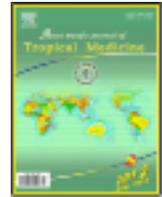




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Combined APACHE II score and arterial blood lactate clearance rate to predict the prognosis of ARDS patients

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ABSTRACT

Objective: To explore the easily applicable indicators of practical value to evaluate the prognosis of acute respiratory distress syndrome (ARDS). **Methods:** Blood and biochemical tests and blood-gas analyses were performed upon entry into the ICUs, 12 h, 24 h, 48 h and 72 h after that in 72 ARDS patients (who were admitted to the ICUs of our hospital from January 2000 to December 2009). Then APACHE II scores were achieved by combining relevant physiological parameters and laboratory results. **Results:** There was a statistical difference between the death group and survival group at different time points upon entering the ICUs in terms of APACHE II score, alveolar-arterial oxygen difference and arterial blood lactate clearance rate. PaO₂/FiO₂ values were recorded to be statistically different between the death group and survival group 24 h, 48 h and 72 h, respectively after entry into the ICUs. In addition, registered linear regression existed between APACHE II score, alveolar-arterial oxygen difference or PaO₂/FiO₂ value and time. APACHE II score 24 h and 72 h after entering ICUs predicted mortality with an area under the ROC curve (AUC) standing respectively at 0.919 and 0.955. Arterial blood lactate clearance rate 12 h, 24 h, 48 h and 72 h after entering ICUs predicted mortality with an area under the ROC curve (AUC) at 0.918, 0.918, 0.909 and 0.991, respectively. **Conclusions:** APACHE II score applied in combination with arterial blood lactate clearance rate is of clinical significance in assessing the prognosis of ARDS patients.

1. Introduction

In recent years, studies on the prognosis of critical diseases have constituted an important area of critical care medicine. It has helped improve medical techniques and service, and has greatly reduced medical risks. Among them, the acute respiratory distress syndrome (ARDS), which was described originally in Lancet in 1967 by Ashbaugh DG and coworkers, has remained a focus and difficulty in critical care medicine^[1]. ARDS is a life threatening respiratory failure due to lung injury from a variety of precipitants. Pathologically, ARDS is characterized by

diffuse alveolar damage, alveolar capillary leakage, and protein rich pulmonary oedema leading to the clinical manifestation of poor lung compliance, severe hypoxemia, and bilateral infiltrates on the chest radiograph. It develops and progresses rapidly, and its prognosis is bad^[2]. Through meta-analysis of clinical study literature from 1967 to 1994 in the international medical community, the mortality stayed around 50% for 3 264 ARDS patients^[3]. However, the ARDS causes 30% to 70% total mortality, which was associated with primary illness and illness severity. Sepsis and aspiration pneumonia have been associated with higher motility, whereas patients with lung injury resulting from major trauma have a lower risk of death. Direct lung injury has also been associated with greater mortality^[4]. Elderly patients (over 65 years old) with ARDS have a poor prognosis^[5]. There were 16% patients die only

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of respiratory failure, while 49% patients die of the multiple organ dysfunction syndrome[6]. Most of ARDS survivors can recover completely, but some of them has lung-fibrogenesis residue[7]. ARDS can affect many groups of patients and is associated with a number of pulmonary and/or extra pulmonary factors, which can impact a patient's prognosis[8]. Thus, it is necessary to build a specific criterion or to find some biochemical markers to predict ARDS prognosis. APACHE II scoring system was regarded as a superior biochemical marker to evaluate the outcomes of critically ill patients and ill severity[9-14]. Lactate clearance, a surrogate for the magnitude and duration of global tissue hypoxia, is used diagnostically, therapeutically and prognostically. Recent several studies have identified that arterial lactate clearance is significantly associated with septic shock severity[15-17], and measurement of serum arterial lactate clearance is helpful to evaluate pressure of global tissue perfusion and to predict patients' prognosis in serving sepsis and septic shock[18-20]. In the current study, we explored the easily applicable biochemical markers of practical value to evaluate ARDS prognosis through observing acute physiological parameters, APACHE II score, alveolar-arterial oxygen difference, $\text{PaO}_2/\text{FiO}_2$ and arterial blood lactate clearance rate.

2. Materials and methods

2.1. Diagnostic criteria

The diagnostic criteria for ARDS (formulated in 1999 by the chapter of Respiratory Diseases, Chinese Medical Association): (i) high risk factors for ARDS; (ii) acute onset with tachypnea and (or) respiratory distress; (iii) hypoxemia: $\text{PaO}_2/\text{FiO}_2 \leq 200$; (iv) chest X-ray: infiltration shadow observed in both lungs; (v) PAWP ≤ 18 mmHg or cardiogenic pulmonary edema being clinically excluded.

2.2. Subjects

72 ARDS patients, who were admitted to the ICUs of our hospital from January 2000 to December 2009, were registered as the study subjects, among whom 49 died at the hospital, 8 were discharged against physician advice and 15 witnessed improvement in their conditions. The 8 discharges against medical advice were counted as subjects in the death group of this study, so there were 57 cases in the death group, which included 39 males and 18 females with the average age standing at 50.75 ± 14.39 , and 15 in the survival group, which was comprised of 10 males and five females with the average age at 49.53 ± 14.01 .

2.3. Analysis methods

Blood and biochemical tests and blood-gas analyses were performed for all subjects upon entry into the ICUs, 12 h, 24 h, 48 h and 72 h after that. Besides, APACHE II scores were achieved by combining relevant physiological parameters and laboratory results.

2.4. Statistics

All data achieved were expressed in the manner of (\pm SD) for statistical analysis by the application of SPSS11.0, the software for running *t*-test, Kruskal-Wallis test, linear regression analysis and ROC analysis.

3. Results

3.1. APACHE II score

The comparison of APACHE II score (*t*-test) achieved at different time frames between the two groups was of statistical difference (Table 1). In addition, APACHE II score ran in a model of linear regression over time (linear regression analysis, $R^2=0.85$) in the death group, meaning that APACHE II score showed no noticeable improvement or even presented a significantly increasing tendency over time in the death group despite of active treatments (Figure 1).

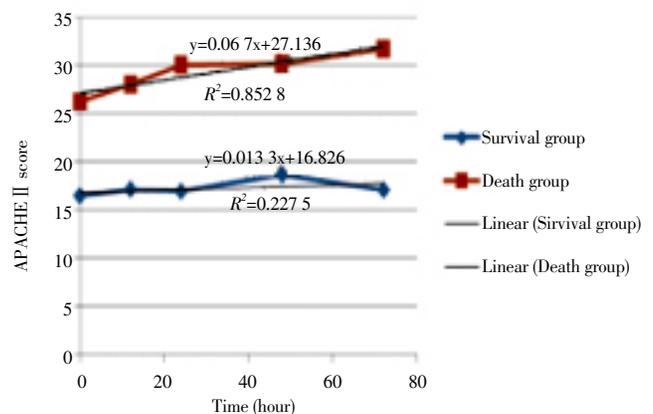


Figure 1. Linear regression drawn from APACHE II score over time in the two groups.

3.2. Alveolar-arterial oxygen difference ($A-aO_2$)

The comparison of $A-aO_2$ (*t*-test) achieved at different time frames between the two groups was of statistical difference (Table 2). In addition, $A-aO_2$ value ran in a model of linear regression over time (linear regression analysis, $R^2=0.98$) in the death group, meaning that $A-aO_2$ value showed no noticeable improvement or even presented a significantly

increasing tendency over time in the death group despite of active treatments.

3.3. PaO_2/FiO_2 value

The comparison of PaO_2/FiO_2 value (*t*-test) achieved at the time points of 24 h, 48 h and 72 h, respectively, between the two groups was of statistical difference (Table 3). In addition, PaO_2/FiO_2 value ran in a model of linear regression over time (linear regression analysis, $R^2=0.95$) in the death group, meaning that PaO_2/FiO_2 showed no noticeable improvement or even presented a significantly decreasing tendency over time in the death group despite of active treatments.

3.4. Arterial blood lactate clearance rate

The determination of arterial blood lactate level was started only from the year of 2007 at our hospital, thus we have only collected such data about 27 patients, consisting of 22 in the death group and 5 in the survival group. The comparison of arterial blood lactate clearance rate (Kruskal–Wallis test) achieved at all the time frames between the two groups was of statistical significance (Table 4).

3.5. ROC Curve analysis of APACHE II score

Areas under the ROC curve drawn from APACHE II scores

were 0.919 and 0.955, respectively at 24 h and 72 h upon entry into the ICUs, which suggested that it was of noticeable significance for the mortality prediction of ARDS patients (Figure 2).

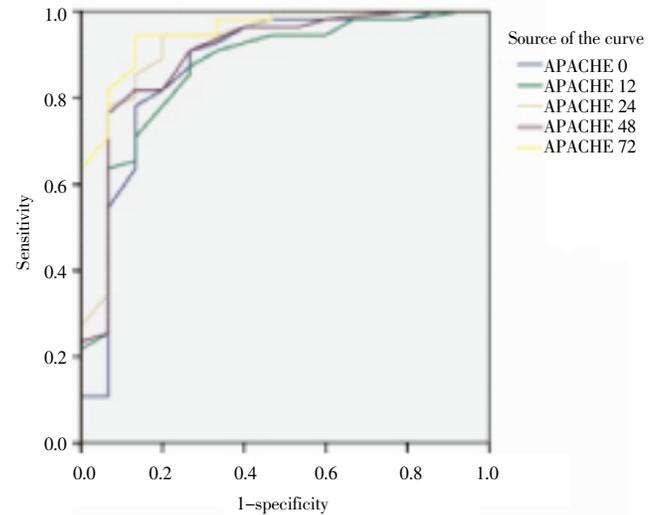


Figure 2. ROC Curve analysis of APACHE II score.

3.6. ROC Curve analysis of $A-aO_2$ and PaO_2/FiO_2

Areas under the ROC curve of $A-aO_2$ and PaO_2/FiO_2 value after patients' entering the ICUs ranged from 0.664 to 0.790 and from 0.242 to 0.351, respectively. Such results demonstrated that $A-aO_2$ and PaO_2/FiO_2 , as independent

Table 1

Comparison of APACHE II score between the 2 groups.

Group	Time of admission to hospital	12 h	24 h	48 h	72 h
Survival group	16.47±7.15 ^a	17.13±6.20 ^a	16.93±6.22 ^a	18.6±6.05 ^a	17.07±4.65 ^a
Death group	26.26±7.15	28.04±8.27	30.05±7.14	30.15±7.68	31.67±7.76

^a*P*<0.05 vs. death group.

Table 2

Comparison of $A-aO_2$ value between the 2 groups.

Group	Time of admission to hospital	12 h	24 h	48 h	72 h
Survival group	250.20±81.16a	276.07±108.35 ^a	272.13±107.13 ^a	304.87±129.57 ^a	286.47±171.97 ^a
Death group	323.65±159.13	364.31±143.51	393.88±158.72	431.13±148.61	472.13±141.71

^a*P*<0.05 vs. death group.

Table 3

Comparison of PaO_2/FiO_2 between the 2 groups.

Group	Time of admission to hospital	12 h	24 h	48 h	72 h
Survival group	157.93±57.48	167.33±98.30	187.20±72.33 ^a	161.87±68.49a	176.27±87.99 ^a
Death group	132.95±96.95	125.12±59.26	115.52±73.01	94.87±43.56	91.41±41.08

^a*P*<0.05 vs. death group.

Table 4

Comparison of arterial blood lactate clearance rate (%) between the 2 groups.

Group	12 h	24 h	48 h	72 h
Survival group	15.49±9.18 ^a	26.75±16.19 ^a	29.61±16.35 ^a	34.39±29.99 ^a
Death group	-29.37±40.39	-31.77±46.05	-57.71±74.19	-109.13±81.98

^a*P*<0.05 vs. death group.

factors, were neither of notable significance for the mortality prediction of ARDS patients.

3.7. ROC Curve analysis of arterial blood lactate clearance rate

Areas under the ROC curve of arterial blood lactate clearance rate 12 h, 24 h, 48 h and 72 h after patients' entering the ICUs were 0.918, 0.918, 0.909 and 0.991, respectively. Such results demonstrated that $A-aO_2$ and PaO_2/FiO_2 were of marked significance for the mortality prediction of ARDS patients (Figure 3).

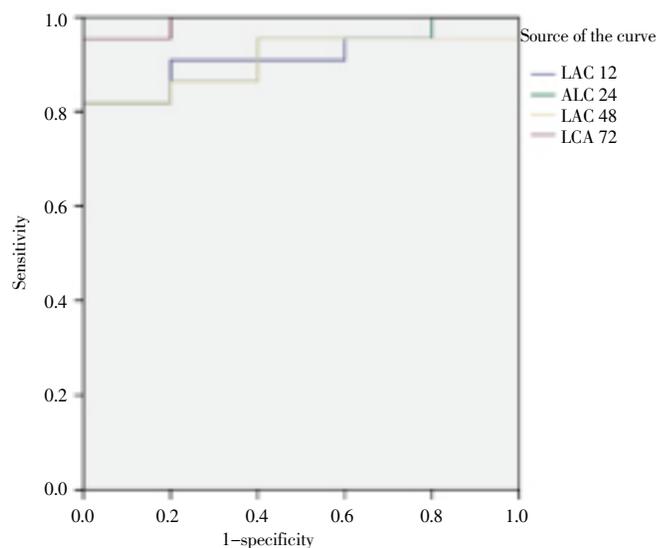


Figure 3. ROC Curve analysis of arterial blood lactate clearance rate.

4. Discussion

ARDS is mainly characterized by alveolar-capillary injury, which is the manifestation of acute respiratory failure[3,4,8]. The difficulty in its treatment lies in the refractory hypoxemia. PaO_2/FiO_2 value, a major indicator for the oxygenating capability of lung, has become a requisite for the diagnosis of ARDS. However, PaO_2 cannot serve as an indicator of tissue cells' demand and utilization of oxygen and is subject to the influence of many factors like the concentration of the oxygen inhaled, cardiac output and oxygen consumption, etc. $A-aO_2$ represents the difference between the oxygen partial pressure in the lung and arterial blood, which is related to arteriovenous anatomical shunt, ventilation/perfusion imbalance and dysfunction of alveolar-capillary diffusion barriers, thus bearing better embodiment of pulmonary ventilation function[21]. The current study suggests that the difference is of statistical significance between the two groups in terms of $A-aO_2$ at all the five time points. No significantly difference could be found in PaO_2/FiO_2 value during the first 24 h upon patients' entry into the ICUs, which may be the result of high concentration of

inhaled oxygen and unstable hemodynamic. It demonstrates that $A-aO_2$ and PaO_2/FiO_2 , as independent factors, is neither of notable value for the prognosis of ARDS patients, indicating that poor oxygenation constitutes a risk factor of poor prognosis but not the only one.

APACHE II scoring system covers a comprehensive multitude of factors like respiration, heart rate, blood pressure, consciousness, tissue perfusion and primary illnesses. It has been commonly applied both at home and abroad in the severity and prognosis assessment of many critical illnesses[9-11]. A variety of studies have proven that there exists the positive correlation between the APACHE II score and patients' mortality[11-14]. The results showed that the difference between the two groups was statistically significant at all the five time points and the score in the death group presents positive correlation with time, which means that the score rises accordingly over time. In addition, the APACHE II scores achieved respectively at 24h and 72h after entering the ICUs have been discovered to be of notable significance in patients' prognosis of mortality (measured by means of areas under ROC curve, $AZ > 0.9$); the areas under ROC curve drawn from APACHE II scores were also running around 0.9 at other time points we set. To sum up, APACHE II score can reflect patients' disease severity and their response to treatments in a timely and accurate manner[21-23].

Furthermore, as ARDS takes its course in patients, lactate accumulates in patients' blood stream[24]. This study also shows us that statistical difference can be observed in terms of patients' arterial lactate clearance rate over time between the two groups and the corresponding areas under ROC curve (AZ) were all higher than 0.9, indicating that this factor can be validly used to predict patient's mortality. As a result, dynamic monitoring of blood lactate clearance rate can be an accurate reflection of tissue perfusion and blood oxygenation level after treatment, and thus it helps to make an effective and objective assessment of patients' prognosis[18-20,25]. The prognosis can be more accurately assessed as long as dynamic monitoring of blood lactate clearance rate is performed in combination with APACHE II scoring.

Conflict of interest statement

We declare that we have no conflict of interest.

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