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An online nomogram of acute respiratory distress syndrome originating from pulmonary disease

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Abstract

Background: Acute respiratory distress syndrome (ARDS) is a highly heterogeneous disease accompanied by high mortality. Our goal was to investigate the risk factors for 28-day mortality and then establish a predictive online nomogram for ARDS originating from pulmonary disease (ARDSp).

Methods: We examined 1087 patients diagnosed with ARDS from January 2010 to December 2019 at the Second Affiliated Hospital of Chongqing Medical University. A total of 185 ARDSp patients were finally enrolled in the training cohort. A total of 43 ARDSp patients from January 2020 to August 2021 in the Second Affiliated Hospital of Chongqing Medical University and the Traditional Chinese Medical Hospital of Jiangbei District were included in the external validation cohort. Fundamental, clinical and laboratory variables at admission were gathered from medical records, and the 28-day prognosis was followed up.

Results: In the training cohort, it was found that age, sex, C-reactive protein, albumin and multiple organ dysfunction syndrome (MODS) were independent risk factors for 28-day mortality via multivariate logistic regression. The online nomogram software for 28-day mortality showed good discrimination, calibration and clinical utility in both the training cohort and external validation cohort.

Conclusions: For ARDSp patients, older males, lower C-reactive protein and albumin levels, and MODS were independent predictors of a poor 28-day prognosis. The online nomogram based on five independent factors could act as a predictive appliance in clinical practice.

KEYWORDS
ARDSp, mortality, nomogram, risk factors

1 | INTRODUCTION

ARDS is an acute and progressive respiratory failure caused by various noncardiogenic factors. The high fatality rate of 45% made ARDS a serious concern. ARDS is a group of highly heterogeneous clinical syndromes with diverse primary aetiologies, complex pathophysiological mechanisms and varying responses to treatment. The American-European Consensus Conference proposed the concept of ARDS subgroups, which, according to the mechanism of lung damage, divided ARDS into direct lung injury (ARDSp) and indirect lung injury (ARDS originating from extrapulmonary disease, ARDSexp) in 1994.[1] The incidence rate of ARDSp accounted for 50–70%,[2] among which pulmonary infection was the most common primary cause.[3-5] There have been several prognostic models for ARDS.[6,7] However, to our knowledge, there is no reliable prediction model for ARDSp.

As a graphical calculation tool created based on a regression model and an intuitive illustration of complex mathematical formulas, the nomogram has become a popular statistical prediction model.[5] Rapid calculations through a user-friendly digital interface provided higher accuracy and easier understanding of prognosis than traditional methods. It realized individualized prediction based on the value of each factor and is now widely used in the study of disease diagnosis and prognosis evaluation.[8,9] The implementation of an online nomogram greatly promoted ease of use and communication.

Therefore, we aimed to develop and validate an online nomogram for predicting 28-day mortality in ARDSp based on 10 years of demographic, clinical and laboratory variables at admission in the Second Affiliated Hospital of Chongqing Medical University and externally validated the nomogram in two clinical centres in China.

2 | METHODS

2.1 | Study design

Multicentre, retrospective cohort research (Registration number: ChiCTR2100046089) was conducted in the Second Affiliated Hospital of Chongqing Medical University and the Traditional Chinese Medical Hospital of Jiangbei District. The Ethical Committee of the Second Affiliated Hospital of Chongqing Medical University approved the research (No. 2021–619). The ethics committee waived the informed consent requirement. Reporting of this study conformed to broad EQUATOR guidelines.[10]All patients diagnosed with ARDS in accordance with the Berlin Definition were included for further screening.[11] The exclusion criteria were as follows: 1) age <18 years; 2) malignant tumours; 3) immunocompromised patients (with transplantation, immunosuppressant therapy); 4) pregnancy; 5) ARDS originating from extrapulmonary disease (sepsis caused by extrapulmonary factors, nonthoracic trauma, transfusion, pancreatitis, burn injury, etc.); and 6) data deficiency. In the end, for the training cohort, we enrolled 185 ARDSp patients diagnosed from January 2010 to December 2019 in the Second Affiliated Hospital of Chongqing Medical University, and 902 patients were excluded (Figure 1). For the external validation cohort, we recruited 43 ARDSp patients in the Second Affiliated Hospital of Chongqing Medical University ($n = 24$) and the Traditional Chinese Medical Hospital of Jiangbei District ($n = 19$) based on the inclusion and exclusion criteria and diagnosed from January 2020 to August 2021 (Figure 1). The severity of the disease was graded according to the oxygenation index based on the Berlin criteria.[11] All patients were treated in line with the medical guidelines in the two hospitals.

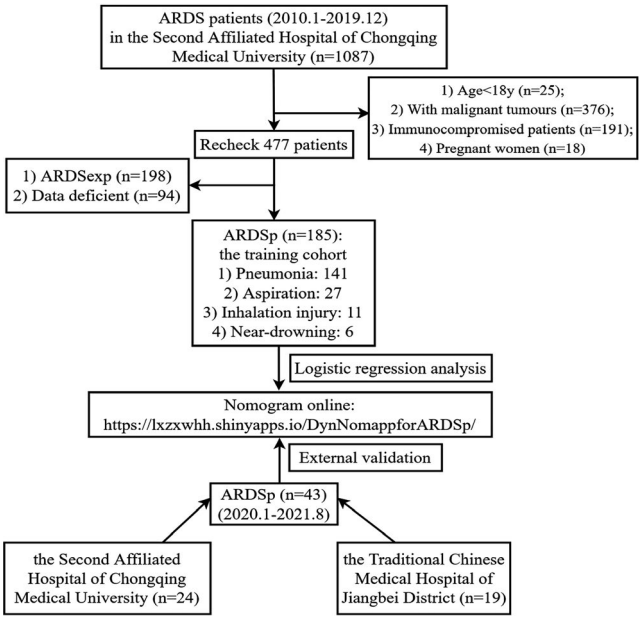


FIGURE 1 Research process diagram

The outcome of our research was mortality at 28 days after admission. Those who were alive 28 days after admission were defined as survivors.

2.2 | Data collection

Those who met the Berlin Definition were diagnosed with ARDS by doctors. We retrospectively searched for patients with an ARDS diagnosis on the first page of their medical records. All clinical and laboratory information and complications were collected from the medical records on the first day of admission. For those who were discharged

within 28 days of admission, our team followed up with the patients' 28-day prognosis by telephone.

2.3 | Statistical analysis

SPSS 26.0 (IBM software) and R 4.1.1 (http://www.R-project.org) were employed for the data analysis and statistical plotting. A two-tailed p value <.05 was defined as statistically significant. After evaluating normality, we presented the continuous variables as the mean ±standard deviation or medians (interquartile ranges). Normally distributed data employed a two-independent sample t test, and inversely, the Mann-Whitney U nonparametric test was executed. The Kruskal-Wallis H test was employed to analyse the differences among continuous variable groups. Frequencies and percentages described the categorical variables. To compare categorical variable differences, the chi-square or Fisher's test was conducted.

To avoid missing important variables, all variables with $p < .2$[12,13] in the univariable logistic regression analysis were screened into multivariable logistic regression analysis. The stepwise method was conducted in the multivariable logistic regression analysis to identify the independent risk factors for a poor 28-day prognosis.

2.4 | Establishment and evaluation of the online nomogram

The nomogram was built according to multivariable logistic regression analysis. The establishment and evaluation of the nomogram proceeded through R 4.1.1. The rms and DynNom packages were employed to establish the nomogram. Tenfold cross-validation was conducted to evaluate the robustness of the nomogram by the caret package. Discrimination was detected via the receiver operating characteristic (ROC) curve by the pROC package. The calibration was evaluated by comparing the predicted and real probability curves via the rms package. Decision curve analysis (DCA) evaluated the clinical utility through the ggDCA package.

3 | RESULTS

3.1 | Basic characteristics of all participants

In the training cohort, 94 survivors and 91 nonsurvivors were enrolled between January 2010 and December 2019. All patients had radiographically pulmonary infiltrations. Pulmonary infection (bacterial, viral, fungal) (141, 76.2%), aspiration of gastric contents (27, 14.6%), toxic inhalation injury (11, 5.9%) and near-drowning (6, 3.2%) were the aetiologies of the 185 ARDSp patients (Additional File 2: Table S1). Table 1 presents the basic information descriptive data, vital signs, laboratory analysis, coexisting conditions and scores at admission. Nonsurvivors were older ($p = .000$) than survivors, and there were more male patients among the nonsurvivors ($p = .041$). There was no significant difference in the onset time, disease severity or vital signs at admission. For laboratory analysis, C-reactive protein (CRP) levels ($p = .002$) and albumin levels ($p = .007$) were associated with significant differences between the two groups. Sequential organ failure assessment (SOFA) scores ($p = .001$) and acute physiology and chronic health evaluation (APACHE) II scores ($p = .006$) revealed differences between survivors and nonsurvivors. Furthermore, nonsurvivors had more complications, especially heart failure ($p = .017$) and MODS ($p = .001$).

For the external validation cohort, 21 survivors and 22 nonsurvivors were admitted to the Second Affiliated Hospital of Chongqing Medical University and the Traditional Chinese Medical Hospital of Jiangbei District from January 2020 to August 2021 (Table 1). Pulmonary infection (bacterial, viral, fungal) (25, 58.1%), aspiration of gastric contents (8, 18.6%), toxic inhalation injury (7, 16.3%), near-drowning (1, 2.3%) and lung contusion (2, 4.7%) were the aetiologies of the 43 ARDSp patients (Additional File 2: Table S1). There were significant differences in age ($p = .027$), neutrophils ($p = .023$), MODS ($p = .000$), SOFA scores ($p = .008$) and APACHE II scores ($p = .006$) between survivors and nonsurvivors. Nevertheless, in general, nonsurvivors had lower CRP and albumin levels and more complications.

3.2 | Univariate and multivariable logistic analyses for 28-day mortality in the training cohort

To determine the risk factors for a poor 28-day prognosis, we performed univariate and multivariable logistic analyses (Additional File 2: Table S2). Given that there was an overlap between vital signs, laboratory analysis and scores, scores were excluded from the multivariable logistic analysis. All the basic information descriptive data, vital signs, laboratory analysis, coexisting conditions and scores at admission were included in the univariable logistic analysis (Table 1). This result indicated that age, sex, CRP, albumin, heart failure and MODS were significantly associated with 28-day mortality ($p < .05$). Then, the primary screening factors ($p < .2$), consisting of age, sex, heart rate, respiratory rate, mean blood pressure, CRP, albumin, heart failure, myocardial infarction and MODS, that may

TABLE 1 Baseline characteristics of ARDSp patients

	Training cohort ($n = 185$)			External validation cohort ($n = 43$)		
	Survivors ($n = 94$, 50.8%)	**Nonsurvivors ($n = 91$, 49.2%)**	***p***	**Survivors ($n = 21$, 48.9%)**	**Nonsurvivors ($n = 22$, 51.2%)**	***p***
Age (year, $\bar{x} \pm s$)	66.88 ± 8.82	75.50 ± 12.18	.000***	56.67 ± 16.96	67.86 ± 14.95	.027*
Female/male (n)	37/57	23/68	.041*	10/11	9/13	.628
Urban/rural (n)	82/12	80/11	.889	18/3	17/5	.698
Onset time (days, $\bar{x} \pm s$)	97.67 ± 18.07	93.16 ± 16.51	.078	15.81 ± 13.82	13.56 ± 19.71	.668
Oxygenation index	173.76 ± 49.01	169.07 ± 63.60	.575	176.44 ± 54.96	179.40 ± 53.44	.859
Mild (n, %)	27 (28.72%)	32 (35.16%)	.09	7 (33.3%)	6 (27.3%)	.943
Moderate (n, %)	60 (63.83%)	45 (49.45%)		12 (57.1%)	13 (59.1%)	
Severe (n, %)	7 (7.45%)	14 (15.38%)		2 (9.5%)	3 (13.6%)	
Vital signs in admission						
Heart rate (bpm, $\bar{x} \pm s$)	102.38 ± 18.62	96.33 ± 18.62	.166	96.24 ± 19.28	105.36 ± 8.04	.116
Respiratory rate (times/min)	23 (20–25.25)	20 (20–25)	.153	22 (20–29)	26 (21.75–30.25)	.212
Mean blood pressure (mmHg)	97.68 ± 18.07	93.16 ± 16.51	.078	90.55 ± 13.23	90.79 ± 19.91	.964
Temperature (°C)	36.8 (36.5–37.83)	36.8 (36.5–37.6)	.592	36.6 (36.4–37.25)	37.15 (36.5–37.85)	.050
Laboratory analysis						
Platelet ($\times 10^9$/L)	162.5 (94–217.5)	175 (101–267)	.412	195 (154–298.5)	171 (97.75–261.5)	.159
Lymphocyte ($\times 10^9$/L, $\bar{x} \pm s$)	0.82 ± 0.40	0.82 ± 0.46	.963	0.84 ± 0.50	1.64 ± 3.67	.325
Neutrophil ($\times 10^9$/L, $\bar{x} \pm s$)	9.88 (6.58–14.58)	10.63 (6.65–15.16)	.487	6.82 (5.27–9.71)	13.87 (6.51–16.66)	.023*
CRP (ng/ml, $\bar{x} \pm s$)	135.42 (65.45–200)	93.37 (28.52–159.32)	.002**	136.12 (113.23–158.39)	96.3 (35.9–156.49)	.084
Procalcitonin (ng/ml)	0.71 (0.21–3.79)	0.50 (0.22–3.3)	.676	0.343 (0.19–0.81)	1.57 (0.16–8.51)	.106
Albumin (g/L)	30.42 ± 5.88	28.16 ± 5.44	.007**	30.09 ± 5.67	29.37 ± 6.39	.701
Blood glucose (mmol/L)	8.05 (6.4–10.25)	8.2 (6.38–10.6)	.869	7.47 (6.05–9.21)	8.9 (7.05–11.6)	.191
Creatinine (μmol/L)	71.75 (55.55–109.55)	85.2 (54.4–126.4)	.311	64.7 (57–78.25)	87.5 (62.5–154.45)	.053
Alanine transaminase (U/L)	21.5 (13–49)	29 (15–51)	.288	27 (16–44)	25.5 (11.75–44.25)	.488
Aspartate transaminase (U/L)	29 (21–65.5)	34 (23–67)	.283	35 (25–58)	37.5 (20–73.25)	.752
Coexisting conditions						
Hypertension (n%)	41.49%	45.05%	.625	38.1%	43.5%	.364
Heart failure (n%)	15.96%	30.77%	.017*	38.1%	31.8%	.755
Myocardial infarction (n%)	2.13%	7.69%	.079	0	1 4.5%	/
Coronary heart disease (n%)	13.83%	14.29%	.929	14.3%	18.2%	1
Chronic obstructive pulmonary disease (n%)	19.15%	19.78%	.914	19.0%	36.4%	.310
MODS (n%)	6.38%	24.18%	.001**	4.8%	54.5%	.000***
Scores						
SOFA, $\bar{x} \pm s$	4.79 ± 1.16	5.25 ± 2.89	.001**	3.33 ± 3.35	7.14 ± 5.27	.008**
APACHEII, $\bar{x} \pm s$	16.25 ± 5.33	18.04 ± 5.30	.006**	13.48 ± 7.60	20.18 ± 7.49	.006**

Note: *$p < .05$, **$p < .01$, ***$p < .001$.

lead to the death of ARDS patients were included in multiple logistic regression analysis. The results showed that elderly (OR 1.050, 95% CI 1.025–1.077), male (OR 2.124, 95% CI 1.009–4.470) and MODS (OR 6.365, 95% CI 2.097–19.319) were independent risk factors for 28-day mortality, while higher CRP (OR 0.990, 95% CI 0.985–0.995) and

higher albumin (OR 0.907, 95% CI 0.850–0.969) were independent protective factors. Heart rate, respiratory rate, mean blood pressure, heart failure and myocardial infarction were refused in the multivariable logistic analysis (Additional File 2: Table S2).

3.3 | Establishment of the online nomogram software

The final 28-day mortality prediction model was established by multivariable analysis and incorporated five independent risk factors: age (y), sex (female: 0; male: 1), CRP (ng/ml), albumin (g/L), and MODS (without MODS: 0; with MODS: 1) (Figure 2). The instructions of the nomogram are reported in detail in the legend of Figure S2 in Additional File 2. Given that the calculation of the nomogram was time-consuming, it was designed for the online predictive nomogram which is available online at https://lxzxwhh.shinyapps.io/DynNomapp-Online/.

The online dynamic nomogram was capable of predicting the prognosis of ARDSp patients under various conditions by conveniently inputting five variables. Figure 3 shows that a 66-year-old man with a CRP level of 113 ng/ml, an albumin level of 29 g/L, and MODS predicted a 28-day mortality rate of 85.6% (95% CI 0.675–0.944).

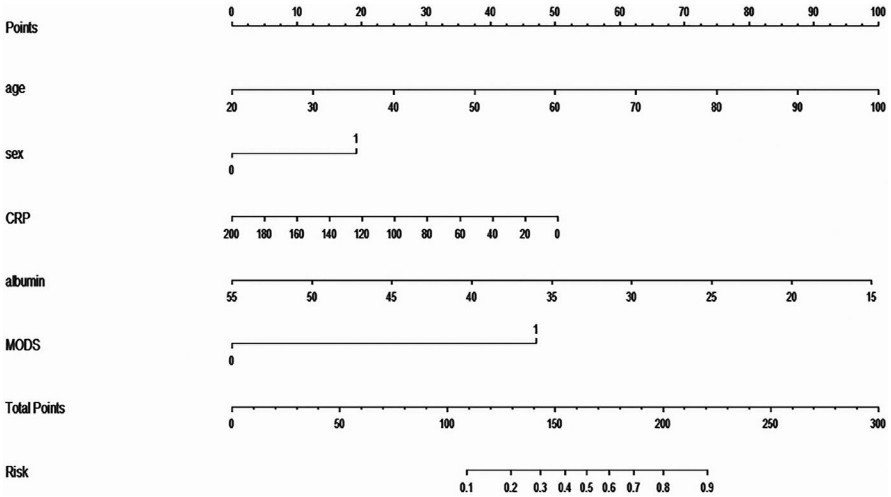


FIGURE 2 The nomogram for predicting ARDSp patients' 28-day mortality based on age, sex, CRP and albumin levels, and MODS. Age: years; sex: 0: female, 1: male; CRP: ng/ml; albumin: g/L; MODS: 0: without MODS, 1: with MODS

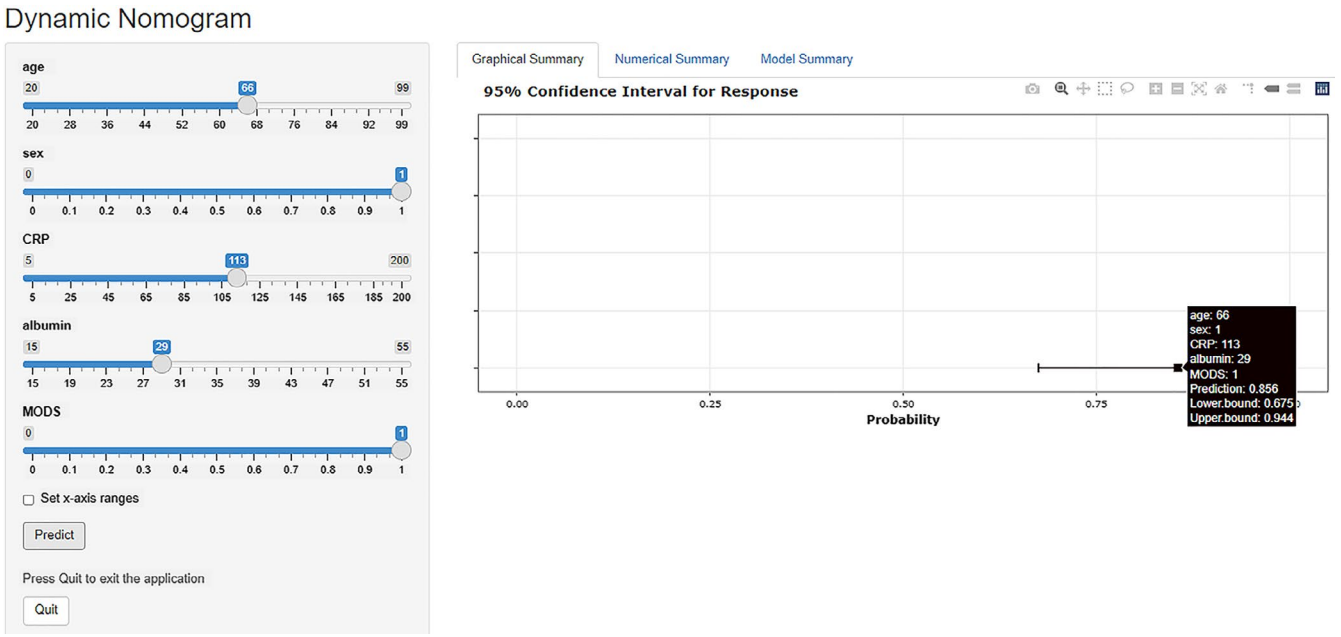


FIGURE 3 Example of the online nomogram. A 66-year-old man with CRP 113 ng/ml, albumin 29 g/L, and MODS had a predicted 28-day mortality rate of 85.6% (95% CI 0.675–0.944)

3.4 | Evaluations of the nomogram performance

The evaluations were conducted on four aspects: validation, discrimination, calibration and clinical usefulness. The nomogram was validated using tenfold cross-validation, and the average area under the curve (AUC) was 0.7804 (Additional File 2: Table S3 and Additional File 1: Figure S1). In the training cohort, nomogram receiver operating characteristic (ROC) curve analysis indicated an AUC of 0.795 (95% CI 0.729–0.850), which was significantly different for age ($p = .0044$), sex ($p < .0001$), CRP ($p < .0001$), albumin ($p < .0001$) and MODS ($p < .0001$) alone using DeLong's test (Figure 4A and Additional File 2: Table S4). In the external validation cohort, the AUC was 0.877 (95% CI, 0.740–0.957). Additionally, significant differences were observed with age ($p = .0492$), sex ($p < .0001$), CRP ($p = .0073$), albumin ($p = .0019$) and MODS ($p = .0065$) alone (Figure 4B and Additional File 2: Table S5). This indicated that the nomogram was efficient in distinguishing between survivors and nonsurvivors. The predicted mortality curves were close to the observed mortality curves in the training cohort and the external validation cohort, with the mean errors of 0.025 and 0.039, respectively (Figure 5). The decision curve analysis showed that clinical decisions could benefit by applying this online nomogram with the extent of the threshold, both in the training cohort (>0.3) and in the external validation cohort (>0.38) (Figure 6).

4 | DISCUSSION

In this study, we found that more nonsurvivors were male, older and had MODS than survivors, which has been validated in various studies.[14,15] The multivariable logistic analysis also suggested that lower albumin and CRP were independent risk factors for a 28-day poor prognosis of ARDSp based on the 10 years of clinical data, especially CRP, which seemed to be a paradox.

Then, we established a convenient and easy online 28-day mortality prediction nomogram for ARDSp after logistic regression. External validation was performed in two centres in China. The nomogram was evaluated by tenfold cross-validation, ROC analysis, calibration curves and DCA.

Given the heterogeneity of ARDSp and ARDSexp, and the few large cohort studies of ARDSp to date, we focused on ARDSp to improve the reliability of the nomogram and fill a vacancy. In 1993, Gattinoni, L et al. first discovered that ARDS caused by pneumonia and abdominal disease had evident differences in pathological changes and the efficacy of positive end-expiratory pressure therapy.[16] A retrospective study of 417 patients compared ARDSp and ARDSexp, the lung injury score was higher and the oxygenation index was lower, suggesting that intrapulmonary injury in ARDSp was more severe.[17] In ARDSp, the extent of alveolar collapse and fibrinous exudation in the alveolar space were more prominent, and interstitial oedema was less prominent. The epithelial cells were mainly

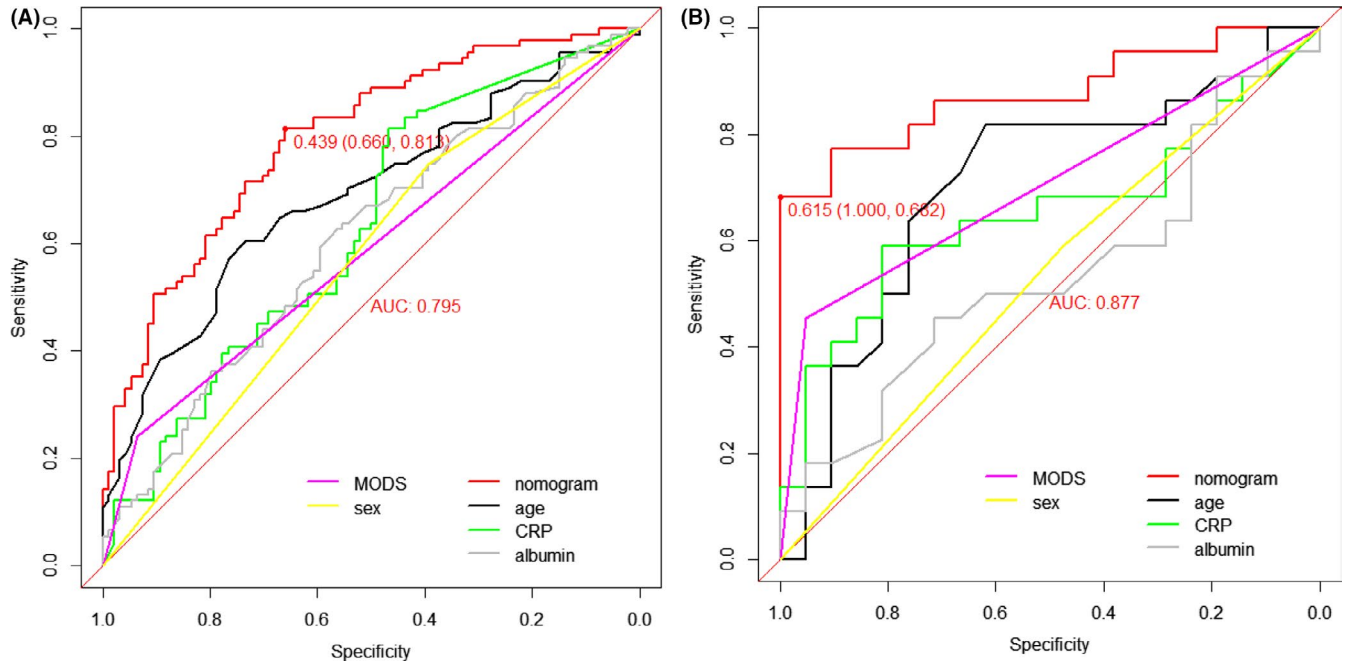


FIGURE 4 ROC curves to predict 28-day mortality in ARDSp patients. A, ROC curve for the training cohort. B ROC curve for the external validation cohort

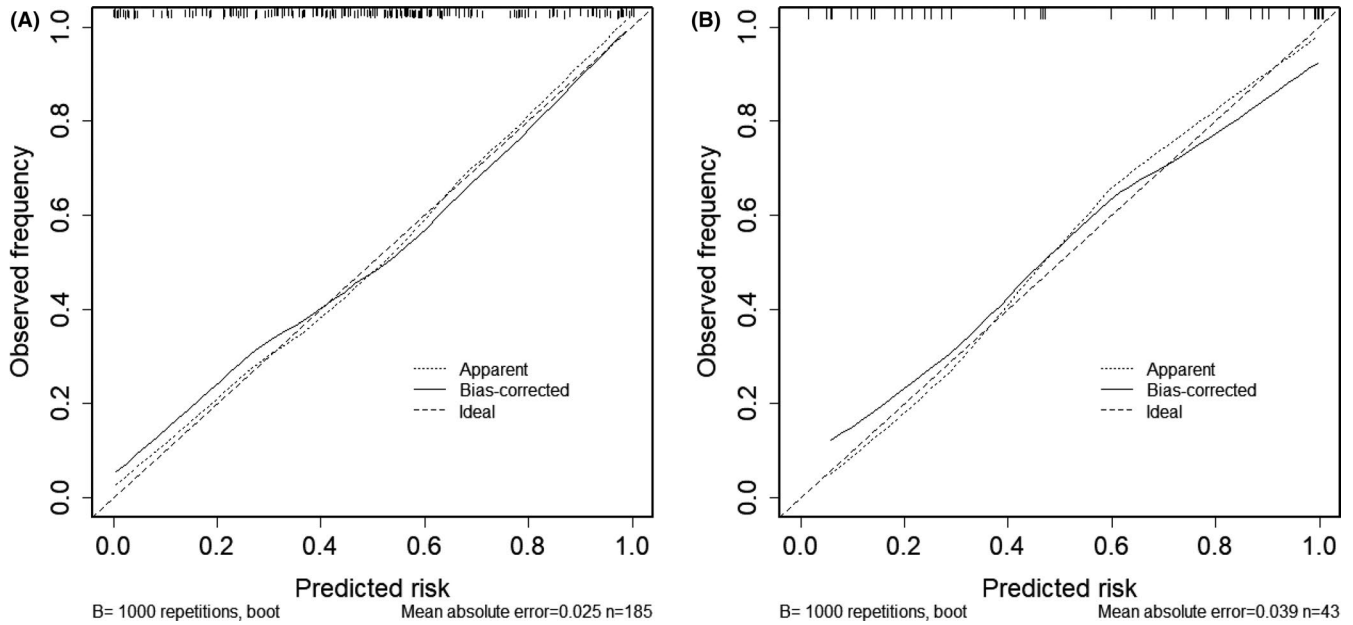
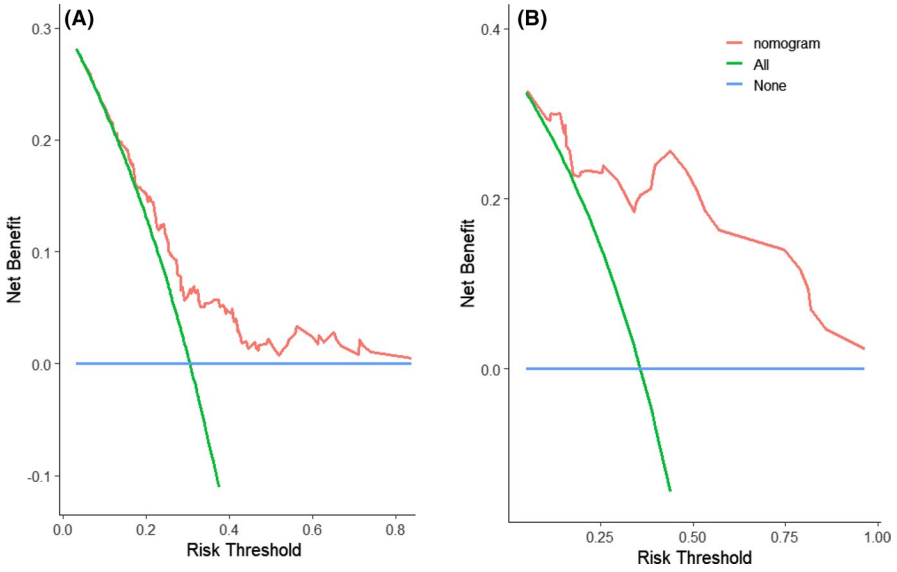


FIGURE 5 Calibration plots of the nomogram. A, The calibration plot for the training cohort; B, the calibration plot for the external validation cohort

FIGURE 6 DCA of the nomogram. A, DCA for the training cohort; B, DCA for the external validation cohort



damaged, and the zona pellucida was thick and inhomogeneous. In ARDSexp, alveolar cavities were slightly affected, and interstitial oedema and alveolar hyperaemia were much more significant.[18-20] Vascular endothelial cell injuries were more prominent, and the zona pellucida was thin and relatively homogeneous.[21] This simple and practical classification had high consistency in the occurrence of diseases, mainly depending on the medical history. Therefore, our model was strictly confined to ARDSp, which limited the sample size to some extent but reduced bias originating from disease heterogeneity.

CRP is a traditional inflammation marker, while in our training cohort, CRP was significantly higher in survivors (135.42 (65.45–200) ng/ml) than in nonsurvivors (93.37 (28.52–159.32) ng/ml), which was one of the independent protective factors for ARDSp. The discrepancies with the conventional clinical concepts were arresting. CRP is an acute-phase protein compounded in the liver. There was a microconcentration in the blood under normal conditions, whereas it increased notably when the body suffered infection, trauma, tumours, surgery and cardiovascular events.[22] Still unclear was its function in ARDS. Sandra H Hoeboer et al. investigated 101 intensive care units and found that CRP levels were positively related to ARDS severity[23]; inversely, another cohort study consisting of 177 ARDS patients indicated that lower CRP levels

were associated with organ failure, requiring for aggressive mechanical ventilation, and poor prognosis.[24] A third view suggested that CRP could not be used as a predictor of ARDS severity or mortality.[25] Unfortunately, to date, there has been no large cohort study focusing on the role of CRP in ARDSp.

In terms of mechanism, CRP inhibited the function of neutrophils in a variety of ways. One proposed mechanism was that the mediation of CRP could inhibit the activity of p38 mitogen-related protein kinase and reduce the chemotactic response of neutrophil signal transduction proteins involved in stimulation.[26] Zhong, W. et al. suggested that CRP might interact with phosphatidylinositol-3 kinase activity,[27] and Dobrinich R. and his colleagues pointed out that CRP played a role in suppressing the respiratory burst of neutrophils.[28] In animal experiments, scientists pointed out that manually stimulating the increase in serum CRP decreased the chemotaxis of neutrophils and improved the consequent alveolar inflammation.[29] They further found that in a rabbit lung injury model overexpressing CRP, the influx of neutrophils and the exudation of alveolar proteins were reduced.[30] Similar experimental phenomena have also been verified in mice.[31] CRP might eliminate the increase in vascular permeability on account of the influence of neutrophil stimulation in rabbit lungs.[32] Therefore, CRP had a protective effect on lung injury in basic experiments and animal experiments. Given that lung injuries were more severe in ARDSp than in ARDSexp, these experimental data appeared to explain our paradox of CRP in ARDSp.

Although hypoproteinaemia has been found in many studies as one of the prognostic factors of ARDS, clinicians tend to pay more attention to conventional inflammatory markers such as leukocytes, neutrophils and procalcitonin, while relatively ignoring albumin in patients. Our research determined that hypoproteinaemia was an independent risk factor for 28-day mortality in ARDSp. Plasma colloid osmotic pressure formed by albumin was the main factor preventing capillary extravasation.[33] Additionally, albumin alleviated the increased vascular permeability due to the inflammatory response by improving capillary endothelial function. In addition, albumin could be regarded as a surrogate marker of the degree of inflammation. Many inflammatory mediators produced during sepsis and ARDS were able to inhibit the production of liver albumin and accelerate protein catabolism.[34] Thus, nutritional evaluations and support were important in ARDSp.

To our knowledge, this was the first large cohort study especially focusing on ARDSp and the first online predictive nomogram for ARDSp. The five independent predictors obtained by regression analysis were utilized to form the predictive model and transformed to a nomogram scoring system. To facilitate clinical use and improve communications, online webpage software was designed. We validated the online nomogram by tenfold cross-validation and evaluated it internally and externally, making our model more reliable. Notably, the nomogram showed excellent discrimination and clinical usefulness, both internally and externally. Perhaps due to the limited number of external cohorts, the calibration was better in the internal group than in the external group. However, in general, the bias was acceptable in both the internal and external validations. Compared with age, sex, CRP, albumin and MODS, the online nomogram was more practical, reliable and accurate. Once data on the five aspects of the patient were available, the model could be applied to estimate the patient's 28-day mortality to aid clinical decision-making. Considering the different medical conditions in different provinces and countries, the online nomogram may need to be further updated when applied to other places.

The research included 185 ARDSp patients from the original 1087 ARDS patients. Regarding the reason why a large number of patients were excluded, on the one hand, as the Second Affiliated Hospital of Chongqing Medical University was a tertiary hospital, most patients with serious and complex conditions, such as malignant tumour patients, patients after organ transplantation and patients receiving immunosuppressive therapy, were often transferred. There were 567 patients who were immunocompromised or had cancers among the 1087 patients. On the other hand, it was reported that ARDSp accounted for approximately 50–70% of ARDS,[2] and the sample size was inevitably reduced after the research scope was limited.

There were 185 patients in the training cohort and 43 patients in the external validation cohort. It seemed that the number of enrolled subjects was not adequate. However, it was of great importance for a robust model to overcome confounding bias, especially for the highly heterogeneous disease ARDS. The primary aetiology of ARDS is diverse, and the pathophysiological mechanism is complex; moreover, the response to treatment varies greatly among patients. The high heterogeneity was one of the principal reasons for the inconsistent results of many clinical trials[7]; hence, there was an urgent need for precision medicine.[35] The nomogram focused on ARDSp, with robust validations both internally and externally; thus, the strict inclusion criteria might largely reduce the defects caused by the insufficient sample size to some extent.

This study has some limitations. First, compared with other ARDS research, we confessed that the number of enrolled participants was relatively small. We selected 43 patients from two hospitals, both located in Chongqing, in southwest China. Second, this was a retrospective study, and 10 years of data were employed to establish the

prediction nomogram. Due to the development of medical science, there might be a difference between the diagnosis and treatment level 10 years ago and the current level, which might constitute the deviation. Our team will enlarge the research and update the nomogram to compensate for the deficiencies in this study in the future.

5 | CONCLUSIONS

Our research demonstrated that sex, age, CRP, albumin and MODS were independent risk factors for 28-day mortality in ARDSp. The nomogram performed well in discrimination, calibration and clinical usefulness in the internal cohort and external validation cohort. Online software was available to provide clinicians with convenient access to evaluating 28-day mortality.

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CONFLICTS OF INTERESTS

The authors have no conflicts of interest with the contents of the article.

AUTHOR CONTRIBUTIONS

Conception and design: HW, YZ and DW; Data acquisition: HW, WT, QH, HH and JD; Data analysis: HW and RT; Drafting and critically revising manuscript: all authors; Final approval for publication: all authors.

DATA AVAILABILITY STATEMENT

The data underlying this article could be acquired from the corresponding author upon reasonable requests.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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