Initial Acute Physiology and Chronic Health Evaluation II score (mean ± SD)	15.5 ± 3.55 (8–65)	14.7 ± 3.25 (8–62)	0.648
Initial computed tomography severity index score (mean ± SD)	8.5 ± 2.45 (6–10)	8.0 ± 3.10 (6–12)	0.576
Initial Ranson score (mean ± SD)	3.0 ± 1.35 (1–8)	3.1 ± 1.27 (1–8)	0.307
Initial Marshall score (mean ± SD)	4.2 ± 1.25 (2–6)	3.8 ± 0.77 (2–6)	0.645
Medical economics (median ± interquartile range)			
Days in hospital	58.9 ± 31.24	63.2 ± 36.15	0.731
Days in ICU	8.3 ± 4.52	8.5 ± 6.75	0.234
Total cost during hospitalization (dollars)	7,615.2 ± 2,475.13	10,013.1 ± 5,041.02	0.003[a]

APD = abdominal paracentesis drainage, PCD = percutaneous catheter drainage, APD + PCD group = patients in this group treated first with APD and followed by PCD, PCD-alone group = patients in this group treated only with PCD without APD, IL = interleukin.

[a]Significant difference.

number of interventional procedures was 167 (Fig. 1). The diameter of the APD catheters varied from 8F to 22F; the size most frequently used in this study was 12F. During interventions under image guidance, either in the radiology suite or at the patient's bedside, the maximum catheter diameter used was 12F initially, followed by upsizing to 16F or 18F, based on the need. Large-bore catheters (22F–32F) were also inserted in the paracolic region at the patient's bedside in patients with gross ascites and abdominal compartment syndrome. Upsizing procedures were performed in 21 patients.

Primary Endpoint

The mortality rate in the PCD-alone group was 4 of 49 patients (8.0%), and disease-specific mortality was 4 of 49 patients; in contrast, the mortality rate in the APD + PCD group (2/53 patients, 3.8%) was lower than in the PCD-alone group ($p < 0.05$). Especially, the disease specific mortality between two groups was significantly different. The causes of death in the patients with disease-specific mortality were mainly from multiple organ dysfunction syndrome and severe infection. Of the four patients who died of disease in PCD-alone groups, two

developed multiple organ failure (MOF) together with persistent/worsening sepsis, one suffered from ongoing sepsis with MOF, and another developed enterocutaneous fistulas with MOF (**Table 2**).

Secondary Endpoints

Clinical and Laboratory Variables. The clinical and laboratory variable data were collected 2 days before initial PCD application (about 20 d from the onset of AP) in both groups. The APACHE II scores, Ranson scores, and Marshall scores were significantly lower in the APD + PCD group compared with the PCD-alone group ($p < 0.05$) (**Table 3**). We also checked the maximum extent of pancreatic necrosis during the stay; the PCD-alone group had a higher number of patients with more than 30% necrosis than the APD + PCD group did (Table 3).

The laboratory variables decreased more rapidly in the APD + PCD group than in the PCD-alone group ($p < 0.05$) (Table 3). For example, in the APD + PCD group, the mean level of serum CRP decreased to 45% (from 146.5 ± 20.53 to 66.3 ± 17.52 mg/L), IL-6 decreased to 23% (from 376.4 ± 63.21 to 86.3 ± 23.11 pg/L), IL-10 decreased to 26% (from 148.7 ± 47.57 to 38.7 ± 16.32 pg/L), and TNF-α decreased to 67% (from 18.3 ± 5.21 to 12.3 ± 4.21 pg/L). These results indicate that a number of inflammatory factors were diminished through drainage of the seroperitoneum by APD.

Infection-Related Variables. A similar number of patients in the APD + PCD group (42/53) had polymicrobial infections compared with the PCD-alone group (39/49). *Escherichia coli* was the most common bacterial isolation in this study, with a significantly higher prevalence in the PCD-alone group compared with the APD + PCD group ($p > 0.05$) (**Table 4**). Fungal isolates were identified in 16 patients; however, there was no statistical difference between the groups. At admission, the mean WBC count in the APD + PCD group (14 ± 2.3 × 10E9/L) was close to that of the PCD-alone group (14 ± 1.7 × 10E9/L); however, WBC recovery took longer in most of the patients in PCD-alone group than in those in the APD + PCD group ($p > 0.05$). Furthermore, the prevalence of sepsis was a little higher in the PCD-alone group (19/49, 38%) compared with the APD + PCD group (16/53, 30%), but not pneumonia or bacteremia. It took more time for the patients in the PCD-alone group (25.7 ± 2.34 d) to gain sepsis reversal than those in the APD + PCD group (21.4 ± 2.16 d) ($p < 0.05$) (Table 4).

Organ Failure. There were significant differences in frequency of organ failure developing at different periods from the onset of the disease between the two groups ($p < \mathbf{0}.05$) (**Table 5**). In addition, the mean number of failed organs and the MOF rate were significantly higher in the PCD-alone group than in the APD + PCD group ($p < 0.05$). The mean duration of organ failure in the PCD-alone group was also higher than in the APD ± PCD group, although the difference did not reach statistical significance ($p \geq 0.05$) (Table 5). The results indicate that the time necessary for reversal of organ failure before PCD insertion was significantly higher in the PCD-alone group than in the APD + PCD group ($p < 0.05$).

Further Interventions. The variables regarding subsequent interventions after APD were observed and evaluated in terms of adjacent PCD and latter necrosectomy. Regarding PCD, first, the interval between the onset of symptoms and the first PCD insertion was a little longer in the APD + PCD group than in the PCD-alone group ($p < 0.05$). Second, the total number of catheters used was 88 in the PCD-alone group and 69 in the APD ± PCD group. Third, the median duration of PCD was significantly higher in the PCD-alone group compared with the APD + PCD group ($p < 0.05$). Fourth, the total number of interventional procedures (repositioning, replacement,

TABLE 2. Primary Clinical Outcomes in Two Groups

Variables	APD + PCD Group	PCD-Alone Group	*p*
Number of patients	53	49	
Mortality (%)	2 (3.8)	4 (8.2)	0.318
Disease specific	0 (0)	4 (8.2)	0.050[a]
Unrelated to disease	2 (3.8)	0 (0)	0.188
Complications in recurrent acute pancreatitis or chronic pancreatitis patients	6 in 4 patients	12 in 8 patients	0.003[a]
Deep venous thrombosis	2	3	
Disease-related colonic fistulas	2	3	
Disease-related duodenal fistulas	1	2	
Intervention-related colonic fistulas	0	2	
Tube drain erosion	1	0	
Intra-abdominal purulent collections	0	1	
Pleural effusion	0	1	

APD = abdominal paracentesis drainage, PCD = percutaneous catheter drainage, APD + PCD group = patients in this group treated first with APD and followed by PCD, PCD-alone group = patients in this group treated only with PCD without APD.

[a]Significant difference.

TABLE 3. Laboratory and Clinical Parameters Between Two Groups

Variable	APD + PCD Group	PCD-Alone Group	p
Number of patients	53	49	
Laboratory variables			
Acidosis (pH < 7.2) (%)	4 (7.5)	4 (8.2)	0.785
Basic deficit (> 5 mEq/L) (%)	6 (13.2)	5 (10.2)	0.527
C-reactive protein (mg/L)	66.3 ± 17.52	93.4 ± 21.62	0.047[a]
IL-6 (pg/L)	86.3 ± 23.11	116.4 ± 25.21	0.032[a]
IL-10 (pg/L)	38.7 ± 16.32	65.3 ± 14.16	0.017[a]
Tumor necrosis factor-α (pg/L)	12.3 ± 4.21	11.7 ± 3.93	0.412
Severity scores (before PCD)			
Acute Physiology and Chronic Health Evaluation II score (mean ± SD)	8.2 ± 2.42 (3–28)	10.7 ± 3.05 (3–30)	0.039[a]
Ranson score (mean ± SD)	2.4 ± 1.02 (1–6)	2.9 ± 1.14 (1–7)	0.041[a]
Marshall score (mean ± SD)	2.9 ± 0.65 (1–6)	3.4 ± 0.72 (1–7)	0.046[a]
Maximum extent of necrosis during the stay (%)			0.032[a]
< 30%	7 (13.2)	5 (10.2)	
30–50%	25 (47.2)	27 (55.1)	
> 50%	21 (39.6)	17 (34.7)	

APD = abdominal paracentesis drainage, PCD = percutaneous catheter drainage, APD + PCD group = patients in this group treated first with APD and followed by PCD, PCD-alone group = patients in this group treated only with PCD without APD, IL = interleukin.
[a]Significant difference.

TABLE 4. Infection-Related Parameters Between Two Groups

Variable	APD + PCD Group	PCD-Alone Group	p
Number of patients	53	49	
Prevalence of infections (%)			0.618
Polymicrobial infections	42 (79.2)	39 (79.6)	
Monomicrobial infections	6 (11.3)	5 (10.2)	
No infection	5 (9.4)	5 (10.2)	
WBC count at admission (× 10E9/L)	14 ± 2.3	14 ± 1. 7	0.058
The recovery of WBC (d)	26.7 ± 11.21	28.6 ± 13.22	0.137
The prevalence of pneumonia (%)	5 (9.4)	4 (8.2)	0.230
The prevalence of bacteremia (%)	26 (49.9)	24 (49.0)	0.275
The recovery of bacteremia	18.0 ± 9.21	17.3 ± 8.93	0.345
The prevalence of sepsis (%)	16 (30.2)	19 (38.8)	0.037[a]
Time for sepsis reversal (d)	21.4 ± 2.16	25.7 ± 2.34	0.031[a]

APD = abdominal paracentesis drainage, PCD = percutaneous catheter drainage, APD + PCD group = patients in this group treated first with APD and followed by PCD, PCD-alone group = patients in this group treated only with PCD without APD.
[a]Significant difference.

flushing, upsizing, and additional catheter placement under imaging guidance) was much higher in the PCD-alone group (280) than in the APD + PCD group (254) (**Table 6**). Fifth, the diameter of the PCD catheters varied from 10F to 22F in both groups, and 12F was the size most frequently used in this study. Upsizing procedures were carried out in 18 patients in the PCD-alone group and in 13 patients in the APD ± PCD group (Table 6). Finally, the rates of total PCD complications were 28.6% and 30.2% in the PCD-alone group and the APD ± PCD group, respectively.

TABLE 5. The Organ Failure–Related Variables Between Two Groups

Variable	APD + PCD Group	PCD-Alone Group	p
Number of patients	53	49	
Number of organs failed per patient			
Mean ± SD	0.8 ± 1.12	1.4 ± 1.34	0.021[a]
Median (range)	1 (0–5)	1 (0–5)	
Organ failures (%)			0.034[a]
No organ failure	16 (30.2)	13 (26.5)	
Single-organ failure	20 (37.7)	18 (36.7)	
Multiple organ failure	17 (32.1)	18 (36.7)	
Onset of organ failure (%)			0.317
Organ failure: 1st week	7 (18.9)	6 (16.7)	
Organ failure: 2nd week	15 (40.5)	15 (41.7)	
Organ failure: 3rd week	10 (27.0)	10 (27.8)	
Organ failure: 4th week	5 (13.5)	5 (13.9)	
Duration of organ failure (d)	23.7 ± 4.25	24.6 ± 7.16	0.058
Reversal of organ failure before PCD (%)	16 (43.2)	11 (30.5)	< 0.001[a]
Acute respiratory distress syndrome (%)	21 (39.6)	25 (51.0)	< 0.001[a]

APD = abdominal paracentesis drainage, PCD = percutaneous catheter drainage, APD + PCD group = patients in this group treated first with APD and followed by PCD, PCD-alone group = patients in this group treated only with PCD without APD.

[a]Significant difference.

Indications for surgical intervention were ongoing sepsis not controlled by interventional radiological management ($n = 14$); persistent/worsening sepsis ($n = 9$); failure to thrive ($n = 4$); colonic gangrene ($n = 3$); gastrointestinal bleeding, including pseudoaneurysm ($n = 3$); and bowel obstruction ($n = 2$). In particular, after initial PCD, 20 patients (40.8%) in the PCD-alone group underwent necrosectomy, compared with 15 patients (28.3%) in the APD + PCD group ($p < 0.05$). In addition, the time from the onset of AP to necrosectomy was longer in the APD + PCD group compared with the PCD-alone group, and the difference was significant (63.4 ± 15.62 d vs 53.6 ± 11.75 d, respectively; $p < 0.05$). However, the interval between the initial PCD and the first necrosectomy was similar between two groups. The number of both endoscopic and open procedures was much higher in the PCD-alone group ($n = 40$) than in the APD + PCD group ($n = 27$) ($p < 0.05$) (Table 6).

DISCUSSION

AP is known as one of the most variable diseases, and it is the leading benign disorder resulting in hospital admission (14). In particular, morbidity and mortality rates associated with AP are still very high (13). There is increasing evidence that minimally invasive approaches, including a step-up approach that incorporates PCD or endoscopic transluminal drainage, followed by video-assisted retroperitoneal debridement or endoscopic debridement, are associated with improved outcomes in AP patients with infected necrosis compared with traditional open necrosectomy (15). Nevertheless, according to the newly published revision of Atlanta classification, some adjustments and improvements of AP treatment are necessary.

The important information of the revised Atlanta AP classification provides rich resources for reconsidering the treatment of AP more appropriately. In particular, the revision puts great emphasis on dealing with types of fluid collections, which can greatly affect the evolvement of AP and the clinical outcome for patients. This current global consensus classification of AP offers a comprehensive classification of collections, which enables us to know these collections well and handle them appropriately. Management options for fluid collections are diverse, including conservative treatment, PCD, open and laparoscopic surgery, and endoscopic drainage (16). Generally speaking, the choice of treatment depends on a correct diagnosis of the type of fluid collection (16). However, within the first week of the disease, it may be difficult to differentiate between APFC and ANC. At this stage, both types of collections may appear as areas with fluid accumulation (4). During this period, we do not think it is necessary to classify the exact type of collection. The importance lies in assessing the volume and distribution of the collections, as doing so can help us decide whether or not APD is indicated. From our point of view, the indication of APD consists of both a volume of more than 50 mL collection and feasible pathways. Therefore, in this study, we have introduced APD in preparation for PCD to better manage the different types of fluid collections defined

TABLE 6. Detailed Information of Further Interventions Between Two Groups

Variable	APD + PCD Group	PCD-Alone Group	p
Number of patients	53	49	
Details for PCD intervention			
Interval between the onset of symptoms and the first PCD insertion (d)	32.3 ± 6.15	24.6 ± 5.62	0.021[a]
Number of PCD catheters per patient			
Mean ± SD	1.3 ± 0.35	1.8 ± 0.61	0.027[a]
Median (range)	1 (1–4)	1 (1–4)	
Total PCD procedures per patient			
Mean ± SD	4.8 ± 2.43	5.7 ± 2.12	0.075
Median (range)	5 (1–11)	6 (1–12)	
Diameter of PCD			0.038[a]
8F	1	0	
10F	51	65	
12F	12	13	
16F	1	0	
20F	0	2	
24F	2	3	
28F	0	2	
32F	2	3	
Upsizing of PCD			0.217
10F–12F	10	11	
12F–16F	1	0	
20F–24F	0	2	
24F–28F	2	3	
28F–32F	0	2	
Site of PCD			0.018[a]
Pancreatic region	33	45	
Left pararenal region	17	22	
Right pararenal region	8	10	
Pelvic region	7	5	
Right subhepatic region	4	6	
PCD catheter duration (d)			< 0.001[a]
Mean ± SD	28.2 ± 7.28	45.1 ± 12.63	
Median (range)	31 (6–192)	43 (11–254)	
Mortality due to PCD or drains	0	0	–
Morbidity due to PCD or drains (%)	16 (30.2)	14 (28.6)	0.317

(*Continued*)

TABLE 6. (*Continued*). Detailed Information of Further Interventions Between Two Groups

Variable	APD + PCD Group	PCD-Alone Group	*p*
Details for necrosectomy			
Number of patients received necrosectomy (%)	15 (28.3)	20 (40.8)	0.028[a]
Ongoing sepsis not controlled	7	10	
Persistent/worsening sepsis	5	6	
Failure to thrive	3	4	
Interval between the onset of symptoms and the first necrosectomy (d)	63.4 ± 15.62	53.6 ± 11.75	0.022[a]
Interval between the initial PCD and the first necrosectomy (d)	27.4 ± 11.21	26.3 ± 8.93	0.205
Total necrosectomy procedures per patient			
Mean ± SD	0.5 ± 0.42	0.8 ± 0.67	0.012[a]
Median (range)	0 (0–8)	1 (0–9)	

APD = abdominal paracentesis drainage, PCD = percutaneous catheter drainage, APD + PCD group = patients in this group treated first with APD and followed by PCD, PCD-alone group = patients in this group treated only with PCD without APD.
[a]Significant difference.

under the revised Atlanta Classification. Combining APD with PCD thoroughly eliminates all types of fluid collections. Our method builds a more complete step-up approach, with more concentration on collections, by inserting APD as the second step between conservative therapy and PCD.

We compared the results of our study with those of the study by Babu et al (2), which is a landmark study in the literature and the first to report on predictors of surgery after PCD. That study reported sepsis reversal in 62.5% of their patients, which compares well with our result of 71.5%. One major reason for these results is that APD was applied before PCD. The disease-specific mortality rate in patients managed with both APD and PCD was 0% (0/53) in our study, compared with 6.8% (2/29) in the study by Babu et al (2). We hold the view that performing APD prior to PCD to treat AP patients with fluid collections results in a better curative effect, for several reasons: 1) easing inflammatory response by eliminating inflammatory factors; 2) preventing new-onset or secondary infection by removing the nutritive medium for bacteria; 3) hampering the development of organ failure by lowering abdominal pressure; and 4) deferring further intervention by serving as a transitional method. Among these contributing aspects, the effectiveness of APD mainly comes from eliminating inflammatory factors and deferring further intervention.

During the first week of AP, cytokine cascades are activated by the pancreatic inflammation, which manifests clinically as systemic inflammatory response syndrome (SIRS) (17, 18). Thus, the main aim of applying APD is to dismiss inflammatory factors to interfere with or even terminate such cytokine cascades. This strategy may weaken the degree of SIRS and benefit patients with AP. In this study, it can be seen that in removing fluid collections by APD, the content of cytokines (such as CRP and ILs) decreased greatly, by almost half. We propose that the elimination of cytokines may be one of the most important functions of APD in aiding in the recovery of patients with AP.

Infections have a significant impact on mortality. The mortality dramatically increases if fluid collections become infected (19, 20), and the secondary infection of fluid collections remains the leading cause of mortality in patients with AP (21). Thus, it is wise to prevent infection by eliminating fluid collections. We proposed that APD might reduce the prevalence of later infection by eliminating fluid collections. However, others have argued that extra puncturation could increase the prevalence of infection (22). In this study, the infection rate in the APD + PCD group was similar to that of the PCD-alone group. That is to say, adding APD to the treatment protocol did not result in more infections. Furthermore, the prevalence of sepsis was lower, and the reversal of sepsis took less time in the APD + PCD group than in the PCD-alone group. Two reasons may explain why adding APD avoids additional infections and might reverse sepsis more effectively. On one hand, APD eliminates fluid collections, which has been reported as a home for microorganisms by providing the necessary conditions for them to thrive (23). On the other hand, APD reduces CRP and leukocyte levels, which are stimulating factors for bacterial growth (23).

It is believed that patients who encounter persistent organ failure within the first few days of AP have an increased risk of death, with a mortality as high as 36–50% (18). Therefore, persistent organ failure is highly recommended to be prevented as early as possible. In this study, early APD can decrease the chance of developing persistent organ failure and achieve organ failure reversal in 38.1% of the patients. This finding implies that APD as the first intervention in the step-up approach alters the natural course of AP in some patients by achieving reversal of organ failure.

Because the risk of postoperative mortality associated with necrosectomy is around 50%, it is advisable to delay necrosectomy when it is compatible with the patient's status (24). In this study, using APD prior to PCD not only postponed necrosectomy for almost 10 days on average but also omitted partial necrosectomy (10% less necrosectomy compared with

PCD-alone). In addition, in this study, APD could also postpone subsequent PCD. APD may serve as a bridge between conservative therapy and PCD in patients with AP.

CONCLUSIONS

In this study, we upgraded the step-up approach by adding APD ahead of PCD as the second step in AP patients with abdominal or pelvic fluid collections whenever indicated. As a result, it is evident that inserting APD into the step-up approach benefits patients mainly in view of decreasing disease-specific mortality. The success of APD in treating AP patients may be due to various factors. One of the factors contributing to the success of APD in this study was the active role played by the radiologist (ultrasound doctor) in catheter management. The other deciding factor was the ability to determine the details of fluid collections, especially their viscosity, volume, and location. The frequency of APD and the size and number of catheters depend on those factors. All in all, the inclusion of APD in the step-up approach alters the natural course of AP, due to its ability to eradicate inflammatory materials, ease organ failure, and postpone further interventions.

Limitations and Prospective Research

Although adding APD as the second step of the step-up approach seems to be beneficial to patients with AP, there are still some limitations to this technique and our study. APD, as an intercurrent approach, carries the risk of introducing additional infection, which is associated with increased morbidity and mortality (19). Thus, we should keep in mind that it is advisable to avoid secondary infection, especially when caused by interventions. Another limitation is that it is still not clear which subset of patients among those managed by APD would require further PCD. In addition, the timing of both APD and PCD remains an issue that needs to be addressed.

To achieve better results with APD application, we are planning to improve the procedure by covering the following aspects in our future research. First, access routes of APD depending on the viscosity, volume, number, and location of fluid collections on a CT scan would improve therapeutic results. In addition, saline irrigation should be used in the APD catheter to achieve better results. Finally, it is important to make sure of the indication for further interventions. In a previous study, it was demonstrated that three factors can be used early in the course to predict necrosectomy after PCD: reversal of sepsis within a week of PCD, an APACHE II score at the first intervention (PCD), and organ failure within 1 week of the onset of disease (2). In our future study, we may also find some early predictors of PCD intervention and investigate the affecting factors in advance to predict treatment with APD alone.

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