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Original Research

Quantification analysis of lactate dehydrogenase and C-reactive protein in evaluation of the severity and prognosis of the acute pancreatitis

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Abstract: To evaluate the value of C-reactive protein (CRP) and lactate dehydrogenase (LDH) in assessing the severity and prognosis of acute pancreatitis (AP). A retrospective analysis was performed with the clinical data of 115 AP patients who were delivered to this hospital between December 2012 and December 2017 for treatment, in which there were 76 patients with mild AP (MAP group) and 39 with moderately severe AP (MSAP) and severe AP (SAP) (non-MAP group). Within 24 h after admission, we detected the levels of CRP, LDH and amylase (AMY) in serum, and according to the sensitivity and specificity of CRP, LDH and AMY, as well as the SROC curve, we evaluated the diagnostic value of these indicators in assessing the severity of AP. In serum, the levels of CRP and LDH in the non-MAP group were significantly higher than those in the MAP group (P <0.05). And in predicting the development of AP, the sensitivity, specificity and accordance rate of CRP were 59.0%, 97.4% and 84.3%, with a cut-off value of 176.00 mg/L; for LDH, these indexes were 94.9%, 88.2% and 90.4%, with a cut-off value of 235.50 U/L. Thus, LDH, combined with the CRP can well predict the incidence rate of the MODS and mortality rate of AP. Finally, we conclude that within 24 h after admission, the levels of CRP and LDH in patients can serve as indicators for evaluating the severity and prognosis of AP.

Key words: C-reactive protein; Lactate dehydrogenase; Acute pancreatitis; Diagnosis; Prognosis.

Introduction

Acute pancreatitis (AP), one of the frequent acute abdominal diseases in clinical practice, is divided into mild acute pancreatitis (MAP), moderately, severe acute pancreatitis (MSAP) and the severe acute pancreatitis (SAP) based upon the severity (1, 2). MSAP and SAP patients are concomitant with the failure in organs, and particularly, SAP is also characterized by the acute onset, rapid progression and complicated pathological changes, concomitant with the SIRS and MODS in an early stage and a mortality rate as high as 20% to 30% (3, 4). Thus, early accurate evaluation of the severity of AP is critical to the clinical treatment and prognosis of AP.

So in this study, we assessed Lactate Dehydrogenase and C - reactive protein retrospectively in the evaluation of the severity and prognosis of the acute pancreatitis the severity and prognosis of the acute pancreatitis.

Materials and Methods

Subjects

In this study, we retrospectively analyzed the clinical data of 115 AP patients who were treated in Tongji Hospital between December 2012 and December 2017. Among these patients, there were 74 males and 41 females, aged between 31 and 78 years old, with an average age of (51.3±16.6) years old. Within 24 h after admission, we detected the levels of CRP and LDH in serum. AP was diagnosed according to the criteria in the *Guidelines for the Diagnosis and Treatment of Acute Pancreatitis* (2014 Edition) stipulated by the Division of Pancreatic Surgery, Society of Surgery, Chinese Medical Association. Inclusion criteria: (i) patients aged between 18 and 40 years old; (ii) patients with onset time < 24 h; (iii) patients with no history of AP; (iv) patients with non-traumatic pancreatitis; (v) patients with no chronic diseases, like chronic pancreatitis or diabetes mellitus; (vi) patients with perfect clinical data. For all subjects, diseases, including other types of acute abdominal diseases, myocardial infarction, immune system diseases, liver cirrhosis, autoimmune liver diseases and hepatobiliary malignancies, were excluded through examination. Patients with chronic diseases (such as tuberculosis, rheumatoid arthritis, etc.), patients who had appendectomy before admission, acute infectious disease (eg, the common cold) have been excluded from the study due to the effect of these diseases on CRP.

Detection methods

Fasting venous blood (5 milliliters) was used for the

Table 1. Comparison of the clinical data of the patients at admission.

Clinical data		MAP group	Non-MAP group	*P*-value
Age (years old)		41.69±12.48	44.11±10.43	0.47
Gender (n of males (%))		43 (56.58)	22 (55.41)	0.95
Body mass index (BMI), kg/m^2		24.8±2.9	24.1±3.7	0.85
History of cholelithiasis (n (%))		9 (11.84)	4 (10.26)	0.91
History of hyperlipidemia (n (%))		9 (11.84)	8 (20.52)	0.51
History of the cholecystectomy (n (%))		9 (11.84)	1 (2.56)	0.17
Within 24 h after admission	CRP (mg/L)	93.28±73.73	215.24±124.93	0.001
	LDH (U/L)	216.62±47.17	468.74±223.77	0.0001
	AMY (U/L)	502.80±397.01	729.50±612.48	0.1825

detection of the CRP and LDH. CRP was detected using Hitachi 7060 automatic biochemical analyzer, while LDH using the VITROS 5600 automatic biochemical and immunological analyzer.

Grouping

According to the *Guidelines for the Diagnosis and Treatment of Acute Pancreatitis in China* (2013, Shanghai), these patients were divided into the MAP group and non-MAP (including the MSAP and SAP) group; based on the existence of multi-organ dysfunction syndrome (MODS), these patients were again grouped into the MODS group and non-MODS group; on the basis of the clinical outcome, these patients were divided into the death group and survival group.

Statistical analysis

SPSS 17.0 software (SPSS Inc., Chicago, IL, USA) was utilized for the data analysis in this study. Measurement data were analyzed using the *t*-test, while enumeration data presented in the form of ratio or rate were compared between groups using the chi-square test. ROC curve was also prepared to analyze the cut-off value, sensitivity and specificity of indicators. $P < 0.05$ suggested that the difference had statistical significance.

Results

General data

From a total of 1573 patients, we finally enrolled 112 patients according to the inclusion criteria, and 48 patients were excluded due to the age, 467 due to the admission time (> 24 h after onset), 49 due to pancreatitis not as the primary disease, 29 due to the diagnosis of traumatic pancreatitis, 709 due to the chronic diseases (like chronic pancreatitis, diabetes mellitus, blood diseases, cardiovascular diseases, renal or hepatic diseases), or administration of the glucocorticoid or anti-tumor preparation, and 156 due to the data loss for transfer to another hospital, pregnancy or refusal to undertake the blood examination. There was no difference in the BMI value of participants in both groups (P>0.05). Among 115 subjects, there were 76 patients with MAP, and 39 with non-MAP, i.e. MSAP or SAP. Gender ratios in MAP group and non-MAP groups were 43:33 and 22:17, respectively, and the average ages were (41.69±12.48) and (44.11±10.43) years old. Both groups did not differ in a statistically significant way for age, sex and history of disease and surgery ($P > 0.05$). Of the LDH and CRP levels, we observed acute decreases in the MAP group, instead of the non-MAP group, and differences had statistical significance ($P < 0.05$) (Table 1).

Value of LDH and CRP in the assessment of AR severity

ROC curve was prepared to calculate the cutoff values of LDH and CRP, which were 235.5 U/L and CRP 176 mg/L. The sensitivity, specificity and accordance rate of these two indicators towards the severity of AP are shown in Table 2. The highest sensitivity and accordance rate were found in LDH in evaluating the severity of AP (AUC=0.972, $P < 0.05$), while the highest specificity was found in CRP (AUC=0.835, $P < 0.05$). Compared to the combination of AMY, LDH and CRP, the sensitivity and accordance rate of CRP were inferior ($P < 0.05$), while the sensitivity, specificity and accordance rate of LDH were also inferior, but the differences had no statistical significance ($P > 0.05$).

Analysis of AP prognosis using LDH and CRP

In the group of patients with CRP, less than 176.00 mg/L, the incidence rate MODS and the mortality rate were all lower than those in those with CRP not less than 176.00 mg/L, while the mortality rate in patients with LDH less than 235.50 U/L was lower than that in those with LDH not less than 235.50 U/L ($P < 0.05$). However, a comparison of the MODS incidence between patients with LDH < 235.50 U/L and those with LDH ≥235.50 U/L showed no statistically significant difference ($P > 0.05$) (Table 3).

Table 2. Analysis of the diagnostic accordance rate in evaluating the severity of AP using different indicators.

Indicators	Cutoff values	Sensitivity (%)	Specificity (%)	Diagnostic accordance rate (%)
LDH	235.5 U/L	94.9	88.20	90.4
CRP	176 mg/L	59.0[ab]	97.4[b]	84.3[ab]
AMY + LDH + CRP	/	97.2	94.9	95.7

[a] $P < 0.05$ *vs.* AMY + LDH + CRP; [b] $P < 0.05$ *vs.* AMY + LDH + CRP.

Table 3. Analysis of the AP prognosis using different indicators (n (%)).

	LDH (U/L)				CRP (mg/L)		
	n	**MODS incidence**	**Mortality**		**n**	**MODS incidence**	**Mortality**
<235.50	69	5(7.25)	3(4.35)	<176.00	90	10(11.11)	2(2.22)
≥235.50	46	18(39.13)	5(10.87)	≥176.00	25	13(52.00)	6(24.00)
χ^2		1.814	17.536			14.336	20.44
P		<0.05	<0.05			<0.05	<0.05

Discussion

AP is a disease accompanying the activation of pancreatic trypsin caused by multiple pathogens, with the local inflammatory responses in the pancreas as the major features, concomitant with or with no alteration in organ functions. Clinically, 20% to 30% of patients have experienced critical signs, with an overall mortality rate of 5% to 10% (5-7). Thus, accurate evaluation of AP severity in an early stage may better guide the clinical therapy, thereby increasing the cure rate and mitigating the pains of patients. At present, in clinical practice, a variety of indicators have been developed for distinguishing the AP severity, including Ranson scale, APACHE II scale, BISAP scale, MCTSI scale, modified Marshall scale, CT Balthszar scale, but these scales are averse to the rapid evaluation of severity for physicians due to the non-uniform standard, or complicated methods, or the long-term observation and comparison (2 to 3 days). In this study, the levels of CRP and LDH in the serum of patients within 24 h after admission can better indicate the severity of AP in an early stage, thereby guiding the clinical treatment, with a decrease in the mortality rate.

CRP is a kind of the non-specific acute-phase reactive protein generated from the hepatocytes under the tumor necrotic factors released by the mononuclear macrophages in case of inflammation and injury of tissues, with the effects to facilitate the phagocytosis, activate the complement and regulate the immune functions. The level of CRP is always in the physiologically normal range, but CRP arises rapidly several hours after any acute infection or tissue injuries, and peak level is attained within 24 and 48 h. CRP serves as an indicator reflecting the inflammation and evaluating the severity of pancreatitis (8-13). CRP > 20 mg/L indicates the possibility of bacterial infection, and at 72 h after onset, CRP exceeds 150 mg/L, indicating the pancreatic tissue necrosis (14). However, the peak level of CRP is usually attained only after 24 h, which, thus, suggests the limitation in early, accurate evaluation of the AP severity. Scholars have found that 24 h following the CRP differentiation, the optimal thresholds in MAP and non-MAP are 150 mg/L and 140 mg/L (15). Additionally, enormous efforts have been devoted to the studies regarding the distinguishing of the severity of AP using CRP (16).

An evident correlation has already been identified between the level of CRP in serum and AP prognosis in previous studies, which, plus the value in prognostic evaluation of disease, makes CRP level a standard for predicting the progression of AP (17, 18). In this study, we found that in the non-MAP group, the increase in CRP level was more significant than that in the MAP group (P <0.05). ROC curve analysis also indicated that the cutoff value of CRP was 176.00 mg/L, with a sensitivity, specificity and accordance rate of 59.0%, 97.4% and 84.3%, and CRP also shows promising value in predicting the incidence of MODS and mortality rate of AP.

LDH, as a kind of glycolytic enzyme, extensively distributes in the cytoplasm of tissues, mainly in the myocardium, skeletal muscle, kidney and liver; as SAP patients are more susceptible to the dysfunctions in heart, lung or kidney, with an increase in the level of LDH. Thus, LDH, in spite of its poor organ specificity, can effectively reflect the pancreatitis-caused damage to other organs, and, accordingly, should be served as an indicator evaluating the progression and severity of AP (19-22). According to the studies in other countries, in distinguishing MAP and non-MAP several days following onset, the optimal thresholds of LDH are 290 U/L and 270 U/L, respectively, with a sensitivity of 88% and an accuracy of 91% (24).

In this study, the cutoff value of LDH was 235.50 U/L, with the sensitivity of 94.9%, specificity of 88.2% and diagnostic accordance rate of 90.4% in evaluating the severity of AP, suggesting that LDH is excellent in sensitivity and specificity in comparison with the CRP and BISAP, respectively ($P < 0.05$). Also, a comparison of the sensitivity, specificity and accordance rate in the evaluation of non-MAP between LDH and combination of AMY, LDH and CRP showed no significant differences ($P > 0.05$). These results suggest that LDH possesses the promising value in diagnosis and prediction of the incidence of MODS and the mortality rate.

Due to the limitation of parameters that we evaluated, it is also recommended that in further studies evaluating the diagnostic accuracy of other laboratory tests like complete blood count, as well as abdominal CT scan as a more definitive method along with CRP and LDH could be helpful.

This study concluded that both LDH and CRP are excellent in the accuracy in evaluating the severity and prognosis of AP in an early stage, and LDH is more efficient in evaluation. However, whether LDH alone can serve as the indicator for assessment of AP prognosis needs to be elucidated in more in-depth, large-sample and multi-center studies.

Interest conflict

none.

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