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Research Article

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Clinical Value of Serum S100A12 in Identifying ARDS Development and Predicting Deterioration in Critically Ill Patients

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Abstract

Objective: *This study aimed to investigate the clinical value of serum S100A12 in identifying the development of acute respiratory distress syndrome (ARDS), its association with subsequent oxygenation deterioration, and its ability to predict 28-day mortality in patients in the intensive care unit (ICU).*

Methods: *Based on the inclusion and exclusion criteria, the demographic data, chronic diseases, and acute physiological indices of ICU patients were collected from two independent general ICUs in the Department of Critical Care Medicine, Jiangnan University Medical Center. Serum S100A12 levels were measured at different time points using an enzyme-linked immunosorbent assay. TS100A12 was derived from serum S100A12 levels and converted to an inverse tangent function in our study. Patients meeting the Berlin definition of ARDS within three days of admission were categorised into ARDS and non-ARDS groups. The ARDS group was further divided into two groups based on the PF (PaO2/FiO2) value at the time of diagnosis: PF < 150 mmHg and PF > 150 mmHg groups. To verify the correlation between serum S100A12 levels and oxygenation deterioration, three grouping sets based on the decrease rate in the oxygenation index within 4 days after ARDS diagnosis were used for substantial analysis: PF decrease rate < 30% group vs. PF decrease rate ≥ 30% group, PF decrease rate < 35% group vs. PF decrease rate ≥ 35% group, and PF decrease rate < 40% group vs. PF decrease rate ≥ 40% group. Additionally, to verify the correlation between serum S100A12 levels and 28-day mortality in patients with ARDS, the ARDS group was divided into survival and non-survival groups. Spearman's correlation analysis was used to assess the association between indicators, logistic regression analysis was used to determine the odds ratios, and receiver operating characteristic curve analysis was used to evaluate predictive efficacy.*

Results: *A total of 144 patients were enrolled in this study from 1 August 2022 to 15 December 2022. At the time of ARDS diagnosis, serum S100A12 levels were significantly higher than those in patients without ARDS, and TS100A12 was identified as a risk factor for the development of ARDS. At the time of ARDS diagnosis, the serum S100A12 levels were significantly higher in the PF < 150 mmHg group than in the PF > 150 mmHg group. Additionally, after ARDS diagnosis, serum S100A12 levels were significantly higher in the group with a higher rate of PF decrease. The PF decrease rate within 4 days was greater with higher serum S100A12 levels at the time of ARDS diagnosis. Additionally, TS100A12 and age were independent risk factors of 28-day mortality, and the combination of serum S100A12 levels and age exhibited a high degree of predictive accuracy for 28-day mortality in patients with ARDS.*

Conclusion: *TS100A12 is a risk factor of ARDS and 28-day mortality. Serum S100A12 levels were associated with a decline in oxygenation within four days of ARDS diagnosis. Additionally, the combination of serum S100A12 levels and age exhibited high efficacy in predicting 28-day mortality.*

Keywords: Acute Respiratory Syndrome Distress, S100A2, Predicting Deterioration, 28-day Mortality.

Introduction

Acute respiratory distress syndrome (ARDS) which can be caused by intrapulmonary or extrapulmonary insults, is a clinical syndrome characterised by acute hypoxaemia, noncardiogenic pulmonary oedema, and dyspnoea [1-4]. Despite the application of multiple techniques, such as lung-protective ventilation strategies, fluid management, and prone ventilation, there is a lack of specialised pharmacological treatments, and the mortality of patients with ARDS remains high [5]. The LUNG SAFE study reported that the 28-day mortality of patients with ARDS was 35%, and that patients with severe ARDS had a mortality rate exceeding 40% [6]. Early identification of ARDS and subsequent oxygenation deterioration in critically ill patients may create opportunities for more aggressive interventions, leading to a reduction in ARDS mortality.

In 2012, the Berlin definition clarified the diagnostic criteria for ARDS, including the time of onset, changes in chest imaging findings, oxygenation index, and the exclusion of cardiogenic pulmonary oedema. In 2023, 32 experts revised the definition of ARDS and proposed a new global definition. The significance of the early identification of ARDS was highlighted by the inclusion of patients receiving high flow oxygenation in the updated definition of ARDS screening [7]. However, serum markers for the early identification of ARDS, subsequent oxygenation deterioration, and 28-day mortality in critically ill patients are currently lacking.

In our previous analysis of proteomic differences between patients with ARDS and healthy individuals, we observed a significant increase in serum S100A12 protein levels in patients with ARDS compared to healthy controls. S100A12 is a protein belonging to the S100 family; it is primarily found in neutrophils and is expressed in small amounts in monocytes. It can be released into body fluids, such as serum and urine, in response to inflammation and is involved in the development of several diseases [8, 9]. S100A12 can mediate intracellular signalling by binding to advanced glycosylation end products (RAGE) receptors on cell membranes, which initiates the intracellular inflammatory signalling pathway, induces the expression of pro-inflammatory cytokines, and participates in immune and inflammatory regulation [10]. It is important to note that RAGE is expressed at low levels in all cells but at higher levels in lung tissues [11-14], and the effects of S100A12 may be more pronounced in the lungs.

Based on the above information, we aimed to investigate the clinical value of serum S100A12 levels in identifying the development of ARDS in patients in the intensive care unit (ICU), its association with the deterioration of oxygenation, and its clinical value in predicting 28-day mortality.

Materials and Methods

Study Population

From 1 August 2022 to 15 December 2022, 241 critically ill patients were admitted to two independent general ICUs in the Department of Critical Care Medicine, Jiangnan University Medical Center. Patients who met the specified criteria were included in this study (Figure 1). This study was approved by the Ethics Committee of Jiangnan University Medical Center (Wuxi No. 2 People's Hospital; approval number: 2016W-001). Each human participant signed an informed consent statement.

Sample Collection

Five millilitres of peripheral venous blood was collected from the patients at the time of ICU admission and 24 and 72 h after ICU admission. The serum was obtained and then stored at -80°C to detect the S100A12 levels.

Clinical Data Collection

Sex, age, and body mass index (BMI) were recorded upon ICU admission. Medical history was obtained from the Hospital Information System. Temperature, heart rate, respiratory rate, blood pressure, blood gas analysis, neutrophils, platelets, creatinine, and total bilirubin were collected at the time of ICU admission (D0), and on the first (D1), third (D3), fifth (D5), and seventh (D7) day in the ICU. Acute physiology and chronic health evaluation II (APACHE II) scores were calculated and recorded [15]. All patients were followed-up with for 28-days after ICU admission, and the survival status at 28 days was recorded. Data collection was completed by two researchers who were blinded to the serum S100A12 levels.

Grouping Criteria

Patients who met the Berlin definition within three days after ICU admission were categorised into the ARDS group, whereas the remaining patients were included in the non-ARDS group. Using the binary classification method, the ARDS group was further divided into two groups based on the oxygenation index at the time of ARDS diagnosis: the PF < 150 mmHg group and the PF > 150 mmHg group. Considering more important value for investigating oxygenation deterioration in mild-moderate ARDS than severe ARDS, patients with mild-moderate ARDS (PF values range from 100 to 300) were divided into three grouping sets based on the decrease rate in the oxygenation index within 4 days after ARDS diagnosis: PF decrease rate < 30% group vs. PF decrease rate ≥ 30% group, PF decrease rate < 35% group vs. PF decrease rate ≥ 35% group, and PF decrease rate < 40% group vs. PF decrease rate ≥ 40% group. Additionally, to verify the correlation between serum S100A12 levels and 28-day mortality in patients with ARDS, the ARDS group was divided into two groups: survival and non-survival.

Biomarker Measurements

Serum S100A12 levels were measured using an enzyme-linked immunosorbent assay (ELISA) kit (Elabscience Biotechnology Co., Ltd., Wuhan, China). The assay was performed according to the manufacturer's instructions. A standard curve was plotted for each enzyme plate using standard samples. The average optical density values of the two wells were substituted into a standard curve to calculate the concentrations of the samples. This ensured the reliability of the experimental data.

Statistical Analysis

SPSS (version 26.0) was used for the data analysis. The data conforming to a normal distribution are expressed as $\bar{x} \pm s$, and

the independent-samples t-test was used for comparison. Data that did not conform to a normal distribution are expressed as the median and quartiles, and the Mann–Whitney U test was used for analysis. The Chi-square test or Fisher's exact test was used to compare dichotomous variables between groups. Survival curve analysis was used to describe the survival status. Spearman's correlation analysis was used to determine the degree of association between indicators. TS100A12 is an arctangent function-transformed variable in our study and was calculated using the following formula: TS100A12 = 1000 × ArcTan (serum S100A12 levels). Odds ratios (ORs) were determined by logistic regression analysis. Receiver operating characteristic (ROC) curves were used to analyse the predictive validity of the variables. Differences were considered statistically significant at $p < 0.05$. Graphs were generated using R 4.3.2 and GraphPad Prism 8.

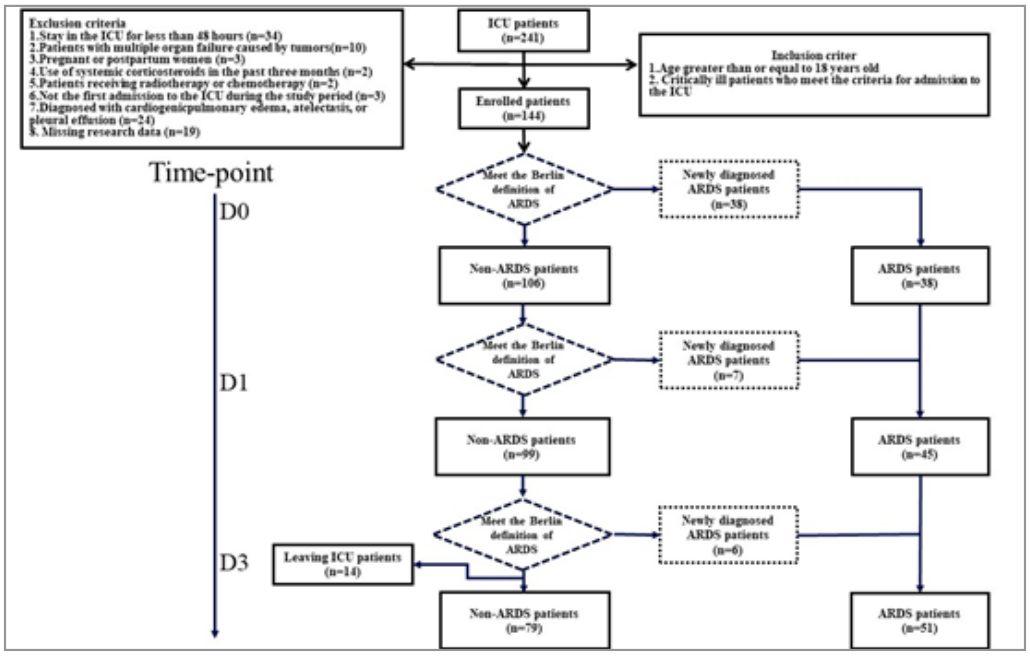

Figure 1: Flow chart of the study population history between the ARDS and non-ARDS groups ($p > 0.05$) (Table 1).

To explore the influence of severity in critically ill patients, the APACHE II scores were compared between patients with and without ARDS, and the results are shown in Table 2. There were no statistically significant differences ($p > 0.05$) in APACHE II scores between patients with and without ARDS at any of the three time points (D0, D1, and D3).

Table 1. Baseline characteristics of patients with and without ARDS

Baseline Characteristics	Patients with ARDS	Patients without ARDS	p-value
Male	38(74.5%)	58(62.4%)	0.139
Age(years)	75 60-82	70 59-80.5	0.215
BMIkg/m²	22.5 20.8-24.4	22.5 20.8-24.5	0.843
Smoke	15(29.4%)	36(38.7%)	0.322
Diabetes	17(33.3%)	25(26.9%)	0.415
Hypertension	32(62.7%)	46(49.5%)	0.126

ARDS, acute respiratory distress syndrome; BMI, body mass index.

Table 2. Comparison of APACHEII scores between patients with and without ARDS

Time-point	Patients with ARDS		Patients without ARDS		p value
	N	APACHE II scores	N	APACHE II scores	
D0	38	19.00 (15.75-23.00)	106	17.00 (14.00-21.00)	0.051
D1	45	19.00 (14.00-23.25)	99	19.00 (12.00-23.00)	0.495
D3	51	16.00 (13.00-22.00)	79	17.00 (12.00-21.00)	0.99

ARDS, acute respiratory distress syndrome; ICU, intensive care unit; APACHEII, Acute Physiology and Chronic Health Evaluation II. D0 refers to the time of ICU admission, while D1 and D3 refer to the first and third day after ICU admission, respectively.

The Serum S100A12 Level was Increased in Patients with ARDS

A comparison of S100A12 levels between patients with and without ARDS at three time points (D0, D1, and D3) revealed significant differences. S100A12 levels were higher in patients with ARDS that in those without ARDS at all three time points (Figure 2)

A. Comparation of the S100A12 level between patients with and without ARDS

Time-point	Patients with ARDS		Patients without ARDS		p value
	N	APACHE II scores	N	APACHE II scores	
D0	38	51.40(41.15-73.64)	106	43.58(33.94-57.81)	0.035
D1	45	53.81(44.66-69.42)	99	40.70(32.57-57.35)	0.001
D3	51	51.11(41.06-69.53)	79	43.66(34.43-58.60)	0.004

Figure 2. Comparison of the S100A12 levels in patients with and without ARDS at different time points. (A) Comparison of the serum S100A12 levels between patients with and without ARDS. (B) The serum levels of S100A12 in 38 patients with ARDS (red box) were higher than those of 106 patients without ARDS (blue box) at the D0 time point. (C) The serum levels of S100A12 in 45 patients with ARDS (red box) were higher than those of 99 patients without ARDS (blue box) at the D1 time point. (D) The serum levels of S100A12 in 51 patients with ARDS (red box) were higher than those of 79 patients without ARDS (blue box) at the D3 time point. ARDS, acute respiratory distress syndrome; ICU, intensive care unit. D0 refers to the time of ICU admission, while D1 and D3 refer to the first and third day after ICU admission, respectively.

TS100A12 is a Risk Factor of the Development of ARDS

In this study, we created a transition variable to amplify the efficiency of identifying

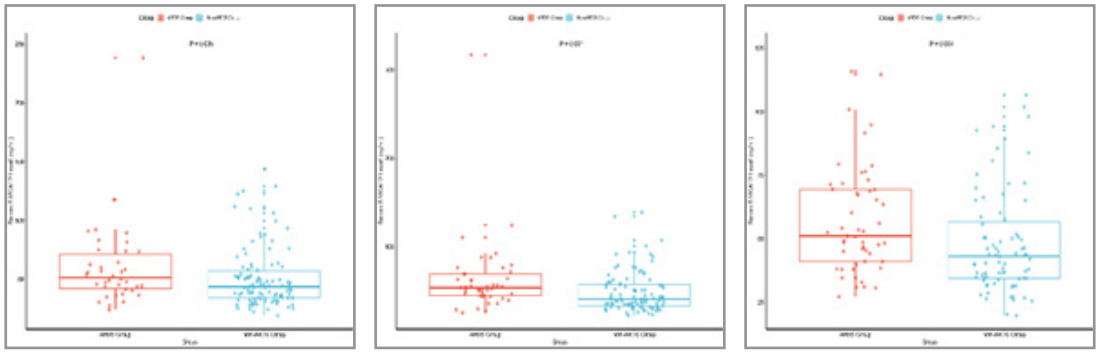

Table 3. Serum S100A12 and TS100A12 level for risk assessment of ARDS development in three time-points after ICU admission

Time-point	S100A12		TS100A12	
	Crude Odds ratio (95% Confidence Interval)	p value	Crude Odds ratio (95% Confidence Interval)	p value
D0	1.011(0.998-1.023)	0.095	1.049 (1.002-1.098)	0.041
D1	1.017(1.002-1.032)	0.027	1.078(1.027-1.131)	0.002
D3	1.021(1.003-1.038)	0.021	1.072(1.021-1.126)	0.005

ARDS, acute respiratory distress syndrome; ICU, intensive care unit. D0 refers to the time of ICU admission, while D1 and D3 refer to the first and third day after ICU admission, respectively. TS100A12 = 1000 × ArcTan (Serum S100A12 levels).

Serum S100A12 Levels were Up-regulated in Patients with ARDS with Poorer Oxygenation

The serum S100A12 level in the PF < 150 mmHg group was significantly higher than that in the PF > 150 mmHg group, indicating that serum S100A12 levels were upregulated in patients with ARDS with poorer oxygenation (Figure 3).

A Comparison of the serum S100A12 level between the PF ≤ 150 mmHg group and PF > 150 mmHg group

Groups	N	Serum S100A12 level (ng/ml)
0<PF≤150	23	56.29(44.22-74.90)
150<PF	28	44.54(35.36-55.27)
p-value	-	0.045

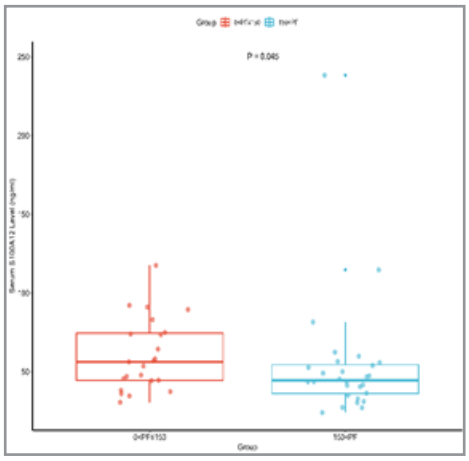

Figure 3: Comparison of serum S100A12 levels between the PF ≤ 150 mmHg group and PF > 150 mmHg group. The serum S100A12 level and PF value were obtained at the time of patient diagnosis. PF = PaO2/FiO2.

Positive Correlation Between Serum S100A12 Levels and Oxygenation Deterioration in Patients with Mild-to-moderate ARDS over Four Days after ARDS Diagnosis

According to the Berlin definition, PF values between 0 and 100 indicate severe ARDS, whereas PF values between 100 and 300 indicate mild-to-moderate ARDS. In this study, 44 patients had mild-to-moderate ARDS, accounting for 86.27% of the total number of patients with ARDS. Figure 4 shows a significant correlation between the serum S100A12 levels and the rate of decrease in PF after ARDS diagnosis ($p < 0.05$). Interestingly, among the different PF decrease rate groups, we did not find any statistically significant differences ($p > 0.05$) in the initial PF values detected at the time of ARDS diagnosis (Table 4). However, comparison of the initial serum S100A12 levels showed a statistically significant difference ($p < 0.05$). In other words, for mild-to-moderate ARDS, the initial PF value cannot be used to assess oxygenation deterioration during the subsequent four days after ARDS diagnosis; however, serum S100A12 levels can be used.

Table 4. Comparison of the serum S100A12 level and PF value between two groups in three different group sets based on the PF value decrease rate

PF value decrease rate	PF value	S100A12 (ng/ml)
<30%(n=32)	169.32(141.0-204.5)	44.40(37.75-53.84)
≥30%(n=12)	216.5(157.5-275.8)	58.17(50.86-77.73)
p-value	0.065	0.033
<35%(n=35)	175.0(141.0-213.5)	44.57(37.75-53.84)
≥35%(n=9)	202.0(159.0-277.5)	59.89(55.70-73.91)
p-value	0.083	0.019
<40%(n=37)	184.0(142.0-220.0)	44.59(37.35-53.97)
≥40%(n=7)	165.0(154.5-262.5)	59.89(56.37-68.16)
p-value	0.312	0.011

The PF values and serum S100A12 levels were measured at the time of ARDS diagnosis. PF = PaO2/FiO2. ARDS, acute respiratory distress syndrome.

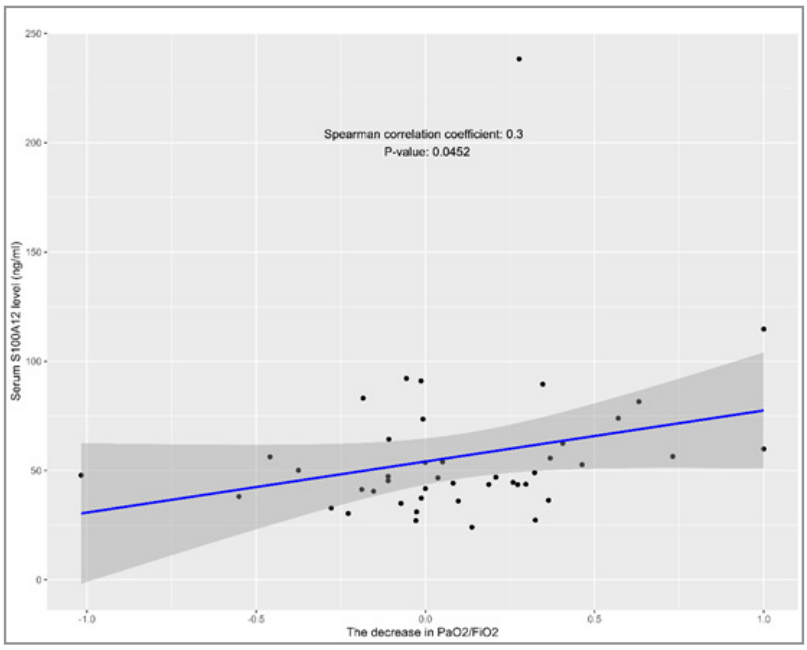

Figure 4. Significant correlation between serum S100A12 levels and the decrease rate in PF value after ARDS diagnosis. PF = PaO2/FiO2. ARDS, acute respiratory distress syndrome.

TS100A12 is an Independent Risk Factor of 28-day Mortality in Patients with ARDS

Table 5 shows that patients in the non-survival group were older than those in the survival group after 28-days of follow-up, and serum S100A12 levels in the non-survival group were higher than those in the survival group. Univariate analysis revealed a statistically significant difference in S100A12 and age between the two groups ($p < 0.05$). Logistic regression analysis revealed that both age and the TS100A12 level were independent risk factors of the 28-day mortality in patients with ARDS (Table 6). Additionally, ROC curve analysis demonstrated that the S100A12 level and age could predict 28-day mortality in patients with ARDS. The figure depicts that the AUC for the S100A12 +Age model was significantly higher than that for the S100A12 or Age model, indicating that the S100A12 +Age model has a better predictive value for predicting 28-day mortality that the S100A12 and Age models. (Figure 5).

Table 5. Comparison of baseline characteristics in patients with ARDS between the survival and non-survival groups

Baseline Characteristics	Non-survival	Survival group	p-value
Male	9(69.2%)	29(76.3%)	0.613
Age(years)	78.92±11.56	68.68±14.74	0.028
BMI (kg/m²)	23.01±2.90	22.82±3.43	0.854
Smoke	5(38.5%)	10(26.3%)	0.487
Diabetes	6(46.2%)	11(28.9%)	0.315
Hypertension	9(69.2%)	23(63.2%)	0.743
PF value	140.0(103.2-234.3)	170.0(139.1-222.6)	0.226
S100A12(ng/ml)	56.29(46.82-86.29)	44.78(36.31-59.22)	0.027

PF and serum S100A12 levels were measured at the time of ARDS diagnosis. BMI, body mass index; ARDS, acute respiratory distress syndrome. PF = PaO2/FiO2.

Table 6. Logistic regression analysis of 28-day mortality in the ARDS group

Index	Crude OR (95% CI)	p value	Index	Corrected OR (95% CI)	p value
Age	1.066(1.004-1.131)	0.037	Age	1.069(1.002-1.140)	0.043
S100A12	0.010(0.992-1.028)	0.283	-	-	-
TS100A12	1.108(1.003-1.224)	0.043	TS100A12	1.118(1.001-1.250)	0.049
S100A12	0.010(0.992-1.028)	0.283	-	-	-

Based on the univariate analysis, age and TS100A12 scores were included in the logistic regression model. These results indicate that both age and the TS100A12 are risk factors for 28-day mortality in patients with ARDS. TS100A12 = 1000 × ArcTan (serum S100A12 level). ARDS, acute respiratory distress syndrome; OR, odds ratio; 95%CI, 95% confidence interval.

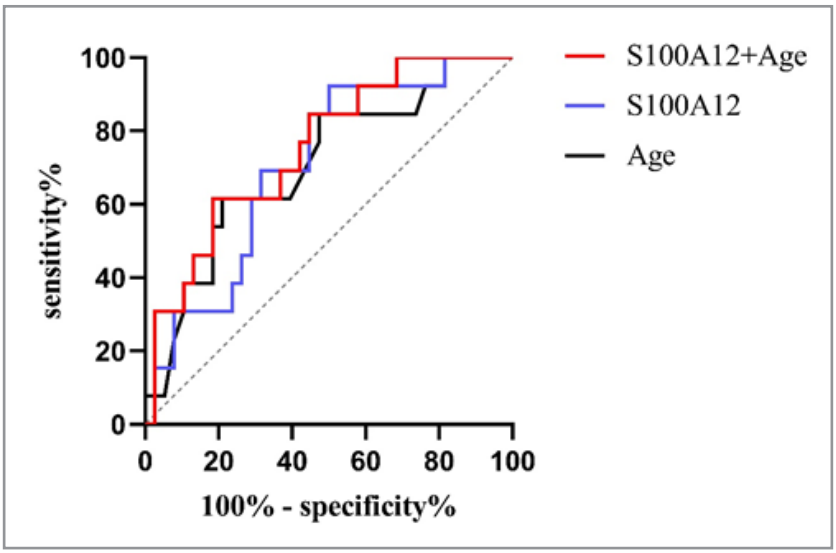

Figure 5. Receiver operating characteristic (ROC) curve analysis of 28-day mortality in patients with acute respiratory distress syndrome. ROC of S100A12 model: Cutoff value: 44.396 ng/ml, sensitivity 92.30%; specificity: 50%, AUC 0.706, p-value 0.027. ROC of Age model: Cutoff value: 78.5 years, sensitivity: 61.5%, specificity: 78.9%, AUC: 0.706, p-value: 0.027. ROC of Age+S100A12 model: Sensitivity: 61.5%, specificity: 81.6%, AUC: 0.753, p-value: 0.007. The AUC for the S100A12+Age model was higher than that for the S100A12 or Age model, indicating that the S100A12+Age model has a better predictive value for 28-day mortality. AUC, area under the ROC curve.

Discussion

Several studies have focused on identifying potential biomarkers to reveal the process of ARDS and prognosis. These are helpful in clinical decision making and treatment optimisation to decrease the mortality rate, especially for the development of ARDS and possible adverse consequences. However, few studies have reported these parameters, especially for early identification of ARDS development, subsequent oxygenation deterioration, and 28-day mortality in ICU patients. This retrospective analysis aimed to assess the clinical application of serum S100A12 in ARDS based on our previous proteomic findings (Supplement 1). Here, we found that TS100A12 was significantly higher in patients with ARDS compared with those without ARDS, and that TS100A12 can be used to identify the risk of ARDS in the early stages after ICU admission. Serum S100A12 levels were upregulated in patients with ARDS with poor oxygenation, and the degree of oxygenation deterioration was positively correlated with serum S100A12 levels in patients with mild-to-moderate ARDS. TS100A12 and age were risk factors of 28-day mortality.

Various insults can induce the release of S100A12 into bodily fluids. S100A12 recognizes and binds to RAGE located on the cell membrane [16-19]. Ligand-receptor binding activates downstream pathways [20]. In a clinical trial involving 14 patients with ARDS, the concentrations of both S100A12 and RAGE in the alveolar lavage fluid significantly increased [21]. Similarly, serum levels of S100A12 and soluble late glycosylation end-product receptors (sRAGE) were significantly elevated in both mouse models and patients with ARDS [22]. Two previous experiments corroborated the discovery of elevated serum S100A12 levels in patients with ARDS, as evidenced in our experiment.

Recent animal studies have demonstrated that S100A12 plays a role in the progression of ARDS by activating the NLRP3 inflammatory pathway by binding to RAGE [23]. Similarly, targeted blockade of the S100A12/NLRP3 axis significantly attenuated lung injury in septic rats [24]. Thus, S100A12 may play a crucial role in the progression of ARDS. Several studies have reported elevated S100A12 levels in inflammatory bowel disease, juvenile rheumatoid arthritis, asthma, leukodystrophy, Kawasaki disease, and adult Still's disease [25-28]. However, few studies have reported its application in the assessment of ARDS development. A previous study measuring serum S100A12 levels in 102 healthy controls and 102 patients with traumatic brain injury (TBI) found that serum S100A12 levels predicted the development of ARDS [29]. In our study, we found that serum S100A12 levels were significantly higher in patients with ARDS compared with those without ARDS, and that TS100A12 can be used to identify patients admitted to the ICU who are at risk of developing ARDS.

Leukocytes are significantly increased in the blood of patients with chronic hypoxic diseases [30]. Animal studies have shown that hypoxia leads to a significant increase in leukocytes in the lung tissues and blood of rats [31]. Similarly, significant neutrophil infiltration was observed in lung tissue samples from patients. Because S100A12 is mainly distributed in neutrophils, S100A12 is associated with respiratory failure in patients with ARDS. In addition, increased leukocyte infiltration depletes the available O2 in tissues, leading to further tissue hypoxia [32]. Neutrophil aggregation in the lung tissue also causes further damage to the lung tissue, leading to further respiratory failure, confirming the experimental conclusion of this study that S100A12 levels are positively correlated with the percentage decrease in oxygenation in patients with ARDS within 4 days.

Both the Berlin definition in 2012 and the new global ARDS definition in 2023 advocate using the PF value to assess ARDS

severity, which is also associated with mortality [33]. A multicentre clinical trial reported that mortality was significantly higher in patients with ARDS with a PF < 150 mmHg than in those with a PF > 150 mmHg at the time of diagnosis [34]. In this study, patients with ARDS with a PF ≤ 150 mmHg had higher serum S100A12 levels those with a PF > 150 mmHg. Moreover, patients with higher serum S100A12 levels experienced a greater decline in oxygenation within 4 days, whereas no significant difference was found in the comparison of PF values at the time of ARDS diagnosis among the three groups. The degree of oxygenation deterioration was positively correlated with serum S100A12 levels in patients with mild-to-moderate ARDS. Furthermore, serum S100A12 levels were significantly higher in the non-survival group than in the survival group in patients with ARDS. The combination of S100A12 and age demonstrated good predictive efficacy in the ROC curve analysis. To the best of our knowledge, this study is the first to describe TS100A12 as an independent risk factor for both ARDS development and 28-days mortality, Daily monitoring of serum TS100A12 levels can provide a better assessment of the risk of ARDS development.

The newly introduced variable, after its conversion through an inverse tangent function, constitutes the mapping relationship with the original variable. Transformation of the arctangent function results in the mapping of the original variable to a specific range of values. This process resulted in data exhibiting a normal distribution and reduced dispersion. Moreover, the newly introduced and transformed variables are positively correlated. Consequently, the variables can be transformed using the inverse tangent function, which fulfils the specific data analysis requirements. To the best of our knowledge, this variable transformation method is not currently employed in ARDS research. This study presents a novel approach to data analysis.

The present study has several limitations. First, to avoid overfitting, only a limited number of clinical variables were included in the logistic regression models. Consequently, potentially relevant variables may not have been evaluated. However, our focus was on study variables that have been previously associated with poor outcomes in ARDS and other critical illnesses. Additionally, the small sample size of patients with ARDS may have limited the identification of prognostic factors in this study. Based on previous animal and clinical studies on the S100A12 protein, we do not believe that the sample size affected our research conclusions. This is because the magnitude of the effect, rather than the sample size, was statistically significant. However, large-scale clinical trials are required to confirm these findings. Owing to the retrospective nature of this study, we could not establish causality between S100A12 protein levels and ARDS. Further studies are required to determine the mechanisms underlying these observations. Given the heterogeneous nature of ARDS, future studies should stratify cohorts according to etiological factors to identify additional confounders. Additionally, the findings cannot be generalised to patients with cardiogenic pulmonary oedema, atelectasis, or pleural effusion because these patients were excluded from the study.

Conclusions

The serum level of TS100A12 can be used to identify ARDS development at an early stage. In our analysis, TS100A12 was identified as a risk factor for ARDS development and mortality within 28 days. The combination of S100A12 and age exhibited high efficacy in predicting the 28-day mortality. Additionally, the changes in oxygenation observed in patients within 4 days post-ARDS diagnosis can be understood based on the levels of S100A12.

Supplementary Information

Acknowledgments

Not applicable.

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Availability of data and Materials

Any data collected during this study can be acquired from the corresponding author upon a reasonable request.

Declarations

Ethics Approval and Consent to Participate

This study adhered to the ethical principles of the 1964 Declaration of Helsinki. The protocol has received approval from the Ethics Committee of Wuxi No. 2 People's Hospital (approval number 2016W-001). Additionally, approvals for the protocol and informed consent documents are obtained from the Institutional Review Board of each participating institution prior to enrolling study participants. Written informed consent is required and obtained from legally authorized representatives at each participating site. Each human participant signed an informed consent statement.

Consent for Publication

Not applicable.

Competing Interests

The authors declare no competing interests

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