Original article

Minimal-access retroperitoneal pancreatic necrosectomy for infected necrotizing pancreatitis: a multicentre study of a step-up approach

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Background: **Various minimally invasive approaches have been described for infected necrotizing pancreatitis. This article describes a modified minimal-access retroperitoneal pancreatic necrosectomy (MARPN) procedure assisted by gas insufflation.**

Methods: **This retrospective, observational study documented patients who had undergone a step-up MARPN between 1 January 2010 and 31 December 2016. A minimum follow-up of 1 year was required for inclusion. The step-up approach involved percutaneous catheter drainage followed by the modified MARPN and necrosectomy. If more than one access site was needed it was categorized as complex MARPN.**

Results: **Of 212 patients with infected necrotizing pancreatitis, 164 (77·4 per cent) underwent a step-up approach. The median number of percutaneous catheter drains and MARPN procedures was 3 (range 1–7) and 1 (1–6) respectively. Ninety patients (54·9 per cent) underwent complex MARPN. For residual necrosis after MARPN, three patients (1·8 per cent) underwent sinus tract gastroscopy, and 11 (6·7 per cent) had sinography combined with a tube change. However, operations in 13 patients (7·9 per cent) required conversion to open surgery. Postoperative complications developed in 103 patients (62·8 per cent). The mortality rate was 6·1 per cent (10 deaths).**

Conclusion: **A step-up approach using a modified MARPN for infected necrotizing pancreatitis is a reasonable option.**

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Introduction

Infected pancreatic necrosis, which often leads to sepsis and multiple organ failure, is one of the most severe complications of necrotizing pancreatitis[1,2]. Infection of necrosis occurs in approximately 30 per cent of patients with necrotizing pancreatitis[3], and the overall mortality rate is approximately 20–30 per cent[3,4]. Currently, treatment of infected necrotizing pancreatitis remains challenging[5–7]. Open necrosectomy has been considered the standard treatment for decades[8]. However, minimally invasive approaches have been increasingly used worldwide, including percutaneous catheter drainage[9,10], laparoscopic necrosectomy[11,12], endoscopic necrosectomy[13–15], video-assisted retroperitoneal debridement[16,17] and minimal-access retroperitoneal pancreatic necrosectomy (MARPN)[18–20]. The advantages of minimally invasive approaches include fewer systemic complications after the intervention and a reduced risk of developing new-onset organ failure[20,21]. Furthermore, these minimally invasive techniques can be performed in a step-up approach: initial percutaneous catheter drainage followed by minimally invasive debridement[7,21].

In the authors' centre, percutaneous catheter drainage has been used for the treatment of infected necrotizing pancreatitis since 2005, and MARPN and video-assisted retroperitoneal debridement since 2008[22–24]. It was noted that necrotic debris floating in saline during MARPN can lead to technical interference and increase the difficulty of debridement. Inspired by laparoscopic surgery and video-assisted retroperitoneal debridement, the MARPN procedure was modified to use gas insufflation instead of saline in 2010[23].

The aim of this study was to describe the technique for a step-up approach (percutaneous catheter drainage followed by modified MARPN) for the management of infected necrotizing pancreatitis, and to evaluate its safety and efficacy.

Methods

A retrospective, observational study was undertaken using information from a prospective database of all patients with infected necrotizing pancreatitis treated by MARPN between 1 January 2010 and 31 December 2016 in two hepatobiliary–pancreatic centres in Beijing, China (People's Liberation Army (PLA) General Hospital and First Affiliated Hospital of Chinese PLA General Hospital). The study followed the STROBE guidelines for observational studies[25]. Patients who underwent percutaneous catheter drainage or video-assisted retroperitoneal debridement alone, or primary open laparotomy, or were treated by other surgical teams, were excluded. The study was approved by the hospital institutional review board (S2019-371-01). Written informed consent was obtained from all patients. Data were collected using the hospital electronic medical record system after institutional review board approval had been obtained.

All computerized medical reports and patient charts were reviewed by two authors, and the following variables were extracted: clinical demographics; aetiology; duration of preoperative and postoperative management; operative characteristics; and short- and long-term outcomes. Preoperative disease severity was evaluated according to Acute Physiology And Chronic Health Evaluation (APACHE) II score, serum C-reactive protein (CRP) level and CT severity index during the 24 h before and after operation.

Imaging

All patients underwent CT before any interventional procedures. CT was used to evaluate the extent of fluid collection and/or pancreatic and peripancreatic necrosis, as well as for targeted radiological intervention and surgical management. MRI or endoscopic ultrasonography was also used to detect necrosis in peripancreatic fluid collections if necessary.

Definitions and treatment strategy

The definition of, and terminology used, for acute pancreatitis and its complications in this study are in accordance with the revision of the Atlanta classification made by the international working group[26]. Infected necrosis was suspected based on the patient's clinical course (sudden-onset fever, and increased CRP and leucocyte levels) or the presence of gas within the fluid collection observed on contrast-enhanced CT[26,27]. Infected necrosis was confirmed by positive culture of pancreatic and/or peripancreatic fluid collected by fine-needle aspiration or during the first drainage procedure[21,28]. The policy was to avoid any intervention in patients treated urgently during the first 4 weeks of the disease, or until infected necrosis had been walled off and demarcated with at least partial liquefaction after a delay of 4–6 weeks. However, for patients with ongoing progressive sepsis and clinical deterioration during this interval, percutaneous drainage was used aggressively under CT guidance. If necessary, more than one drain was placed at the same procedure.

Postoperative complications were assessed according to the Clavien–Dindo classification[29]. Major complications were defined as those with a Clavien–Dindo grade of III or IV. Mortality was defined as death during the hospital admission or during the 3 months after discharge. After discharge, all patients were followed up.

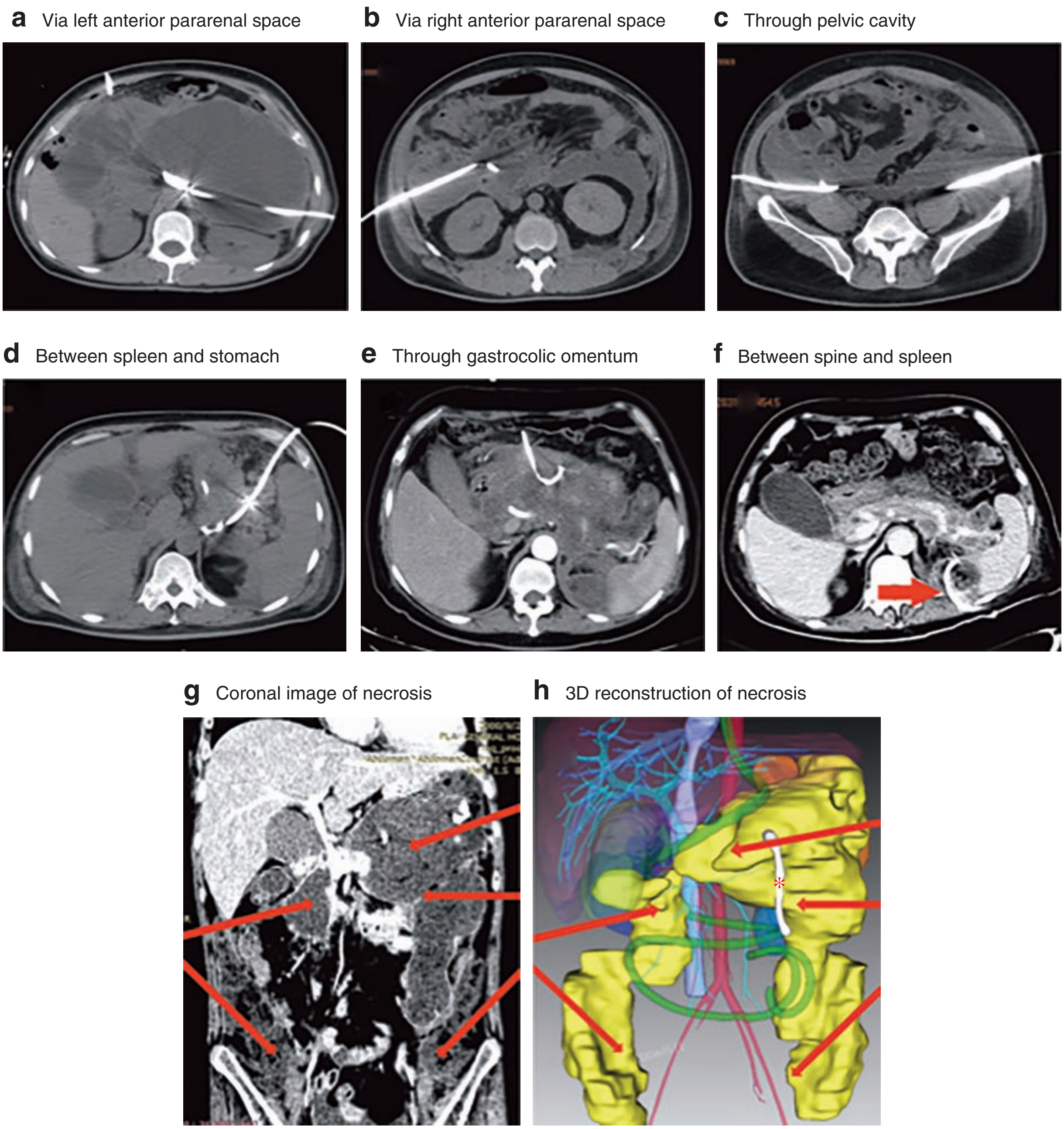
One-year follow-up

Long-term outcomes were assessed, including the development of pancreatic fistula, new-onset diabetes mellitus, pancreatic exocrine insufficiency, and recurrence of acute pancreatitis with or without residual fluid collection.

Radiological techniques

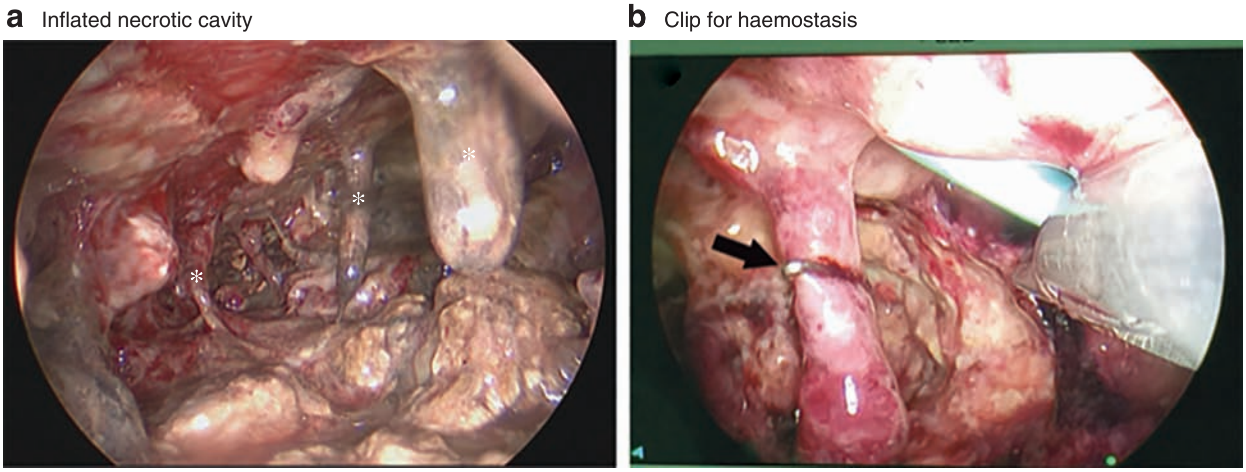
The step-up principle was used[7], with initial percutaneous catheter drainage followed by minimally invasive debridement. The minimum drain size was usually 12 Fr. The puncture route for percutaneous catheter drainage was

Fig. 1 Six percutaneous catheter drainage routes used as access tracks for minimal-access retroperitoneal pancreatic necrosectomy, and images of horseshoe-shaped necrosis



a Route through left anterior pararenal space, **b** route through right anterior pararenal space, **c** bilateral routes through pelvic cavity, **d** transabdominal route through space between spleen and stomach, **e** transabdominal route through gastrocolic omentum and **f** back route (arrow) between spine and spleen. **g** Coronal CT image and **h** three-dimensional (3D) reconstruction of infected necrotizing pancreatitis with horseshoe-shaped necrosis. Red arrows represent five retroperitoneal percutaneous catheter drainage routes; the asterisk shows a transabdominal percutaneous catheter drain.

Fig. 2 Intraoperative views of modified minimal-access retroperitoneal pancreatic necrosectomy



a Pneumoperitoneum inflates the necrotic cavity and facilitates debridement. Vessels (asterisk) in the necrotic tissue are well preserved. **b** A titanium clip (arrow) for haemostasis is shown.

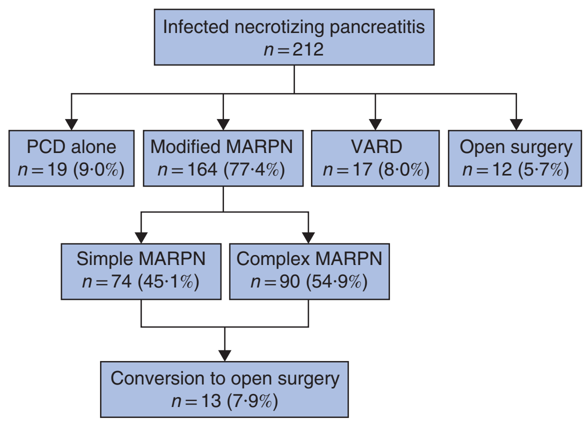
determined by the location of necrosis under CT guidance. Overall, there were six route choices (*Fig. 1*). First, as most of the infected necrosis was in the left retroperitoneal space, access to the necrotic cavity was often obtained via the left flank (between the lower pole of the spleen and the left pararenal space). If peripancreatic necrosis extended towards the lower abdomen, a second percutaneous catheter drain next to the lower pole of the kidney might be needed. Second, the route through the right anterior pararenal space was indicated for right-sided necrosis around the pancreatic head. Third, a route through the pelvic cavity was used in extensive bilateral retroperitoneum necrosis (horseshoe-shaped necrosis) or left-sided necrosis along the retrocolic space. Fourth, in patients with predominant necrosis of the pancreatic head and lesser sac, a route through the gastrocolic omentum was often used. As a transabdominal route, if needed for debridement, sequential dilatation of the sinus tract within 2–3 weeks was necessary to prevent peritoneal contamination by infected necrosis. The fifth route, indicated for peripancreatic necrosis located above the splenic hilus, was also a transabdominal route, through the space between the spleen and stomach. The sixth route was through the back of the body between the spine and spleen; this route was indicated for deep retropancreatic infection.

Strategies for placing percutaneous catheter drains

Retroperitoneal access was preferred over transabdominal access. The percutaneous catheter drainage route was established along the longitudinal axis of the necrotic cavity to achieve the largest range of debridement at a later stage. The puncture angle was slanted slightly to the bottom of the necrotic cavity to avoid a gastrointestinal fistula owing to compression of the drainage tube (*Fig. 1a*). The puncture point was as close to the necrotic cavity as possible to facilitate establishment of an access track for MARPN. If there was extensive pancreatic/peripancreatic necrosis, multiple drains were placed during the first procedure. Finally, based on the percutaneous catheter drainage route and number of drains, the range of debridement was assessed using a two-dimensional picture archiving and communication system (PACS) or a three-dimensional virtual system[30]. If there was an area in the necrotic cavity not visible by nephroscopy, percutaneous catheter drainage planning was revised to achieve complete removal of infected necrosis.

Based on their role in debridement, access tracks can be classified as a main, accessory[31] or alternative. Debridement was predominately performed using the main track. The accessory track supplemented the main track and was used to remove a relatively small amount of necrosis. The alternative track was used to remove residual necrosis located in blind areas of the main/accessory track, as well as to irrigate the necrotic cavity after debridement. The main track usually included left and right routes through the anterior pararenal space. A left- and/or right-sided pelvic cavity route was often used as an accessory track. Two types of transabdominal route and the back route were used as an alternative track. Right-sided MARPN and necrosectomy undertaken through more than one access site was classified as complex MARPN[31].

Fig. 3 Study flow chart



PCD, percutaneous catheter drainage; MARPN, minimal-access retroperitoneal pancreatic necrosectomy; VARD, video-assisted retroperitoneal debridement.

Table 1 Demographic and preoperative data

	No. of patients* ($n = 164$)
Age (years)†	48 (22–84)
Sex ratio (M : F)	117 : 47
Aetiology	
Stones	94 (57·3)
Alcohol	30 (18·3)
Hyperlipidaemia	26 (15·9)
Other	14 (8·5)
Tertiary referral	136 (82·9)
Preoperative antibiotic therapy	121 (73·8)
Extent of pancreatic necrosis (%)	
< 30	38 (23·2)
30–50	33 (20·1)
> 50	42 (25·6)
Peripancreatic necrosis alone	51 (31·1)
Necrosis > 5 cm down paracolic gutter	110 (67·1)
Preoperative organ failure	
Single	19 (11·6)
Multiple	22 (13·4)
Preoperative ICU admission	55 (33·5)
Confirmed infection	151 (92·1)

*With percentages in parentheses, unless indicated otherwise; †values are median (range).

Surgical techniques

Surgical debridement was generally performed 1–2 weeks after percutaneous catheter drainage. The related technique employed for MARPN has been reported previously[18–20]. Briefly, patients were placed in a supine position under general anaesthesia. A 1·5-cm skin incision was made centred on the percutaneous catheter drain. Then, the drain catheter was exchanged over a guidewire for serial renal dilators. Notably, fluoroscopy was not required for drain catheter exchange in this series. If there were multiple percutaneous catheter drains on one side, the main track was usually dilated first. The other tracks were dilated under nephroscopy and used as accessory tracks. Amplatz renal dilators (Cook Urological, Bloomington, Indiana, USA) were used serially to create a 30-Fr tract, and a 10-mm trocar was inserted. A percutaneous nephroscope (Hopkins telescope; Karl Storz Endoskope, Tuttlingen, Germany) with a 6-mm working channel was then passed along the trocar into the necrotic cavity, and suction used to remove pus. Samples were sent for microbiological examination.

Next, during the classical MARPN procedure, copious irrigation and suction was required to create a cavity. Typically, 10–20 litres of irrigation fluid were required[19].

Modified minimal-access retroperitoneal pancreatic necrosectomy

In the modified approach, carbon dioxide was infused to inflate the necrotic cavity instead of saline solution (*Fig. 2*). Retroperitoneal insufflation was set up at a maximum pressure of 8 mmHg to avoid high pressure promoting bacterial translocation. Piecemeal removal of solid necrosis was then performed repeatedly using a fenestrated grasper through the working channel. To avoid bleeding, especially in patients who were within 4 weeks of onset of the disease, debridement was relatively conservative and limited to the removal of loose, easily debrided necrotic tissue. Finally, a 10-Fr catheter sutured to a 28–30-Fr tube drain was placed into the distal end of the necrotic cavity to allow continuous lavage after surgery. All patients underwent CT on postoperative days 5–7 to evaluate the results of necrosectomy and drainage. A video of the modified MARPN procedure is available online (*Video S1*, supporting information).

Treatment of residual necrosis

If residual infected necrosis was suspected, debridement through the main track and/or accessory track was repeated at approximately 7-day intervals. Sinography was preferred for residual necrosis located in blind areas of MARPN, and a new catheter was placed into the residual cavity of infected necrosis under X-ray screening. A small area of isolated infection was addressed by adequate drainage (*Fig. S1*, supporting information). Gastroscopic debridement through the sinus tract was another option for residual necrosis. In contrast to rigid endoscopes, flexible endoscopes could offer various visual angles and thus improve the outcome of endoscopic necrosectomy. Finally,

Table 2 Technical data for step-up approach

	No. of patients* (*n* = 164)
Time to first PCD in the authors' centre (days)†	54 (6–182)
PCD > 28 days after onset	140 (85·4)
No. of percutaneous catheter drains per patient†	3 (1–7)
1	37 (22·6)
2	41 (25·0)
3	52 (31·7)
≥ 4	34 (20·7)
Patients with PCD-related complications	0 (0)
Interval from drainage to surgery (days)†	10 (0–46)
Interval from onset of necrotizing pancreatitis to surgery (days)†	64 (18–193)
Surgery > 28 days after onset	158 (96·3)
Duration of surgery (min)†	70 (30–240)
Intraoperative transfusion of blood products	5 (3·0)
No. of modified MARPN procedures per patient†	1 (1–6)
1	89 (54·3)
2	47 (28·7)
≥ 3	28 (17·1)
Patients having complex modified MARPN procedures	90 (54·9)
Multiple left-sided necrosectomy	25 (15·2)
Bilateral necrosectomy	49 (29·9)
Right-sided necrosectomy	16 (9·8)
Emergency conversion to open surgery	3 (1·8)
Additional PCD needed after MARPN	11 (6·7)

*With percentages in parentheses, unless indicated otherwise; †values are median (range). PCD, percutaneous catheter drainage; MARPN, minimal-access retroperitoneal pancreatic necrosectomy.

open debridement with a small incision (5–7 cm) under CT guidance (*Fig. S2*, supporting information) was used for the management of residual necrosis in some refractory cases. Whenever possible, traditional open necrosectomy was avoided.

Statistical analysis

Continuous variables are expressed as median (range) and were compared using the Wilcoxon signed-rank test. Categorical variables were analysed using McNemar's test. For all tests, statistical significance was set at $P < 0{\cdot}050$. Data were analysed using SPSS® version 17.0 for Windows® (IBM, Armonk, New York, USA).

Results

During the study interval, an intervention, including percutaneous catheter drainage alone, modified MARPN, video-assisted retroperitoneal debridement or open surgery, was undertaken in 212 patients with signs of infected necrotizing pancreatitis (*Fig. 3*), of whom 164 had modified MARPN. Overall, MARPN was performed increasingly, and the role of open surgery gradually declined (*Fig. S3*, supporting information).

Table 3 Findings before and after percutaneous catheter drainage

	Initial period (before drainage)	Preoperative period (after drainage)	*P*†
CT severity index score	9 (4–10)	8 (4–10)	< 0·001
APACHE II score	12 (2–23)	7 (1–26)	< 0·001
C-reactive protein (mg/l)	212 (24–586)	165 (10–473)	< 0·001
Organ failure*	58 (35·4)	41 (25·0)	< 0·001‡

Values are median (range) unless indicated otherwise; *values in parentheses are percentages. APACHE, Acute Physiology And Chronic Health Evaluation. †Wilcoxon signed-rank test, except ‡McNemar's test.

Table 4 Postoperative outcomes after modified minimal-access retroperitoneal pancreatic necrosectomy

	No. of patients* (*n* = 164)
Conversion to open surgery	13 (7·9)
Emergency laparotomy	4 (2·4)
Elective laparotomy	4 (2·4)
Small-incision necrosectomy	5 (3·0)
Sinus tract gastroscopy	3 (1·8)
Sinography combined with a tube change	11 (6·7)
Major complications related to surgery	45 (27·4)
New-onset organ failure	8 (4·9)
Intra-abdominal bleeding	13 (7·9)
Enterocutaneous fistula	29 (17·7)
Others	10 (6·1)
Death	10 (6·1)
Patients with complications	103 (62·8)
Clavien–Dindo grade of complications	
I	48 (29·3)
II	36 (22·0)
III	30 (18·3)
IV	21 (12·8)
Postoperative duration of hospital stay (days)†	20 (5–174)
Long-term complications	65 (39·6)
Persistent pancreatic fistula	15 (9·1)
Incisional hernia	0 (0)
New-onset diabetes	16 (9·8)
New-onset pancreatic exocrine insufficiency	7 (4·3)
Pseudocyst	12 (7·3)
Recurrent pancreatitis	6 (3·7)
Regional portal hypertension	18 (11·0)

*With percentages in parentheses, unless indicated otherwise; †values are median (range).

Demographic data for patients who underwent MARPN are shown in *Table 1*. Preoperative disease severity was assessed within 24 h before operation. Notably, peripancreatic necrosis alone occurred in 51 patients (31·1 per cent). *Table 2* shows detailed data regarding percutaneous catheter drainage and the modified MARPN procedure. A median of 1 (range 1–6) MARPN procedures was performed in each patient. The severity of disease declined significantly after percutaneous catheter drainage (*Table 3*). Postoperative complications developed in 103 patients (62·8 per cent) (*Table 4*). No complications related to pneumoperitoneum were recorded. Ten patients (6·1 per cent) in this study died within 90 days after surgery. Causes of death were ongoing multiple organ failure (8) and postoperative bleeding (2). Eight patients (4·8 per cent) underwent traditional open laparotomy after modified MARPN for the following reasons: abdominal bleeding (4), colonic fistula (2), gallbladder perforation (1) and bowel obstruction (1). Median duration of follow-up was 41 (range 13–96) months. Long-term complications typically associated with necrosectomy were assessed. Regional portal hypertension and new-onset diabetes were the two most common complications.

Discussion

A staged multidisciplinary step-up approach is being used increasingly in the management of infected necrotizing pancreatitis[7,32–34]. In the present study, patients had a significantly decreased APACHE II score, incidence of organ failure, CT severity index and CRP level after undergoing percutaneous catheter drainage, in accordance with previous reports[10,35]. John and colleagues[36] first reported a patient with infected necrotizing pancreatitis managed with a step-up approach using the MARPN technique.

The site of percutaneous catheter drain placement is a key factor in determining the extent of MARPN. However, percutaneous catheter drainage route choices have seldom been reported in previous studies[9,19,37–39]. Six percutaneous catheter drainage routes have been summarized systematically here, contributing to broadening the indication for MARPN and improving the efficacy of debridement. A consensus on the strategy for percutaneous catheter drainage placement is lacking[27,40], and percutaneous catheter drains have usually been placed one by one after an interval of 72 h for observation[21]. In the authors' experience, if there is extensive necrosis, multiple drains should be placed at the first procedure. Multiple drains and adequate drainage have four advantages over a single drain and inadequate drainage. Above all, they help in controlling sepsis as soon as possible[35]. Adequate drainage may also promote fluid collection wall maturation and necrotic tissue demarcation, thereby increasing surgical safety and the possibility of a single debridement procedure[17]. In addition, multiple percutaneous catheter drains are helpful for postoperative retroperitoneal irrigation and thereby accelerate patient recovery[35]. More importantly, if a single percutaneous catheter drain is placed, or unreasonable percutaneous catheter drainage procedures are undertaken in patients with extensive peripancreatic necrosis, the necrotic cavity will collapse to some extent after drainage, potentially leading to isolated areas of necrosis and an inability to establish the access track for subsequent MARPN. Therefore, a proactive percutaneous catheter drainage strategy is recommended for infected necrotizing pancreatitis[10]. No percutaneous catheter drainage-related complications occurred in the present series. In a systematic review[38] of percutaneous catheter drainage as a primary treatment for necrotizing pancreatitis, nine percutaneous catheter drainage procedure-related complications were described (2·5 per cent).

It was reported by the Liverpool team[31] that a median of three procedures was needed for adequate necrosectomy using the MARPN technique. The median CT severity index score, which indicates the extent of pancreatic and peripancreatic necrosis, was 9 in their series. In the present study, a median of one MARPN procedures was performed, and the median preoperative CT severity index score was 8. Notably, the present study included 90 patients (54·9 per cent) who had a complex MARPN procedure, which reflects the high level of difficulty in treating patients in this series. The authors believe that the main reason for this is the high incidence of extensive peripancreatic necrosis in the present study. In other studies[35,41], extrapancreatic necrosis was significantly associated with grade of acute pancreatitis and surgical intervention. MARPN became difficult and time-consuming because of the spatial separation of necrotic tissue in these patients. Combined use of main, accessory and alternative tracks contributes to decreasing the blind zone in debridement and residual necrosis, improving the efficacy of the necrosectomy.

MARPN[20] and video-assisted retroperitoneal debridement[21] are landmark techniques for minimally invasive retroperitoneal necrosectomy, and have gained widespread acceptance. To improve the efficacy and safety of classical MARPN, carbon dioxide gas was used instead of saline during debridement. This modified technique can be considered a hybrid between classical MARPN and laparoscopy/video-assisted retroperitoneal debridement. There are four major advantages of the above modification in the authors' experience. First, a clear field of view without necrotic debris floating in saline makes the technique easier. Second, the necrotic cavity is inflated during pneumoretroperitoneum facilitating detection of hidden focal infection. Third, the modification allowed better control of intraoperative bleeding; bleeding points could be identified, grasped or coagulated and titanium clips could be used for haemostasis during debridement. In the present series, five patients received a blood transfusion during necrosectomy, and conversion to open surgery was required in three patients because of intraoperative bleeding. Fourth, video-assisted retroperitoneal debridement involves a 5–7-cm incision, whereas MARPN uses a 1·5-cm incision, which is less invasive and helps prevent incisional hernia.

In the present study, postoperative complication and mortality rates were 62·8 and 6·1 per cent respectively. The Liverpool team[31] reported corresponding rates of 64·4 and 11·2 per cent between 2009 and 2013 using the MARPN technique. Both studies included a high-risk group. In recent reports[17,20,21,27,31] of various minimally invasive retroperitoneal approaches, the postoperative morbidity and mortality rates of infected necrotizing pancreatitis ranged from 30 to 90 per cent and from 0 to 20 per cent respectively, depending on the severity of disease at the time of necrosectomy. However, it is difficult to compare these outcomes because of heterogeneous patient populations. The authors believe that the low mortality rate in the present series can be attributed mainly to the step-up approach and the low incidence of new-onset organ failure after MARPN (4·9 per cent)[21,42].

Residual necrosis after minimally invasive necrosectomy is a challenging problem[17]. In the present study, three minimally invasive approaches to removal of residual necrosis were used: sinography combined with a tube change, sinus tract gastroscopy and small-incision necrosectomy. Sinus tract endoscopy with a flexible endoscope for necrosectomy in patients with infected pancreatic necrosis was first reported by Carter and colleagues in 2000[18]. The present study indicates that sinus tract gastroscopy can play a role in the management of residual necrosis after MARPN. Sinography combined with percutaneous catheter drainage is a common technique used for the treatment of enterocutaneous fistula and intra-abdominal abscess. For small-incision necrosectomy under CT guidance, it is an effective method for removing an isolated infection. Here, these adjuvant techniques were used successfully in 19 patients (11·6 per cent) and decreased the rate of conversion to traditional open necrosectomy owing to residual necrosis.

Some limitations should be mentioned. This retrospective study lacked controls treated with classical MARPN using direct necrosectomy instead of a step-up approach. Recently, Kumar and co-workers[43] reported that direct endoscopic necrosectomy may be superior to a step-up approach for walled-off pancreatic necrosis with suspected or established infection. To further establish the value of the step-up approach using MARPN and improve the stratification of patients for management, an RCT is being considered in the authors' centre. The technical details are still being refined and the present study reflects the learning-curve stage. Full standardization and further randomized prospective evaluations of the present techniques are necessary in the future[32].

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Z.-W.L., S.-Z.Y. and P.-F.W. contributed equally to this work. S.-C.L., S.-W.C. and J.-H.D. are joint senior authors.

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Supporting information

Additional supporting information can be found online in the Supporting Information section at the end of the article.