

## Review Article

## New Paradigm of Diagnosis of Severe Acute Necrotizing Pancreatitis

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## Introduction

About 20-30% of patients with acute pancreatitis have a severe disease and mortality rate among inpatients were 15%. Globally, the incidence of Acute Pancreatitis (AP) is increasing year by year, but its complications and mortality are not decreasing. There are many causes of AP, but most common cause of AP is an alcohol. According to some studies in our country, alcohol is the number one cause of acute pancreatitis and the mortality rate is 15.3%. Mortality rates in the event of acute pancreatitis caused by complication which is the pancreatic necrosis, intoxication, hemorrhage and multiple organ failure [1,2]. Diagnosis of AP, optimal choice of treatment tactics at different stages of the peritoneal inflammatory process, early detection of the type and location of necrotic inflammation, detection of infectious evidence of necrosis, objective assessment of the nature of the injury, as well as the severity of the patient (intoxication syndrome) are very important factors to identify course of the disease and prognosis [3,4]. In addition to the detection of pancreatic infection, it is important to evaluate the patient's physical condition using the most commonly used Ranson criteria, APACHE II and SAPS criteria when selecting surgical indications and comprehensive treatment regimens [5,6]. In our country, the ability to determine some of the indicators of these evaluation systems is limited to province and district hospitals. There is no systematic assessment system for differentiating ANP in our country, and no research has been conducted when selecting the treatment options, assessing the course of the disease and prognosis. Therefore, based on the above, there is an urgent need to conduct research to address important issues and to improve the diagnosis and treatment of acute alcohol-induced necrotizing pancreatitis.

## Goal

Determine the importance of early diagnostic assessment of alcohol-induced severe acute necrotizing pancreatitis

## Materials and Methods

We conducted our research using an observational research model and a factual research method. Sampling of research materials

will be carried out by targeted sampling. From November 1, 2008 to January 1, 2020, 122 patients who were hospitalized with alcohol-induced AP were selected and archival documents or medical histories were selected. Data were retrospectively collected based on medical history analysis using a specially designed 90-question card. In the first quarter of 2018, our research team developed a new 90-question card and new recording system for determining necrosis, stage and prognosis of acute pancreatitis Table 1.

No	Hospitalization	NO	YES
1	WBC > 16*10 <sup>9</sup> L	0	1
2	Abdominal bloating, Abdominal tenderness, Abdominal pain +1 >2 symptom	0	1
3	Serum LDH > 450 u/l	0	1
4	Serum Amylase >1000 u/l or <50 u/l	0	1
5	Blood Glucose >200 mg/dl (> 11 mmol/l)	0	1
6	SIRS-Systemic inflammatory response syndrome	0	1
<b>Within 24-48 hours after hospitalization</b>			
7	Serum Ca <sup>2+</sup> < 8 mg/dl (< 2.0 mmol/l)	0	1
8	BUN > 5 mg/dl (>1,98 mmol/l)		1
9	C-Reactive protein test >120 mg/l		1
10	Procalcitonin -PCT > 0.8 ng/l	0	1
11	Serum Lipase > 200 u/l	0	1
12	Balthazar grade C,D,E	0	1
Total -12			

## Version of Table 1:

- Score of from 1 to 3 indicates -A- Mild acute pancreatitis.
- Score of from 4 to 6 indicates -B- Moderate acute pancreatitis and suspected acute necrotizing pancreatitis.
- Score of 7 or more indicates -C- Severe acute necrotizing pancreatitis.

**Table 1:** New recording system for determining necrosis, stage and prognosis of acute pancreatitis.

### Statistical Analysis

Statistical analysis was performed using correlation analysis of the causative factors, outcomes, or prognosis of the disease. Also statistical analysis was performed using averages, ANOVA test, regression analysis methods to calculate the clinical signs and changes in the analysis related to the new evaluation system.

### Results

The minimum age of patients with ANP was 25 and the maximum was 71, with the majority (87.4%) aged 26 to 60 years.

Data	Number	Lower limit	Upper limit	Average	Std. Deviation
Age	122	25	71	44.8852	10.65088
Valid N)	122				

**Table 2:** The average age of the patients in the study.

The amount of alcohol		Count		Total
		Died	Cured	
Alcohol volume	Standard alcohol intake	0	1	1
	More than standard alcohol intake	1	33	34
	Twice as much as standard alcohol intake	7	47	54
	4 times or more than standard alcohol intake	23	10	33
Total		31	91	122

**Table 3:** The amount of alcohol and Prognosis.

When the Person Correlation method calculates the relationship between alcohol consumption and mortality, it is assumed that the weaker the correlation, the higher the amount of alcohol consumed, the lower the cure and the higher the mortality ( $P < 0.05$ ).

Period of drinking alcohol		Prognosis		Total
		Died	Cured	
The time from the onset of the disease to hospitalization	Delayed	24	40	64
	On time	7	51	58
Total		31	91	122

**Table 4:** The time from the onset of the disease to hospitalization \* prognosis.

Of the 31 deaths reported in the study, 24 (77.4%) were hospitalized more than 72 hours after the onset of the disease. Late hospitalization and late treatment of patients with ANP disease have been shown to adversely affect the prognosis of the disease.

Blood tests	New recording system				P -value
	Mild 1	Moderate 2	Severe 3	Total	
	(n=12)	(n=69)	(n=41)	(n=122)	

	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	
White blood cells(hospitalization)	12.12 ± 5.2	14.54± 3.9	18.62± 4.9	15.7 ± 4.9	0
White blood cells(48-72 h)	11.34± 4.7	14.24± 4.2	15.30± 3.2	14.32 ± 4.1	0.005
Neutrophils	74.9 ± 11.4	78.5 ± 18.8	84.8 ± 11.0	80.3 ± 16.2	0.021
Thrombocyt	212.1 ± 94.6	313.1 ± 174.3	231.3 ± 87.4	275.7 ± 149.3	0.299
Hemoglobin	14.9 ± 1.39	13.2 ± 2.70	14.5 ± 1.26	13.8 ± 2.29	0.372
Hematocrit(hospitalization)	44.3 ± 5.21	42.7 ± 11.6	42.9 ± 8.1	42.3 ± 10.0	0.829

**Table 5:** Blood analysis results of the participants.

Biochemical tests	New recording system				p-value
	A	B	C	Total	
	(n=12)	(n=69)	(n=41)	(n=122)	
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	
Serum amylase	937.2 ± 1183.9	1058.8 ± 1280.6	1701.5 ± 1016.7	1262.8 ± 1220.8	0.008
Serum LDH	367.0 ± 135.9	509.3 ± 235.3	570 ± 98.2	515.8 ± 198.0	0.003
Blood sugar	7.05 ± 3.73	7.24 ± 4.1	8.9 ± 6.19	7.8 ± 4.88	0.098
Serum calcium	2.10 ± 0.29	1.99 ± 0.23	1.78 ± 0.11	1.93 ± 0.23	0
Serum calcium (48 h)	2.05 ± 0.26	1.9 ± 0.21	1.7 ± 0.15	1.87 ± 0.22	0
C-reactive protein	95.83 ± 45.21	170.29 ± 59.59	180.13 ± 67.01	166.27 ± 65.05	0.001
Serum lipase	130.9 ± 35.2	200.6 ± 41.3	240.2 ± 120.0	195.5 ± 70.8	0.002
Procalcitonin test	0.55 ± 0.95	1.10 ± 1.75	2.96 ± 1.73	1.67 ± 0.95	0.043
Blood urea nitrogen	11.09 ± 15.9	5.84 ± 6.22	6.31 ± 4.84	6.52 ± 7.42	0.209
Total proteins	67.9 ± 8.1	63.7 ± 8.1	65.5 ± 6.8	64.7 ± 7.7	0.882
Albumins	41.7 ± 7.5	37.2 ± 9.9	40.6 ± 8.6	38.8 ± 9.4	0.547
Serum GPT	66.5 ± 99.1	69.6 ± 71.2	80.7 ± 73.6	73.0 ± 74.6	0.439
Serum GOT	61.0 ± 89.4	63.4 ± 59.5	95.1 ± 89.8	73.9 ± 74.9	0.041
Creatinine	110.9 ± 38.2	73.6 ± 44.6	99.3 ± 120.0	141.5 ± 80.9	0.002

**Table 6:** Biochemical analysis results of the participants.

In our study, all parameters were significant, but White blood cells, neutrophils, serum amylase, serum LDH, Procalcitonin test, serum lipase, Creatinine, C-reactive protein, serum GOT was found to be higher than the value specified in the evaluation system for the variable ( $P < 0.05$ ). (For determining pancreatic necrosis). Regression analysis showed that white blood cells, Procalcitonin, serum LDH, serum lipase, C-reactive protein and serum amylase were higher than those specified in the evaluation system, and that the level of significance for the variable (indicating a severe pancreatitis or poor prognosis) was higher than other test results ( $P < 0.05$ ). According to the new evaluation system, 12 out of 122 patients were classified as A class or 0-3, 69 (56.5%) patients were class B or 4-6, and 41 (33.6%) patients were class C or  $> 7$  points. Of the total cases, 90.1% were rated as severe form of ANP and pancreatic necrosis by the classification system we developed.

New recording system		Biopsy			Total
		Edematous pancreatitis	Pancreo necrosis	Purulent pancreonecrosis	
Classification	0-3 A	1	0	0	1
	4-6 B	1	21	29	51
	>7 C	0	19	22	41
Total		2	40	51	93

**Table 7:** New recording system \* Biopsy.

After evaluating the subjects by the evaluation system and comparing them with the biopsy, it was confirmed that the patients belonging to the B and C categories of the evaluation system had pancreatic necrosis and inflammation.

New recording system		Prognosis		Total
		Died	Cured	
Classification system	0-3 A	0	12	12
	4-6 B	7	62	69
	Higher than 7 C	24	17	41
Total		31	91	122

**Table 8:** New recording system\*Prognosis.

When we assessed the prognosis with the new assessment system, we found that 100 percent of patients in category A were cured, 89.8 percent of patients in category B were cured, and 41.5 percent of patients in category C were cured and 58.5 percent died. Statistical calculations using the correlation analysis method for the correlation between the score and the cure of the evaluation system shows negative correlation ( $P < 0.05$ ). In other words, the higher the score of the evaluation system, the lower the cure rate and the higher the mortality rate.

## Discussion

Serum pancreatic enzyme measurement is the “gold standard” for the diagnosis of AP [7]. In an episode of AP, amylase, lipase, elastase, and trypsin are released into the bloodstream at the same time but the clearance varies depending on the timing of blood sampling. Amylase is an enzyme secreted by the pancreas, and also salivary glands, small intestine, ovaries, adipose tissue, and skeletal muscles. There are two major isoforms of amylase: pancreatic and salivary, and the leading function is digestion of starch, glycogen, and related poly- and oligosaccharides, by hydrolysis [9]. In AP, serum amylase levels usually rise within 6 to 24 h, peak at 48 h, and decrease to normal or near normal levels over the next 3 to 7 days [4-6]. Lipase is another enzyme secreted by the pancreas. AP is the main reason for an increase in lipase, and many investigators emphasize that lipase is more specific, but can be found elevated also in non-pancreatic diseases such as renal disease, appendicitis, acute cholecystitis, chronic pancreatitis,

bowel obstruction, etc. [4]. In AP, serum lipase remains elevated for a longer period than serum amylase. It rises within 4 to 8 h, peaks at 24 h, and decreases to normal or near normal levels over the next 8 to 14 days [5,6]. A Cochrane revision with the aim to compare the diagnostic accuracy of different pancreatic enzymes in the diagnosis of AP showed a sensitivity and specificity of 72% and 93% for serum amylase, and 79% and 89% for serum lipase, respectively [8]. Our study found an increase in lipase during SANP, which is of diagnostic value or statistically significant, especially in the diagnosis of necrotic inflammation ( $P < 0.05$ ).

Many textbooks consider the C-reactive protein (CRP) as the gold standard for disease severity assessment [9]. Using a cut-off value from 110 to 150 mg/l, the sensitivity and specificity ranged from 38 to 61%, and 89 to 90%, respectively, at the time of hospital admission [9]. The major drawback of C-reactive protein is that peak levels are reached only after 48 to 72 h. In our study, C-reactive protein was one of the most important tests for severe disease and necrosis in the SANP. Some studies have shown that procalcitonin is important in determining the severity of acute pancreatitis and in predicting the risk of infecting pancreatitis [10]. Procalcitonin is indicated in patients with confirmed pancreatic necrosis to predict necrotic infection [10-14]. A procalcitonin value of 3.8 ng/ml or higher within 96 h after onset of symptoms indicated a pancreatic necrosis with a sensitivity and specificity of 93% and 79% [10,13]. In our study, an increase in procalcitonin levels was statistically significant ( $P < 0.05$ ) in determining the severity and severity of the disease. Studies by Staubli SM [16]

and Yang CJ [11] have shown that pancreatic necrosis is 93% and 79% sensitive and specific if procalcitonin levels are 3.8 ng/mL or higher within 96 hours of onset of symptoms [6,11]. Studies by Valverde-Lopez F [12] have shown that a drop in blood calcium levels (1.8 mmol/l) occurs during ACS, which is often seen as a symptom of ASA necrosis [12].

In our study, it was possible that the level of calcium in the blood was reduced ( $P < 0.05$ ) in the necrotic form of ANP compared with non-necrotic necrosis. Therefore, blood calcium levels are considered to be one of the most important tests to be performed in patients with ANP. The PPV for the Ranson score ranges from 28.6 to 49% (sensitivity 75–87%, specificity 68–77.5%), for the Glasgow score from 59 to 66% (sensitivity 61–71%, specificity 88–89%), for the APACHE II score, 55.6% after 48 h (sensitivity 83.3%, specificity 91%), and for the APACHE-O score 54–80% (sensitivity 69–74%, specificity 86–90%). All these scores can only be assessed after 48 h, and thus do not enable risk stratification on admission. Despite their weaknesses, these scores are still useful to prove or exclude severe disease [14]. A study of 161 patients evaluated the assessment and comparison of the early predictability of various parameters most widely used in AP. They found the significant cutoff values for prediction of severe AP were Ranson  $\geq 3$ , BISAP  $\geq 2$ , APACHE-II  $\geq 8$ , CTSI  $\geq 3$ , and CRP at 24 h  $\geq 21$  mg/dl ( $> 210$  mg/l). They concluded that different scoring systems showed similar predictive accuracy for severity of AP, but that APACHE-II demonstrated the highest accuracy for the prediction of SAP [15]. According to evaluated our new scoring system, 69 (56.5%) patients were in category B ( $> 3$  scores) of 122 patients and 41 (33.6%) patients in category C or above 7 scores. 90.1% of all cases were evaluated by our new scoring system in severe AP, necrotizing pancreatitis.

The patients who classified A category by new scoring system were 100% cured and 89.8% of patients classified B were healed, while 41.5% of the patients classified C category were healed and mortality rate was 58.5%. The correlation between new scoring system and recover of patient is evaluated based on statistical calculations using the correlation analysis method, the variable was negative ( $P < 0.05$ ). Comparing to other scoring systems, our scoring system is equally effective. But it is easy to use in the hospitals of developing countries because of using few high-sensitive indicators. Comparing to other researches, difference of our research is in creating new scoring system of acute pancreatitis, especially first time in Mongolia [16-30].

## Conclusion

- In Mongolia, relatively young men suffer from alcohol-induced pancreatitis. Factors contributing to the development of necrosis in acute pancreatitis include alcohol abuse, prolonged alcohol use, delayed hospitalization, and delayed treatment.

- In our study, following clinical signs and laboratory findings are effective in distinguishing severe forms of acute pancreatitis, early diagnosis, assessment of prognosis, and development of surgical treatment tactics. Laboratory tests include: increase in white blood cells, neutrophils, serum amylase, Procalcitonine, serum LDH, serum lipase, C-reactive protein and a decrease in hematocrit, serum calcium.
- The new recording system that we have developed for early diagnosis, progression and prognosis of severe forms of acute pancreatitis is easy to evaluate, and it is possible to determine the criteria included in the evaluation system in the secondary and tertiary hospitals of Mongolia.

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