

# Severe acute pancreatitis in the elderly: Etiology and clinical characteristics

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## Abstract

**AIM:** To investigate the etiology and clinical characteristics of severe acute pancreatitis (SAP) in elderly patients ( $\geq 60$  years of age).

**METHODS:** We reviewed retrospectively all the SAP cases treated in Xuanwu Hospital in Beijing between 2000 and 2007.

**RESULTS:** In 169 patients with SAP, 94 were elderly and 16 died. Biliary and idiopathic etiologies were the first two causes that accounted for over 90% of SAP in the elderly. Biliary, hyperlipemic and alcoholic etiologies were the first three causes in the young. The proportion of co-morbidity of cholelithiasis, biliary infection, hypertension and coronary heart disease in the aged was significantly higher than that in their young partners. The scores of APACHE II and Ranson were also significantly higher in the elderly except the CT score. Organ failures were more common in the elderly, but the local pancreatic complications were not different between the two groups. Mortality of the aged was correlated with the severity of SAP, multiple co-morbidity and incidence of multiple organ dysfunction syndrome (MODS). MODS was the main cause of death.

**CONCLUSION:** The etiology of SAP in the elderly is quite different from that in the young. Biliary and unknown factors are main causes in the aged. The elderly are subject to major organ failures but there is no difference in the occurrence of local pancreatic complications between the elderly and the young. It is crucial to monitor and improve the functions of major organs so as to prevent MODS in the aged with SAP.

## INTRODUCTION

Severe acute pancreatitis (SAP) refers to the acute pancreatitis (AP) associated with organ failure and/or local complications such as necrosis, pseudocyst or abscess. The overall mortality of SAP has decreased in recent years to around 15%-20%<sup>[1,2]</sup>. Tenner<sup>[3]</sup> has shown in the aged, the presence of complications like infected pancreatic necrosis can increase the mortality to 50%. Fan<sup>[4]</sup> investigated the AP in the elderly ( $> 75$  years old) patients and indicated that the high mortality of this group is probably due to a higher prevalence of cardiopulmonary diseases and biliary stones. However, in China, the elderly refers to people aged 60 or over 60 years clinically. Few studies have compared the clinical characteristics between the elderly ( $\geq 60$  years old) and the young patients with SAP. In this retrospective study, we aimed to investigate whether there is a difference in etiology and clinical characteristics between the aged and its younger partners with SAP, and to analyze the factors that attribute to the high mortality in the elderly.

## MATERIALS AND METHODS

### Patients

Between January 2000 and January 2007, 169 patients with SAP were treated in the surgery intensive care unit (SICU) and the Department of General Surgery at Xuanwu Hospital of Capital Medical University in Beijing, China. All patients' medical charts were reviewed retrospectively and the relative clinical data were collected. Acute pancreatitis was diagnosed based on the facts of the elevation of serum amylase to more than 3 times the upper normal limit and a typical clinical picture, and the

diagnostic criteria of SAP were the APACHE II score of more than 8 within 72 h after admission<sup>[5]</sup>. Clinical severity evaluations were carried out by APACHE II and Ranson's scoring systems within 48 h after admission<sup>[6,7]</sup>. A serial abdominal contrast-enhanced CT (CECT) was performed in each patient and the findings were graded according to the Balthazar classification<sup>[8]</sup>.

On admission, all patients were treated medically according to generally accepted principles consisting of withholding oral intake, inserting a nasogastric tube for drainage, providing pain relief, restoring fluid and electrolytes intravenously, and administration of prophylactic antibiotics. A proton pump inhibitor and somatostatin were given to prevent stress ulcers and to inhibit pancreatic excretion. The Dachengqi decoction (a Chinese herbal medicine in fluid form) was given through the nasogastric tube twice a day to improve gastrointestinal function.

Patients with gallstones were evaluated by sonography routinely. Endoscopic retrograde cholangiopancreatography (ERCP) was performed in cases of biliary etiology, as proven by ultrasonography, or magnetic resonance cholangiopancreatography and elevated bilirubin, alkaline phosphatase and aspartate aminotransferase. A papillotomy was done if stones and sludge were present in the common bile duct and some were followed by an endoscopic nasobiliary drainage. Surgical intervention (necrosectomy with drainage and continuous postoperative lavage) was performed if infected pancreatic necrosis was clinically suspected or confirmed by positive bacteriologic results of CT-guided fine-needle aspirations.

Patients consuming large amounts of alcohol were considered as having alcoholic pancreatitis. Serum triglyceride level more than 11.3 mmol/L (1000 mg/dL), and exclusion of other etiologies were accepted as the hyperlipidemic etiology<sup>[9]</sup>. Patients were classified as having an idiopathic etiology if the history and laboratory findings ruled out any known etiologic factors, and ultrasonography revealed a normal biliary tract.

Co-morbidity was defined as a pre-existing disease or a condition in addition to the acute pancreatitis. Co-morbidity was diagnosed if the condition was an active problem and/or need routine treatment prior to the onset of acute pancreatitis. The assessment of organ function and diagnosis of multiple organ dysfunction syndrome (MODS) was performed on the basis of the Marshall multiple organ dysfunction score<sup>[10]</sup>.

### Statistical analysis

Statistical evaluation was performed with SPSS 11.0 for Windows. The significant differences of clinical characteristics of the aged and young SAP patients were tested with the  $\chi^2$  test. Clinical severity scoring of SAP, such as Ranson, APACHE II and CT scorings, was described with mean  $\pm$  SD. The differences between the two groups were tested through independent samples *t* test. *P* < 0.05 was considered statistically significant.

## RESULTS

### General clinical characteristics

Patient general characteristics are summarized in Table 1.

**Table 1** General clinical characteristics of patients with severe acute pancreatitis

	Elderly ( $\geq 60$ yr) ( <i>n</i> = 94)	Young (< 60 yr) ( <i>n</i> = 75)	<i>P</i> value
Mean age (yr, range)	70.9 (60-87)	44.2 (17-59)	-
Male	44 (46.8%)	49 (65.3%)	0.0197
Female	50 (53.2%)	26 (34.7%)	0.0197
Medium ICU stay in days (range)	8 (2-56)	8 (2-90)	-
Medium hospital stay in days (range)	21 (13-64)	19 (12-90)	-
Hospital deaths	16 (17.0%)	4 (5.3%)	0.0291

**Table 2** Etiology of severe acute pancreatitis *n* (%)

	Elderly ( $\geq 60$ yr)	Young (< 60 yr)	<i>P</i> value
Biliary	61 (64.9)	28 (37.3)	0.0006
Alcohol	2 (2.1)	15 (20.0)	0.0001
Hyperlipemia	3 (3.2)	22 (29.3)	< 0.0001
Abdominal surgery	2 (2.1)	1 (1.3)	1
Drug-induced	1 (1.1)	0 (0.0)	1
Idiopathic	25 (26.6)	9 (12.0)	0.021
Total	94	75	-

There were 169 patients with SAP in this study, including 94 aged ( $\geq 60$  years old) and 75 young (< 60 years old). The mean age of the aged was 70.9 years (range 60-87) and the young was 44.2 years (range 17-59). Of the 94 elderly patients, 44 (46.8%) were men, and 50 (53.2%) women. In patients younger than 60 years old, 49 (65.3%) were men, and 26 (34.7%) women. Medium stay in SICU was 8 d (2-56 d) in the aged and 8 d (2-90 d) in the young patients. Medium hospital stay was 21 d (13-64 d) in the aged and 19 d (12-90 d) in the young. The mortality rate of SAP was 17.0% (16 cases) in the aged and 5.3% (4 cases) in the young.

### Etiology

The two major etiological factors responsible for acute pancreatitis were biliary and alcohol, although the proportions of pancreatitis attributed to these two factors varied considerably in different countries and regions. In our 169 SAP patients, biliary pancreatitis was the first common etiology in both the aged and the young groups (Table 2), but it was more common in the elderly (64.9% *vs* 37.3%, *P* = 0.0006). Interestingly, the idiopathic pancreatitis was the second most common etiology in the aged patients, significantly more common than in its younger counterparts (26.6% *vs* 12.0%, *P* = 0.0210). In patients younger than 60 years of age, the second and third causes were hyperlipemia (29.3%) and alcohol (20.0%) respectively. However, in the elderly, these two etiologies were less common (3.2% and 2.1% respectively). Two cases of pancreatitis underwent abdominal surgery in the elderly and one in the young. The operations were esophageal cancer resection, cholecystectomy and gastrectomy, respectively. One elderly woman experienced drug-induced SAP while taking Methotrexate.

Table 3 Co-morbidity of severe acute pancreatitis *n* (%)

	Elderly (≥ 60 yr)	Young (< 60 yr)	<i>P</i> value
Cholelithiasis	47 (50.0)	18 (24.0)	0.0008
Biliary infection	20 (21.3)	5 (6.7)	0.0087
Hypertension	20 (21.3)	4 (5.3)	0.0035
Coronary heart diseases	14 (14.9)	4 (5.3)	0.0490
Previous stroke	5 (5.3)	0 (0.0)	0.0667
Previous myocardial infarction	4 (4.3)	1 (1.3)	0.3836
Diabetes mellitus	8 (8.5)	9 (12.0)	0.6079
Liver cirrhosis	3 (3.2)	2 (2.7)	1.0000
Malignant diseases	4 (4.3)	1 (1.3)	0.3836
Autoimmune diseases	0 (0.0)	1 (1.3)	0.4438

Table 4 Clinical scoring of severe acute pancreatitis (mean ± SD)

	Elderly (≥ 60 yr, <i>n</i> = 94)	Young (< 60 yr, <i>n</i> = 75)	<i>P</i> value
Ranson	3.4 (1.7)	2.8 (1.6)	0.0069
APACHE II	14.0 (7.6)	9.9 (6.6)	0.0003
CT score	4.0 (1.9)	4.8 (1.8)	0.0020

### Co-morbidity

Co-morbidity was defined as a pre-existing disease or condition in addition to the current onset of pancreatitis (Table 3). The morbidity of cholelithiasis, biliary infection, hypertension and coronary heart disease in the aged was significantly more common than in the young. Previous stroke was diagnosed in five aged patients but none in the young (5.3% *vs* 0%, *P* = 0.0667). Diabetes mellitus, previous myocardial infarction, liver cirrhosis, malignancies and autoimmune diseases might be seen in both groups.

### Clinical scoring of SAP

In our study, three clinical scores, APACHE II, Ranson's and CT score, were collected (Table 4). The scores of APACHE II and Ranson were significantly higher in the aged than in the young ( $3.4 \pm 1.7$  *vs*  $2.8 \pm 1.6$ , *P* = 0.0069). Surprisingly, the CT score was higher in the younger patients ( $4.8 \pm 1.8$  *vs*  $4.0 \pm 1.9$ , *P* = 0.0020).

### Organ failures and complications of SAP

Organ failures and complications were two major characteristics of SAP distinguished from mild pancreatitis. As shown in Table 5, the most frequent complications of SAP in the aged are acute lung injury (ALI) and/or acute respiratory distress syndrome (ARDS) (30.9%), followed by MODS (26.6%), electrolyte disturbances (21.3%), renal failure (18.1%), pancreatic encephalopathy (17.1%) and cardiovascular insufficiency (17.0%). Except for metabolic disorders and cardiovascular insufficiency, the incidences of ALI/ARDS, MODS, renal failure and pancreatic encephalopathy in the elderly were significantly higher than those in the young. The other complications, such as GI bleeding, paralytic ileus, pancreatic pseudocyst, pulmonary infection, fungous infection, abdominal compartment syndrome (ACS) and disseminated intravascular coagulation (DIC), occurred less frequently (< 15%) in both the elderly and the young.

Table 5 Organ failures and complications in severe acute pancreatitis *n* (%)

	Elderly (≥ 60 yr)	Young (< 60 yr)	<i>P</i> value
Total	94 (100)	75 (100)	
ALI/ARDS	29 (30.9)	13 (17.3)	0.0498
Renal insufficiency	17 (18.1)	5 (6.7)	0.0375
Cardiovascular insufficiency	16 (17.0)	11 (14.7)	0.8331
Pancreatic encephalopathy	16 (17.0)	4 (5.3)	0.0291
Hepatic insufficiency	8 (8.5)	5 (6.7)	0.7754
Metabolic disorders	20 (21.3)	12 (16.0)	0.4334
DIC	5 (5.3)	4 (5.3)	1.0000
GI bleeding	5 (5.3)	5 (6.7)	0.7521
With single organ failure	42 (44.7)	16 (21.3)	0.0019
With MODS	25 (26.6)	10 (13.3)	0.0374
Pancreatic abscess	13 (13.9)	13 (17.3)	0.6685
Pancreatic pseudocyst	11 (11.7)	8 (10.7)	1.0000
Ileus	9 (9.6)	6 (8.0)	0.7909
ACS	5 (5.3)	4 (5.3)	1.0000
Fungous infection	4 (4.3)	1 (1.3)	0.3836
Sepsis	8 (8.5)	6 (8.0)	1.0000

ALI/ARDS: Acute lung injury or acute respiratory distress syndrome; MODS: Multiple organ dysfunction syndrome; GI: Gastrointestinal; ACS: Abdominal compartment syndrome; DIC: Disseminated intravascular coagulation.

Table 6 Clinical characteristics of dead and survived cases in the aged with severe acute pancreatitis *n* (%)

		Death ( <i>n</i> = 16)	Survival ( <i>n</i> = 78)	<i>P</i> value
Gender	Male	9 (56.3)	35 (44.9)	0.4255
	Female	7 (43.7)	43 (55.1)	0.4255
Etiology	Biliary	10 (62.5)	51 (65.4)	1.0000
	Idiopathic	5 (31.3)	20 (25.6)	0.7570
Scoring (mean ± SD)	Ranson	5.6 ± 1.8	3.1 ± 1.3	< 0.0001
	APACHE II	26.3 ± 9.3	11.9 ± 4.7	< 0.0001
	CT score	5.6 ± 2.1	3.7 ± 1.7	0.0001
Co-morbidity	Single	4 (25.0)	28 (35.9)	0.5647
	Multiple	12 (75.0)	24 (30.8)	0.0015
Organ dysfunction	Single	1 (6.3)	16 (20.5)	0.2882
	MODS	15 (93.8)	10 (12.8)	< 0.0001

### Mortality of SAP in the elderly

The mortality of SAP in the aged was significantly higher than that of the young in our data (17.0% *vs* 5.3%, *P* = 0.0291, Table 1). We further compared the clinical characteristics of the dead and the surviving patients of the elderly (Table 6). We found no difference in either gender or etiologies between the two subgroups. Only the severe scores, multiple co-morbidities and MODS were significantly higher in the subgroup of the dead patients and almost all of this subgroup died of MODS.

## DISCUSSION

In most studies, the two major etiological factors, biliary disease and alcohol abuse together account for more than 80% of AP patients<sup>[11,12]</sup>. Studies in the United Kingdom reveal that 40%-57% of patients with AP have small gallstones<sup>[13,14]</sup>.

In our study, biliary pancreatitis was the most common

cause for SAP in both aged and young patients. However, biliary etiology in the elderly is as high as 64.9%, we thought it was because very few patients were addicted to alcohol and the incidence of cholelithiasis increased in this subgroup. Meanwhile, unknown etiology, or idiopathic pancreatitis accounted for 26.6% of the elderly and ranked second, quite different from the etiologies in the young patients. This is similar with other reports in which 30%-40% of elderly patients with acute pancreatitis have an unclear etiology<sup>[15]</sup>. Interestingly, the second more common etiology was not alcohol abuse but hyperlipemia in the young patients in our study. Although alcoholism was associated with over 80% of patients in studies from New York and around 70% in Scandinavian countries, in the Beijing area, it seems not a major concern.

Many drugs are associated with the development of acute pancreatitis. These include didanosine, furosemide, corticosteroids, azathioprine and sodium valproate<sup>[16]</sup>. However, there is no clinical feature that can differentiate drug-induced pancreatitis from other factor caused-pancreatitis. Drug-induced pancreatitis is usually diagnosed using the following criteria: pancreatitis developed during treatment, resolved following the discontinuation of the drug, and re-developed following re-challenge of the offending drug<sup>[17]</sup>. Because no causal factor for pancreatitis was found after the initial work-up, acute pancreatitis induced by Methotrexate was suspected in a 63 years old woman who took it for a week and her symptom was relieved after cessation of the drug.

Even though the mortality of SAP is around 22%-30%, few data showed the mortality of SAP in the elderly. A Japanese survey done from 1991 to 1995 showed that the mortality of SAP is greater than 20% in patients over 50 years of age<sup>[18]</sup>. Andersson reported that the hospital mortality of AP in a university hospital in Sweden decreased slightly, from 4.7% (1975-1985) to 3.7% (1986-1996), and that the average age of the dead patients markedly increased from 59.2 to 73.6 years<sup>[19]</sup>. This suggested that the older the patients, the higher mortality they have. Fan<sup>[4]</sup> has concluded that mortality from AP was related to coexisting diseases in the elderly, not to the severity of acute pancreatitis and reported a 21.3% mortality from AP in patients aged above 75 years. Browder<sup>[15]</sup> also believed organ function compromise correlates with mortality and appears more significant than severity of pancreatic disease. In our study, the co-morbidities, including cholelithiasis, biliary infection, hypertension and coronary heart disease were more common in the aged. The mortality of SAP in this group was 17%, but 5.3% in the young.

Recently, Kaya<sup>[20]</sup> demonstrated that the APACHE II score is the best predictor of mortality among Ranson, Imrie and APACHE II scores. We found that both APACHE II and Ranson's criteria were of significance in predicting mortality in the aged. Unexpectedly, the CT score was different from the two above scores, and it was lower than in the aged patients. This seems that the average local pathological conditions in the aged were less serious than that in the young patients. To explain this data with caution and to exclude the heterogeneity of the aged group, we further analyzed the dead and the living cases in the elderly. The CT score was markedly higher

in the deceased cases, suggesting that it is still a sensitive predictor for mortality from SAP. Leung<sup>[21]</sup> reported that the sensitivity of CT severity index (CTSI) is higher than Ranson score and APACHE II score, although they are also the predictors for complications, mortality and the length of AP course. Some researches suggest that MRI seems to be a reliable method of staging AP severity in comparison with CECT scan<sup>[22]</sup>. Otherwise, C-reactive protein (CRP) is a useful indicator for assessing severity and recommended to apply in clinical practice<sup>[23,24]</sup>.

The most frequent complication of SAP in the aged in our study is ALI/ARDS (29 cases, 30.9%), followed by MODS (25, 26.6%), electrolyte disturbances (21.3%), renal failure (17, 18.1%), pancreatic encephalopathy (16, 17.0%) and shock (16, 17.0%). Currently, there are no specific examinations or unified diagnostic standards for pancreatic encephalopathy. It results from the combined actions of multiple factors based on cerebral demyelination due to pancreatin<sup>[25]</sup>. In our study, it was diagnosed according to clinical symptoms and electroencephalogram or MRI.

The local pancreatic complications, such as pancreatic abscess, pancreatic pseudocyst and ACS, are not different between the two groups. It supports the opinion that the local pathological condition is not the critical factor but organ dysfunction, especially cardiovascular, pulmonary, renal and cerebellar function, for the high incidence of death in the elderly. This phenomenon could be related to the progressive decline in physiological function of major organs with aging. The other complications, such as alimentary tract hemorrhage, pulmonary infection, fungous infection and disseminated intravascular coagulation (DIC), do not occur so frequently (< 15%) and there is no difference between the elderly and the young. We suggest that in treatment of SAP in the aged, priority should be given to monitoring and improving the functions of major organs so as to prevent MODS. At the same time, it is necessary to find out the origin of SAP and remove it early by minor-injury method. Additionally, the fluid quantity and speed of transfusion should be decreased in the aged and the dose of medicine should be used properly in order to avoid injury of the organ function.

In our study, the incidence of paralytic ileus was less than 10%. It may be associated with the gastrointestinal functions. SAP patients admitted to our intensive care unit were given purgatives, such as magnesium sulfate, Mannitol, lactulose and Dachengqi decoction (Chinese herbal medicine). These drugs could promote gastrointestinal motility, ameliorate intestinal permeability and decrease bacterial translocation<sup>[26,27]</sup>. They can also improve bile discharge and decrease effusion in the abdominal cavity. Rhubarb is the main constituent of Dachengqi decoction. Rhubarb can exert protective effects on SAP by inhibiting the inflammation of pancreas in rats, improving pancreatic microcirculation and altering exocrine secretion<sup>[28]</sup>. Wu<sup>[29,30]</sup> also reported the benefit from Chinese herbal medicine in treatment of SAP and recommended the regimen for clinical use.

In conclusion, SAP in the aged had obviously different features from the young. Both of biliary and unknown etiological factors result in over 90% of SAP in elderly. The co-morbidities of cholelithiasis, biliary

infection, hypertension and coronary heart disease are more common than in the young. APACHE II scores and Ranson's criteria are markedly higher in the elderly and CT scores much higher in the elderly who died in the hospital. Therefore, the mortality of the aged patients is correlated with the severity of SAP, and co-morbidity and incidence of MODS are not relevant to patients' gender or etiologies. Importance should be attached to monitoring and improving the functions of major organs so as to prevent MODS in the aged with SAP.

## COMMENTS

### Background

The overall mortality of severe acute pancreatitis (SAP) has decreased in recent years to around 15%-20%. Few studies compared the clinical characteristics between the elderly ( $\geq 60$  years old) and the young patients with SAP.

### Research frontiers

Some researches have shown that the presence of complications such as infected pancreatic necrosis, in the aged ( $> 75$  years old) can increase the mortality of AP to 50%, probably due to a high prevalence of cardiopulmonary diseases and biliary stones.

### Innovations and breakthroughs

The authors retrospectively reviewed the SAP cases that were treated in a hospital in Beijing between 2000 and 2007 to investigate the etiology, clinical characteristics and outcomes of SAP in the elderly patients.

### Applications

The authors suggest that importance should be attached to monitoring and improving the functions of major organs so as to prevent MODS in the aged with SAP.

### Peer review

This article reviews the experience with elderly patients in China with SAP. This is an interesting and well-written paper.

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