Biomedical Research 2016; 27 (2): 328-335 *ISSN 0970-938X*
www.biomedres.info

Study on the relationship between the common clinical index changes of emergency critically ill patients and the APACHE II score and prognosis.

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Abstract

Objective: To study the relationship between the changes of blood lactic acid (LAC) levels, serum C-reactive protein (CRP) levels, red cell distribution width (RDW) levels of emergency critically ill patients and the APACHE II score and prognosis.

Methods: Data were collected prospectively on 228 EICU admissions from March 2011 to December 2011. The Acute Physiology And Chronic Health Evaluation (APACHE) score was calculated within the first 24 hours after admission and monitored LAC, CRP, RDW levels on admission to 0 hour, 24 hours, 48 hours, 72 hours. Also recording the LAC, CRP, RDW levels in the end (patients leave hospital or die), defining these values as the end point values in this study. 228 patients were divided into three groups according to their APACHE scores: Group I 15 points (n=50); Group II 16 to 30 points (n=84); Group III>30 points (94 cases). And according to 28 days whether death, divided into the death group (n=124) and the survival group (n=104). Through the statistical methods, analyzing the clinical value of early dynamic changes of LAC, CRP, RDW in pathogenic condition and prognosis assessment of critically ill patients.

Results: The mortality rates were increased with the increasing of APACHE score. Pearson correlation analysis found that: At different time points, LAC levels and APACHE scores are positively correlated (r=0.602, 0.552, 0.523, 0.494, P all<0.01); At different time points, CRP levels and APACHE scores are positively correlated (r=0.198, 0.287, 0.346, 0.384, P all<0.01); At different time points, RDW-CV levels and APACHEscores are not correlated (P all>0.05). The tendency charts of LAC, CRP, RDW-CV levels on admission to 0 hour, 24 hours, 48 hours, 72 hours and in the end of critically-ill patients: The LAC levels on admission to 0 hour are the most highest, and then gradually declined, the end to the lowest; The CRP levels after admission gradually raised, the peak on admission to 48 hours, and then gradually declined, the end to the lowest; The RDW-CV levels after admission gradually raised, the peak on admission to 72 hours, the end to the lowest. ICU mortality in Critically-ill patients further on-line multivariate logistic analysis, the results showed that: among the age, sex, APACHE score and the LAC, CRP, RDW-CV levels on admission to 0 hour, 24 hours, 48 hours, 72 hours, the variables that have a significant influence on death are APACHE score, the LAC levels on admission to 72 hours, the CRP levels on admission to 48hours. (PAPACHE=0.000, PLac=0.002, PCRP=0.002).

Conclusion: Blood LAC, serum CRP level and APACHE score arepositively correlated. They are good indicators of evaluating the severity and prognosis in critically-ill patients. Dynamic monitoring blood LAC, serum CRP levels may be more meaningful than a single monitoring, helps to find the disease twist. RDW level and APACHE score have no linear relationship, cannot be used to evaluate critical illness, but this research affirms the significance that apply to the cardiovascular system diseases and the blood system diseases.

Keywords: Critical illness, Lactic acid, C-reactive protein, Red cell distribution width, Acute physiology and chronic health evaluation II.

Accepted on January 20, 2016

Background

Critically ill patients have serious disease, poor prognosis, high mortality, and difficulty treatment. Many studies showed that the severity of the disease was closely related with prognosis. In view of the changeable condition of critically ill patients and the rapidly progress, the treatment need to make timely adjustment according to the illness. Knowing the severity of the disease and making a preliminary prediction of the prognosis of the disease can help to make the best clinical

therapeutic regimen, delay the progress of the disease, and prevent the occurrence of certain complications [1].

Acute physiology and chronic health evaluation (APACHE II) [2] scoring system is proposed by the research team led by Professor Knaus of the Medical Center of Washington University, which can access the severity of the patients' condition with critical disease. But, due to the disadvantages of APACHE II score, such as the complex composition and complicated clinical application, as well as the rapid changes and progress of the disease of critically ill patients, the simple and accurate clinical markers are needed to determine and predicted the development of the disease.

The purpose of this study is to explore the correlation between lactic acid (LAC), C-reactive protein (CRP), red blood cell distribution width (RDW) and APACHE score and to assess the prognostic effect through monitoring the early dynamic changes of LAC, CRP and RDW of emergency critically ill patients. In this study, we collected the dynamic monitoring data of lactic acid, CRP and RDW levels, as well as the APACHE II score, and the statistical analysis on these indicators has important significance in evaluating the disease severity, guiding clinical treatment, and reducing the mortality of the patients.

List of Abbreviations

LAC: lactic acid; CRP: C-reactive protein; RDW: red blood cell distribution width; APACHE II: acute physiology and chronic health evaluation; APS: acute physiology score; CHS: chronic health score; ICU: Intensive Care Unit

Materials and Methods

Clinical data

Case selection criteria

Inclusion criteria: The patients should consistent with the intensive care unit (ICU) treatment scope proposed by China ICU Construction Management Guidelines (2006). Acute, reversible, specific standard is as follows: (1) has a life-threatening organ dysfunction, the ICU intensive monitoring. Protect and strengthen treatment, is likely to get this short-term rehabilitation of patients. There are many risk factors, (2) has the potential In life, the ICU closely monitoring and timely and effective treatment, may reduce the risk of death of patients. (3) Based on chronic organ dysfunction, the occurrence of acute aggravating and life-threatening, through monitoring and ICU

Exclusion criteria: The patients who in line with the criteria above but dead within 72 hours after hospital admission, and the patients with incomplete information were excluded.

Source of cases

A total of 228 patients who treated in the Emergency ICU of the First Affiliated Hospital of Dalian Medical University from March 2011 to December 2011 were selected, including 117 male patients and 111 female patients, the age was 17-88 years old, average (58.89 ± 17.39) years old. The monitoring and treatment methods in this study have been agreed, and all the patients have signed the informed consent, and this study has achieved the ethics approval from the ethics committee of Affiliated Hospital of Dalian Medical University (Table 1).

Table 1: *Correlations between Acute Physiology and Chronic Health Evaluation II (APACHE II)1 score and plasma concentrations of lactic acid, CRP and RDW-CV in critically ill patients (n=228).*

Parameter	Time point							
	Admission		24 h		48 h		72 h	
	r	P	r	P	r	P	r	P
LAC	0.602	<0.01	0.552	<0.01	0.523	<0.01	0.494	<0.01
CRP	0.198	<0.01	0.287	<0.01	0.346	<0.01	0.384	<0.01
RDW-CV	0.963	<0.01	0.973	<0.01	0. 972	<0.01	0. 963	<0.01

Grouping

The 228 critically ill patients were divided into three groups according to APACHE II score, APACHE II score ≤ 15 in I group (n=50), APACHE II score was 16-30 in II group (n=84), and APACHE II score 30 in III group (n=94). And the patients were divided into death group (n=124) and survial group (n=104) based on the death or the survive within 28 days.

Research methods

The arterial LAC, serum CRP and RDW-CV levels were tested after hospital admission immediately, 24, 48 and 72 hours after hospital admission, and the APACHE II score of all the patients were evaluated.

The arterial blood lactate (LAC), serum C- reactive protein (CRP) and red blood cell distribution width (RDW) levels of all critically ill patients were detected at the time of admission, 24 hours after admission, 48 hours after admission and 72 hours after admission; the LAC, CRP and RDW levels at the end time (discharge or death) were recorded, and used as the end value of the study; the acute physiology and chronic health evaluation score (APACHEscore) of all subjects were evaluated.

Blood LAC test: LAC was measured using GEM Premier 3000 blood gas analyzer produced by US IL Company. Serum CRP: CRP was measured by immune response turbidimetry which provided by Roche Company.

RDW test: RDW measurement using American COULTER Company produced blood cell analyzer, in this study, the RDW level was expressed with coefficient of variation of RDW (RDW-CV), its part of complete routine blood test.

APACHE score: After all patients admitted to the emergency room of ICU, the worst value of various physiological parameters and laboratory findings within its first 24 hours

were collected, and recorded the age and chronic health conditions.

Statistical analysis

SPSS11.5 software was used to analyze the data, and the general data were expressed with ($\bar{x} \pm s$), the comparison of normality measurement data between groups was analyzed with variance analysis, the comparison between survival group and death group used independent samples t-test, Pearson correlation analysis was used for measurement data correlation analysis; Multivariate logistic regression analysis was used to analyze the death of the critically ill ICU patients; $P<0.05$ indicates there is significant difference, and $P<0.01$ suggests that there is very significant difference.

Results

Pearson linear correlation analysis was used to analyze the correlation between the APACHE II score and the LAC, CRP and RDW-CV levels measured at different time points of the 228 critically ill patients, and found that the LAC level at different time points was correlated with APACHE II score ($P<0.01$)the CRP level at different time points was correlated with APACHE II score ($P<0.01$); The RDW-CV level at different time points was negatively correlated with APACHE II score ($P<0.01$, Table 1).

Homogeneity test was conducted on the collected LAC, CRP and RDW-CV levels at different time points based on the standard of $\alpha=0.05$, and found LAC showed the heterogeneity among different groups at the same time point, CRP showed homogeneity among different groups at the same time point, and RDW-CV showed homogeneity among different groups at the same time point. Further q test or Dunnett T3 method was conducted based on the standard of $\alpha=0.05$, and found that (1) the serum LAC levels of different groups at the same time point were increased with the increasing of APACHE II score, and the comparison of every two means among multple sample means showed that there was no significant difference between I group and II group ($P>0.05$), there was significant difference between I group and III group ($P<0.05$), and there was significant difference between II group and III group ($P<0.05$). (2) The serum CRP levels of different groups at the same time point were increased with the increasing of APACHE II score, and the comparison of every two mean among multple sample mean showed that there was no significant difference between groups when hospital admission, there was no significant difference between I group and II group at 24 and 72 hours after hospital admission ($P>0.05$), and there was significant difference between I group and II group at 48 hours after hospital admission ($P<0.05$). Meanwhile, there was significant difference between I group and III group at 24, 48 and 72 hours after hospital admission ($P<0.05$), and there was significant difference between II group and III group ($P<0.05$). (3) The RDW-CV levels of different groups at the same time point were decreased with the increasing of APACHE II score, and there was significant difference between I group and II group at 0, 24 and 72 hours after hospital admission ($P<0.05$), there was significant difference between I group and III group at 0, 24 and 48 hours after admission ($P<0.05$), and there was significant difference between II group and III group at 0, 24, 48 and 72 hours after hospital admission ($P<0.05$, Table 2).

Table 2: *Plasma concentrations of LAC, C-reactive protein and RDW-CV in patients, stratified according to Acute Physiology and Chronic Health Evaluation II (APACHE II)2 score.*

Parameter	APACHE II score		
	≤ 15 n=50	15–25 n=84	>25 n=94
Plasma Lac, mmol/L			
Admission to ICU	2.75 ± 2.69	3.69 ± 3.22	6.85 ± 4.20[a,b]
24 h	2.29 ± 1.99	2.84 ± 2.23	5.09 ± 3.78[a,b]
48 h	2.07 ± 1.55	2.41 ± 1.59	3.76 ± 2.27[a,b]
72 h	1.77 ± 1.08	2.17 ± 1.32	2.97 ± 1.65[a,b]
Plasma C-reactive protein, mg/L			
Admission to ICU	60.3 ± 3.26	67.1 ± 4.82	78.5 ± 6.47
24 h	67.2 ± 3.67	84.6 ± 6.58	107.3 ± 8.05[a,b]
48 h	59.1 ± 4.76	86.1 ± 5.44a	123.7 ± 6.16[a,b]
72 h	55.8 ± 6.82	74.9 ± 5.01	122.8 ± 4.02[a,b]
Plasma RDW-CV, (%)			
Admission to ICU	17.6 ± 0.81	14.3 ± 0.76	13.2 ± 1.76[a,b]
24 h	17.2 ± 1.35	14.1 ± 1.02	12.8 ± 1.10[a,b]
48 h	17.4 ± 0.89	13.9 ± 0.40	12.6 ± 1.24[a,b]
72 h	17.1 ± 0.54	13.7 ± 0.51	11.5 ± 0.67[a,b]

Data presented as mean ± SD. [a]P<0.05 vs APACHE II score ≤ 15 at same time point; [b]P<0.05 vs APACHE II score 15-25 at same time point; Kruskal-Wallis or Mann-Whitney U-test. ICU: intensive care unit.

The t test was used to compare the APACHE II score of the critically ill patients between survival group and death group, and found that the APACHE II score of the death group was higher than that of the survial group, and the difference was statistically significant; the LAC, CRP and RDW-CV levels at different time points of the death group were higher than those of the survival group, and there were statistical significant differences (Tables 3 and 4).

Table 3: Plasma concentrations of LAC, C-reactive protein and RDW-CV in patients, stratified according to survival or death.

Parameter	Survival group	Death group
	N=104	N=124
Plasma Lac (mmol/L)		
Admission to ICU	3.29 ± 2.72	6.04 ± 4.39[c]
24 h	2.71 ± 2.23	4.43 ± 3.61[c]
48 h	2.12 ± 1.24	3.54 ± 2.32[c]

72 h	1.74 ± 0.95	2.98 ± 1.89 [c]
Plasma C-reactive protein (mg/L)		
Admission to ICU	59.6 ± 53.2	79.3 ± 61.7 [c]
24 h	73.2 ± 55.8	104.4 ± 66.7[c]
48 h	67.7 ± 49.0	119.1 ± 80.0[c]
72 h	61.2 ± 46.5	114.7 ± 83.0[c]
Plasma RDW-CV (%)		
Admission to ICU	17.4 ± 1.34	14.5 ± 1.23[c]
24 h	17.6 ± 1.89	13.4 ± 0.82[c]
48 h	17.6 ± 1.93	12.8 ± 0.95[c]
72 h	17.7 ± 1.78	11.4 ± 0.72[c]

Data presented as mean ± SD. [c:] P<0.05, compared between the survival group and the death group at same time point; Kruskal–Wallis or Mann-Whitney U-test. ICU: intensive care unit.

Multivariate logistic regression analysis on the death of the ICU critically ill patients

Logistic regression analysis was used to analyze the data, Forward Likelihood Ratio method (Forward LR) was used for the stepwise selection of variables, multivariate Logistic regression analysis was conducted on the ICU critically ill patients, and the results showed that among the indicators of gender, age, APACHE II score and the LAC, CRP, and RDW-CV levels at 0, 24, 48, and 72 hours after hospital admission, variable APACHE II score, LAC level at 72 hours after hospital admission and CRP level at 48 hours after hoapital admission had significant influence on death (Table 5).

Table 4: *Comparison of APACHE II score of critically ill patients between survival group and the death group ($\bar{x}$ ± s).*

Groups	N	APACHE II score
Survival	104	19.97 ± 10.47
Death	124	32.90 ± 11.34
P value		<0.01

Accuracy test (Receiver Operating Characteristic Curve) showed that the LAC level after hospital admission and the CRP level at 72 hours after hospital admission had the best sensitivity and specificity, and the RDW-CV level at 48 hours after hospital admission was correlated with the disease, but had no correlation with the mortality rate (Figure 1).

Based on the category of the disease in this study, the 228 critically ill patients were divided into three groups, A group was other system diseases (n=175), B group was hematological disease (n=14), and C group was cardiovascular disease (n=39). Homogeneity of variance test was conducted to test the RDW-CV levels at different time points based on the standard of α=0.05, the results found that there were significant difference on RDW-CV levels at 0, 24, 48 and 72 hours after hospital admission between A group and B group (P<0.05); there were significant differences between A group and C group at all the time points (P<0.05); and there were significant differences between B group and C group at 72 hours after hospital admission, and there were no significant differences between B group and C group at other three time points (P>0.05) (Table 6).

Table 5: *Multivariate Logistic regression analysis on death risk factors of ICU critically ill patients.*

Variable	Regression coefficient (B)	Standard error (SE)	Wald value (X2)	P	OR	95% confidence interval Lower limits	Upper limits
Constant term	-3.832	0.571	44.952	0.000*	0.022		
APACHEII score	0.087	0.017	25.432	0.000*	1.090	1.054	1.128
CRP level	0.009	0.003	9.635	0.002*	1.009	1.003	1.015
48 hours CRP							
72 hours LAC	0.411	0.133	9.482	0.002*	1.508	1.161	1.958

*P<0.05, means the partial regression coefficient of this cariable has statictical significance.

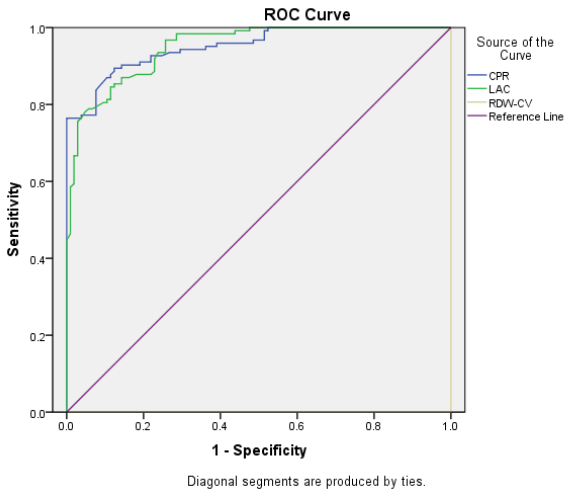

Figure 1: *Receiver operating characteristic curve.*

Table 6: *Comparison of serum RDW-CV levels between groups at different time points ($\bar{x}$ ± s, %).*

Groups	Hospital admission	24 hours after hospital admission	48 hours after hospital admission	72 hours after hospital admission
A	14.0 ± 1.23	14.2 ± 1.65	14.3 ± 1.72	14.4 ± 1.89
B	16.3 ± 1.48*	16.5 ± 1.73*	16.9 ± 1.79*	17.1 ± 1.60[*]
C	16.1 ± 1.45*	16.0 ± 1.38*	16.0 ± 1.38*	15.9 ± 1.31[*#]

*P<0.05, compared with I group; #P<0.05, compared with II group.

Discussions

The APACHE II score is the currently most widely and authoritative critical illness condition evaluation system used in ICU. The assessment of the disease of ICU patients and the prediction of mortality can help to objectively draw up and develop the medical care plan, thus providing objective and scientific basis for the development of medical quality, rational application of medical resources and the confirmation of optimal timing of discharge or the choice of treatment time. The APACHE score can not only used in the comparison between single disease patients, but also can be used for the evaluation of mixed disease [3]. The score is closely related with the severity of the disease, the higher the score, the more serious the illness is, the greater the risk of death. APACHE II score <10, the possible of death in hospital was small; the APACHE II score between 10-20, the mortality rate was 50%; the APACHE II score>20, the mortality was 80%-100% [1]. In this study, we found that the mortality were 16%, 50% and 78.7% respectively when the APACHE II scores were ≤ 15, 16-25 and >25, and with the increasing of the score, the disease was more serious, and the mortality will be higher, and this result was consistent with the literature. This study also showed that the APACHE II score of the survival group was significantly lower than that of the death group, and the difference was significant. In addition, in the multivariate Logistic regression analysis on the prognosis of critical illness patients, APACHE II score was incorporated into the main factors that influencing the prognosis of the patients. All these showed that APACHE II score has important significance in the evaluation of ICU patients with critical illness and indicating the prognosis [3].

Critically ill patients often have lactic acid metabolism disorders and hyperlactacidemia, and the reasons are as follow [4]: (1) Whole body tissue hypo perfusion, tissue cell perfusion deficiency will inevitably lead to cell hypoxia [5], which is the main cause of lactic acid increasing. (2) The decreasing of the metabolism and scavenging ability of lactic acid: liver and kidney, as the two important organs of lactic acid metabolism, its dysfunction can cause lactic acid metabolism and scavenging obstacles, accumulating in the body and leading lactic acid increasing. (3) High catecholamine hyperlipidemia induced by stress. (4) Congenital metabolic disorders: congenital metabolic disorders may result in the gluconeogenesis pathway abnormality or mitochondrial enzyme deficiency; the enhanced glycolysis may lead to increased lactic acid. (5) Drugs affection: such as metformin and sodium nitrate. The results indicated that lactic acid level can reflect energy metabolism of cell level, and correlated with the function of each organ, hyperlactacidemia is the risk factor of multiple organ dysfunction syndrome. This study found that with the increasing of APACHE score of critically ill patients, the severity of the disease will be increased gradually, and the lactic acid content of different groups at different time points was increased. There lactic acid content of 16-25 score group was increased significantly when compared with >25 score group, and the difference was significant (P<0.05), indicating that the lactic acid content was closely related with the severity of disease. The lactic acid contents were increased both in the ≤ 15 score group and the 16-30 score group, but there was no significant difference, this may be related with the small sample size. Related researches showed that there was good linear relationship between lactic acid levels at different time points and APACHE II score (r=0.602, 0.552, 0.523 and 0.494, P<0.01). The results of this study were consistent with the previous report [6, 7], indicating that lactic acid content can be used to evaluate the severity of critical ill. Analysis from the correlation coefficient, and found that the LAC level of critically ill at 0 hour after hospital admission has good relationship with APACHE score. The lactic acid levels at different time points of the death group were increased significantly when compared with the survival group (P<0.01). This result was consistent with the related literatures [8]. In addition, the multivariate Logistic regression analysis on the prognosis of critically ill patients includes the LAC level into the factors that can affect the prognosis of the patients. Dynamic monitoring of LAC level is more valuable than single monitoring in reflecting body oxygen, severity of disease and prognosis [9]. Studies have reported that the duration of lactic acid increasing is an important factor related to the prognosis, Abramson et al [10] found that the survival rates of the patients when the lactic acid reduced to the normal level within 24, 24-48 and >48 hours were 100%, 75% and 13.6%, respectively. Husain FA [11] also has the similar findings. Although, in this study, we did not observed the mortality at the time points that the lactic acid reduced to the normal level, from the bar chart of lactic acid level at different time points of different groups, we found that the lactic acid level of >25 score group was back to the normal level at 72 hours after hospital admission, the lacic acid level of 16-25 score gorup was back to the normal level at 48 hours after hospital admission, and the level of ≤ 15 score group was back to the normal level at 24 hours after hospital admission. Observation from the bar chart of lactic acid levels at different time points of the death group and the survival group can found that the duration of lactic acid increased in the death group was longer than that in the survival group. The results showed that the longer the duration of lactic acid increasing, the longer the duration of tissue and organ hypoxic hypo perfusion, the higher the occurrence rate of MODS, the more serious the patients are, and the worse the prognosis is.

Serum C-reactive protein (CRP) is an acute phase protein which synthesized with liver induced by cytokine interleukin-6 (IL-6), and it is the trace protein presents in serum or plasma. The CRP concentration in normal human blood is generally <8 mg/L and the concentration will be increased significantly when inflammation, tissue damage, ischemia and malignant tumor exist. More and more studies showed that CRP is an important sign of tissue damage, infection, inflammation, necrosis and malignant tumors [12]. Studies have showed that the decreasing of CRP will not be infected by chemotherapy, radiotherapy and hormone therapy, and keep relatively stable

[13]. In view of the characteristics of serum CRP, it has been used in the clinical detection of many diseases [14]. In this study, we found that with the increasing of APACHE II score, the disease will be more serious, and the serum CRP levels at different time points of different groups were increased. The statistical analysis showed that there was no significant difference in CRP level between groups, and this may be related with the increasing of CRP level within 4-8 hours after onset. At 24, 48 and 72 hours after hospital admission, the CRP level in the 16-25 score group was increased significantly when compared with the >25 score group ($P<0.05$), and the difference was significant. Therefore, it is not difficult to summary that serum CRP level is related with the severity of critical ill. While there was significant difference in CRP level between ≤ 15 score group and 16-25 score group at 48 hours after hospital admission ($P<0.05$), and there was no significant difference between other groups, considered that this may be related with the peak of CRP level at 48 hours after increasing. Relative researches showed that there was liner correlation between serum CRP levels at different time points and the APACHE II score ($r=0.198$, 0.287, 0.346 and 0.384, $P<0.01$). The results of this study are consistent with the relative studies [15, 16], indicating that serum CRP level can be used to assess the severity of critical disease. From the correlation coefficient, the CRP level of critically ill patients at 72 hours after hospital admission has the best correlation with APACHE score. The serum CRP level at different time points of the death group was increased significantly when compared with the survival group ($P<0.01$), and the difference was significant. In addition, the multivariate Logistic regression analysis on the prognosis of critically ill patients included the CRP level at 48 hours after hospital admission into the factors that can affect the prognosis of the patients. The results above suggested that serum CRP level was closely related with severity of critical disease, and is the good index used to predict the prognosis of critically ill patients. Studies of Suzana et al. [17] suggested that serum CRP level of critically ill patients was positively correlated with organ failure and the risk of death, and the result was consistent with the result of this study. Dynamic monitoring of serum CRP level has greater significance in comprehensive evaluation of the severity of disease and the prognosis. On one hand, if the serum CRP level maintained in a high level, meaing poor prognosis, and the dynamic monitoring can help to analyze and find the changes of the disease timely, and then adjust the treatment plan timely. On the other hand, if the optimal critical value can be determined, the dynamic monitoring of CRP level can improve the prefiction efficiency of CRP on critical illness. But the reports about this are rare, so better evidence is expected to be obtained from the high quality researches in the future.

Red blood cell distribution width (RDW) is the objective index that reflects red cell heterogeneity, and it is also an important parameter to reflect the variation of the volume of red blood cells. The increasing of RDW is mainly correlated with the proliferation and acceleration of red blood cells. It is reported that some inflammatory factors, such as G-CSF and EPO etc, also can stimulate the proliferation of red blood cells, leading to the increasing of RDW [18,19]. In recent years, some domestic and foreign researchers found that RDW is a new prognostic factor in selective cardiovascular disease patients (chronic or acute heart failure [20,21], stroke [22] or pulmonary hypertension [23], coronary artery disease [24]) and non-selective cardiovascular disease patients [25-26]. Some studies reported that the increasing of RDW can also reflect the body potential inflammatory state.

In recent years, the research on RDW has attracted more and more attention, and the research field is continuously extended, but there is no correlative report on critical disease. A prospective study is employed in this study, the serum RDW values of critically ill patients at different time points were collected, and the statistical analysis showed that with the increasing of APACHE II score, the RDW level at different time points was not increased. The RDW levels at different time points of death group were higher than those of the survival group, but there was no significant difference ($P>0.05$). Relative studies showed that the correlation coefficients of RDW levels at different time points and APACHE II score were 0.963, 0.973, 0.972 and 0.963 ($P<0.01$), indicating that RDW level was negatively correlated with APACHE II score, and the RDW level was highest at 48 hours after hospital admission, this suggested that with the disease progress of the critically ill patients, the consumption of red blood cells reached maximum value, at this time, the increasing of red blood cells means there may be compensation, and the disease condition had a turnover, but has no correlation with mortality. The results above showed that RDW-CV can be used for the evaluation of critical illness, but cannot be used for the determination of prognosis. The results were not consistented with literatures, so we divided the 228 cases of critically ill patients again, A group was the control group (175 cases of other system diseases), B group was the hematological diseases (n=14), and C group was cardiovascular diseases (n=39). The analysis results showed that the comparison between A group and B group at hospital admission, 24, 48 and 72 hours after hospital admission showed there was significant difference ($P<0.05$); there was significant difference between A group and C group ($P<0.05$). There was signigicant difference between B group and C group at 72 hours after hospital admission ($P<0.05$), and there was no significant difference between B group and C group at other three time points ($P>0.05$). The results showed that RDW has significant effect in evaluating hematological diseases and cardiovascular diseases. The results of North American CHARM (Candesartan for the treatment of heart failure to reduce incidence rate and mortality) in 2007 showed that the increasing of RDW-CV was closely related with the incidence rate and mortality of cardiovascular events, and suggested that high RDW level may be one of the predictive factors of cardiovascular events [21]. Another study of CARE related data found that RDW was also related with the incidence of cardiovascular events in patients with coronary heart disease [27]. Therefore, for the critically ill patients with cardiovascular disease, RDW-CV determination can provide objective risk stratification for clinical treatment, but opposite

in the critically ill patients, the lower the RDW-CV level, the worse and the disease condition.

Conclusions

- The LAC level and APACHE scores were positively correlated, and they are good indicator for evaluating the severity and judging prognosis of critically ill patients; Dynamic monitoring of LAC level is more worth than single monitoring,. The longer the duration of LAC increasing, the poor the prognosis, the higher the mortality.
- The serum CRP level is positive correlated with APACHE scores, serum CRP level changes will help to assess the severity of critically ill patients and judging prognosis; The dynamic monitoring of serum CRP level may be more meaningful then single monitoring, and could help find condition turn.
- There is no-linear correlation between RDW and APACHE score, so RDW cannot be used in comprehensive evaluation of critical ill, but in this study, we confirmed its great significance in detection of cardiovascular system diseases and blood system disease.
- Compared with the APACHE score with the difficulty of data collection, blood LAC and serum CRP detection has the characteristics of quick, simple, easy to repeat, and cheap, which is the early and sensitive indicator of severity evaluation of critical care.
- For some special diseases, the combination of blood LAC, serum CRP, inspection of RDW and APACHE score can improve the prognosis effect on critical ill to some extent.
- Blood LAC, serum CRP and RDW may become a new clinical evaluation method in the future, but there still some problems need to be researched, more proactive, reasonable design and large sample researches are needed.

Competing Interests

The author(s) declare that they have no competing interests.

Authors' Contribution

(1) JL have made substantial contributions to conception and design, revising it critically for important intellectual content; (2) GDN have analysis and interpretation of data; (3) DS have been involved in drafting the manuscript and acquisition of data; (4) ZY have given final approval of the version to be published.

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