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Mortality Indicators and Risk Factors for Intra-Abdominal Hypertension in Severe Acute Pancreatitis

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This study assessed the risk factors associated with mortality and the development of intra-abdominal hypertension (IAH) in patients with severe acute pancreatitis (SAP). To identify significant risk factors, we assessed the following variables in 102 patients with SAP: age, gender, etiology, serum amylase level, white blood cell (WBC) count, serum calcium level, Acute Physiology and Chronic Health Evaluation II (APACHE-II) score, computed tomography severity index (CTSI) score, pancreatic necrosis, surgical interventions, and multiple organ dysfunction syndrome (MODS). Statistically significant differences were identified using the Student *t* test and the χ^2 test. Independent risk factors for survival were analyzed by Cox proportional hazards regression. The following variables were significantly related to both mortality and IAH: WBC count, serum calcium level, serum amylase level, APACHE-II score, CTSI score, pancreatic necrosis, pancreatic necrosis >50%, and MODS. However, it was found that surgical intervention had no significant association with mortality. MODS and pancreatic necrosis >50% were found to be independent risk factors for survival in patients with SAP. Mortality and IAH from SAP were significantly related to WBC count, serum calcium level, serum amylase level, APACHE-II score, CTSI score, pancreatic necrosis, and MODS. However, Surgical intervention did not result in higher mortality. Moreover, MODS and pancreatic necrosis >50% predicted a worse prognosis in SAP patients.

Key words: Severe acute pancreatitis – Intra-abdominal hypertension – Risk factors – Mortality

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Acute pancreatitis (AP) most commonly presents with acute abdominal pain and is diagnosed on the basis of increased serum concentrations of amylase and lipase. Approximately 80% of AP patients recover, without complications, because the disease is mild and self-limiting in these patients. However, the mild, self-limiting form of AP may progress to severe AP (SAP) in approximately 20% of patients. SAP is characterized by pancreatic necrosis, local complications, and systemic organ failure; is associated with high morbidity; and has a considerably higher mortality rate (up to 30%) than mild AP.[1] A deeper understanding of the pathophysiology of SAP and a better assessment of disease severity will improve the management and outcomes of this complex disease.[2] The treatment for mild disease is supportive, whereas that for SAP involves management by a multidisciplinary team that includes gastroenterologists, interventional radiologists, and surgeons. In SAP patients, intra-abdominal hypertension (IAH) has drawn more attention. High IAH levels can significantly decrease perfusion of abdominal viscera and make tissues suffer hypoxic injury, which aggravates systemic inflammatory response syndrome.[3] Persistent, elevated intra-abdominal pressure (IAP) could lead to a series of consequences, including cardiovascular and renal dysfunction and intestinal and hepatic ischemia, which could lead to a worse prognosis in patients with SAP.[4] It has been shown that IAH is related to higher mortality and morbidity rates compared to patients with no IAH.[5] However, the detailed mechanism underlying IAH in patients with SAP is still unclear. In this retrospective study, we identified the risk factors for mortality and the development of IAH in patients with SAP.

Methods

This study involved 102 patients with SAP who were admitted between January 2007 and December 2011 to Peking Union Medical College Hospital within 24 hours after symptom onset. SAP was diagnosed on the basis of the Atlanta criteria,[6] and patients were included in the study if one or more of the following were present: (1) organ failure, as indicated by shock (systolic blood pressure < 90 mmHg), respiratory insufficiency (PaO2 < 60 mmHg), or renal dysfunction (serum creatinine $>$ 200 umol/L); (2) an Acute Physiology and Chronic Health Evaluation II (APACHE-II) score ≥ 8; and (3) local complications such as pancreatic necrosis, abscess, or pseudocyst. All selected patients underwent computed tomography (CT) and a blood test that included serum calcium and serum amylase 72 hours after admission. The CT findings were graded using the CT severity index (CTSI).[1] A jejunal feeding tube was inserted for nutritional support.

IAP was measured with a catheter inserted into the bladder according to the standard technique established by The World Society of Abdominal Compartment Syndrome (WSACS) in 2006.[7] All patients performed consecutive IAP monitoring for at least 3 days. IAH was defined as a sustained, elevated IAP of more than 12 mmHg, and abdominal compartment syndrome (ACS) was defined as a sustained IAP of more than 20 mmHg in association with new organ dysfunction or failure.

The types of surgical intervention in our study included necrosectomy and drainage of infected, acute, necrotizing pancreatitis, which was performed with different approaches such as radiology, endoscopy, and open abdominal decompression. The decision of which surgical intervention to perform was made according to these factors: progressive IAH, infected pancreatic necrosis, and end-organ dysfunction that is refractory to these nonoperative therapies.

The study protocol was approved by the ethics committee of Peking Union Medical College Hospital.

Data collection

The study parameters included age, gender, etiology, white blood cell (WBC) count, serum calcium level, serum amylase level, APACHE-II score, CTSI score, pancreatic necrosis, surgical intervention, and multiple organ dysfunction syndrome (MODS). All parameters were measured at Peking Union Medical College Hospital.

All patients received follow-up. The mean follow-up at the time of the last follow-up was 36.6 days (range, 14–76 days).

Statistical analysis

The Student t test and χ^2 test were used to analyze the differences between the two groups by the following factors: age, gender, etiology, WBC count, serum calcium level, serum amylase level, APACHE-II score, CTSI score, pancreatic necrosis, surgical intervention, and MODS. All tests were 2-tailed, and only $P < 0.05$ was considered significant

Table 1 Comparative analysis of various factors related to mortality rate in patients with SAP

	Survivors (n = 81)	Nonsurvivors (n = 21)	*P* value
Mean age, y	46.43 ± 12.34	48.81 ± 14.50	0.450
Gender			
Male	53 (65.4%)	11 (52.4%)	0.27
Female	28 (34.6%)	10 (47.6%)	
Etiology			
Gallstones	40 (49.4%)	12 (57.2%)	0.219
Alcoholism	19 (23.5%)	7 (33.3%)	
Hyperlipidemia	22 (27.1%)	2 (9.5%)	
APACHE-II score	14.28 ± 4.73	17.62 ± 2.09	< 0.001
WBC count ($\times 10^9$/L)	18.38 ± 4.14	20.42 ± 2.64	0.035
WBC count > 20×10^9/L			
Yes	23 (28.4%)	12 (57.1%)	0.013
No	58 (71.6%)	9 (42.9%)	
CTSI score	6.42 ± 1.53	7.38 ± 0.97	0.001
Serum amylase level, IU/L	1858.3 ± 646.6	2163.7 ± 427.8	0.013
Serum calcium, mmol/L	1.76 ± 0.14	1.67 ± 0.11	0.014
Pancreatic necrosis			
Yes	53 (65.4%)	21 (100%)	0.002
No	28 (34.6%)	0 (0 %)	
Pancreatic necrosis >50%			
No	24 (29.6%)	18 (85.7%)	< 0.001
Yes	57 (70.4%)	3 (14.3%)	
MODS			
Yes	34 (42.0%)	19 (90.5%)	< 0.001
No	47 (58.0%)	2 (9.5%)	
Surgical intervention			
Yes	33 (40.7%)	12 (57.1%)	0.177
No	48 (59.3%)	9 (42.9%)	

APACHE-II, Acute Physiology and Chronic Health Evaluation II; CTSI, computed tomography severity index; MODS, multiple organ dysfunction syndrome; SAP, severe acute pancreatitis; WBC, white blood cell.

in all cases. Binary logistic regression was used to examine the independent effects of each significant variable. Data were analysed using SPSS software (version 16.0, SPSS Inc, Chicago, Illinois).

Results

The mean age of the 102 study patients was 46.92 ± 12.77 years (25–77 years); the study included 64 (62.7%) men and 38 women. The cause of AP was gallstones in 52 patients (51.0%), alcoholism in 26 patients (25.5%), and hyperlipemia in 24 patients (23.5%). The WBC count in 35 patients (34.3%) was $>20 \times 10^9$/L, including 12 nonsurvivors. Pancreatic necrosis occurred in 74 patients, and >50% of the pancreas range was found in 42 of these patients. Fifty-three patients, including 19 nonsurvivors, developed MODS. Surgical interventions were performed in 45 patients.

Twenty-one patients (20.6%) died during hospitalization. The clinical prognostic factors associated with patient outcomes are shown in Table 1. The WBC count ($P = 0.035$) and serum amylase level ($P = 0.013$) were higher and serum calcium level was lower ($P = 0.014$) in the nonsurvivors than in the survivors. The following factors were significantly associated with a high mortality rate: APACHE II score ($P < 0.001$), WBC count $>20 \times 10^9$/L ($P = 0.013$), CTSI score ($P = 0.001$), pancreatic necrosis ($P = 0.002$), pancreatic necrosis >50% ($P < 0.001$), and MODS ($P < 0.001$). However, it was found that surgical intervention had no statistically significant relation to mortality ($P = 0.177$).

In all, 36 patients developed IAH; the association of various clinical parameters with IAH is shown in

Table 2 Comparative analysis of various factors related to the development of IAH in patients with SAP

	IAH (n = 36)	Non-IAH (n = 66)	*P* value
Mean age, y	45.39 ± 12.65	47.76 ± 12.85	0.373
Gender			
Male	19 (52.8%)	45 (68.2%)	0.124
Female	17 (47.2%)	21 (33.8%)	
Etiology			
Gallstones	20 (55.6%)	32 (48.5%)	0.308
Alcoholism	6 (16.7%)	10 (15.3%)	
Hyperlipidemia	10 (27.7%)	14 (21.2%)	
APACHE-II score	17.72 ± 3.71	13.47 ± 3.22	< 0.001
WBC count ($\times 10^9$/L)	20.20 ± 3.36	18.04 ± 4.07	0.008
CTSI score	7.44 ± 1.00	6.17 ± 1.51	< 0.001
Serum amylase level, IU/L	2178.3 ± 597.86	1780.97 ± 588.02	0.002
Serum calcium, mmol/L	1.65 ± 0.10	1.79 ± 0.13	< 0.001
Pancreatic necrosis			
Yes	35 (97.2%)	39 (59.1%)	< 0.001
No	1 (2.8%)	27 (40.9%)	
Pancreatic necrosis >50%			
Yes	27 (75%)	15 (22.7%)	< 0.001
No	9 (25%)	51 (77.3%)	
MODS			
Yes	24 (11.8%)	29 (44.1%)	0.028
No	12 (88.2%)	37 (55.9%)	

APACHE-II, Acute Physiology and Chronic Health Evaluation II; CTSI, computed tomography severity index; IAH, intra-abdominal hypertension; MODS, multiple organ dysfunction syndrome; SAP, severe acute pancreatitis; WBC, white blood cell.

Table 2. The following variables were significantly associated with the occurrence of IAH: WBC count ($P = 0.008$), serum amylase level ($P = 0.002$), serum calcium level ($P < 0.001$), APACHE-II score ($P < 0.001$), CTSI score ($P < 0.001$), pancreatic necrosis ($P < 0.001$), pancreatic necrosis >50% ($P < 0.001$), and MODS ($P = 0.028$).

However, the mean age, gender, and etiology were not significantly related to patient survival or the development of IAH. We used binary logistic regression to do a multivariate analysis and found that MODS and pancreatic necrosis >50% (hazard ratio, 2.666; $P = 0.025$) were independent predictors of survival in patients with SAP (Table 3).

Table 3 Multivariate analysis of prognostic factors for overall survival

Variable	Hazard ratio (95% CI)	*P* value
WBC count >20 $\times$ 10^9/L	0.912 (0.196–4.254)	0.907
Serum amylase level, IU/L	1.000 (0.999–1.001)	0.905
Serum calcium, mmol/L	0.292 (0.000–341.408)	0.733
APACHE-II score	0.904 (0.664–1.230)	0.520
CTSI score	1.937 (0.731–5.133)	0.184
Pancreas necrosis >50%	0.059 (0.006–0.549)	0.013
MODS	0.113 (0.021–0.608)	0.011
IAH	1.414 (0.343–5.831)	0.632

APACHE-II, Acute Physiology and Chronic Health Evaluation II; CTSI, computed tomography severity index; IAH, intra-abdominal hypertension; MODS, multiple organ dysfunction syndrome; WBC, white blood cell.

Discussion

Most clinical prognostic scores that aim to predict the severity and mortality rate of AP focus on the systemic response to the disease. The use of scoring systems helps to evaluate organ failure in AP patients. APACHE-II is the most widely used system for the evaluation of patients with SAP. Higher APACHE-II scores indicate greater severity of AP, with a corresponding increase in morbidity and mortality.[8] In this study, we found that APACHE-II scores significantly differed between survivors and nonsurvivors. Recently, a new prognostic scoring system, the bedside index for severity in AP, has been proposed as an accurate method for the early identification of patients at risk for mortality.[9–11] This bedside index is based on five points: urea nitrogen >25 mg/dL, impaired

mental status as evidenced by disorientation or disturbed mentation, systemic inflammatory response syndrome, age >60 years, and pleural effusion. Good-to-excellent discrimination between survivors and nonsurvivors has been reported with this index.[12]

Another new scoring system that has been used is the CTSI, which has some advantages over other systems in the prediction of AP severity.[13–15] CTSI scores are significantly correlated with mortality, and higher scores correlate with greater mortality rates. Patients with a CTSI score of 0, 1, or 2 exhibited nearly no mortality, whereas those with a score of 7 to 10 had a mortality rate of 17%.[16] In this study, we found that CTSI scores significantly differed between survivors and nonsurvivors.

Multiple organ failure is the most common and most severe factor that leads to death from SAP.[17] Renal and pulmonary failure were the most frequent complications in the present study. Patients with MODS had a significantly higher mortality than those without MODS. Furthermore, we found that MODS was an independent prognostic factor of survival in patients with SAP.

The extent of pancreatic necrosis also proved to be of major importance. Patients with necrosis of <30% of the pancreas exhibited no mortality, whereas those with larger areas of necrosis (30%–50% and >50%) had mortality rates of 11% to 25%.[18] In a multivariate analysis by Ocampo et al.,[19] the extent of pancreatic necrosis was related to the development of infected pancreatic necrosis. Another study showed that pancreatic necrosis was associated with higher morbidity and mortality rates.[20] In this study, we found that pancreatic necrosis was associated with higher mortality, and pancreatic necrosis >50% was an independent prognostic factor of survival in patients with SAP.

Furthermore, we found that WBC count, WBC count $>20 \times 10^9$/L, serum amylase level, and serum calcium level were significantly associated with mortality, which is consistent with previously reported results,[21] but were not associated with surgical intervention. In our study, age, gender, and etiology were not associated with mortality.

Early recognition and treatment of IAH and ACS significantly improves patient survival and decreases morbidity from AP.[22,23] In the present study, we evaluated the risk factors for IAH in patients with SAP. Like mortality, the development of IAH was significantly associated with WBC count, serum amylase level, serum calcium level, APACHE-II score, CTSI score, pancreatic necrosis, and MODS.

Conclusion

We demonstrated that the risk factors for both mortality and IAH from SAP are WBC count, serum calcium level, serum amylase level, APACHE-II score, CTSI score, pancreatic necrosis, and MODS, but that surgical intervention was not associated with high mortality rate. Furthermore, WBC count $>20 \times 10^9$/L and pancreatic necrosis of >50% were associated with a high mortality rate. The development of IAH was only related to pancreatic necrosis of >50%. MODS and pancreatic necrosis >50% were found to be independent risk factors for survival in patients with SAP and predicted a worse prognosis.

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