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Original article

Step-up mini-invasive surgery for infected pancreatic necrosis: Results from prospective cohort study

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ABSTRACT

Objectives: To investigate the clinical efficacy and success predictors of mini-invasive techniques in the treatment of infected pancreatic necrosis (IPN).
Methods: IPN patients admitted to our clinic for treatment by mini-invasive techniques were included in this study prospectively. Treatment was divided into four sequential phases: percutaneous catheter drainage (PCD), mini-incision drainage (MID), video assisted debridement (VAD) and open surgery. Patients progressed to next phase if the infection cannot be controlled. The frequency of surgery, treatment duration, cure rate, incidence of complication and overall mortality were recorded. Risk factors for failure of PCD and MID procedures were detected by logistic regression including demographics, disease severity and morphologic characteristics.
Results: From January 2012 to March 2015, a total of 54 consecutive IPN patients were treated, with an average age of 51.2 ± 3.1 years. Of the 54 cases, 18 (33.3%) were cured after PCD; 13 (24.1%) with uncontrolled infection were cured after MID; and the remaining 19 cases (35.2%) were cured after VAD. No open surgery was performed. Overall mortality was 7.4% (4/54), and the incidence of complications was 12.9% (7/54). In multivariable regression, the following factors were associated with high failure rate for both PCD and MID: heterogeneous fluid collection (odds ratio (OR) = 3.14; 95% confidence interval (CI): 1.32 ~ 4.25, P = 0.001 for PCD; OR = 2.99; 95% CI: 1.52 ~ 5.10, P = 0.006 for MID), multiple infected collections (OR = 4.51; 95% CI: 2.94 ~ 8.63; P = 0.000 for PCD; OR = 4.17; 95% CI: 2.77 ~ 8.12, P = 0.000 for MID), CT severity index (0 ~ 3/4 ~ 6/7 ~ 10: OR = 2.16; 95% CI: 1.83 ~ 3.62, P = 0.031 for PCD; OR = 2.72; 95% CI: 1.78 ~ 4.10, P = 0.005 for MID).
Conclusions: Step-up mini-invasive techniques can be considered a first choice in the treatment of IPN. CT is effective to predict success of PCD and MID.

Introduction

Secondary infection of pancreatic or peripancreatic necrosis is an important cause of mortality in acute pancreatitis (AP), and is an acknowledged indication for surgical intervention [1]. Mortality rates for open necrosectomy treatment of pancreatic necrosis are as high as 11.4–39.1%, mainly due to the deterioration of general condition with operating on such acute patients and postoperative complications [2]. Therefore, mini-invasive techniques are more and more employed in the treatment of IPN in order to overcome the shortcomings of open surgery and reduce postoperative mortality. Despite the lack of high-quality evidence, minimally invasive methods of necrosectomy are preferred to open necrosectomy, percutaneous catheter or endoscopic transmural drainage was recommended as the first step in the treatment of patients with suspected or confirmed walled-off IPN [3]. In this prospective cohort study, we have analyzed the clinical outcome and efficacy of mini-invasive techniques for the treatment of IPN in patients presenting at our center over a thirty-nine months period. The risk factors for failure of mini-invasive approaches are also explored to guide prognostication in clinical practice and risk stratification in clinical studies.

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Materials and methods

Case selection

The patients with IPN who were treated at our center between January 2012 and March 2015 were included in our study. Diagnosis of AP was made according to standards defined in the American College of Gastroenterology Guidelines, pancreatic and peripancreatic necrosis was diagnosed by contrast-enhanced computerized tomography (CT) scanning [1]. Infected necrotic tissue was defined as persistent sepsis or progressive clinical deterioration despite maximal support in the intensive care unit (ICU), or the presence of gas in fluid observed on contrast-enhanced CT scans.

Organ failure was defined as a score of 2 or more organ systems using the modified Marshall scoring system [4].

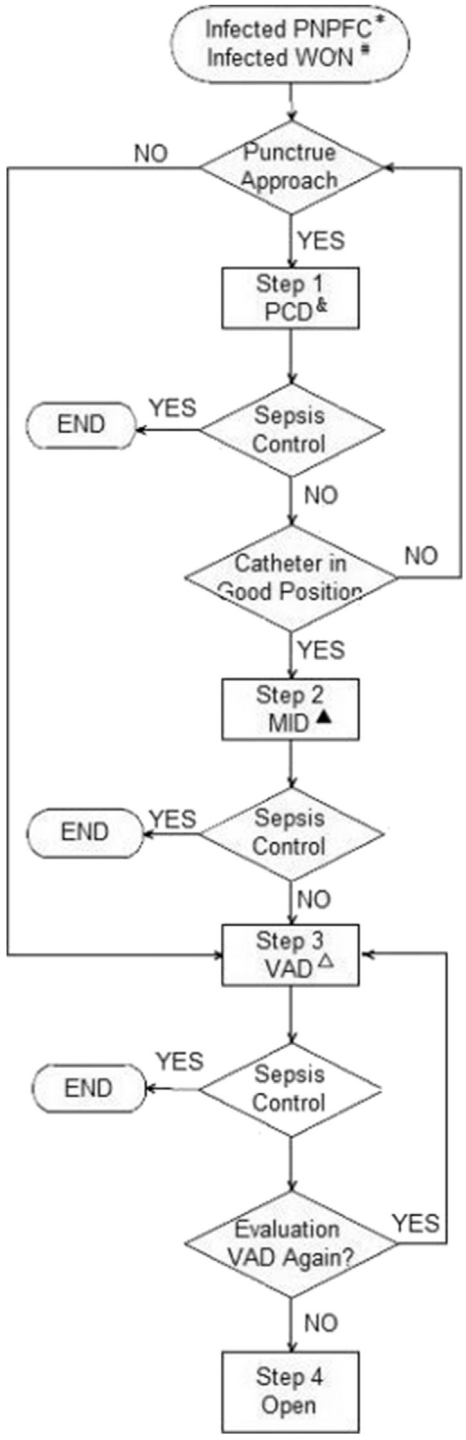

Fig. 1. Treatment process of infected pancreatic/peripancreatic necrosis. *ANC acute necrotic collection; # WON walled-off necrosis; & PCD percutaneous catheter drainage; ▲ MID mini-incision drainage; △ VAD video assisted debridement.

Therapeutic methods

Once the infection was diagnosed, the patients were enrolled in the treatment protocol (Fig. 1). During this process, contrast-enhanced CT scanning was used for evaluation of treatment effect. Treatment was divided into four sequential phases, with patients progressing through phases as necessary, according to the success of treatment at each phase.

Phase one comprised ultrasound or CT-guided percutaneous catheter drainage (PCD) under local anesthesia. If there was no suitable puncture approach available, treatment phase three was performed directly. Where infection did not improve significantly, or symptoms recurred despite a controlled infection, a further CT scan was performed. If the drainage catheter was incorrectly placed, PCD was repeated with a repositioned catheter. However, if the infection was not controlled due to inadequate drainage, the patient progressed to the second phase of treatment.

Phase two, mini-incision drainage (MID) was performed by making a 3–4 cm incision surrounding the percutaneous catheter, followed by a layered incision to the abscess cavity along the line of the catheter. Mature pancreatic and peripancreatic necrotic tissues with clear margins were excised with sponge forceps, and several large-diameter catheters placed to enable vacuum drainage. Where infection did not improved after MID, patients progressed to phase three.

Phase three of the treatment process comprised video assisted debridement (VAD), using either nephroscopy via retroperitoneal approach or laparoscopy via intraperitoneal approach. Under general anesthesia, the video equipment was placed via a sinus tract adjacent to the MID drainage tube, and biopsy forceps or sponge forceps used to remove necrotic tissue. For patients who did not receive the first two treatment phases and progressed straight to VAD, retroperitoneoscopy was performed. A retroperitoneal space was created and a trocar placed according to the methods of laparoscopic adrenalectomy [5]; perinephric retroperitoneal tissue was then gradually separated as far as the abscess cavity. Pancreatic and peripancreatic necrotic tissue was removed, and drainage performed. If clinical manifestations of infection showed no improvement following the procedure, a CT scan was performed to assess whether further VAD was appropriate. In cases refractory to treatment by VAD, open pancreatic necrosectomy was performed.

Phase four, open pancreatic necrosectomy, was performed as follows: using an upper abdominal midline incision, or a bilateral subcostal incision approach, the gastrocolic ligament was divided, or the pancreatic bed exposed through the transverse mesocolon. Blunt dissection was used to probe pancreas and peripancreatic areas, and pancreatic and peripancreatic necrosis removed, followed by the placement of multiple drainage tubes for closed drainage [6].

Patient characteristics, frequency of surgery, treatment duration, cure rate, incidence of complication (enterocutaneous fistula, perforation of a visceral organ, intraabdominal bleeding and pancreatic leakage during admission or during the 3 months after discharge) and overall mortality were recorded.

Possible risk factors

Possible risk factors for failure of PCD and MID procedures are divided into three groups: demographic factors, disease severity factors and morphological factors on CT.

Table 1
Treatment results of mini-invasive surgery for infected pancreatic necrosis.

	PCD	MID	VAD
No. of procedures	1–3	1–2	1–4
Overall cure rate	33.3% (18/54)	24.1% (13/54)	35.2% (19/54)
Drainage duration, median (range)	46 (32–116) days	39 (28–69) days	56 (41–87) days
Tube diameter	8.5–16 Fr	16–36 Fr	30–36 Fr
Complication rate	2% (1/50)	9.4% (3/32)	14.3% (3/21)
Mortality	0	6.3% (2/32)	9.5% (2/21)
Treatment interval, median (range)	8 (4–14) days	12 (7–19) days	–

PCD percutaneous catheter drainage; MID mini-incision drainage; VAD video assisted debridement.

Demographic factors: (1) age; (2) sex; (3) etiology; and (4) ECOG score.

Disease severity factors: (1) serum leukocytes; (2) serum creatinine level; (3) serum procalcitonin (PCT); (4) Acute Physiology And Chronic Health Evaluation (APACHE) II score; (5) Ranson score; and (6) organ failure.

Morphological factors on CT: (1) percentage of pancreatic necrosis; (2) contents of the collection (Homogeneous collection: collection consisting of a single density; Heterogeneous Collection: collection consisting of multiple densities); (3) size of the collection; (4) spread of the infected collection and (5) CT severity index.

Statistical analysis

Continuous data are presented as mean ± standard deviation. The logistic regression analysis was used to identify variables associated with failure of PCD or MID. All variables with univariable $p < 0.1$ were considered for the multivariable model. All variables with an adjusted $p < 0.05$ were retained in the final model. Results are presented as odds ratios (ORs) with 95% confidence intervals (CI). A 2-tailed $P < 0.05$ was considered statistically significant. Statistical analysis was performed with SPSS version 17.0 (SPSS Inc., Chicago, IL, USA).

Results

Patients

From January 2012 to March 2015, a total of 54 consecutive patients with IPN were treated at our center, including 39 males and 15 females, with an average age of 51.2 ± 3.1 years (range 27–84 years). There were 25 patients transferred from other hospitals including tertiary medical centers. According to accepted definitions of local pancreatic complications [1], four cases comprised acute necrotic collection (ANC) and 50 cases, walled-off necrosis (WON). The duration of AP on admission ranged from six hours to five months, and was less than one week for 17 cases. Of the 54 cases, nine cases had organ failure over 48 h with one case of multiple-organ failure.

Treatment outcome

The median time between onset of pancreatitis and timing of first intervention was 47 days (11–154days). The treatment result was shown in Table 1. A total of 50 cases were given PCD treatment in the first phase, with 27 cases showing disease duration of less than four weeks. Four cases were given VAD directly due to the

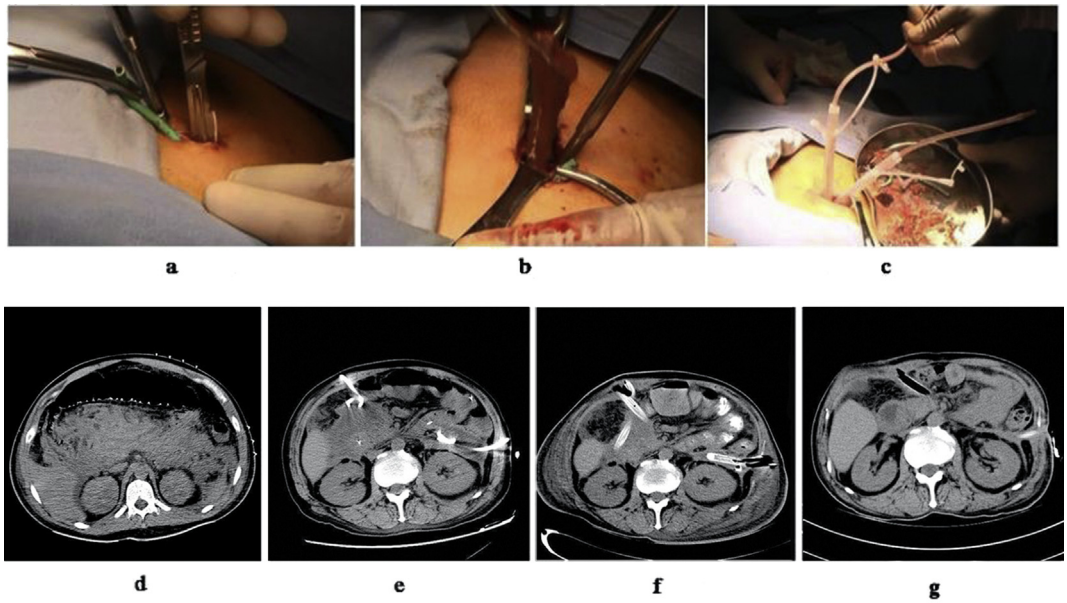

Fig. 2. MID in a 53-year-old male with a disease duration of two months; CT scan showing infection of WON in the pancreatic body, as well as the head and tail of pancreatic body. a. Layered incision guided by PCD; b. Extraction of necrotic tissue with sponge forceps; c. Placement of two 30 Fr drainage tubes; d. Before PCD; e. Placement of 8.5 Fr drainage tube by PCD before MID treatment; f. The use of a 30 Fr drainage tube after MID; g. CT scan showing the majority of infected necrosis absorbed 52 days following placement of MID drainage tube. PCD, percutaneous catheter drainage; MID, mini-incision drainage; ECOG Eastern Cooperative Oncology Group.

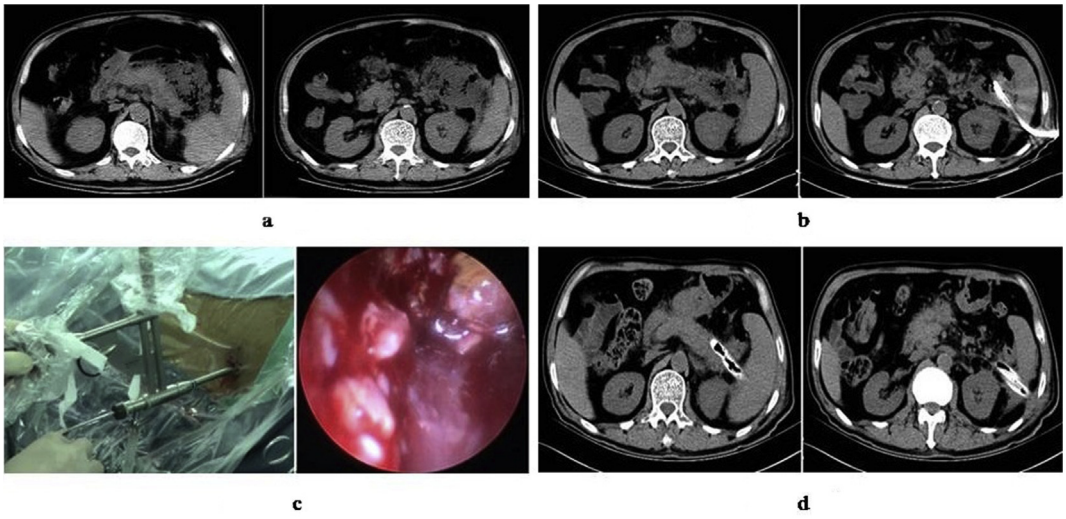

Fig. 3. VAD (nephroscope) in a 71-year-old male with a disease duration of two weeks. a. CT scan showing secondary infection of WON at the tail of pancreatic body; b. CT scan showing infected necrosis after PCD drainage (9 days) and MID drainage (7 days); c. Pancreatic necrosis and fester seen during VAD under nephroscope; d. CT scan showing successful absorption of IPN 36 days after VAD. PCD, percutaneous catheter drainage; MID, mini-incision drainage; VAD, video assisted debridement; WON, walled-off pancreatic necrosis.

absence of a safe puncture approach, with both these cases showing disease duration of greater than four weeks. Of the 50 cases, 42 were via retroperitoneal approach and 8 were via intraperitoneal approach. The 32 patients in whom infection was not controlled after PCD received MID treatment (Fig. 2). Two patients out of 19 unhealed patients died of persistent respiratory and circulatory failure, and the remaining 17 patients progressed to the third phase. A nephroscope or laparoscopy was placed via the sinus tract established in the second phase and necrotic tissues removed (Fig. 3). Following MID, eleven patients had a retroperitoneal sinus tract, and six patients had intraperitoneal sinus tracts. Four patients did not have a suitable approach for PCD and entered the third phase directly for removal of pancreatic necrosis via retroperitoneoscopy (Fig. 4). Two patients died of persistent respiratory and renal failure.

In our study, no patient received fourth phase treatment of open pancreatic necrosectomy. Overall mortality was 7.4% (4/54) and the incidence of complications during the perioperative period was 12.9% (7/54). Complications included two cases of postoperative bleeding, one case of duodenum fistula, and four cases of pancreatic fistula, all of which were cured by non-surgical treatment.

Bacterial culture

There were 116 pus samples obtained from the IPN patients and 94.8% (110/116) were positive for bacterial culture. Of the 54 patients, 11 were infected with gram-positive germs (5 *Staphylococcus aureus*, *3 Pseudomonas aeruginosa*, 2 *Enterococcus faecium*, *1 Staphylococcus haemolyticus*), 27 g-negative germs (15 *Escherichia coli*, *8 Klebsiella pneumoniae*, *4 Enterobacter cloacae*,), and 1 fungi (*Candida albicans*). Multiple infection was occurred in 15 patients. Multidrug resistant (MDR) microorganisms was found in 28 (51.9%) patients and the most frequent MDR bacteria was methicillin-resistant *S. aureus* (39.3%, 11/28). Success rate for PCD treatment was not significantly different in the patients with MDR infections *vs*. those without it (33.3% *vs* 34.2%, P = 0.700).

Risk factors for failure of PCD and MID

Risk factors for failure of PCD and MID included in this study were presented in Table 2. In our study cohort, the most common cause of pancreatitis was biliary stone (35, 64.9%). Nine (16.7%) patients had persistent organ failure and 29 (53.7%) had multiple infected collections. Results of logistic regression are summarized in Tables 3 and 4. The following parameters were associated with failure of PCD in multivariable analyses: persistent organ failure > 48 h (OR = 1.09, 95% CI 1.07 ~ 3.38; P = 0.049); percentage of pancreatic necrosis (OR = 2.18, 95% CI 1.29 ~ 7.36; P = 0.004); heterogeneous collection (OR = 3.14, 95% CI 1.32 ~ 4.25; P = 0.001; multiple infected collections (OR = 4.51, 95% CI 2.94 ~ 8.63; P = 0.000), CT severity index (OR = 2.16, 95% CI: 1.83 ~ 3.62; P = 0.031). When concerning about MID, the following parameters

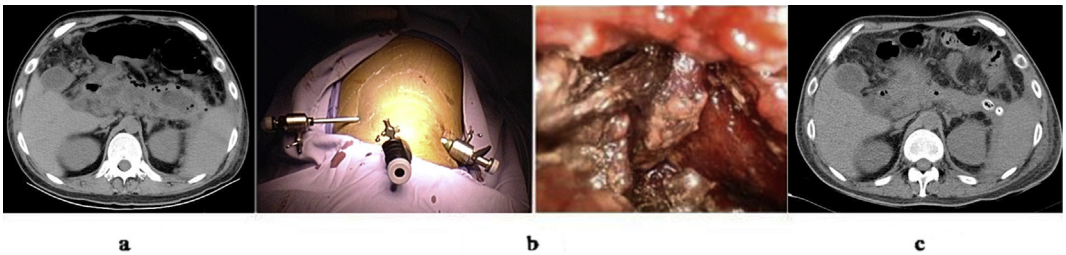

Fig. 4. VAD (retroperitoneoscopy) in a 28-year-old male with a disease duration of four weeks. a. CT scan showing secondary infection of WON at the tail of pancreatic body, where a safe PCD approach could not be confirmed. b. Retroperitoneoscopy showing location of trocar (right lateral position) and pancreatic necrosis. c. CT scan showing substantial improvement 48 days after retroperitoneoscopy. PCD, percutaneous catheter drainage; VAD, video assisted debridement; WON, walled-off necrosis.

Table 2
Possible predictors for failure of PCD and MID in patients with IPN.

Risk factors	Outcome
Demographics	
Age, mean ± standard deviation	51.2 ± 3.1 years
Sex	
male	39
female	15
Etiology	
Biliary	35
High triglyceride	9
Alcoholic	6
Others	4
ECOG score	3.2 ± 0.6
Disease severity factors	
White blood cell count, median (range)	14.3 (4.1–34.5) × 10^9/L
Serum creatinine level, median (range)	125 (53–326) mg/L
Serum procalcitonin, median (range)	1.2 (0.31–5.56) ng/ml
APACHE II score, median (range)	12 (6–21)
Ranson score, median (range)	5 (2–7)
Persistent organ failure > 48 h[a]	9
Morphological factors on CT	
Percentage of pancreatic necrosis	
< 30%	25
30% ~ 50%	18
> 50%	11
Contents of the collection	
homogeneous	6
heterogeneous	45
Maximal length of the collection	15.4 ± 7.7 cm
Spread of infected collections	
solitary	25
multiple	29
CT severity index	
0 ~ 3	5
4 ~ 6	29
7 ~ 10	20

[a] According to modified Marshall score. PCD percutaneous catheter drainage; MID mini-incision drainage; IPN infected pancreatic necrosis; ANC acute necrotic collection; WON wall-off necrosis; ECOG Eastern Cooperative Oncology Group.

were associated with failure of MID in multivariable analyses: heterogeneous collection (OR = 2.99, 95% CI 1.52 ~ 5.10; P = 0.006), multiple infected collections (OR = 4.17, 95% CI 2.77 ~ 8.12; P = 0.000), CT severity index (OR = 2.72, 95% CI 1.78 ~ 4.10; P = 0.005). Taken together, heterogeneous collection, multiple infected collections, CT severity index are the risk factors for failure of both PCD and MID. CT is effective to predict success of such mini-invasive procedures.

Follow-up

For all 54 patients who entered the clinical pathway, the median follow-up time was 22 (2–40) months. There was no recurrent retroperitoneal collection and late complication occurred.

Discussion

A great variety of mini-invasive techniques have been reported for treatment of IPN, including PCD, nephroscope, peritoneoscope and flexible endoscope, all superior to traditional open pancreatic necrosectomy in terms of clinical efficacy, although opinion differs regarding their impact on mortality reduction [2,7–12]. Further, there are no accepted criteria available to aid in the selection of mini-invasive technique, due to advantages and disadvantages of each method. Therefore, the clinical indication for each technique, and single or combined usage of these, requires further investigation.

PCD, with the advantage of being a non-surgical method suitable for critical patients [13], is the most commonly used mini-invasive technique for the treatment of infected pancreatic/peripancreatic necrosis. Since PCD was first reported by Freeny et al. in 1998 [14], a great number of related reports have emerged detailing its use. In 2011, a systematic retrospective analysis [15] showed that the incidence of complications and cure rate of PCD in the treatment of IPN were 21.2% and 55.7%, respectively. However, the report also highlighted the possibility that the efficacy of PCD may be overestimated due to selection bias. The only randomized controlled trial [16] in the report revealed a 35% efficacy rate, similar to the results we present in this study, in which 37.5% (12/32) of patients were cured after PCD, and no complications were found except one case of pancreatic fistula.

The drainage tubes most frequently used for PCD range in caliber from 8 to 28 Fr [15], and one reason for treatment failure is blockage of small caliber tubes, as well as separation of the necrotic area resulting in inadequate drainage. To circumvent this disadvantage, we used MID, which allows the placement of several

Table 3
Results of univariable and multivariable regression for failure of PCD in patients with IPN.

Risk factors	Univariable regression		Multivariable regression	
	OR (95% CI)	P value	OR (95% CI)	P value
Persistent organ failure > 48 h[a]	1.16 (1.08 ~ 3.22)	0.041	1.09 (1.07 ~ 3.38)	0.049
Percentage of pancreatic necrosis (< 30%/30% ~ 50%/ > 50%)	2.21 (1.36 ~ 7.08)	0.005	2.18 (1.29 ~ 7.36)	0.004
Heterogeneous collection	3.08 (1.27 ~ 4.33)	0.002	3.14 (1.32 ~ 4.25)	0.001
Multiple infected collections	4.72 (3.10 ~ 8.73)	0.000	4.51 (2.94 ~ 8.63)	0.000
CT severity index (0 ~ 3/4 ~ 6/ > 7)	2.11 (1.72 ~ 3.19)	0.029	2.16 (1.83 ~ 3.62)	0.031

[a] According to modified Marshall score. PCD percutaneous catheter drainage; IPN infected pancreatic necrosis; ANC acute necrotic collection; WON wall-off necrosis.

Table 4
Results of univariable and multivariable regression for failure of MID in patients with IPN.

Risk factors	Univariable regression		Multivariable regression	
	OR (95% CI)	P value	OR (95% CI)	P value
Persistent organ failure > 48 h[a]	1.10 (1.02 ~ 3.22)	0.044	1.06 (0.91 ~ 3.18)	0.065
Percentage of pancreatic necrosis (< 30%/30% ~ 50%/ > 50%)	1.14 (1.15 ~ 3.08)	0.045	1.05 (0.90 ~ 3.19)	0.061
Heterogeneous collection	2.89 (1.42 ~ 5.91)	0.006	2.99 (1.52 ~ 5.10)	0.006
Multiple infected collections	4.10 (2.54 ~ 7.96)	0.001	4.17 (2.77 ~ 8.12)	0.000
CT severity index (0 ~ 3/4 ~ 6/ > 7)	2.56 (1.70 ~ 4.86)	0.007	2.72 (1.78 ~ 4.10)	0.005

[a] According to modified Marshall score. MID mini-incision drainage; IPN infected pancreatic necrosis; ANC acute necrotic collection; WON wall-off necrosis.

drainage tubes of large caliber (30–36 Fr), improving drainage compared to smaller tubes and resulting in the successful treatment of a further seven patients. Despite the limited sample size, MID is considered safe and simple, and can offset the disadvantages of PCD, as well as avoiding the risk of open surgery.

VAD can be performed using various approaches and endoscopes [7,17–19]. The retroperitoneal approach with nephroscope for pancreatic necrosectomy was first reported by Connor et al. [20], although in that study 5/24 patients still required open surgery following the VAD procedure. In 2010, Lakshmanan et al. [21] cured five IPN patients by nephroscope without open surgery, using similar methods. The ten patients in our study were also cured by nephroscope without open surgery. Whether nephroscopic surgery can fully replace open surgery should be determined by large scale cohort studies, however we believe that fluid inside the abscess cavity can be effectively drained by this method. Where infection is not controlled by MID, it is usually because non-liquefied pancreatic and peripancreatic necrotic tissues in the cavity cannot be adequately drained. However, such necrotic tissue can be completely removed by surgical instruments with the assistance of video under nephroscope, which we believe is likely to achieve the same effect as open surgery.

A further disadvantage of VAD by nephroscope is the lack of a safe retroperitoneal approach: only 53% of the patients in the report by Connor et al. [20] were suitable for mini-invasive surgery by this method. However, in our study the approach was established after PCD and MID, where a complete sinus had been formed, and therefore VAD was not restricted to a retroperitoneal approach, and an intraperitoneal approach could also be used. Retroperitoneoscopic VAD can also effectively remove pancreatic necrotic tissue, as demonstrated by the four cases in our study unsuitable for PCD and MID which progressed straight to this technique, and from other reports in the literature [22–24]. The advantages and disadvantages of retroperitoneoscopic VAD surgery require further investigation due to the limited sample size in the current reports.

In the last two decades, endoscopic therapy of patients with symptomatic walled-off necrosis has been used more and more in clinic practices and with a high rate of efficiency [25–27]. However, endoscopic transmural drainage was associated with higher rate of complication when compared with percutaneous drainage [27] and it also may lead to a deterioration of infection due to the multidrug resistant bacterial from digestive tract. In addition, the ability of debridement under endoscopy is limited. For these reasons, endoscopic treatment was not included in our clinic pathway.

Overall, there are still disadvantages in the use of mini-invasive techniques for the treatment of IPN. First, there are no defined criteria for the clinical indication of mini-invasive techniques. For instance, in our study the time interval between PCD and MID was 4–14 days, and the interval between MID and VAD was 7–19 days, however, elsewhere the time interval between initial PCD and open surgery ranges from 1 to 600 days [15], a considerable difference compared with our study. Second, mini-invasive surgery may need repetition and open surgery may still be necessary. Even though open surgery was not performed on the patients receiving pancreatic necrosectomy using nephroscope and retroperitoneoscopy in this study, the average frequency of surgery was three times, similar to that seen in previous studies of 3–4 interventions [20,21]. Therefore, whilst mini-invasive techniques may reduce the possibility of open surgery, the indication for the use of these techniques and whether they extend hospital stay, increase cost of treatment and delay eventual open surgery all require further investigation.

Nowdays, the predictive factors for successful mini-invasive treatment for IPN are still unclear. Study form *Dutch Pancreatitis Study Group* including 130 patients randomized in the PROPATRIA and the PANTER trials showed that male sex (OR = 0.27; 95% CI: 0.09–0.55; P < 0.01), multiple-organ failure (OR = 0.15; 95% CI: 0.04–0.62; P < 0.01), percentage of pancreatic necrosis (<30%/30%–50%/>50%:OR = 0.54; 95% CI: 0.30–0.96; P = 0.03), and heterogeneous collection (OR = 0.21; 95% CI: 0.06–0.67; P < 0.01) are negative predictors for success of catheter drainage in IPN [28]. Similarly, in our study, we found that heterogeneous fluid collection (OR = 3.14; 95% CI: 1.32 ~ 4.25, P < 0.01 for PCD; OR = 2.99; 95% CI: 1.52 ~ 5.10, P < 0.01 for MID), multiple infected collections (OR = 4.51; 95% CI: 2.94 ~ 8.63; P < 0.01 for PCD; OR = 4.17; 95% CI: 2.77 ~ 8.12, P < 0.01 for MID), CT severity index (0 ~ 3/4 ~ 6/7 ~ 10: OR = 2.16; 95% CI: 1.83 ~ 3.62, P = 0.03 for PCD; OR = 2.72; 95% CI: 1.78 ~ 4.10, P < 0.01 for MID) were the risk factors for failure of both PCD and MID.

Patient mortality in this study was low (7.4%, 4/54). Mini-invasive techniques can significantly reduce the incidence of postoperative organ failure [16], and patients avoid the need for open surgery, which may delay recovery and lead to postoperative complications. Another possible reason for the relatively low mortality in our study may be the small sample size, and only 48.1% (26/54) of the patients having disease duration of more than one week, with the longest being five months on admission.

We conclude that mini-invasive techniques can be regarded as the preferred surgical method for the treatment of AP associated with IPN, and may replace traditional open necrosectomy for pancreatic necrosis. However, whether the application of mini-invasive techniques can reduce mortality requires further study. Due to the complexity of IPN, a combination of multiple mini-invasive techniques may hold the key to improved clinical efficacy in the treatment of this condition.

Acknowledgments

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