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Comparison between minimally invasive and open surgical treatment in necrotizing pancreatitis

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ARTICLE INFO

Article history:
Received 10 July 2016
Received in revised form
20 September 2016
Accepted 26 October 2016
Available online 2 November 2016

Keywords:
Acute pancreatitis
Open necrosectomy
Percutaneous catheter drainage
Endoscopic drainage
Minimally invasive treatment

ABSTRACT

Background: Minimal access techniques have gained popularity for the management of necrotizing pancreatitis, but only a few studies compared open necrosectomy with a less invasive treatment. The aim of this study was to evaluate the outcomes of minimally invasive treatment for necrotizing pancreatitis in comparison with open necrosectomy.

Materials and methods: This retrospective study included 70 patients who underwent minimally invasive intervention or open surgical debridement for necrotizing pancreatitis between January 2007 and December 2014. Data were analyzed for postoperative morbidity and outcome.

Results: Of 70 patients, 22 patients underwent primary open necrosectomy and 48 patients were treated with minimally invasive techniques. Percutaneous and endoscopic drainage were successful in 34.9% and 75.0% of patients, respectively. The rates of postoperative new-onset organ failure and intensive care unit stay were significantly lower in the minimally invasive group (25.0% *versus* 54.5%; $P = 0.016$, and 29.2% *versus* 54.5%; $P = 0.041$, respectively). Gastrointestinal fistulas occurred more frequently after primary open necrosectomy (36.4% *versus* 10.4%; $P = 0.009$). Mortality was comparable in both groups (18.6% *versus* 27.3%; $P = 0.420$). Mortality for salvage open necrosectomy was similar to that for primary open debridement (28.6% *versus* 27.3%; $P = 0.924$). The independent risk factors for major postoperative complications were primary open necrosectomy ($P = 0.028$) and shorter interval to first intervention ($P = 0.020$). Mortality was independently associated only with older age ($P = 0.009$).

Conclusions: Minimally invasive treatment should be preferred over open necrosectomy for initial management of necrotizing pancreatitis.

This study was presented in part at the 67th Congress of the Polish Surgical Association on September 10, 2015 in Lublin, Poland.

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http://dx.doi.org/10.1016/j.jss.2016.10.022

Introduction

In the early 1990s, Bradley *et al.*[1] suggested that some patients with sterile pancreatic necrosis recover without surgery. Since then medical management of necrotizing pancreatitis (NP) has been generally adopted. However, a considerable number of patients with NP still require intervention. Traditionally, these patients underwent open necrosectomy which is a morbid operation leading to the complication rates of 43%-89% and mortality of 9%-39%.[2-7] Open necrosectomy, once considered the "*gold standard*" procedure for infected pancreatic necrosis, has been increasingly challenged by less invasive methods. Minimal access techniques have been developed to reduce surgical stress, and thereby limit its deleterious influence on patient's condition. Several case series of minimally invasive treatment for NP showed relatively low morbidity and mortality,[8-11] but one of the concerns was selection bias which might be a confounding factor favoring less invasive approach. The minimally invasive techniques used in NP include percutaneous catheter drainage (PCD), endoscopic drainage, and retroperitoneal necrosectomy under videoscopic guidance. The most common technique used as first intervention is percutaneous drainage. PCD was shown to be the definitive and only treatment in 55.7% of cases of NP.[12] There are two basic modifications of retroperitoneal necrosectomy: video-assisted retroperitoneal debridement (VARD) and minimal access retroperitoneal pancreatic necrosectomy (MARPN). The average efficacy of retroperitoneal necrosectomy by either of these techniques varied between 60% and 88%.[9,11,13,14] Similarly, endoscopic procedures for walled-off necrosis achieved a high success rate of 75%-100%.[10,15,16] Despite encouraging outcomes from minimally invasive case series, prolonged ineffective treatment and ultimate conversion to open necrosectomy might result in increased mortality.[17,18] Furthermore, the factors which allow prediction of success of minimally invasive techniques remain unclear, and we are still unable to identify *a priori* patients who are poor candidates to less invasive treatment that would otherwise benefit from a forefront open necrosectomy.

To date, there have been published only a few studies comparing minimal access techniques with open necrosectomy,[13,19-23] two of which were randomized clinical trials.[19,21] One of these was the Pancreatitis, Necrosectomy Versus Step Up Approach (PANTER) trial which compared the "*step-up*" approach with open necrosectomy.[19] The step-up arm included percutaneous or endoscopic drainage followed by VARD, if necessary. This seminal study showed that the minimally invasive step-up approach was associated with a reduced rate of the composite end point of major complications or death, compared with open necrosectomy (40% *versus* 69%, $P = 0.006$). The other study was the Pancreatitis, Endoscopic Transgastric Versus Primary Necrosectomy in Patients with Infected Necrosis (PENGUIN) trial which evaluated endoscopic necrosectomy in comparison with surgical necrosectomy.[21] Of 10 patients, four patients in the primary necrosectomy arm underwent laparotomy, whereas the remaining patients had VARD. One of the inclusion criteria was eligibility for both endoscopic and open necrosectomy, which also created a selection bias and significantly limited the applicability of the results from this study only to a highly selected group of patients. In addition, the study was criticized for excessive mortality in the surgical necrosectomy arm which reached 40%.

The purpose of this study was to evaluate the outcomes of minimally invasive treatment in comparison with primary open necrosectomy for symptomatic NP.

Materials and methods

Patients

Between January 2007 and December 2014, 392 patients were admitted to our department with the diagnosis of acute pancreatitis. One hundred forty-seven patients (37.5%) had NP. The study included all the consecutive patients who had NP and required interventional or surgical treatment. The patients treated surgically for abdominal compartment syndrome during the early phase of disease were excluded. Patients who had already undergone surgical debridement or percutaneous drainage in the referring hospital or had a past history of pancreatic partial resection or necrosectomy were not included in the study either. Excluded from the study were also patients referred as outpatients for the management of longstanding sequelae of acute pancreatitis such as walled-off necrosis or pancreatic pseudocysts which had persisted for months since the index episode of the disease. The demographic, clinical, perioperative variables and outcomes were compared between the group treated with minimally invasive techniques (MIN) and the group undergoing primary open necrosectomy (OPEN). Major postoperative complications included new-onset organ failure, postoperative hemorrhage, and gastrointestinal fistula. Organ failure was regarded as organ dysfunction score of ≥ 2 points in modified Marshall scale.[24] New-onset organ failure was recognized if it was not present on the day of initial invasive treatment and occurred anytime thereafter. Persistent organ failure was defined as one lasting longer than 48 h. Postoperative pancreatic fistula was not regarded as a major postoperative complication for two reasons. First, with modern techniques of surgical necrosectomy, only demarcated and loose necrosis is bluntly removed, and thus subsequent pancreatic fistula results from the underlying disease process and ductal disruptions rather than from the operation itself. Second, the incidence of pancreatic fistula after necrosectomy or PCD might approach 91% and to a certain degree, depends on its definition.[7,25] Pancreatic fistula was defined in this study as an amylase-rich fluid outflow through a drain or surgical wound at the time of discharge or requiring interventional treatment.

The study was approved by the Institutional Ethics Committee Board.

Invasive treatment of NP

Routine medical treatment for acute pancreatitis consisted of intravenous fluids, analgesics, and nutritional support

preferably by enteral route. Prophylactic antibiotics were used in 58.6% of cases, and for 34.3% of patients, this information was not available. Invasive treatment was postponed for as long as possible. Fine needle aspiration for confirmation of infection was not practiced routinely. The indications for intervention were suspected infection of pancreatic necrosis, bleeding into the necrotic collections, pressure symptoms due to expanding collections such as persistent abdominal pain or gastric outlet syndrome. Up to 2006, most patients with acute NP, who required invasive treatment, were managed with open necrosectomy in our institution. Since 2007, patients have been considered for minimally invasive treatment. We use the minimally invasive techniques such as PCD, endoscopic drainage or necrosectomy, and MARPN. The initial procedure is usually PCD. The access site depends on the location of the necrotic collections and multiple catheters are placed if necessary. The preferred percutaneous access is through the left retroperitoneum or anteriorly through the gastrocolic omentum. Endoscopic drainage is chosen in patients with necrotic collections limited to the lesser sac in whom PCD access is deemed difficult or there is an underlying disconnected duct syndrome. Endoscopically, the collections are drained through the stomach or duodenum using one access site for 1-2 stents. Endoscopic necrosectomy is performed for poorly resolving collections with abundant particulate debris. Failed percutaneous drainage is an indication for MARPN if feasible. Our modified technique of MARPN has been described in detail elsewhere.[26] In short, we use a single-access port (SILS; Covidien Inc, Norwalk, CT) placed through a short incision in the left lumbar region. Necrotic collections are accessed through the left retroperitoneum, and loose necrotic debris is removed piecemeal by means of laparoscopic grasping forceps under visual guidance of a laparoscope. Open necrosectomy is performed as upfront management or as a salvage operation for failed minimally invasive treatment. Our technique of pancreatic necrosectomy is tailored to the extent of pancreatic and peripancreatic necrosis. Bilateral subcostal or midline incisions are used according to the surgeon's preference. The preferred approach is through the gastrocolic omentum. Necrotic debris is removed bluntly, and the retroperitoneum is copiously irrigated. Drains are left for gravitational drainage.

Statistical analysis

Statistical analysis was performed using Stata 14 software (Stata Corp, College Station, TX, 2015). Descriptive statistics were presented as medians and interquartile ranges (IQR) or number and proportions. The Student's *t*-test or Mann–Whitney U tests were used for continuous data, and the Fisher exact test or Chi-square Pearson tests were used for categorical data analysis where appropriate. Two-sided *P*-value of < 0.05 was regarded statistically significant. Trends over time were assessed using the linear trend regression. Multivariate logistic regression was used to assess which factors were significant for the prediction of major postoperative complications and mortality in patients with NP who required intervention. The factors significant in the univariate analysis ($P \leq 0.1$) were included in the multivariate analysis. A forward stepwise selection analysis was carried out. If data were missing, the cases were excluded from the analyses for the specific parameters in the case of descriptive statistics and tests, and the whole cases needed to be excluded from the regression analysis.

Results

Treatment modality selection for NP

Of 70 patients with symptomatic NP who required intervention, 22 patients underwent primary open necrosectomy and 48 patients received minimally invasive treatment. The proportion of patients managed initially with minimally invasive techniques increased from 50% in 2007 to 83% in 2014 (Fig. 1). However, there was no clear pattern with regard to changes in the ratios of utilization of minimally invasive therapy over time which was evidenced by the coefficient of determination of the linear trend regression of merely 0.03.

Primary open necrosectomy was selected because of the following reasons: surgeon's preference ($n = 11$), percutaneously or endoscopically inaccessible necrotic collection ($n = 7$), and concomitant complications not amenable to minimally invasive treatment ($n = 4$). Complications requiring open surgery were active bleeding into the necrotic collection ($n = 3$) and toxic megacolon ($n = 1$).

Demographic and clinical characteristics of the study groups

The study groups did not differ with regard to demographic and clinical variables (Table 1). Computed Tomography Severity Index score, extent and location of necrosis, and frequency of preinterventional organ failure were all comparable in both groups. Most patients were referrals (78.6%). The most common indication for invasive treatment was suspected or proven infection of pancreatic necrosis (82.9%); 41 of 48 patients in the MIN group and 17 of 22 patients in the OPEN group (85.4% *versus* 77.3%, $P = 0.401$). Two of these patients in the OPEN group had concomitant septic bleeding into the necrotic collection, and one patient had toxic megacolon. Other indications for intervention were persistent pressure symptoms: 7 of 48 patients and 5 of 22 patients in the MIN and OPEN groups respectively (14.6% *versus* 22.7%, $P = 0.486$). One patient from the OPEN group underwent operation because of acute bleeding into a sterile necrotic collection. Culture of the specimens collected at the first invasive procedure was positive in 72.8% of patients. Infection was monomicrobial in 66.7% of cases. The timing of the initial procedure was comparable in both groups. The median interval from the onset of acute pancreatitis to intervention was 34.5 d (IQR: 24-53 d; Table 2).

Primary open necrosectomy

A median of two surgical debridements (IQR: 1-7) was performed per patient. The percentage of patients who required subsequent relaparotomies was 54.5%. Apart from debridement and drainage, an additional procedure was necessary in 27.3% of patients at the initial operation or re-explorations. These procedures included splenectomy ($n = 2$), partial

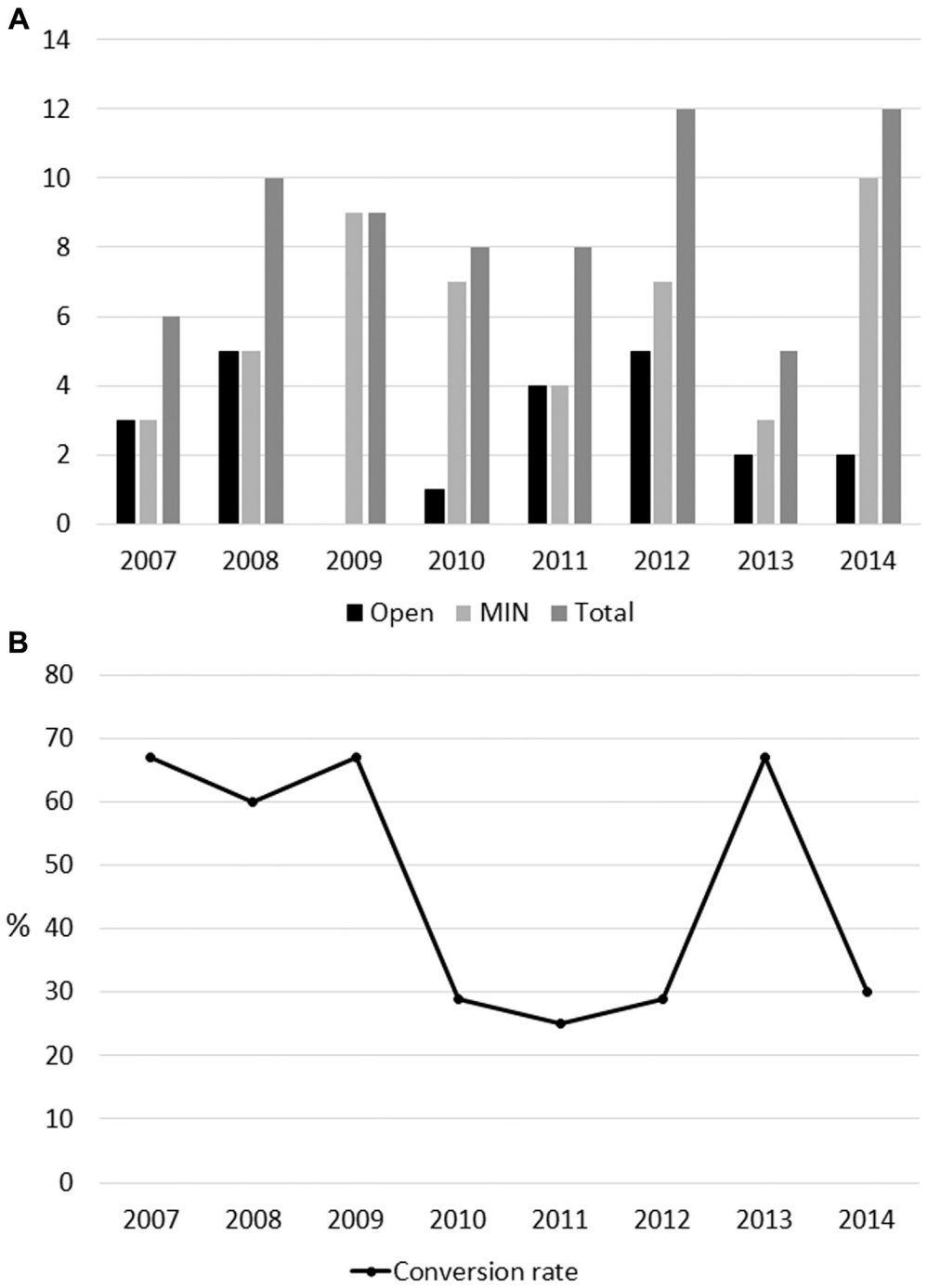

Fig. 1 – Trends in minimally invasive and open surgical treatment for necrotizing pancreatitis over an 8-y period: (A) proportion of minimally invasive procedures (MIN) and open necrosectomies (OPEN) in the consecutive years; (B) rate of conversion from minimally invasive treatment to open surgery.

resection of the small and/or large intestine ($n = 3$), and antrectomy combined with segmental colectomy ($n = 1$). The median duration of the first necrosectomy was 117.5 min (IQR: 90-130 min).

Minimally invasive treatment

Figure 2 summarizes interventions in the group of minimally invasive treatment. All but one patient selected for minimally invasive treatment were managed according to the "*step-up*" approach. One patient had MARPN done as the first procedure. Of 48 patients, 43 patients underwent initially PCD, and four patients had endoscopic therapy. A median of one access site (IQR: 1-2) was used per patient at the time of the first percutaneous drainage. Additional percutaneous procedures were necessary in 32.6% of these patients. A median of one PCD (IQR: 1-2) was performed per patient. Conversion from PCD to salvage open necrosectomy was required in 19 of 43 patients

Table 1 – Baseline characteristics of the patients with NP who underwent interventional or operative treatment.

Characteristic	Overall	Minimally invasive treatment ($n = 48$)	Primary open necrosectomy ($n = 22$)	P value
Median age, y (IQR)	50 (37-61)	50.5 (37-59.5)	49 (36-61)	0.960
Male sex, No (%)	54 (77.1)	38 (79.2)	16 (72.7)	0.551
Etiology, No (%)				
Alcohol	43 (61.4)	31 (64.6)	12 (54.6)	
Lithiasis	13 (18.6)	9 (18.8)	4 (18.2)	0.577
Other	14 (20.0)	8 (16.7)	6 (27.3)	
Median BMI, kg/m^2 (IQR)	26 (24-30)	26 (23-30.5)	27 (26-30)	0.400
Tertiary referrals, No (%)	55 (78.6)	36 (75.0)	19 (86.4)	0.282
Median CTSI*, points (IQR)	8 (4.5-10)	8 (4-10)	8 (6-10)	0.607
Necrosis of pancreatic parenchyma*, No (%)				
No necrosis	16 (23.5)	12 (26.1)	4 (18.2)	
<30%	13 (19.1)	8 (17.4)	5 (22.7)	0.824
30-50%	10 (14.7)	6 (13.0)	4 (18.2)	
>50%	29 (42.6)	20 (43.5)	9 (40.9)	
Extrapancreatic necrosis alone*, No (%)	16 (23.5)	12 (26.1)	4 (18.2)	0.472
Central necrosis*, No (%)	19 (27.9)	10 (21.7)	9 (40.9)	0.099
Necrotic collection extending along the mesentery root, No (%)	17 (24.3)	9 (18.8)	8 (36.4)	0.111
Necrosis extending into the pararenal regions, No (%)	49 (70.0)	34 (70.8)	15 (68.2)	0.822
WON*, No (%)	51 (75.0)	37 (80.4)	14 (63.6)	0.134
Infected necrosis, No (%)	58 (82.9)	41 (85.4)	17 (77.3)	0.401
Severe acute pancreatitis, No (%)	10 (14.3)	8 (16.7)	2 (9.1)	0.400
Organ dysfunction at any time before intervention, No (%)	12 (17.1)	8 (16.7)	4 (18.2)	0.876
Multiple organ dysfunction at any time before intervention, No (%)	6 (8.6)	4 (8.3)	2 (9.1)	0.916
Persistent organ dysfunction before intervention, No (%)	10 (14.3)	8 (16.7)	2 (9.1)	0.400
Organ dysfunction on the day of intervention, No (%)	5 (7.1)	4 (8.3)	1 (4.5)	0.568
Median CRP, mg/L (IQR)	222 (151-268)	222.5 (160.5-275)	217 (144-268)	0.987
Median WBC, $\times 10^9$/L (IQR)	12.2 (8.1-17.5)	12.4 (8.1-18.3)	10.3 (7.8-16.7)	0.210
Median serum albumin, g/dL (IQR)	2.4 (2.1-3.0)	2.35 (2.2-3.0)	2.4 (1.95-3.0)	0.392
ICU before intervention, No (%)	11 (15.7)	6 (12.5)	5 (22.7)	0.275

BMI = body mass index; CRP = C-reactive protein; CTSI = Computed Tomography Severity Index; ICU = Intensive Care Unit; WBC = white blood cell count; WON = walled-off necrosis.
*Excluded two patients who did not have contrast-enhanced computed tomography because of allergy to contrast media.

(44.2%). The reasons for conversion were ongoing sepsis ($n = 13$), hemorrhage ($n = 3$), and intraperitoneal leakage ($n = 3$). Three patients died while treated with PCD and did not undergo open surgery. These patients were not regarded as candidates to open surgery because of poor general condition, and other minimally invasive procedures were not feasible. Six of 43 patients (13.9%) were assigned to MARPN because of ongoing local sepsis despite percutaneous drainage. In one of these patients, there was a need for conversion to salvage open necrosectomy because of intraperitoneal leakage. Overall, one or two MARPN sessions were necessary for recovery. Endoscopic therapy was performed only in patients in whom the necrotic collections were confined to the lesser sac. One of the four patients required conversion to open necrosectomy because of intraperitoneal leakage. In all, the rate of conversion to open necrosectomy decreased from 66.7% to below 30% after 3 y of our experience with minimally invasive techniques and remained stable thereafter except for the year 2013. However, there was no clear pattern with regard to the rate of conversions over time. The coefficient of determination for the linear trend regression was 0.24 for conversions to open necrosectomy in the consecutive years.

Outcomes of minimally invasive and open surgical treatment

Minimally invasive treatment was successful in 24 of 48 patients (50.0%) selected for such a management. The success rates for percutaneous and endoscopic drainage were 34.9% (in 15 of 43 patients) and 75.0% (in three of four patients), respectively. There was a trend toward a decreased rate of major postoperative complications in the MIN group in comparison with OPEN group (41.7% *versus* 63.6%; $P = 0.088$). The incidence of postoperative new-onset organ failure was significantly lower in patients who underwent primarily minimally invasive treatment (25.0% *versus* 54.5%; $P = 0.016$).

Table 2 – Management and outcomes in patients with NP who underwent minimally invasive or open surgical treatment.

Variable	Overall	Minimally invasive treatment ($n = 48$)	Primary open ($n = 22$)	P value
Median time to first intervention, d (IQR)	34.5 (24-53)	31.5 (24-50.5)	40.5 (27-71)	0.628
Reintervention, No (%)	46 (65.7)	34 (70.8)	12 (54.5)	0.183
Median number of reinterventions per patient, (IQR)	2 (1-2)	2 (1-2)	2 (1-2.5)	0.472
Conversion to open necrosectomy, No (%)	–	21 (43.8)	n/a	–
Postoperative new-onset organ failure, No (%)	24 (34.3)	12 (25.0)	12 (54.5)	0.016
Postoperative ICU, No (%)	26 (37.1)	14 (29.2)	12 (54.5)	0.041
Medical morbidity, No (%)	17 (24.3)	14 (29.2)	3 (13.6)	0.187
Major postoperative complications, No (%)	34 (48.6)	20 (41.7)	14 (63.6)	0.088
Bleeding, No (%)	14 (20.0)	8 (16.7)	6 (28.6)	0.258
Pancreatic fistula, No (%)	17 (24.3)	10 (20.8)	7 (31.8)	0.320
GI fistula, No (%)	13 (18.6)	5 (10.4)	8 (36.4)	0.009
Mortality, No (%)	15 (21.4)	9 (18.8)	6 (27.3)	0.420
Postoperative LOS, d (IQR)	48.5 (28-70)	49 (26-72)	40.5 (29-53)	0.467

GI = gastrointestinal; ICU = intensive Care Unit; LOS = length of stay; n/a = not applicable.

Similarly, a lower proportion of patients required intensive care treatment after minimally invasive management (29.2% *versus* 54.5%; $P = 0.041$). Gastrointestinal fistulas occurred more frequently after primary open necrosectomy (36.4% *versus* 10.4%; $P = 0.009$). There were no statistical differences in mortality between the MIN and OPEN groups (18.8% *versus* 27.3%; $P = 0.420$). The mortality rate in patients from the MIN group who eventually required salvage open necrosectomy was comparable with that for primary open debridement (28.6% *versus* 27.3%; $P = 0.924$). Overall mortality was 28.6% for patients intervened within the first 4 wk, and thereafter decreased to 16.7% ($P = 0.234$).

The results of univariate and multivariate analyses are shown in Tables 3-5. In the univariate analysis, the risk factors significant for major postoperative complications were presence of organ failure at any time before intervention ($P = 0.017$), persistent organ failure ($P = 0.047$), unsuccessful minimally invasive treatment ($P = 0.001$), preoperative intensive care unit stay ($P = 0.013$), shorter time interval to intervention ($P = 0.024$), necrosis extending along the paracolic gutters ($P = 0.009$) or the mesenteric root ($P = 0.012$), and the disconnected pancreatic duct syndrome ($P = 0.019$). Whereas a high body mass index ($P = 0.082$) and primary open necrosectomy ($P = 0.092$) showed a trend toward significance for major postoperative complications. In the multivariate analysis, only primary open necrosectomy ($P = 0.028$) and a shorter time interval to intervention ($P = 0.020$) were significant. All patients who had organ failure present on the day of the first intervention developed major postoperative complications, and therefore this variable could not be included in the multivariate analysis because of its non-zero variance in the subsamples.

The risk factors significant for mortality in the univariate analysis were age ($P = 0.035$), body mass index ($P = 0.016$), NP without parenchymal necrosis ($P = 0.022$), and necrosis extending along the mesenteric root ($P = 0.028$). While presence of organ failure on the day of intervention ($P = 0.051$) showed a trend toward significance for mortality. However, increased mortality remained independently associated only with older age ($P = 0.009$) in the multivariate analysis.

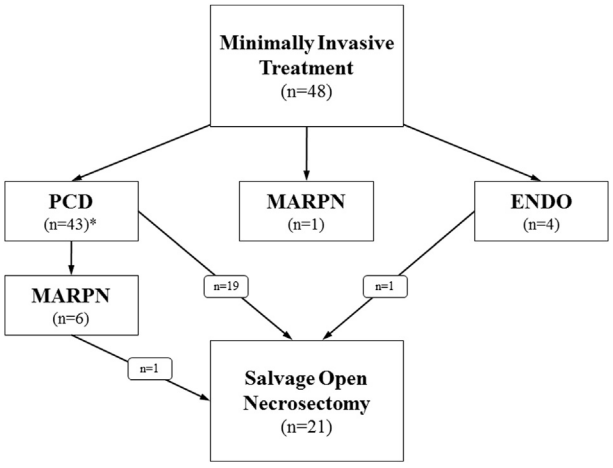

Fig. 2 – The flowchart summarizes the minimally invasive management in patients with necrotizing pancreatitis. *Three patients died without open surgery.

Discussion

In recent decades, we have witnessed a change in the treatment of NP from open necrosectomy toward minimally invasive techniques. This strategy was summarized in the last International Association of Pancreatology/American Pancreatic Association guidelines for the management of acute pancreatitis which recommend initial percutaneous or endoscopic drainage followed by endoscopic or surgical necrosectomy if necessary.[27] The choice of initial intervention in NP depends on location and extension of the necrotic collections, timing of intervention, and expertise of the treating

Table 3 – Univariate logistic regression analysis predictors for major postoperative complications.

Variables	OR	95% CI	P value
Minimally invasive treatment	0.408	−1.937, 0.145	0.092
Age (y)	0.994	−0.038, 0.026	0.719
BMI, kg/m^2	1.112	−0.013, 0.225	0.082
CTSI, point	0.890	−0.311, 0.079	0.242
Pancreatic necrosis (%)	0.993	−0.022, 0.008	0.358
Necrotic collection limited to lesser sac	0.216	−2.689, −0.380	0.009
Preoperative organ failure*	7.083	0.352, 3.563	0.017
Preoperative multiple organ failure*	6.034	−0.405, 4.000	0.110
Preoperative persistent organ failure*	5.231	0.023, 3.286	0.047
Preoperative ICU stay*	14.583	0.560, 4.800	0.013
ICU (d)*	0.919	−0.351, 0.182	0.533
Successful minimally invasive treatment	0.088	−3.829, −1.043	0.001
Interval to intervention (d)	0.978	−0.041, −0.003	0.024
EXPN	2.774	−0.170, 2.211	0.093
Necrotic collection along the mesentery	4.952	0.351, 2.848	0.012
Disconnected duct syndrome	0.246	−2.570, −0.232	0.019
Infected pancreatic necrosis	2.143	−0.544, 2.068	0.253

BMI = body mass index; CI = confidence interval; CTSI = Computed Tomography Severity Index; EXPN = NP without parenchymal necrosis; ICU = intensive care unit; OR = odds ratio.
*Anytime in the period preceding the first intervention.

Table 4 – Univariate logistic regression analysis predictors for mortality.

Variables	OR	95% CI	P value
Minimally invasive treatment	0.615	−1.671, 0.700	0.422
Age (y)	1.046	0.003, 0.087	0.035
BMI (kg/m^2)	1.188	0.032, 0.314	0.016
CTSI	0.865	−0.376, 0.087	0.220
Pancreatic necrosis (%)	0.990	−0.028, 0.008	0.290
Necrotic collection confined to lesser sac	0.291	−2.822, 0.356	0.128
Preoperative organ failure*	2.136	−0.609, 2.127	0.277
Preoperative multiple organ failure*	1.962	−1.130, 2.477	0.464
Preoperative persistent organ failure*	1.714	−0.954, 2.032	0.479
Preoperative ICU stay*	2.494	−0.479, 2.306	0.198
ICU (d)*	0.967	−0.154, 0.086	0.581
Organ failure on day of intervention	6.625	−0.005, 3.787	0.051
Interval to intervention (d)	0.980	−0.046, 0.007	0.140
EXPN	4.278	0.211, 2.696	0.022
Necrotic collection along the mesentery	3.937	0.146, 2.595	0.028
Disconnected duct syndrome	0.578	−1.942, 0.846	0.441
Infected pancreatic necrosis	1.444	−1.271, 2.007	0.660

BMI = body mass index; CI = confidence interval; CTSI = Computed Tomography Severity Index; EXPN = NP without parenchymal necrosis; ICU = intensive care unit; OR = odds ratio.
*Anytime in the period preceding the first intervention.

team. In this series, half of the patients who underwent minimally invasive treatment avoided open surgery. A 34.9% success rate of PCD in this study is similar to that reported in other series.[19,28] Although endotherapy was successful in a relatively high proportion of patients (75.0%), this modality was used only in four selected patients who had the necrotic collections confined to the lesser sac, and all of them were intervened later than 6 wk from the onset of disease. In general, we are reluctant to intervene endoscopically earlier than 6 wk of disease for fear of perforation of the necrotic collection into the peritoneal cavity. Despite careful patient selection, this complication occurred in one of our patients.

To date, there is paucity of studies that compared minimally invasive treatment with open necrosectomy for NP.[13,17,19-21] The majority of these studies derive from a few centers of excellence for pancreatic surgery, and their findings also require validation from other institutions, including lower volume hospitals before we will be able to apply them to general practice. This study represents our initial experience with minimally invasive techniques in patients with NP, and thus partially covers the stage of a learning curve. Selection criteria for both minimally invasive therapy and conversion to open necrosectomy in our series were, to a certain degree, subjective and biased. At the very beginning, some in our team felt skeptical toward application of minimally invasive therapy in NP. This attitude is reflected by the fact that half of the patients who underwent primary open necrosectomy were selected for such modality because of the treating surgeon's preference. Over time, our confidence in minimally invasive therapy increased, so that at present, no one in our team questions its role. However, when to advance from minimally invasive therapy to open surgery in patients with persistent local sepsis remains the open question. Our impression was that minimally invasive therapy would be more effective in collections containing a considerable amount of fluid. In our previous study, we showed that a reduction in size of the necrotic collection by a median of 76% shortly after PCD was associated with its success, compared with only 16% decrease for failed PCD.[29] Similarly, Horvath *et al.*[9] reported that a 75% decrease in collection size within 2 wk after PCD predicted its success. Since 2010, we have offered MARPN to patients with necrotic collections persistent despite percutaneous drainage, if retroperitoneal access was possible. Otherwise, conversion to open necrosectomy was required. The reasons for conversion in eight of 24 patients who failed minimally invasive therapy were complications regarded as not amenable to minimally invasive techniques. In hindsight, we believe that some of these complications could have been managed by less invasive techniques, e.g., intravascular interventions could be used to arrest effectively bleeding into the necrotic collections. At the beginning of our experience, we were anxious that prolonged, and eventually unsuccessful, minimally

Table 5 – Multivariate logistic regression analysis predictors for major postoperative complications and mortality.

Variable	Coefficient (β)	SE	OR	95% CI	P value
Major postoperative complications					
Minimally invasive treatment	−1.388	0.632	0.250	−2.627, −0.149	0.028
Necrotic collection confined to the lesser sac	−1.180	0.661	0.307	−2.475, 0.115	0.074
Persistent organ failure	1.855	1.008	6.394	−0.120, 3.831	0.066
Interval to intervention	−0.025	0.011	0.975	−0.047, −0.004	0.020
Intercept	2.127	0.750		0.656, 3.598	0.005
Mortality					
Minimally invasive treatment	−1.182	0.819	0.307	−2.787, 0.423	0.149
Age	0.080	0.031	1.083	0.020, 0.140	0.009
Organ failure on the day of intervention	2.300	1.309	9.976	−0.265, 4.866	0.079
Necrotic collection confined to the lesser sac	−1.459	0.969	0.232	−3.358, 0.440	0.132
BMI	0.159	0.088	1.172	−0.013, 0.330	0.070
Intercept	−8.885	3.300		−15.352, −2.417	0.007

BMI = body mass index; CI = confidence interval; OR = odds ratio.

invasive treatment for infected pancreatic necrosis might be associated with increased mortality which could possibly have been avoided if we had performed open necrosectomy instead. Hence, we initially set a low threshold for conversion, and more often resorted to open necrosectomy (Fig. 1). Nevertheless, our study demonstrated that salvage open necrosectomy was equally safe in patients who failed minimally invasive treatment by showing the comparable mortality rates for salvage and primary open necrosectomy (28.6% *versus* 27.3%; $P = 0.924$). Similarly, van Santvoort *et al.*[30] reported a mortality rate of 20% if PCD was performed as first intervention, whereas mortality for primary necrosectomy was 18% ($P = 0.71$). However, 13% of primary necrosectomies were minimally invasive, endoscopic, or retroperitoneal (VARD). In contrast, Babu *et al.*[17] reported a 48.1% mortality in patients who ultimately required open necrosectomy after unsuccessful PCD. This rate of mortality was much higher than those from recent series of open necrosectomy. In line with this finding, Gomatos *et al.*[18] showed that conversion from MARPN to open necrosectomy was an independent predictor for mortality in patients with NP (odds ratio = 3.51; 95% confidence interval = 1.05-11.13; $P = 0.035$). Higher mortality in patients who require conversion to salvage open necrosectomy might be attributed to metabolic deterioration and severe depletion of the physiological reserves after a protracted disease with persistent local sepsis and increased catabolism. Open surgery in such debilitated patients carries invariably a high risk of death. Consequently, a judicious and timely use of open necrosectomy is warranted to avoid excessive mortality. The remaining predictive factors for mortality in the study by Gomatos *et al.*[18] were age, admission after September 2008, preoperative intensive care unit stay, and preoperative multiple organ failure. In comparison, only older age was associated with increased mortality in the multivariate analysis from our study. On the other hand, age is one of the strongest independent predictors for mortality in acute pancreatitis, regardless of treatment.[4,7,13,18] Mortality for open necrosectomy fluctuates around 20%, although some case series reported one-digit mortality rates.[2,5,7,17,18,30-32] Madenci *et al.*[7] published a contemporary series of open surgical debridement for NP with an overall mortality of 8.8%. However, as much as 78% of patients underwent necrosectomy after the fourth week of disease. Currently, it is widely accepted that the outcomes of surgical treatment for NP are closely related to the timing of intervention. Interventions at later stages of disease, irrespective of technique used—minimally invasive or open, result in lower morbidity and mortality rates.[30,33,34] In accordance with other studies, the mortality rate in our series decreased over time; from 28.6% for interventions within the first month to 16.7% if invasive treatment was undertaken thereafter. Moreover, a longer interval to first intervention was one of two factors independently associated with a decreased rate of major postoperative complications in this study. Interestingly, Sugimoto *et al.*[25] proposed proactive clinically based PCD to control pancreatic juice leakage and thus decrease disease severity. There was no hospital mortality in their series, and none of the patients with NP required necrosectomy.

The predictors for success of minimally invasive treatment remain unclear. Hollemans *et al.*[28] showed that poor success of PCD was associated with male gender, multiple organ failure, increasing percentage of pancreatic necrosis, and heterogeneity of the collections. In comparison, Babu *et al.*[17] found that renal failure, Acute Physiology and Chronic Health Evaluation II score, and number of bacteria were independent predictors of conversion from PCD to open necrosectomy. However, the majority of these factors represent the predictors for mortality of NP in general, and thus their usefulness for selection to minimally invasive treatment might be limited.

One of the most important advantages of minimal access techniques for the management of NP appears to be a lower incidence of new-onset organ failure which reflects less severe second hit caused by surgical trauma. Gomatos *et al.*[18] reported a lower frequency of postoperative multiorgan failure (20.4% *versus* 35%; $P = 0.001$) and a decreased Acute Physiology and Chronic Health Evaluation II score (median 8 *versus* 9 points; $P < 0.001$) in MARPN patients, compared with

patients who underwent open necrosectomy. van Santvoort *et al.*[19] found out a lower incidence of new-onset multiple organ failure in patients assigned to the step-up approach in comparison with primary open necrosectomy arm (12% *versus* 40%; $P = 0.002$). Similarly, the rate of new-onset organ failure in this series was lower for the minimally invasive group (25.0% *versus* 54.5%, $P = 0.016$). Given that these rates were calculated per study arm, a proportion of newly occurring organ failure in the minimally invasive group has to be attributed to salvage open necrosectomy in patients who required conversion after failed less invasive treatment. van Santvoort *et al.*[30] observed fewer complications in patients who had PCD performed as first intervention in comparison with primary open necrosectomy (42% *versus* 64%, $P = 0.003$). Likewise, there was a trend toward a decreased rate of major postoperative complications in patients who were initially managed by minimally invasive techniques in this study (41.7% *versus* 63.6%; $P = 0.088$). Of procedure-related complications, gastrointestinal fistulas were significantly more common in open necrosectomy group (36.4% *versus* 10.4%; $P = 0.009$). This finding might be attributed to a more extensive dissection during open surgical debridement. In contrast, Raraty *et al.*[13] reported a comparable rate of enteric fistulas in patients managed by MARPN or open necrosectomy (7.3% *versus* 9.6%; $P = 0.86$).

This study has some limitations. First, it is retrospective with a moderate number of patients and thus with a limited power for statistical analysis, especially in terms of mortality. Because of its nature, a selection bias was unavoidable in this study, although the baseline characteristics were comparable between the groups. Second, the study represents our initial experience with minimally invasive treatment for acute pancreatitis including the stage of a learning curve. Third, the mortality rate was relatively high. However, the mortality rates for both minimally invasive and open surgical treatment in this series still fell within the range reported in other recent series.[2,5,17,18,30,31]

Conclusion

Minimally invasive treatment should be preferred over open necrosectomy for initial management of NP because these techniques are associated with a decreased rate of some postoperative complications, although mortality remains comparable. Mortality of salvage open necrosectomy after failed minimally invasive treatment is not increased, compared with primary open necrosectomy.

Acknowledgment

Authors' contribution: M.W. designed the study, collected and interpreted data, and drafted the article. W.C. designed the study, collected and interpreted data, and revised the article, B.W. analyzed statistically data and revised the article. M.J., A.K., I.W.K., and M.S. collected data and revised the article. All authors approved the final version of the article.

Disclosure

The authors report no proprietary or commercial interest in any product mentioned or concept discussed in this article.

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