World Journal of Gastroenterology

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DOI: 10.3748/wjg.v22.i9.2828

World J Gastroenterol 2016 March 7; 22(9): 2828-2836
ISSN 1007-9327 (print) ISSN 2219-2840 (online)

ORIGINAL ARTICLE

Retrospective Study

Early complications after interventions in patients with acute pancreatitis

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Author contributions: Wei AL, Guo Q, Hu WM and Zhang ZD conceived and designed the study; Wei AL and Wang MJ performed the study; Wei AL and Guo Q analyzed the data; Wei AL wrote the paper; all authors have read and approved the final version to be published.

Institutional review board statement: The study was reviewed and approved by the West China Hospital of Sichuan University Institutional Review Board.

Informed consent statement: All study participants, or their legal guardian, provided informed written consent prior to study enrollment.

Conflict-of-interest statement: All authors declare no conflicts of interest.

Data sharing statement: No additional data are available.

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Received: September 1, 2015
Peer-review started: September 1, 2015
First decision: October 15, 2015
Revised: November 4, 2015
Accepted: November 24, 2015
Article in press: November 24, 2015
Published online: March 7, 2016

Abstract

AIM: To identify the possible predictors of early complications after the initial intervention in acute necrotizing pancreatitis.

METHODS: We collected the medical records of 334 patients with acute necrotizing pancreatitis who received initial intervention in our center. Complications associated with predictors were analyzed.

RESULTS: The postoperative mortality rate was 16% (53/334). Up to 31% of patients were successfully treated with percutaneous catheter drainage alone. The rates of intra-abdominal bleeding, colonic fistula, and progressive infection were 15% (50/334), 20% (68/334), and 26% (87/334), respectively. Multivariate analysis indicated that Marshall score upon admission, multiple organ failure, preoperative respiratory infection, and sepsis were the predictors of postoperative progressive infection ($P < 0.05$). Single organ failure, systemic inflammatory response syndrome upon admission, and C-reactive protein level upon admission were the risk factors of postoperative colonic fistula ($P < 0.05$). Moreover, preoperative Marshall score, organ failure, sepsis, and preoperative systemic inflammatory response syndrome were the risk factors of postoperative intra-abdominal bleeding ($P < 0.05$).

CONCLUSION: Marshall score, organ failures, preoperative respiratory infection, sepsis, preoperative systemic inflammatory response syndrome, and C-reactive protein level upon admission are associated with postoperative complications.

Key words: Acute necrotizing pancreatitis; Intervention complications; Intra-abdominal bleeding; Colonic fistula; Progressive infection

Core tip: Intra-abdominal bleeding, colonic fistula, and progressive infection are the three major early post-procedural complications in patients with acute necrotizing pancreatitis regardless of the selected approach. Possible predictors, accurate diagnosis, and appropriate management methods are beneficial to decrease the mortality rate and convalescence, as well as promote the life quality of patients with acute pancreatitis. In this study, Marshall score, organ failures, preoperative respiratory infection, sepsis, preoperative systemic inflammatory response syndrome, and C-reactive protein level upon admission are associated with post-procedural complications. Proper and gentle intervention process, and close monitoring and evaluation of patients who are prone to suffer from postoperative complications may increase the therapeutic efficiency.

Wei AL, Guo Q, Wang MJ, Hu WM, Zhang ZD. Early complications after interventions in patients with acute pancreatitis. *World J Gastroenterol* 2016; 22(9): 2828-2836 Available from: URL: http://www.wjgnet.com/1007-9327/full/v22/i9/2828.htm DOI: http://dx.doi.org/10.3748/wjg.v22.i9.2828

INTRODUCTION

Acute pancreatitis (AP) presents a high mortality rate of up to 30% and is one of the most common diseases requiring multidisciplinary management. In the United States and in other pancreatitis centers worldwide, billions of dollars are spent annually for this life-threatening disease[1]. With increased knowledge on AP and ICU management, guidelines were recently revised in different countries[2]. Stratifying the severity of AP is necessary to identify AP patients requiring intervention. Organ failure and infected necrosis are important criteria to evaluate the severity of AP[3]. The revised Atlanta classification unequivocally defined severe AP as persistent organ failure (> 48 h). In our center, we also found that organ failure, and not infection, primarily causes mortality in patients with necrotizing pancreatitis[4]. The peri-pancreatic fluid collection, especially that with necrosis, is easily infected because of the transmural migration of bacteria from the intestinal wall[5]. Infection or suspended infection usually indicates the need for intervention. Endoscopic necrosectomy[6-10], laparoscopic necrosectomy[11], percutaneous catheter drainage (PCD)[12-15], and minimal access retroperitoneal pancreatic necrosectomy[16] are consistently studied in intervention research. Approximately 18% to 100% of patients survived by minimally invasive treatment alone, with a complication rate of 0% to 17% and overall mortality rate of 0% to 34%, indicating that minimally invasive approach is safe and feasible[17,18]. However, many trials were limited to a small number of patients.

Early complications after the intervention include intra-abdominal bleeding, colonic fistula (CF), and progressive infection, which may require subsequent intervention. Most reports used complication rate as an index for a successful management protocol[6,18]; however, few studies focused on the primary causes of these intractable complications. Babu *et al*[13] found that the increased APACHE Ⅱ score prior to the first PCD, the onset of organ failure in the first week of AP attack, and the failure of sepsis reversal within a week of PCD were the indicators of surgery for progressive infection. To our knowledge, no previous studies have focused on the predictors of intra-abdominal bleeding and CF after surgery.

In this study, we investigated the incidence, management and outcome of intra-abdominal bleeding, CF, and progressive infection, and mainly analyzed the possible predictors of early complications after the initial intervention in acute necrotizing pancreatitis.

MATERIALS AND METHODS

Patient and design

Patients diagnosed with necrotizing AP in West China Hospital from January 2009 to December 2013 were included in this study. These patients had undergone surgical intervention (percutaneous catheter drainage, minimally invasive necrosectomy, or open necrosectomy). Data were recorded from admission until discharge. Infected pancreatic necrosis was confirmed by positive culture obtained from either PCD or specimen during surgery. Gas bubble signs in the retroperitoneal space as revealed by CECT were also ascribed to infection.

Management protocol and data collection

APACHE-Ⅱ score, modified Marshall score, and organ failure including respiratory failure, circulatory failure, and renal failure (definitions are shown in Table 1) were evaluated upon admission, a week after the attack of the disease and before operation, respectively. Persistent organ failure is considered when organ failures cannot be reversed within 48 h. Ventilation and continuous renal replacement therapy (CRRT) were administered to patients with respiratory failure and renal failure, respectively, as necessary. Citric acid was employed as anticoagulant in CRRT when no contraindications were identified. CTSI was recorded before surgery.

We observed the possible onset of early complications in each patient after the first intervention. The complications are presented in Table 1. If PCD failed,

Table 1 Definitions

Systemic inflammatory response syndrome	Occurrence of 2 or more of the followings for > 48 h: pulse > 90 beats/min; rectal temperature < 36 ℃ or > 38 ℃; white blood cell count < 4000 or > 12000/mL; and respirations > 20/min or pCO_2 < 32 mmHg
Renal failure	Creatinine level > 177 μmol/L (2 mg/dL) after rehydration or hemofiltration or hemodialysis
Circulatory failure	Systolic blood pressure < 90 mmHg despite adequate fluid resuscitation
Respiratory failure	PaO_2 60 mmHg or less despite FiO_2 of 0.30, or need for mechanical ventilation
Multiple organ failure	Two or more organs failed
Preoperative respiratory infection	Positive sputum culture with or without clinical symptoms
Colonic fistula	Discharge of large-bowel contents from a drain or a drain site or from the surgical wound
Progressive infection	Simmering infection in which the patient has intermittent low-grade fever, with or without leukocytosis and imaging showing incomplete resolution of the necrosis, which may not be accompanied by purulent discharge from the drains
Intra-abdominal bleeding	New fresh blood coming from drainage or wound and blood loss more than 500 mL in 24 h
Respiratory infection	New positive microbiological results of sputum culture after surgery with or without clinical symptoms
Postoperative sepsis	New positive blood culture/aspirate and more than one of the following clinical signs: rectal temperature < 36 ℃ or > 38 ℃, tachycardia > 90/min, tachypnea (respiratory rate > 20/min) or hyperventilation ($paCO_2$ < 4.3 kPa), white blood cell count < 4×10^9/L or > 12×10^9/L, or the presence of more than 10% immature neutrophils

the patients received minimally invasive necrosectomy or open necrosectomy. The following factors were considered as the possible predictors of the occurrence of CF: sex, age, BMI, time from onset of symptoms to surgery, CRP, preoperative systemic disorders (*e.g.*, hypocalcemia, hypoproteinemia, acidosis, base deficit), APACHE-Ⅱ score, Marshall score, organ failures, morphological assessments based on CECT before surgery (*e.g.*, percentage of pancreatic necrosis, gas bubble signs), preoperative CTSI, ASA classification, operation approaches, length of operation, blood transfusion volume, and infected pancreatic necrosis. Additional administration of CRRT was considered one of the possible predictors of intra-abdominal bleeding after necrosectomy, besides the predictors presented previously. Preoperative sepsis and respiratory infection and systemic inflammatory response syndrome (SIRS) upon admission and that before operation were also considered possible risk factors for postoperative progressive infection.

When postoperative intra-abdominal bleeding occurred, radiologic embolization procedure or laparotomy was performed to stop the bleeding. Ileostomy was performed when CF occurred. Another necrosectomy was subsequently performed in patients with intractable progressive infection.

Statistical analysis

Complication and mortality rates were the major outcomes of this study. Data are presented as median (range). Multivariate analysis results of the different predictors of postoperative intra-abdominal bleeding, CF, and progressive infection were presented as 95% confidence interval (CI) and odds ratio (OR); and *t* test was employed to analyze the normally distributed ordinal data. Nonparametric test such as rank test was used for ordinal data without normal distribution. χ^2 test was used to compare categorical variables. Two-sided *P* value < 0.05 was considered statistically significant.

RESULTS

Patient characteristics

A total of 334 patients with acute necrotizing pancreatitis received initial intervention in our center from January 2009 to December 2013. Among these patients, 50 underwent minimally invasive retroperitoneal necrosectomy (three of them underwent laparoscopic debridement), and 102 underwent initial PCD management. And the other 182 patients received open necrosectomy. Table 2 presents the detailed characteristics of the patients. The postoperative mortality rate was 16% (53/334), whereas the rates of early complications, including intra-abdominal bleeding, CF, and progressive infection, were 15% (50/334), 20% (68/334), and 26% (87/334), respectively. Among the 53 death cases, 19 (36%) patients died because of multiple organ failure, 5 (9%) of them died of hemorrhagic shock and other 29 (55%) patients died of septic shock. Among the patients with intra-abdominal bleeding, 10 received radiologic intervention, 5 received hemostasis by compression through the incision on the loin with gauze bandage, and 35 patients received another laparotomy. Other complications included postoperative sepsis (13%), respiratory infection (12%), ileus (4%), alimentary tract hemorrhage (4%), intestinal leakage (4%), and incisional infection (9%). Two patients with postoperative ileus suffered from enterolysis.

Severity of acute pancreatitis

To date, organ failure and infection are the two main indexes to evaluate the prognosis of acute necrotizing pancreatitis. The median (range) Marshall score upon admission and preoperation score were 2(0-12) and 2(0-12), respectively. The median APACHE-Ⅱ score upon admission was 8. As shown in Table 2, 201 (60%) patients suffered from organ failures, and 117 of them presented single organ failure. The onset of single or multiple organ failures during the first week

Table 2 Characteristics and outcomes of patients with necrosectomy *n* (%)

Characteristics	Outcomes
Demographics	
Age (yr)	46 (21-74)
Male sex	220 (66)
BMI (kg/m^2)	28 (19-35)
Etiology	
Biliary	167 (50)
Alcoholic	43 (13)
Others	124 (37)
Onset of symptoms to first intervention	
< 2 wk	58 (17)
2-4 wk	124 (37)
> 4 wk	152 (46)
Severity of disease	
APACHE-II score at admission	8 (2-32)
Marshall score at admission	2 (0-12)
Preoperative Marshall score	2 (0-12)
SIRS at admission	157 (47)
SIRS before operation	177 (53)
Organ failure, *n*	
Single organ failure at any time before surgery	117 (35)
Single organ failure started at first week	71/117
Persistent organ failure	101/117
MOF at any time before surgery	84 (25)
MOF started at first week	46/84
Persistent MOF	70/84
Laboratory parameters	
CRP at admission (mg/L)	200 (17-535)
CRP before surgery (mg/L)	151 (8-478)
Preoperative acidosis pH < 7.2	67 (20)
Preoperative basic deficit > 5 mEq/L	120 (36)
Preoperative hypocalcemia (calcium level < 1.87 mmol/L)	148 (44)
Preoperative hypoproteinemia (albumin level < 30 g/L)	171 (51)
Morphological criteria on CECT	
Pancreatic necrosis	285 (85)
Extrapancreatic necrosis only	49 (15)
Percentage of necrosis, *n*	
< 30%	161/285
30%-50%	75/285
> 50%	49/285
CTSI before surgery	8(4-10)
Gas bubble signs in the retroperitoneal space	69 (21)
Microbiological data, *n*	
Infected pancreatic necrosis	214 (64)
Escherichia coli	77/214
Enterococcus	64/214
Klebsiella	13/214
Baumanii	19/214
Other bacillus	15/214
Fungal infection	15/214
Staphylococcus	9/214
Pseudomonas aeruginosa	2/214
Preoperative sepsis	107 (32)
Operation data	
Type of surgery	
PCD	102 (31)
Minimally invasive necrosectomy	50 (16)
Open necrosectomy	182 (53)
ASA classification	
Ⅰ	88 (26)
Ⅱ	168 (50)
Ⅲ	78 (24)
Operation time, min	138 (20-360)
Blood transfusion during operation	91 (27)
Blood transfusion on the first day after surgery	79 (23)
Postoperative data	
Mortality	53 (16)
Postoperative ICU stay (d)	11 (0-170)
Whole hospital stay (d)	53 (5-220)
Intra-abdominal hemorrhage	50 (15)
Colonic fistula	68 (20)
Progressive infection	87 (26)

BMI: Body mass index, calculated as weight in kilograms divided by height in meters squared; APACHE: Acute physiology and chronic health examination; ICU: Intensive care unit; CRP: C-reactive protein; MOF: Multiple organ failure; CECT: Contrast-enhanced computed tomography; CTSI: Computed tomography severity index; SIRS: Systemic inflammatory response syndrome; PCD: Percutaneous catheter drainage.

of the disease was observed in 17 out of 201 patients. Up to 171 out of the 201 patients showed persistent organ failures (either single or multiple). SIRS, which was considered as an initial reaction to inflammation but eventually causing organ failure and death, was observed in 157 patients upon admission and in 177 patients before intervention.

The CRP levels at admission and preoperation were 200 and 151 mg/L, respectively. Systemic disorders were observed, including severe metabolic disturbance (hypocalcemia), as well as severe acid and base disturbance. Approximately 20% of the patients experienced preoperative acidosis, and 36% suffered from base deficit of about 5 mEq/L before intervention. In addition, 148 of 334 (44%) patients suffered from hypocalcemia, whereas 171 of 334 (51%) patients had hypoproteinemia.

The legible presentation of CECT can help us to evaluate the extent of the collections and the rates of peri-pancreatic and pancreatic necrosis. Gas bubble signs in the retroperitoneum may prompt infection. Median CTSI was 8 (4-10). A total of 285 out of 334 (85%) patients had pancreatic necrosis; out of these 285 patients, 161 had < 30% necrosis, 75 had necrosis ranging from 30% to 50%, and 49 had > 50% necrosis. The remaining 49 out of 334 patients showed extra pancreatic necrosis alone.

The onset of infection indicates the need for intervention, especially when the medical management failed. We collected the fluid around the pancreas during PCD or during the operation and sent the specimens for microbiological analysis. A total of 214 out of 334 (64%) patients were confirmed to suffer from infected pancreatic necrosis; the relative abundance of bacteria is shown in Table 2. *Escherichia coli*, *Enterococcus*, and *Bacillus* were the most common bacteria in this study, constituting about 88% of the total bacterial population. Increasing cases of fungal infection (15/214) suggested that we should be cautious when using antibiotics, especially for extended periods. Up to 32% of the patients had sepsis before necrosectomy.

Reversal from PCD alone was observed in 31% of the patients. ASA classification of patients is presented in Table 2. The median operation time was 138 min (20 - 360 min). A total of 91 (27%) and 79 (23%) patients had blood transfusion during operation and on the first day of surgery, respectively.

Table 3 Factors predicting progressive sepsis

Factors	P_1 value	Odd ratio (lower-upper)	P_2 value
Onset of symptoms to the first intervention			
< 2 wk	0.093		
2-4 wk	0.938		
> 4 wk	0.176		
APACHE-Ⅱ score at admission	0.150		
Marshall score at admission	0.015	1.723 (1.526-2.995)	0.046
Preoperative Marshall score	0.042	0.885 (0.607-1.290)	0.524
SIRS at admission	0.076		
Preoperative SIRS	0.001	0.644 (0.210-1.976)	0.442
Single organ failure at any time before surgery	0.510		
MOF at any time before surgery	0.041	2.031 (3.410-10.054)	0.038
CRP at admission	0.600		
CRP before surgery	0.172		
Morphological criteria on CECT			
Pancreatic necrosis	0.157		
Extrapancreatic necrosis	0.157		
Percentage of necrosis			
< 30%	0.157		
30%-50%	0.526		
> 50%	0.245		
Gas bubble signs	0.351		
CTSI before surgery	0.030	1.063 (0.811-1.393)	0.66
Infected pancreatic necrosis	0.274		
Sepsis before surgery	0.0001	11.165 (5.384-23.153)	0.0001
Preoperative respiratory infection	0.0001	4.304 (2.085-8.884)	0.0001
Operation type	0.082		

P_1 indicated two-sided P value of univariate analysis; P_2 indicated two-sided P value of multivariate analysis. APACHE: Acute physiology and chronic health examination; ICU: Intensive care unit; CRP: C-reactive protein; MOF: Multiple organ failure; CECT: Contrast-enhanced computed tomography; CTSI: Computed tomography severity index; SIRS: Systemic inflammatory response syndrome.

Predictors of complications

The median Marshall scores at admission (P = 0.015) and pre-operation (P = 0.042) were higher in the progressive infection group than in the infection-free group, as indicated by univariate analysis (Table 3). In addition, no significant differences of APACHE Ⅱ score between the two groups were observed. MOF at any period before surgery was observed in 24 patients in the progressive infection group and 46 patients in the infection-free group (P = 0.041). Patients with postoperative progressive infection showed increased CTSI (P = 0.03). Increased incidences of respiratory infection and sepsis (P < 0.0001), as well as preoperative SIRS (P = 0.001), were observed in patients with progressive infection. Multivariate analysis revealed that Marshall score upon admission (OR = 1.723,95%CI: 1.526-2.995, P = 0.046), MOF at any time before surgery (OR = 2.031,95%CI: 3.410-10.054, P = 0.038), preoperative respiratory infection (OR = 4.304,95%CI: 2.085-8.884, P < 0.0001), and sepsis before surgery (OR = 11.165, 95%CI: 5.384-23.153, P < 0.0001) were the predictors of postoperative progressive infection.

Table 4 Factors predicting colonic fistula

Factors	P_1 value	Odd ratio (lower-upper)	P_2 value
Onset of symptoms to surgery			
< 2 wk	0.432		
2-4 wk	0.945		
> 4 wk	0.595		
APACHE-Ⅱ score at admission	0.005	0.955 (0.837-1.090)	0.497
Marshall score at admission	0.007	0.849 (0.582-1.239)	0.397
Preoperative Marshall score	0.019	1.045 (0.733-1.491)	0.807
SIRS at admission	0.0001	2.927 (1.102-7.776)	0.031
Preoperative SIRS	0.015	0.554 (0.170-1.806)	0.327
Single organ failure at any time before surgery	0.001	6.289 (1.652-23.948)	0.007
MOF at any time before surgery	0.222		
CRP level at admission	0.001	1.005 (1.001-1.009)	0.010
CRP level before surgery	0.0001	1.003 (0.998-1.008)	0.321
Hypoproteinemia before surgery	0.0001	1.564 (0.750-3.265)	0.233
Pancreatic necrosis	0.708		
Extrapancreatic necrosis only	0.708		
Percentage of necrosis			
< 30%	0.829		
30%-50%	0.738		
> 50%	0.762		
CTSI before surgery	0.249		
Gas bubble signs	0.047	2.150 (0.933-4.955)	0.321
Infected pancreatic necrosis	0.506		
Preoperative Sepsis	0.519		
Preoperative respiratory infection	0.179		
Preoperative ICU stay	0.014	1.016 (0.973-1.060)	0.472
Type of surgery	0.328		

P_1 indicated two-sided P value of univariate analysis; P_2 indicated two-sided P value of multivariate analysis. APACHE: Acute physiology and chronic health examination; ICU: Intensive care unit; CRP: C-reactive protein; MOF: Multiple organ failure; CECT: Contrast-enhanced computed tomography; CTSI: Computed tomography severity index; SIRS: Systemic inflammatory response syndrome; PCD: Percutaneous catheter drainage.

We compared the parameters that can potentially predict CF in patients with acute necrotizing pancreatitis (Table 4). The median APACHE Ⅱ score upon admission (P = 0.005) and Marshall scores at admission (P = 0.007) and pre-operation (0.019) were higher in the CF group. CF patients showed higher CRP levels both at admission and before operation. Thirty-five of 68 patients with postoperative CF had single organ failure, whereas 82 of 266 patients in the non-CF group had single organ failure (P = 0.001). However, no significant difference in the frequency of MOFs was observed between the two groups. The incidences of SIRS at admission and pre-operation were higher in CF patients (P < 0.05). Moreover, CECT revealed no significant difference in necrosis between the groups, except that more patients in the CF group showed gas

Table 5 Factors predicting intra-abdominal hemorrhage

Factors	P_1 value	Odd ratio (lower-upper)	P_2 value
APACHE-Ⅱ score at admission	0.004		
Marshall score at admission	0.0001	0.882 (0.626-1.243)	0.474
Preoperative Marshall score	0.0001	1.560 (1.003-2.426)	0.048
SIRS at admission	0.001	0.774 (0.274-2.185)	0.628
Preoperative SIRS	0.0001	1.294 (1.086-2.002)	0.050
Single organ failure at any time before surgery	0.0001	5.287 (1.524-7.369)	0.031
MOF at any time before surgery	0.003	4.327 (1.325-6.548)	0.041
CRP before surgery	0.273		
Base deficit before surgery, > 5 mEq/L	0.741		
Hypoproteinemia before surgery	0.854		
Hypocalcemia before surgery	0.006	1.576 (0.723-3.438)	0.253
Acidosis at admission pH < 7.2	0.693		
Pancreatic necrosis	0.148		
< 30%	0.724		
30%-50%	0.346		
> 50%	0.923		
Extra-pancreatic necrosis only	0.148		
Gas bubble signs	0.901		
CTSI before surgery	0.053		
Operation time	0.218		
Blood transfusion during operation	0.635		
Blood transfusion on the first day after surgery	0.472		
Pancreatic infection	0.140		
Preoperative sepsis	0.048	1.227 (1.089-1.578)	0.002
Preoperative respiratory infection	0.240		
Preoperative ICU stay	0.055		
CRRT	0.010	0.810 (0.353-1.861)	0.620
Type of surgery	0.245		

P_1 indicated two-sided P value of univariate analysis; P_2 indicated two-sided P value of multivariate analysis. APACHE: Acute physiology and chronic health examination; ICU: Intensive care unit; CRP: C-reactive protein; MOF: Multiple organ failure; CECT: Contrast-enhanced computed tomography; CTSI: Computed tomography severity index; SIRS: Systemic inflammatory response syndrome; CRRT: Continuous renal replacement therapy; PCD: Percutaneous catheter drainage.

bubble signs in the retroperitoneal space (P = 0.047). Multivariate analysis revealed that single organ failure at any time before surgery (OR = 6.289, 95%CI: 1.652-23.948, P = 0.007), SIRS at admission (OR = 2.927, 95%CI: 1.102-7.776, P = 0.031), and CRP level at admission (OR = 1.005, 95%CI: 1.001-1.009, P = 0.010) were the risk factors of postoperative CF.

As shown in Table 5, the median Marshall scores upon admission and before operation were higher in the bleeding group than in the non-bleeding group (P < 0.0001). Significant differences in the incidence of single organ failure and MOFs (P < 0.05) were observed. The incidence of hypocalcemia was significantly higher in the bleeding group (P = 0.006). The incidences of sepsis and SIRS at admission and before operation were significantly higher in the bleeding group than in the non-bleeding group. CRRT was administered in more patients of the bleeding group to temporarily replace renal function (P = 0.01). Multivariate analysis revealed that preoperative Marshall score (OR = 1.560, 95%CI: 1.003-2.426, P = 0.048), single organ failure at any time before surgery (OR = 5.287, 95%CI: 1.524-7.369, P = 0.031), MOF at any time before surgery (OR = 4.327, 95%CI: 1.325-6.548, P = 0.041), preoperative sepsis (OR = 1.227, 95%CI: 1.089-1.578, P = 0.002), and preoperative SIRS (OR = 1.294, 95%CI: 1.086-2.002, P = 0.050) were the risk factors of postoperative intra-abdominal bleeding.

DISCUSSION

Intra-abdominal bleeding, CF, and progressive infection are the three major early-postoperative complications in patients with acute necrotizing pancreatitis. In the past few decades, interventions mainly comprise open necrosectomy and minimally invasive necrosectomy. Step-up approach has been established as a management regimen of the disease. By using this method, approximately 40%-50% (severe) of pancreatitis patients showed reversal from PCD alone, and the mortality and complication rates decreased[13,14,18]. However, most studies mainly focused on the reversal and mortality rates by this method. Few studies reported about the pathophysiology and predictors of complications. We initially thought that the different interventions might influence the complication rate because either open necrosectomy or minimally invasive debridement *via* lumbar incision exposes the organs or vessels of the abdomen. However, the current results indicated that no significant differences in the rate of complication arising from the conduct of the different interventions were observed between the complication and non-complication groups. To our knowledge, this study is the first to investigate the predictors of early AP complications after initial intervention.

SIRS, a sterile response without sepsis or infection, is a systemic action of cytokines released from damaged pancreatic cells during the first week up to the second week from attack. If SIRS is severe, MOF triggered by these inflammatory mediators occurs[19]. During the latter phase, patients are at risk for infections because of intestinal flora translocation. Sepsis is a SIRS associated with bacterial infection occurring at late onset of MOF. Thus, we compared some indexes of severity of pancreatitis, including organ failures (single or multiple)[20], Marshall score, SIRS, and sepsis. We found that all these predictors were associated with an increased incidence of postoperative intra-abdominal bleeding; multivariate analysis confirmed that high preoperative Marshall score, organ failures (either single or multiple) at any

time before surgery, sepsis, and preoperative SIRS contributed to postoperative intra-abdominal bleeding. The main possible explanation is that bleeding is uncontrolled when patients have shock or disseminated intravascular coagulation (DIC). In addition, direct erosion of the vessels, primarily the splenic artery, may cause postoperative intra-abdominal bleeding during the course of AP[21]. We also found that CRRT was administered in 30% of the bleeding group compared with 11% of the non-bleeding group. Citric acid was used as anticoagulant. Thus, patients were in the easy-to-bleed condition. However, receiving CRRT was not among the predictors based on the results of multivariate analysis in this study.

Colonic leakage or fistula is one of the threatening postoperative complications with severe abdominal and wound infection. Studies reported that the incidence of colonic complications in acute necrotizing pancreatitis is 10% to 44%, and most of these occur in the transverse colon[22-25]. Necrosis, fistula, and stricture are the main forms of colonic complications resulting from pancreatitis. The reasons of CF possibly include pancreatic fluid erosion, vascular complications (embolism or embolus), and intervention-related drain erosion. In our study, 68 patients suffered from colonic complications, 29 of which had drain erosion. Tubes were withdrawn from the 29 patients, and five of them naturally recovered, whereas the 24 other patients received ileostomy. Higher CRP level[26] and higher incidence of gas bubble signs as revealed by CECT indicated that patients with CF may have suffered from severe infections before surgery. Compared with the non-CF group, patients with postoperative CF had a higher incidence of organ failure (51% *vs* 31%), and SIRS upon admission (68% *vs* 42%) and before operation (66% *vs* 50%). Embolism might cause colon ischemia and necrosis when inflammation and coagulation disorder occurred in patients. Leak and fistula might form because of edema and fragile colon wall in patients with hypoproteinemia (72% *vs* 46%). In this situation, drainage tubes easily invaded the colon wall.

Progressive infection after intervention was also a challenge to surgeons because the onset of progressive infection requires subsequent surgical necrosectomy. Recent prospective clinical trials on sepsis reversal through the step-up approach aimed to reduce the progressive infection rate and reoperation rate. However, reversal from PCD alone is still not achieved in 50% of the patients, thus requiring subsequent necrosectomy. Few reports on predicting the success rate of PCD based on the risk factors exist, except that of Babu *et al*[13]'s and Hollemans *et al*[14]'s teams. Hollemans *et al*[14] reported that patients with characteristics such as male gender, MOF, increasing percentage of necrosis, and heterogeneous collection on CT, were related to the poor success rate of PCD. Similarly, we found that preoperative MOF patients had a risk of progressive infection. In addition, we found that Marshall score upon admission, preoperative respiratory failure, and sepsis before intervention were the predictors of progressive infection after the initial intervention. In some instances, untreated respiratory infection or sepsis results in pancreatic infection. We deduced that in some cases, the bacteria from the peri-pancreatic fluid after the intervention were the same as the bacteria found in sputum culture (*Klebsiella*) or blood culture but different from the intestinal translocation bacteria such as *Enterococcus*. Thus, to avoid progressive infection after intervention, respiratory infection and sepsis before intervention should be controlled.

This research had a number of limitations. First, the retrospective nature of this study may have led to a potential bias in data collection, especially with the very large sample size. Second, we were not able to complete all the values of procalcitonin and IL-6, which were important to evaluate the prognosis of AP, because procalcitonin and IL-6 tests were not routinely performed for the past several years. In addition, some patients had more than one complication. For patients who had two or more complications, all the predicting factors were inhibited at the time of first occurrence of complication. The interaction of two complications or the intervention we performed to treat the complications was not considered in the analysis, although few patients had this condition.

In summary, the possible predictors, accurate diagnosis, and appropriate management methods are beneficial to decrease the mortality rate and convalescence, as well as promote the life quality of acute pancreatitis patients. High preoperative Marshall score, organ failures (single or multiple) at any time before surgery, sepsis, and preoperative SIRS are associated with postoperative intra-abdominal bleeding. Single organ failure, SIRS upon admission, and CRP level upon admission may possibly indicate the occurrence of CF. Marshall score upon admission, preoperative respiratory failure, and sepsis were the predictors of progressive infection after the initial intervention. Proper and gentle intervention process, close monitoring, and evaluation of patients prone to suffer from postoperative complications may increase the therapeutic efficiency.

COMMENTS

Background

Acute pancreatitis (AP) remains one of the most common diseases with high mortality. Organ failure and infected necrosis are important criteria to evaluate the severity of AP. Invasive interventions are required when medical managements failed. Post-procedural complications including intra-abdominal bleeding, colonic fistula (CF), and progressive infection may require subsequent intervention and thus affect the prognosis.

Research frontiers

According to the authors of this study, no previous studies have focused on the predictors of intra-abdominal bleeding and CF after pancreatic surgery. Hence, proper prediction of risk factors for post-procedural complications will

direct our management.

Innovations and breakthroughs

These trials first analyzed the predictors of complications after the first intervention in acute necrotizing pancreatitis patients, although most reports used complication rate as a success index for a management protocol instead of focusing on the primary causes of these intractable complications.

Applications

These reports can help facilitate the diagnosis and management of post-procedural complications in patients with acute necrotizing pancreatitis. Optimal protocol management, gentle and careful operational process, close monitoring and evaluation of patients who are prone to suffer postoperative complications may increase the therapeutic efficiency.

Peer-review

This study provides a very good review regarding early postoperative complications of acute pancreatitis and relevant information about the clinical history of the disease in China. This study also highlights the importance of using clinical laboratory indicators in the possible prevention of complications.

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P- Reviewer: Cosen-Binker L, Fujino Y, Soares RLS
S- Editor: Ma YJ **L- Editor**: Ma JY **E- Editor**: Wang CH

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ISSN 1007-9327