

New Recording System of Diagnosis of Acute Necrotizing Pancreatitis

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Abstract

About 20%-30% of patients with acute pancreatitis have a severe disease and mortality rate among inpatients were 15%. There are many causes of Acute Pancreatitis (AP), but most common cause of AP is an alcohol. 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 necrotizing pancreatitis, early diagnosis, and assessment of prognosis. Laboratory tests parameters include of new recording system: increase in white blood cells, procalcitonin, serum amylase, serum LDH, serum lipase, C-reactive protein and a decrease in hematocrit, serum calcium.

Keywords: Neutrophils • Serum amylase • Serum lipase • C-reactive protein • Procalcitonin

Introduction

Pancreatitis is a pathological condition where the pancreas becomes inflamed, and its cells are damaged. There are two types of pancreatitis, acute and chronic. Globally, the incidence of Acute Pancreatitis (AP) is increasing year by year, but its complications and mortality are not decreasing. It has been suggested that about 40% of the AP is caused by excessive alcohol consumption, while another 40% is due to gallstones. The severity of AP ranges from mild to severe and life-threatening. Usually, mild AP has a low mortality rate (less than 1%), whereas the mortality rate of severe AP can be up to 30%. The prospective cohort study of Pang et al. showed that weekly drinkers and heavy drinking episodes were associated with a 50% excess risk of acute pancreatitis compared to that with non-drinkers. Further, individuals with diabetes had a 34% higher risk of acute pancreatitis [1]. Razvodovsky et al. also reported the highest age-standardized sex-specific male and female pancreatitis mortality caused by alcohol was 63.1% and 26.8%, respectively [2-5]. According to WHO statistics, almost one in five Mongolian men binge-drink weekly, and this high consumption has become the primary cause of acute pancreatitis. Domestic reports reveal that the mortality rate of AP due to the excess use of alcohol is 15.3% in Mongolia [6].

Mortality due to acute pancreatitis is caused by complications arising from several pathological conditions, including pancreatic necrosis, intoxication, hemorrhage and multiple organ failure [6,7]. Pancreatic necrosis is complex and especially challenging, occurring in 40% to 70% of patients. Necrotizing Pancreatitis (NP) can be divided into 2 phases. In the early phase, an inflammatory response syndrome occurs, caused by pro-inflammatory cytokines. The second phase is dominated by sepsis-related complications such as pulmonary, renal and cardiovascular failure arising from the infection of the necrotic pancreas. The diagnosis of acute necrotizing pancreatitis, the 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 essential factors to identify the course of the disease and have prognostic significance [8-10].

In addition to the detection of pancreatic infection, it is important to evaluate the patient's physical condition using the most commonly Ranson, APACHE II, and SAPS criteria when selecting surgical indications and comprehensive treatment [11,12]. Unfortunately, in our country, the ability to determine some of the indicators of these evaluation systems is limited in the aimag and district hospitals. Therefore, there is no systematic assessment system for differentiating acute necrotic pancreatitis usable throughout our country. Therefore, the study's objective is to propose and demonstrate a new scoring system based on the clinical features and readily available diagnostic parameters for acute alcohol-induced pancreatic necrosis to develop diagnostic and treatment algorithms and aid with prognosis (Table 1 and 2).

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

At the hospitalization			
No		NO	YES
1	WBC>16 × 10 ⁹ 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
Within 24-48 hours after hospitalization			
7	Serum Ca ²⁺ <8 mg/dl (<2.0 mmol/l)	0	1
8	BUN>5 mg/dl (>1.98 mmol/l)	0	1
9	C-Reactive protein test >120 mg/l	0	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			

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 and Score of 7 or more indicates-C- Severe acute necrotizing pancreatitis.

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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 3).

Exclusion criteria

WPatients who presented with unconsciousness, concomitant multiple organ disease or chronic multiple organ failure, cancer, acute non-alcoholic pancreatitis, chronic organ system disease with increased levels of C-reactive protein, and systemic inflammatory response syndrome caused by infectious diseases were excluded.

Statistical analysis

Descriptive statistics, including frequency, percentages, mean, Standard Deviation (SD), median and range were calculated to evaluate demographic and clinical characteristics. For continuous variables, ANOVA tests with Tukey's multi-comparison test were used. For categorical variables, Chi-square and Fisher's exact tests were carried out to determine statistically significant differences. For hypothesis testing, the critical p-value was set at 0.05. The statistical analysis was performed using Stata MP Version 16.0.

Ethical statement

The study was approved by the Ethical Review Sub-Committee of Ach Medical School on May 15, 2020 (Table 4). In the study, the medical histories of patients admitted to the hospital with AP diagnosis were obtained from the archives of The First Central Hospital and Third State Central Hospital. The patient's name was encrypted, no personal identifying information was used, and confidentiality was maintained.

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. 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 Acute Necrotizing Pancreatitis (ANP) disease have been shown to adversely affect the prognosis of the disease (Table 5). In our study, all parameters were significant, but procalcitonin, serum amylase, serum lipase, serum LDG8 C-reactive protein, serum glucose was found to be higher than the value specified in the evaluation system for the variable (in determining pancreatic necrosis) (Table 6). ANOVA analysis test showed that white blood cells, procalcitonin, serum amilza, serum lipaza, serum glucose, serum LDG, C-reactive protein 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 ($p < 0.01$). Of the total cases, 90.1% were rated as severe form of ANP and pancreatic necrosis by the classification system we developed. The 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 ($p < 0.05$) (Table 7). in other words, the higher the score of the evaluation system, the lower the cure rate and the higher the mortality rate.

The average age of the patients in the study					
	Number	Lower limit	Upper limit	Average	Std. Deviation
Age	122	25	71	44.8852	10.6509
Valid N)	122				

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

Alcohol volume*Prognosis				
	Count	Prognosis		Total
		Died	Cured	
		Standard alcohol intake	0	
More than standard alcohol intake	1	33	34	
Alcohol volume	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. When the Person Correlation method calculates the relationship between alcohol 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 ($p < 0.05$).

The time from the onset of the disease to hospitalization * prognosis				
		Prognosis		Total
		Died	Cured	
		The time from the onset of the disease to hospitalization	Delayed	
	On time	7	51	58
Total		31	91	122

Table 4. 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	12.12 ± 5.2	14.54 ± 3.9	18.62 ± 4.9	15.7 ± 4.9	0.000
(hospitalization)					
White blood cells	11.34 ± 4.7	14.24 ± 4.2	15.30 ± 3.2	14.32 ± 4.1	0.005
(48-72 h)	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	44.3 ± 5.21	42.7 ± 11.6	42.9 ± 8.1	42.3 ± 10.0	0.829
(hospitalization)					

Table 5. Blood analysis results of the participants.

Biochemical tests	New recording system				p-value
	(n=12)	B (n=69)	C (n=41)	Total (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. 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, Proclaciton in, 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.

Classification	New recording system * Biopsy			Total
	Biopsy		Purulent pancreonecrosis	
	Edematous pancreatitis	Pancreo necrosis		
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. 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.

Discussion

Serum pancreatic enzyme measurement is the “gold standard” for the diagnosis of AP [8]. In an episode of AP, amylase, lipase, elastase, and trypsin are released into the bloodstream simultaneously, but the clearance varies depending on the timing of blood sampling. Amylase is an enzyme secreted mainly by the pancreas and salivary glands, but also the small intestine, ovaries, adipose tissue, and skeletal muscles. There are two major iso forms of amylase: pancreatic and salivary, and its leading function is the 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 [10-12]. Late hospitalization and late treatment of patients with ANP disease have been shown to affect the prognosis of the disease adversely (Table 8).

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

Table 8. 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.

Lipase is another enzyme secreted by the pancreas. AP is the main reason for an increase in lipase. Many investigators emphasize that lipase is more specific but can also be found elevated in non-pancreatic diseases such as renal disease, appendicitis, acute cholecystitis, chronic pancreatitis, bowel obstruction, etc. [10,11]. 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 [13].

A Cochrane review comparing 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 [14]. Our study found an increase in lipase during ANP, which is of diagnostic value or statistically significant, especially in the diagnosis of necrotic inflammation (p<0.01).

Many textbooks consider the C-reactive protein (CRP) as the gold standard for disease severity assessment [15]. 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 [15]. 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 ANP. Some studies have shown that procalcitonin is important in determining the severity of acute pancreatitis and in predicting the risk of infecting pancreatitis [16]. Procalcitonin is indicated in patients with confirmed pancreatic necrosis to predict necrotic infection [16-19]. A procalcitonin value of 3.8 ng/ml or higher within 96 h after onset of symptoms indicated pancreatic necrosis with a sensitivity and specificity of 93% and 79% [16,17].

In our study, an increase in procalcitonin levels was statistically significant (p<0.01) in determining the severity and severity of the disease. Studies by Staubli et al. [12] and Yang [18] have shown that pancreatic necrosis is 93% and 79% sensitive and specific if procalcitonin levels are 3.8ng/mL or higher within 96 hours of the onset of symptoms [13,17]. Studies by Valverde-Lopez F 17 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 [19].

It was possible that the serum calcium level was reduced (p<?0.01) in the necrotic form of ANP compared with normal tissue as non-necrotic necrosis. Therefore, blood calcium levels are considered one of the most important tests for patients with ANP in our study. The positive predictive value 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 [20].

One study of 161 patients evaluated using the parameters for early predictability most widely used in AP. The authors determined the significant cut off values for prediction of severe AP were Ranson ≥ 3 , BISAP ≥ 2 , APACHE-II ≥ 8 , CTSI ≥ 3 , and CRP at 24 h ≥ 21 mg/dl (> 210 mg/l). They concluded that different scoring systems showed similar predictive accuracy for the severity of AP, but APACHE-II demonstrated the highest accuracy for predicting severe acute pancreatitis [21-24].

Using our new scoring system, 69 of 122 (56.5%) patients were category B (score >3) and 41 (33.6%) patients in category C (score >7). By our new system, 90.1% of all cases were in severe acute necrotizing pancreatitis. Of the patients classified A category by our new scoring system, 100% survived, and 89.8% of patients in class B survived, while less than half (41.5%) of the patients classified in category C survived. The correlation between our new scoring system and the patient's survival was evaluated using the correlation analysis and found to be significant ($p < 0.001$) [25-30].

Our scoring system is equally effective compared to others. But it is easier to use in the hospitals of developing countries because it uses only a few highly sensitive indicators. We note that our study has limitations, namely, a small sample size and limited follow-up. The sampling was conducted mainly in Third and First Central Hospitals located in Ulaanbaatar. Thus, the future direction of this study includes the application of the scoring system to other hospitals, especially in central hospitals of 21 province as well as district hospitals in Ulaanbaatar.

Conclusion

In Mongolia, relatively young men suffer from alcohol-induced pancreatitis. Factors contributing to necrosis in acute pancreatitis include alcohol abuse, prolonged alcohol use, delayed hospitalization, and delayed treatment. In our study, clinical signs and laboratory findings effectively distinguish severe forms of acute pancreatitis, early diagnosis, assessment of prognosis, and development of surgical treatments. Clinical signs include abdominal pain, bloating, and abdominal muscle stiffness. Laboratory tests include an increase in white blood cells, neutrophils, serum LDH, serum lipase, C-reactive protein and a decrease in hematocrit, serum calcium. The new evaluation system that we have developed for early diagnosis, progression and prognosis of severe forms of acute pancreatitis is easy to evaluate. The criteria used in the evaluation system are available in the secondary and tertiary hospitals of our country.

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