Establishment and Evaluation of a Simplified Evaluation System of Acute Respiratory Distress Syndrome

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Purpose: In recent years, a variety of acute respiratory distress syndrome (ARDS) evaluation systems have been developed worldwide; however, they are not so convenient for the doctors clinically, we decided to establish and evaluate a simplified evaluation system of ARDS (SESARDS). Materials and Methods: Data from 140 ARDS patients (derivation data set) were collected to screen for prognostic factors affecting outcomes in ARDS patients. By logistic regression analysis, scores were allocated to corresponding intervals of the variables, respectively, by means of analysis of the frequency distribution to establish a preliminary scoring system. Based on this primary scoring system, a definitive evaluation scheme was created through consultation with a panel of experts. The scores for the validation data set (92 cases) were assigned and calculated by their predictive mortality with the SESARDS and acute physiology and chronic health evaluation II (APACHE II). The performance of SESARDS was compared with that of APACHE II by means of statistical analysis. Results: The factors of age, pH, Glasgow coma scale (GCS), oxygenation index (OI), and the lobes of lung were associated with prognosis of ARDS respectively. The sensitivity and specificity of SESARDS for the validation data set were 96.43% and 58.33%, respectively. On the AUC, no significant difference between APACHE II and SESARDS was detected. There were no significant differences between the prediction and the actuality obtained by SESARDS for the validation data set the SESARDS scores were positively correlated with the actual mortality. Conclusion: SESARDS was shown to be simple, accurate and effective in predicting ARDS progression.

Key Words: Acute respiratory distress syndrome, evaluation of severity, scheme evaluation

INTRODUCTION

Presently, the mortality for acute respiratory distress syndrome (ARDS) is high.1,2 Ji-ang and Hu1 proposed that the currently available methods for evaluating ARDS disease severity are not reflective of the actual severity and can be inconsistent. However, these evaluation systems can be effective in indicating the degree of critical illness as well as in evaluating treatment and outcomes. In recent years, a variety of ARDS
posed at the American-European Consensus Conference on ARDS in 1994. In all 232 eligible patients, diagnostically, the ratio of the partial pressure of arterial oxygen (PaO\textsubscript{2}) to the fraction of inspired oxygen was less than 200 (adjusted if the altitude exceeded 1000 m), and bilateral infiltrations were evident on chest radiography, consistent with the presence of pulmonary edema without evidence of left atrial hypertension.

Methods

Data collection

Physiological measurements, age and previous health status were used to calculate APACHE II score. Clinical parameters for ARDS were obtained within the first 24 hours after the diagnosis of ARDS was made, and included 1) age, sex, and comorbidities; 2) respiratory rate, blood pressure, body temperature, and heart rate; 3) white cell count and hematocrit; 4) serum level of sodium, potassium, creatinine and glucose; 5) arterial blood gas including pH, PaO\textsubscript{2}, PaCO\textsubscript{2}, and oxygenation index (OI); 6) Glasgow coma scale (GCS); 7) presence of ARDS (p); 8) number of risk factors for ARDS; 9) number of lobes involved; 10) amount of extra-pulmonary organ dysfunction or failure; and 11) vital status at discharge.

Assignment for indexes

In 1998, Gattinoni, et al.\textsuperscript{6} reported that pathological changes in pneumonia-induced ARDS were significantly different, in addition to the effects on PEEP from ARDS caused by abdominal disease. Accordingly, he classified ARDS into two categories: ARDS (p) and ARDS (exp), and then assigned scores of 1 to the former and 0 to the latter, when applying them to statistical treatment. For our statistical purpose, likewise, we handled the score assignments in this study for the four lobes of the lung (left-up, left-down, right-up and right-down) according to the standards for evaluating acute lung lesions. According to the scope of inflammation on chest imaging, we assigned scores of 1-4 for the four lobes, respectively. Then, we assigned scores of 1-5 for the total number of indicators of nonpulmonary organ dysfunction present, including alimentary tract hemorrhage, acute renal failure, liver function failure, nervous function failure, and function failure of the hematological system.

Statistical analysis

Statistical analysis was conducted based on the retrospective case-control study, and results of the descriptive statis-
tics were presented as means±SD. The comparison between two means was analyzed by independent-sample t-test, and the frequency distributions in categorized variables were compared using Pearson’s chi-square test. The risk factors affecting ARDS prognosis were screened by univariate logistic regression and multivariate logistic regression (forward conditional). Then, a probabilistic equation for a simplified evaluation system of acute respiratory distress syndrome (SESARDS) was established by full-factor logistic regression, and thereafter, the quartile frequency distribution method was used to establish a preliminary valuation system, from which a definitive evaluation scheme of SESARDS was developed and revised after consultation with a panel of experts. Finally, SESARDS and APACHE II were compared in regarding to validity, sensitivity, and specificity using receiver operating characteristics curves (ROC) curves. SPSS software version 13.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis and plotting of graphs, scatter plots and ROC curves, as well as calculation of the AUC of ROCs.

**RESULTS**

**Baseline demographics**
Statistically, the differences between the two sets were in-

| Table 1. Baseline Demographics for Both Data Sets |
|-----------------------------------------------|
| Variables | Derivation data set (n=140) | Validation data set (n=92) | p value |
| Age (yrs)  | 46.05±16.24 | 48.08±19.66 | 0.409 |
| Female sex | 44 | 28 | 0.656 |
| ARDS (p)  | 104 | 73 | 0.375 |
| APACHE II score | 20.48±7.09 | 21.92±9.80 | 0.064 |
| Death  | 90 | 56 | 0.667 |

ARDS, acute respiratory distress syndrome; APACHE, acute physiology and chronic health evaluation.

**Table 2. Results of Univariate Logistic Regression Analysis**

| Variables | B    | Wald | p value | OR      | 95% CI Lower | Upper |
|-----------|------|------|---------|---------|--------------|-------|
| Age (yrs) | 0.026 | 5.513 | 0.023 | 1.027   | 1.004        | 1.050 |
| GCS       | -0.148 | 5.958 | 0.015 | 0.862   | 0.765        | 0.971 |
| pH        | -6.362 | 11.818 | 0.001 | 0.002   | 0.000        | 0.065 |
| OI        | -0.013 | 8.519 | 0.004 | 0.987   | 0.979        | 0.996 |
| lobes of lung | 0.804 | 15.330 | 0.000 | 2.235   | 1.494        | 3.344 |
| P(A-a)O₂   | 0.005 | 7.909 | 0.005 | 1.005   | 1.002        | 1.009 |
| NONPORG*   | 0.471 | 7.643 | 0.006 | 1.601   | 1.147        | 2.235 |
| DBP       | -0.026 | 4.981 | 0.026 | 0.975   | 0.953        | 0.997 |
| Hct       | -3.998 | 4.428 | 0.035 | 0.018   | 0.000        | 0.760 |
| MBP (mm Hg)| -0.021 | 4.106 | 0.043 | 0.979   | 0.960        | 0.999 |

GCS, Glasgow coma scale; OI, oxygenation index; DBP, diastolic blood pressure; MBP, mean blood pressure; Hct, hematocrit.

*Amount of nonpulmonary organ dysfunction.

**Results of Univariate Logistic Regression Analysis**

**Factors influencing ARDS prognosis**
After univariate logistic regression analysis, the variables of diastolic blood pressure, P(A-a)O₂, pH, hematocrit, GCS, OI, the sum of lung field, amount of nonpulmonary organ dysfunction and MBP were used in a logistic regression model to screen for factors influencing the prognosis of ARDS, which included age, pH, GCS, OI and lobes of the lung (Table 3).

**Development of SESARDS**

**Frequency analysis**
The five factors for the derivation data set were treated with frequency analysis for their respective values when the percentiles were set at 25%, 50% and 75%.
The results of frequency analysis were used to establish the grades of each factor, taking into consideration the actual values of all five factors. For the actual age and lobes of the lung, we assigned to 0-25% a score of 0, 25-50% a score of 1, 50-75% a score of 2 and to 75-100% a score of
numbers: from number 1 (as the most important) to number 5 (as the least important). To calculate the weight of each variable, we combined the serial numbers (1 to 5) with the Weight Calculation Sheet and used the following formula:

\[ F = \Sigma [(n+1-i)\cdot fi] \]

where \( n = 5 \), \( i = \) serial number and \( fi = \) the frequency of rank \( i \) (Table 6).

### Establishment of SESARDS

All the weights of the variables together with their grades were revised to establish the final SESARDS (Table 7).

### The probability of death equation

Subsequently, the scores of SESARDS, as an independent
variable, were applied to logistic regression using the possibility of death as a dependent variable, to work out the probability of death equation:

\[
R = \frac{e^{-2.702 + 0.406 \times \text{SESARDS}}}{1 + e^{-2.702 + 0.406 \times \text{SESARDS}}}
\]

Comparisons between SESARDS and APACHE II

The Validity of SESARDS

The ROC curves of SESARDS and APACHE II ROC was used to test the validity of SESARDS. The results showed no significant differences between SESARDS and APACHE II, statistically (Fig. 1).

The sensitivities, specificities and accuracies of SESARDS and APACHE II SESARDS and APACHE II were used on the validation data set for the comparisons of prediction of survival/death and actuality of survival/death (Table 8).

The reliability of SESARDS

Comparisons between SESARDS and APACHE II were made in regards to their reliability by way of Lemshow-Hosmer test.

The relationship between SESARDS score and actual mortality

SESARDS was used to evaluate and score the cases studied from which actual mortalities were calculated. Finally, the SESARDS scores and the actual mortalities were compared, shown to be positively correlated (Table 10, Fig. 2).

Table 7. The SESARDS Severity of Disease Classification System

| Variables      | 0   | 1   | 2   | 3   | 4   | 5   | 6   | 7   |
|----------------|-----|-----|-----|-----|-----|-----|-----|-----|
| Age (yrs)      | ≤34 | 35-44 | 45-58 | ≥59 |
| pH            | ≥7.447 | 7.372-7.446 | 7.281-7.371 | ≤7.280 |
| GCS          | 15  | ≤14  |     |     |     |     |     |     |
| OI (mm Hg)    | ≥149.76 | 120.73-149.76 | 86.20-120.72 | ≤86.19 |
| Lobes of lung | ≤2  | 3    | 4   |     |     |     |     |     |

GCS, Glasgow coma scale; OI, oxygenation index.

Table 8. Comparisons between SESARDS and APACHE II in Sensitivity, Specificity and Accuracy

| Variables | Sensitivity% | Specificity% | Accuracy% | Kappa |
|-----------|--------------|--------------|-----------|-------|
| SESARDS   | 96.43        | 58.33        | 81.52     | 0.585 |
| APACHE II | 67.86        | 91.67        | 77.17     | 0.554 |

SESARDS, simplified evaluation system of acute respiratory distress syndrome; APACHE, acute physiology and chronic health evaluation.

Table 9. The Reliabilities of SESARDS and APACHE II Via Lemshow-Hosmer Test

| Variables | \( \chi^2 \) | \( p \) value |
|-----------|--------------|---------------|
| SESARDS   | 8.543        | 0.382         |
| APACHE II | 13.369       | 0.100         |

SESARDS, simplified evaluation system of acute respiratory distress syndrome; APACHE, acute physiology and chronic health evaluation.

Table 10. The Relationship between SESARDS Score and Actual Mortality

| SESARDS score | Actual mortality (%) |
|---------------|----------------------|
| 0-4           | 6.25                 |
| 5-8           | 50.67                |
| 9-12          | 77.92                |
| 13-16         | 95.45                |
| 17-18         | 100                  |

\( \chi^2 = 78.632 \), \( p = 0.000 \)

SESARDS, simplified evaluation system of acute respiratory distress syndrome.

Fig. 1. ROC curves of SESARDS and APACHE II, ROC, receiver operating characteristics curves; SESARDS, simplified evaluation system of acute respiratory distress syndrome; APACHE, acute physiology and chronic health evaluation.
It is characterized by excellent performance in predicting mortality in ARDS patients over lung injury score, focusing only on the severity of respiratory failure. APACHE II and SAPS II scores have been previously reported to be independent predictors of hospital mortality in ARDS patients. According to Oh, et al., APACHE II score is closely related to mortality in patients in the Intensive Care Unit ($r=0.81$). However, APACHE II is obtained by dividing the aggregate sum by the number of components used, and the 14 components used in this system may make it more difficult for doctors to use it clinically.

After development, we applied SESARDS to the validation data set for evaluation of its reliability and validity in comparison to APACHE II, and found that there were no significant differences in accuracy in predicting ARDS incidence, nor sensitivity or specificity. Importantly, the AUC of the ROC for SESARDS was not different from that of APACHE II statistically. Moreover, it was found that there was no significant difference between the predictive results and the actual results when SESARDS was used on the validation data set, indicating that SESARDS was satisfactory in regards to goodness-of-fit. At last, our study provided evidence that SESARDS score was positively correlated with the actual mortality ratio. Moreover, SESARDS is relatively simpler than APACHE II (5 variables compared to 14).

It should be emphasized that in the first 24 hours SESARDS did not perfectly predict death rates in individual patients. However, our data indicated that misclassification rates became smaller as the probability of death increased (Fig. 1). Nevertheless, the specificity of SESARDS (58.33%) was unsatisfactory, though it is based on a larger number of samples, compared to several other ARDS-specific studies.

In conclusion, SESARDS was shown to be simple, accurate and effective in predicting ARDS progression.

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