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Serum lactate dehydrogenase is predictive of persistent organ failure in acute pancreatitis

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ABSTRACT

Purpose: Elevated serum lactate dehydrogenase (LDH) has been reported in a serious of clinical diseases. However, the relationship between LDH and the incidence of persistent organ failure (POF) in acute pancreatitis (AP) has not been characterized.

Materials and methods: A total of 105 patients with AP who presented within 72 h from symptom onset between 2014 and 2015 were included in this retrospective study. Demographic parameters and laboratory data on admission were compared between patients with and without POF. Multivariable logistic regression analyses were utilized to evaluate the prognostic value of LDH for predicting POF.

Results: 21 patients were diagnosed with POF. Compared to non-POF, patients with POF showed a significantly higher value of serum LDH on admission (741.57 ± 331.72 vs. 296.08 ± 135.73 U/L, $P < 0.001$). After multivariate logistic analysis, LDH remained an independent risk factor for POF (Hazard ratio 4.38, 95%CI: 1.42–13.47; $P = 0.010$). A LDH value of 647 U/L predicted POF with an area under the curve (AUC) of 0.876, a sensitivity with 76.2% and specificity with 98.8%, respectively.

Conclusions: Our results indicate that serum LDH on admission is independently associated with POF in AP and may serve as a potential prognostic factor.

1. Introduction

Acute pancreatitis (AP) is an inflammatory disorder characterized by local and systemic immuno-inflammation, which is observed clinically as a spectrum ranging from local pancreatitis to systemic inflammatory response, organ failure (OF) and death. Most patients suffer from a mild, self-limiting inflammatory derangement, but the remaining will develop a severe disease associated with local or systemic complications and/or OF [1]. According to 2012 revised Atlanta classification for AP, severe AP (SAP) has been redefined as AP with persistent OF (OF lasts >48 h) with a lethality rate of 20–60% [2-6].

Early assessment of disease severity is pivotal for the determination of therapeutic strategy since effective treatment could significantly decrease mortality of patients with severe pancreatitis [7,8]. Lactate dehydrogenase (LDH) is a cytoplasmic enzyme that is widely expressed in tissues. The enzyme converts pyruvate, which is the final product of glycolysis, to lactate when oxygen is in short supply [9]. Elevated LDH is observed in disease conditions such as tissue injury, necrosis, hypoxia, hemolysis or malignancies [10-12]. LDH is clarified as a prognostic factor for severe type of AP (1992 Atlanta criteria), pancreatic necrosis (PNec), infection and mortality in AP [13-15]. However, the association underlying LDH and POF in the AP pathophysiology has not been elucidated yet.

2. Materials and methods

2.1. Patients

Consecutive adults (aged 18 years and above) admitted to the Pancreatic Disease Institute of Wuhan Union Hospital with a confirmed diagnosis of AP between January 2014 and January 2015 were included in this study. Diagnosis of AP was based on the presence of two or more of the following three criteria: 1) abdominal pain consistent with AP; 2) serum amylase and/or lipase elevation ≥ three times the upper limit of normal; and/or 3) computed tomography (CT) findings characteristic of AP [2]. The exclusion criteria included any of the following: the time from abdominal pain onset to hospital admission ≥ 72 h, age younger than 18 years, pancreatitis induced by trauma, chronic pancreatitis, and unavailable laboratory measurements or medical records. Laboratory data were obtained from the blood screening test at hospitalization. Blood samples were collected within 2 h after hospitalization and analyzed using an automated clinical chemical analyzer within 6 h

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of sampling in the same core clinical laboratory in Union Hospital (Wuhan, China). LDH levels were measured enzymatically using kits (Roche Diagnostics, Basel, Switzerland). The reference values of LDH levels with this assay are 109 to 245 U/L. Patients' electronic medical records and paper charts were reviewed by one independent physician for information on demographics, physiologic variable, and disease severity. The study was conducted according to the principles of the Declaration of Helsinki. Informed consent for individual patient was not obtained since all data were retrieved retrospectively from the laboratory test information system without additional blood samples or laboratory analysis. The ethics review board of Wuhan Union Hospital approved this study.

2.2. Definitions

Disease severity was determined according to the revised 2012 Atlanta classification [2]. OF was diagnosed when the following cutoffs were exceeded: 1) cardiovascular failure if systolic blood pressure was <90 mm Hg despite fluid replacement; 2) respiratory failure if the ratio of PaO2/FiO2 was <300 mm Hg; and 3) renal failure if serum creatinine was ≥170 umol/L (1.9 mg/dL). POF was identified if OF lasts for >48 h. PNec was defined as appearance of pancreatic parenchymal and/or peripancreatic necrosis on CECT images [2].

2.3. Statistical analysis

Statistical analysis was performed using SPSS 20.0 (SPSS Inc., Chicago IL, USA). Continuous data are presented as means and standard deviation (SD). Categorical variables are reported as number (frequency). Student's *t*-test and Mann-Whitney *U* test were used to evaluate the differences of baseline characteristics between the study cohort and the control group. Multiple group comparisons were performed using the Chi-square test for categorical variables and the Kruskal-Wallis test for continuous data. Univariate analysis was performed using log-rank test. All variables with statistically significant prognostic value in univariate analysis were selected for further multivariate analysis. Multivariate analysis was undertaken with a Cox regression model. Hazard ratios (HRs) and 95% confidence intervals (95% CIs) are presented. Receiver-operator curves (ROC) were constructed to evaluate the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of the parameters in predicting persistent organ failure. A P value < 0.05 was considered a statistically significant difference.

3. Results

3.1. Patients

A total of 105 patients with confirmed AP admitted to Union hospital (Wuhan, China) during the period were included in this study. Baseline characteristics of these patients according to LDH levels (elevated or normal) are presented in Table 1. The mean age was 48.97 years and 62 (59%) of the patients were male. Overall, 21 (20%) patients were identified with POF. There were 14 patients developing solitary POF (all of respiratory system). Multiple POF was observed in 7 patients (5 of lung and kidney, 1 of lung and heart, and 1 of lung, kidney and heart). During hospitalization, 6 patients with POF died with an overall mortality of 5.7%. No death was observed in patients without POF (Table 2).

3.2. Comparison between patients with different LDH levels

Compared to patients with normal or low LDH (n = 39), patients with high LDH (n = 66) show significantly higher incidences of developing POF (28.8% vs. 5.1%; P = 0.003), PNec (35.0% vs. 20.5%; P = 0.001) and higher (but not significant) in-hospital mortality (9.1% vs. 0.0%; P = 0.052).

Table 1
Basic characteristic of AP patients according to LDH level (normal range < 245 U/L).

No.	LDH < 245 U/L 39	LDH ≥ 245 U/L 66	P-value
Age, years	50.92 ± 13.30	47.82 ± 13.37	0.252
Male gender	22 (56.4%)	40 (60.6%)	0.673
Daily drinker	17 (43.6%)	30 (45.5%)	0.853
Current smoker	18 (46.2%)	34 (51.5%)	0.595
Etiology			0.629
Biliary	24 (61.5%)	33 (50.0%)	
Alcoholic	8 (20.5%)	20 (30.3%)	
Hyperlipidemia	6 (15.4%)	10 (15.2%)	
Idiopathic	1 (2.6%)	3 (4.5%)	
Outcomes			
POF	2 (5.1%)	19 (28.8%)	0.003
PNec	8 (20.5%)	35 (35.0%)	0.001
In-hospital mortality	0 (0.0%)	6 (9.1%)	0.052

Abbreviations: AP, acute pancreatitis; ICU, intensive care unit; LDH, lactate dehydrogenase; PNec, pancreatic necrosis; POF, persistent organ failure.

3.3. Comparison between patients with and without POF

Compared to patients without POF, patients with POF were much older, had elevated rates of pancreatic necrosis, and in-hospital mortality (Table 1). Conventional severity scores such as Ranson and SIRS were significantly higher in POF ones. The level of serum LDH was significantly lower, while the levels of white blood count, glucose, urea and creatinine were statistically higher in patients with POF (Table 3).

3.4. Admission serum LDH as an independent prognostic factor for POF

In order to further investigate the association between serum LDH and incidence of POF, we used multivariate Cox regression model. Univariate analysis suggested serum glucose, albumin, urea, creatinine, calcium, LDH, SIRS score and Ranson score correlated significantly with the incidence of POF. Multivariate analysis was performed using the characteristics shown to have statistical significance (P < 0.05) by univariate analysis.

On multivariate analysis, only serum LDH ≥ 647 U/L was identified as an independent prognostic factor (HR: 4.38, 95%CI 1.42–13.47; P = 0.010) (Table 4). As shown in Table 5 and Fig. 1, serum LDH on admission had an area under curve of the receiver operating characteristic of (AUC) of 0.876 (95%CI: 0.767–0.985) for prediction of POF, with a sensitivity of 76.2%, specificity of 98.8%, PPV of 94.1%, and NPV of 94.3%. The optimal threshold was 647 U/L. The AUC of SIRS score and Ranson score for predicting POF were 0.749 (95%CI: 0.643–0.855) and 0.768 (95%CI: 0.663–0.872), respectively.

Table 2
Types of POF and the corresponding in-hospital mortality.

	POF	In-hospital mortality
Solitary POF	14	2 (14.3%)
Respiratory	14 (100.0%)	2 (14.3%)
Renal	0 (0.0%)	0 (0.0%)
Cardiovascular	0 (0.0%)	0 (0.0%)
Multiple POF	7	4 (57.1%)
Respiratory + renal	5 (71.4%)	2 (40.0%)
Respiratory + cardiovascular	1 (14.3%)	1 (100.0%)
Respiratory + cardiovascular + renal	1 (14.3%)	1 (100.0%)

Abbreviations: POF, persistent organ failure.