THE RELATIONSHIP BETWEEN SOLUBLE CD74, SCD14 AND SEVERITY AND PROGNOSIS IN PATIENTS WITH ACUTE RESPIRATORY DISTRESS SYNDROME

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ABSTRACT

Objective: To investigate the relationship between soluble leukocyte differentiation antigen 74 (sCD74) and soluble leukocyte differentiation antigen 14 (sCD14) and severity and prognosis in patients with acute respiratory distress syndrome (ARDS).

Methods: A total of 96 patients with ARDS were randomly divided into mild, moderate and severe groups according to differences in their oxygenation index (OI): mild group (n=19), moderate group (n = 44) and severe group (n=33). Moreover, 35 healthy subjects were selected as the normal group. The serum sCD74 and sCD14 levels were measured by enzyme-linked immunosorbent assay (ELISA), and the changes in APACHE II scores were also compared in each group. According to the outcome of prognosis, patients were divided into either the death group (n=22) or survival group (n=74). Changes in serum sCD74 level, sCD14 level and APACHE II score were measured in these two groups. The correlation between serum sCD74 and sCD14 level, as well as ARDS severity, were analysed according to the Pearson correlation test.

Results: Compared to the normal group, the serum sCD74 levels, sCD14 levels and APACHE II scores in the study group were significantly higher than those in the normal group (P<0.05). Serum sCD74 level, sCD14 level and APACHE II score increased significantly (P<0.05) with the increasing ARDS severity of patients, among which the mild group had the lowest level and the severe group had the highest level. Compared to the survival group, the serum sCD74 levels, sCD14 levels and APACHE II scores of the death group were significantly higher than those of the survival group (P<0.05). The areas under the curve of serum sCD74, sCD14 and sCD74/sCD14 in patients with ARDS were 0.823, 0.746 and 0.933, respectively. The combined detection of serum sCD74 and sCD14 was more valuable in evaluating the prognosis of patients with ARDS. The Pearson correlation test indicated a significant positive correlation between serum sCD74 levels, sCD14 levels and APACHE II scores in patients with ARDS (r=0.325, P<0.05 and r=0.469, P<0.05, respectively).

Conclusion: The serum levels of sCD74 and sCD14 in patients with ARDS are significantly higher than that in patients with ARDS. Moreover, their levels can exhibit certain values that can be used to judge the severity and prognosis of patients with ARDS.

Keywords: Acute respiratory distress syndrome, severity, prognosis, correlation, soluble CD74, sCD14.

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Introduction

Acute respiratory distress syndrome (ARDS) is a type of clinical syndrome[1] that is primarily characterised by increased pulmonary alveolar capillary permeability, diffuse alveolar infiltration, progressive hypoxemia, and the development of respiratory failure due to various internal and external factors. ARDS is a clinically common critical illness; according to statistics, there are tens of thousands of annual cases worldwide. The incidence and mortality of 80 of every 100,000 people were ARDS[2]. The main issue for patients with ARDS is an imbalance between the anti-inflammatory and inflammatory mediators of the body[3]. Notably, this imbalance of inflammatory mediators and anti-inflammatory mediators can cause damage to the tissues and organs, thereby resulting in systemic inflammatory response syndrome, which leads to ARDS and may cause multiple organ failure[4]. The main method for treating ARDS is mechanical ventilation. However, with the development of mechanical ventilation

equipment and the application of various modern ventilation monitoring techniques, patient mortality remains high[5]. Therefore, it is of great significance to find relevant factors, early prevention and timely treatment to evaluate the severity of the disease and predict the prognosis of patients. In the present study, 96 patients with ARDS were studied. The purpose of this study was to determined whether soluble leukocyte differentiation antigen 74 (sCD74) and soluble leukocyte differentiation antigen 14 (sCD14) in patients with ARDS are associated with the severity of the disease and its prognosis.

Data and methods

Basic information

The study of this group was approved by the Ethics Committee of the hospital and complied with medical ethics. A total of 96 patients with ARDS were randomly selected as the study group.

Inclusion criteria:

• All patients met the diagnostic criteria for ARDS formulated by the Chinese Medical Association[6];

• Clinical onset or respiratory symptoms are newly developed or exacerbated within 1 week;

• Double lung plaque cannot be completely interpreted by exudation, lobe/lung collapse or nodule;

• All study subjects and their families provided informed consent and signed informed consent.

Exclusion criteria:

• Patients with incomplete medical records or exiting for any reason;

• Patients with severe cardiac function, liver and kidney insufficiency and/or complicated infectious disease;

• Patients with lactation or pregnancy;

• Those who cannot cooperate with the treatment.

A total of 62 males and 34 females were included in the study group, which had a mean age and body mass index (BMI) of 56.33 ± 6.31 years and 25.57 ± 5.34 kg/m^2, respectively.

Mild group

Oxygenation index (OI)=200~30mmHg, positive end-expiratory pressure or continuous positive airway pressure ≥5cmH$_2$O;

Moderate group

OI=101~200mmHg and end-expiratory positive pressure ≥5cmH$_2$O;

Severe group

OI<100mmHg and end-expiratory positive pressure ≥5cmH$_2$O.

The mean age was 55.31 ± 7.29 years. BMI (24.03 ± 3.88kg/m^2), moderate group, 44 cases (27 males, 17 females); the mean age was 56.73 ± 6.02 years. BMI 23.81 ± 3.16kg/m^2, 33 cases in the severe group (21 males and 12 females); the mean age was 54.95 ± 7.67 years. BMI 24.19 ± 2.99kg/m^2).

Simultaneously, 35 healthy subjects were selected as the normal group, which included 24 males and 11 females with a mean age of 54.71 ± 5.28 years and BMI of 22.69 ± 3.97kg/m^2.

No statistically significant difference was observed between age and the other basic data in each group (P>0.05).

Observation index

Serum sCD74 and sCD14 levels: serum sCD74 and sCD14 levels were measured by enzyme-linked immunosorbent assay (ELISA). The testing methods were performed in strict accordance with the instructions of the kit.

Changes in the APACHE II scores of each group: APACHE II score has often been used to evaluate the severity of a patient.

The APACHE II score includes acute physiological score (Acute Physiological Rating, APS), age (age points) and chronic health status. APACHE II score = APS + age + chronic health status.

According to the prognosis of patients that were followed up for 30 days, patients were divided into death (n=22) and survival (n=74) groups. Changes in serum sCD74 level, sCD14 level and APACHE II score were measured in the two groups.

The correlation between serum sCD74 level, sCD14 level and the severity and prognosis of patients with ARDS was analysed according to the Pearson correlation test.

Statistical methods

In the present study, the SPSS10.0 software package was used for statistical data analysis.

The data were compared using the sample t-test. The levels of sCD74 and sCD14 in each group were determined by enzyme-linked immunosorbent assay.

The correlation of serum sCD74 and sCD14 level with the severity and prognosis the patients with ARDS were analysed according to the Pearson correlation test. The statistical difference test standard was P<0.05.

Results

Comparison of serum sCD74 level, sCD14 level and APACHE II score between study and normal groups

Compared to the normal group, the team patients' serum sCD74 levels, sCD14 levels, APACHE II scores were significantly higher (P<0.05) (see Table 1).

Group	n	sCD74 (ng/mL)	sCD14 (µg/L)	APACHE II score
Study group	96	75.37±11.43	49.91±12.35	24.46±4.22
Normal group	35	26.85±9.31	12.22±3.43	12.58±3.21
t		22.521	17.767	15.123
P		<0.001	<0.001	<0.001

Table 1: Comparison of serum sCD74 levels, sCD14 levels and APACHE II scores ($\bar{x}$±s).

Comparison of serum sCD74 and sCD14 levels in patients with different conditions

With the increasing severity of symptoms among patients, serum sCD74, sCD14, APACHE II score levels were significantly higher (P<0.05). Among them, the mild group had the lowest levels, whilst the severe group exhibited the highest level (Table 2).

Group	n	sCD74 (ng/mL)	sCD14 (µg/L)	APACHE II score
Mild group	19	42.28±8.18	23.32±3.41	17.63±2.59
Moderate group	44	74.39±11.45	42.45±15.53	23.28±5.45
Severe group	33	94.42±15.35	58.94±18.43	32.49±2.84
F		106.06	33.79	84.33
P		<0.001	<0.001	<0.001

Table 2: Comparison of serum sCD74 and sCD14 levels ($\bar{x}$±s).

Comparison of serum sCD74 level, sCD14 level and APACHE II score between death and survival groups

When compared to the survival group, the serum sCD74 levels, sCD14 levels and APACHE II scores of death group patients were significantly higher (P<0.05) (Table 3).

Group	n	sCD74 (ng/mL)	sCD14 (µg/L)	APACHE II score
Death group	22	96.18±14.49	59.14±13.14	46.68±12.14
Survival group	74	55.38±10.54	34.13±9.03	22.37±8.64
t		15.237	10.389	10.873
P		<0.001	<0.001	<0.001

Table 3: Serum sCD74 level, sCD14 level and APACHE II score comparison between survival and death groups ($\bar{x}$±s).

The value of serum sCD74 and sCD14 in the prognosis evaluation of patients with acute respiratory distress syndrome

The ROC curve was established, and the results showed that the areas under the curve for serum sCD74, sCD14 and sCD74+sCD14 were 0.823, 0.746 and 0.933, respectively, in patients with ARDS.

The combined detection of serum sCD74 and sCD14 had a higher prognostic value in patients with ARDS (see Table 4).

Index	ROC	Sensitivity (%)	Specificity (%)	APACHE II score
sCD74	0.823	82.63	77.86	24.46±4.22
sCD14	0.746	81.99	71.91	12.58±3.21
Joint detection	0.933	92.31	93.42	15.123

Table 4: The value of sCD74 and sCD14 in the prognosis evaluation of patients with acute respiratory distress syndrome.

The correlation between sCD74, sCD14 and the severity of acute respiratory distress syndrome

The present study utilised APACHE II score evaluation of the disease severity of patients.

Scores were checked by Pearson correlation analysis and ARDS patients' serum sCD74 levels, sCD14 levels and APACHE II scores had significantly positive correlations (r=0.325, P<0.05 and r=0.469, P<0.05, respectively).

Conclusion

ARDS is an acute, disseminated and inflammatory lung injury that is presently a common, critical and serious disease. According to statistics, the mortality of patients with ARDS in the intensive care unit and under regular hospitalisation remained over 40% under low tidal volume lung-protection ventilation[7]. ARDS is often complicated by multiple organ dysfunction syndrome, and the occurrence and development of both ailments are closely related to the runaway of systemic inflammatory response syndrome. At present, the treatment of ARDS is primarily based on low tidal volume lung-protective ventilation, limited fluid input and other comprehensive treatment, while the key to reducing ARDS mortality is early prevention[8]. Therefore, identifying indexes closely related to the occurrence, development and prognosis of ARDS for the early diagnosis, prevention and treatment of ARDS is of great importance to reducing the mortality in patients with ARDS.

Developed by Knaus in 1978, the APACHE II score is mainly composed of APS, age and chron-

ic health status. After three years of research, a set of objective evaluation systems including primary disease, respiration, heart rate, blood pressure, consciousness, tissue perfusion and other factors, was put forward in 1981, which has the advantages of simplicity and reliability. APACHE II score has become the most widely used and authoritative method to evaluate the severity of critical diseases and predict their prognosis[9]. According to related reports, the APACHE II score has an important relationship with the prognosis of patients with ARDS[10]. In the present study, the APACHE II scores of the study group were significantly higher than that of the normal group, while the APACHE II score of the death group was significantly higher than that of the survival group. The results indicate that the APACHE II score was related to the severity of ARDS. Therefore, the dynamic monitoring of the APACHE II score could reflect the severity of ARDS.

sCD74 is a single transmembrane protein on the cell membrane and is the constant chain of human histochemical compatibility complex type II molecule. sCD74 on the cell membrane is a high-affinity receptor of macrophage migration inhibitor that binds to itself and has an important relationship with the occurrence of ARDS[11]. Moreover, sCD74 is the outer segment of the CD74 molecule. In the study of ARDS mouse model, Tahir et al.[12] found that sCD74 exists in the peripheral serum and alveolar lavage fluid of mice. Furthermore, the level of CD14 is closely related to the severity of ARDS in mice. CD14 is mainly expressed on the surface of monocytes/macrophages, with sCD14 and additional variants (e.g., monocyte surface CD14, mCD14 on monocytes)[13]. sCD14 is the main form of CD14 in vivo and a marker of immune response in the body, thereby serving an important role in the systemic inflammatory response[14]. The results of the present study suggest that serum sCD74, sCD14 and APACHE II scores are independent risk factors for prognosis. Serum sCD74 has a certain diagnostic value in the prognosis of patients with acute respiratory distress syndrome, and its combined detection is more valuable.

In summation, the levels of serum sCD74 and sCD14 in patients with ARDS were significantly elevated, thus making these values useful in judging the severity and prognosis of patients with ARDS.

References

1) Sinha P, Calfee CS, Beitler JR, Soni N, Ho K, et al. Physiologic Analysis and Clinical Performance of the Ventilatory Ratio in Acute Respiratory Distress Syndrome. Am J Respir Crit Care Med 2019; 199: 333-341.

2) Li RHL, Tablin F. A Comparative Review of Neutrophil Extracellular Traps in Sepsis. Front Vet Sci 2018; 5: 291.

3) O'Halloran KD, Lewis P. Respiratory muscle dysfunction in animal models of hypoxic disease: antioxidant therapy goes from strength to strength. Hypoxia (Auckl) 2017; 5: 75-84.

4) Menk M, Giebelhäuser L, Vorderwülbecke G, Gassner M, Graw JA, et al. Nucleated red blood cells as predictors of mortality in patients with acute respiratory distress syndrome (ARDS): an observational study. Ann Intensive Care 2018; 8: 42.

5) Semler MW, Marney AM, Rice TW, Nian H, Yu C, et al. B-type Natriuretic Peptide, Aldosterone, and Fluid Management in Acute Respiratory Distress Syndrome. Chest 2016; 150: 102-111.

6) Zhang ZZ. Dexmedetomidine For the Treatment Of Acute Lung Injury: A Fact Or Fiction? J Invest Surg 2019; 23: 1-3.

7) Thompson BT, Chambers RC, Liu KD. Acute Respiratory Distress Syndrome. New Engl J Med 2017; 377: 562-572.

8) Tao W, Yang LQ, Gao J, Shao J. Neuromuscular Blocking Agents for Adult Patients with Acute Respiratory Distress Syndrome: A Meta-Analysis of Randomized Controlled Trials. J Trauma Acute Care Surg 2018; 85: 1102-1109.

9) Huda AQ, Karim MR, Mahmud MA, Islam MS, Haque MF, et al. Use of Acute Physiology and Chronic Health Evaluation (APACHE)-II and Red Cell Distribution Width (RDW) for Assessment of Mortality of Patients with Sepsis in ICU. Mymensingh Med J 2017; 26: 585.

10) Wan B, Xu WJ, Xu WN, Zhan P, Wu GN, et al. Plasma long noncoding RNA IL-7R as a prognostic biomarker for clinical outcomes in patients with acute respiratory distress syndrome. Clin Respir J 2018; 12: 1607-1614.

11) Kim BS, Stoppe C, Grieb G, Leng L, Sauler M, et al. The clinical significance of the MIF homolog d-dopachrome tautomerase (MIF-2) and its circulating receptor (sCD74) in burn. Burns 2016; 42: 1265-1276.

12) Tahir SA, Gao J, Miura Y, Blando J, Tidwell RSS, et al. Autoimmune antibodies correlate with immune checkpoint therapy-induced toxicities. Proc Natl Acad Sci U S A 2019; 116: 22246-22251.

13) Wu CC, Lan HM, Han ST, Chaou CH, Yeh CF, et al. Comparison of diagnostic accuracy in sepsis between presepsin, procalcitonin, and C-reactive protein: a systematic review and meta-analysis. Ann Intensive Care 2017; 7: 91.

14) Xia K, Zhang P, Hu J, Hou H, Xiong M, et al. Synergistic effect of receptor-interacting protein 140 and simvastatin on the inhibition of proliferation and survival of hepatocellular carcinoma cells. Oncol Lett 2018; 15: 4344-4350.

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