Original Article



# A combination of the APACHE II score, neutrophil/lymphocyte ratio, and expired tidal volume could predict non-invasive ventilation failure in pneumonia-induced mild to moderate acute respiratory distress syndrome patients

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**Background:** Noninvasive ventilation (NIV) failure rate is relatively high in patients with acute respiratory distress syndrome (ARDS). Currently the data regarding prediction of NIV failure of pneumonia-induced mild to ARDS patients were scarce.

**Methods:** A total of 364 patients (from January 2016 to December 2020) diagnosed with hypoxemic respiratory failure and managed with NIV were initially included and finally 131 pneumonia-induced mild to moderate ARDS patients were enrolled in this study. Electronic medical records were reviewed to determine whether NIV succeeded or failed for each patient. The relationship between the Acute Physiology And Chronic Health Evaluation II (APACHE II) score , neutrophil/lymphocyte ratio (NLR), expired tidal volume (Vte) and NIV failure were specifically analyzed. Multivariate logistic regression analyses were conducted to identify the independent factors of NIV failure. Receiver-operating characteristic curves were used to assess the efficacy of the variables in predicting NIV failure. Kaplan-Meier curves for 28-day survival were used to compare the mortality rates of different groups.

**Results:** Of the patients, 64 (48.9%) experienced NIV failure, APACHE II score [odds ratio (OR) =0.77; P=0.002], NLR (OR =0.838; P=0.046), and Vte (OR =0.343; P=0.009) were independent factors for predicting NIV failure. A combined value comprising the APACHE II score, NLR, and Vte had better efficacy at predicting NIV failure [area under the curve (AUC) =0.9; 95% confidence interval (CI): 0.845–0.955] than the APACHE II score (AUC =0.818; 95% CI: 0.745–0.891), NLR (AUC =0.839; 95% CI: 0.765–0.913), or Vte (AUC =0.805; 95% CI: 0.729–0.881) alone. The cumulative survival probability within 28 days was lower in patients with a combined value >59.17 (P<0.001 by the log-rank test), an APACHE II score >16.5 (P<0.001 by the log-rank test), an NLR >7.22 (P<0.001 by the log-rank test), and a Vte >8.96 mL/kg (P<0.001 by log-rank test).

**Conclusions:** A combined value comprising an APACHE II score >16.5, a NLR >7.22, and a Vte >8.96 mL/kg may be a useful surrogate for predicting NIV failure among pneumonia-induced ARDS patients, and patients with a combined value >59.17 should be cautiously monitored during NIV. A further study with a larger sample size is warranted.

**Keywords:** Neutrophil/lymphocyte ratio (NLR); expired tidal volume (Vte); acute respiratory distress syndrome (ARDS); predictor

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## Introduction

The use of non-invasive ventilation (NIV) is dramatically increased in patients with acute respiratory failure (1), as it significantly reduces the work of breathing, thereby reducing the need for intubation (2,3). Compared to NIV, intubation via invasive mechanical ventilation is associated with many complications, such as diaphragmatic weakness and ventilator-associated pneumonia (4,5). However, the NIV failure rate is around 50% in patients with hypoxemic respiratory failure (6,7), and patients who experience NIV failure are more likely to die in hospital than those who are NIV success (8,9). Thus, the accuracy of early methods for identifying acute respiratory distress syndrome (ARDS) patients who may not benefit from NIV needs to be improved.

Despite improvements in treatments, such as the use of low tidal volume ventilation, ARDS is still associated with high mortality (10). A number of studies have attempted to identify the possible factors of NIV failure, but with conflicting results (7,11,12). One reason for the conflicting results reported in the studies is that the different underlying etiologies of ARDS may have variable clinical phenotypes, and different risk and prognostic factors (13,14). There is significant heterogeneity between pulmonary and extrapulmonary ARDS in terms of the pathology, inflammation response, and respiratory mechanics (15,16). Previous studies utilized inflammatory biomarkers, which were not collected bedside routinely, to stratify ARDS patients and predict the prognosis (17,18) with high cost and inconvenience. There is an urgent need to develop clinical accessible variables to predict NIV failure.

Pulmonary infections account for the vast majority of ARDS risk factors (19). We performed this study to examine variables that could be easily measured at the bedside to predict NIV failure among pneumonia-induced mild to moderate ARDS patients. We present the following article in accordance with the STARD reporting checklist (available at https://atm.amegroups.com/article/view/10.21037/atm-22-536/rc).

## Methods

### *Subjects and study design*

This single-center retrospective observational study, which comprised 131 pneumonia-induced ARDS patients, was conducted at the Department of Respiratory and Critical Care Medicine, Beijing Chao-Yang Hospital, West Campus, from January 2016 to December 2020. This study was approved by the Institutional Review Board of the Beijing Chao-Yang Hospital (No. 2016-KE-95). Since the current study did not impose any diagnostic and therapeutic influence on patients, the Institutional Review Board of Beijing Chao-Yang Hospital approved the study with a waiver of informed consent. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

The patient selection process is shown in *Figure 1*. The Berlin definition of ARDS (20) was adopted to evaluate the patients, and 234 patients were diagnosed with ARDS (mild to moderate). A total of 103 patients were excluded from the study, as the underlying cause of ARDS was not pneumonia, and 8 patients were excluded from the study, as they were NIV intolerant.

NIV failure was defined as a failure to maintain an arterial oxygen tension ($PaO_2$)/fraction of inspired oxygen ($FiO_2$) of <100 mmHg, a respiratory rate >40 breaths/min, inability to protect the airway (due to coma or seizure disorders), inability to clear the viscous secretions, inability to correct dyspnea, lack of improvement of signs of a high respiratory muscle workload, respiratory or cardiac arrest, or hemodynamic instability without any response to fluids or vasoactive agents (21).

The bi-level or CPAP (continuous positive airway pressure) mode was applied to patients. The airway pressure and other ventilator parameters were set according to clinical practice and patients' tolerance, and these parameters were adjusted according to arterial blood gas. An oronasal mask was used on all patients. Supplemental oxygen flow was adjusted to maintain an oxygen saturation >90%.

The primary outcome of the current study was NIV failure, and the secondary outcome was 28-day survival.

### *Measurements*

Patients' baseline characteristics were recorded, including age, gender, length of stay in hospital, Acute Physiology And Chronic Health Evaluation II (APACHE II) score, the use of glucocorticoid before admission, and comorbidities (including kidney failure, respiratory diseases, malignancy, heart failure, liver function impairments, gastrointestinal bleeding, diabetes, and hypertension). Patients' vital signs (including heart rate, temperature, respiratory rate, systolic pressure) were recorded. Arterial blood gas and peripheral venous blood were obtained at the time of admission. Data on treatment and the NIV condition used were obtained by reviewing the medical charts.

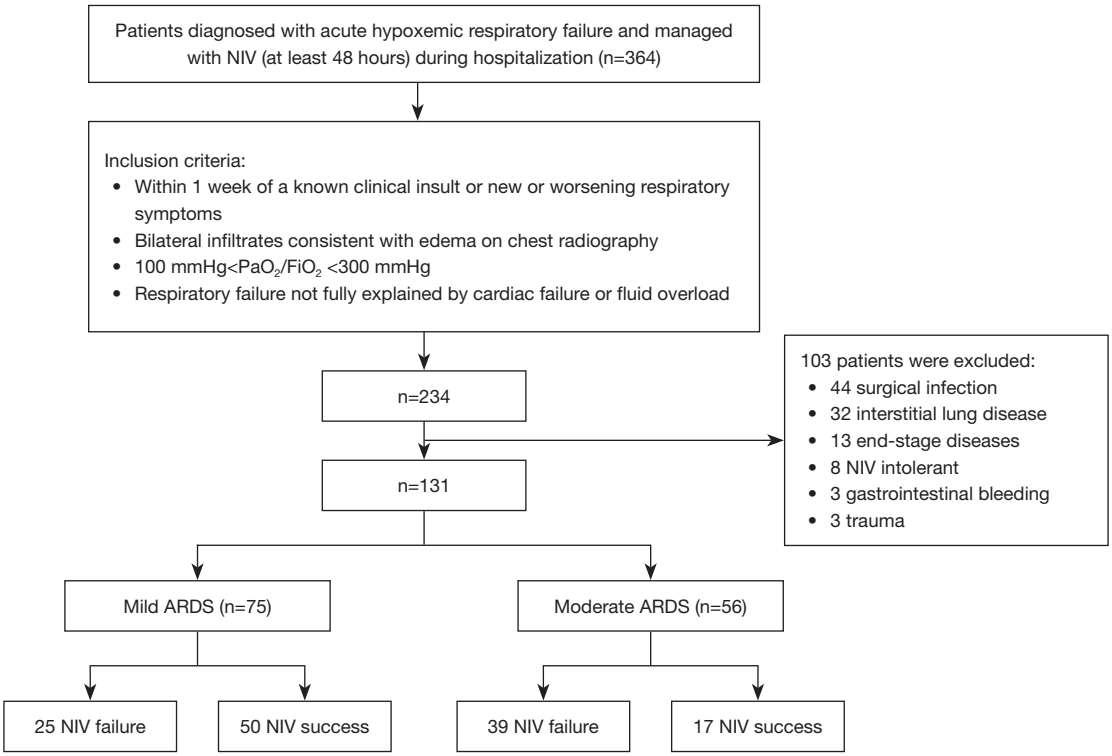


**Figure 1** Patient selection chart. NIV, non-invasive ventilation. ARDS, acute respiratory distress syndrome.

### *Statistical analyses*

To compare the continuous variables, the Kolmogorov-Smirnov test was used to test the normality of the data, and Levene's test was applied to assess the homogeneity of variance. The continuous data are expressed as the median with the interquartile range, or the mean ± standard deviation as appropriate and the categorical data are expressed as a number with a percentage. The normally distributed continuous variables were analyzed using the unpaired Student's *t*-test (including APACHE II, Vte, pH, $PaO_2/FiO_2$). The non-normally distributed continuous variables were analyzed using the Mann-Whitney *U*-test (including age, gender, LOS, heartbeat, systolic pressure, temperature, respiratory rate, $PaCO_2$, $HCO_3^-$, leukocyte count, neutrophil count, lymphocyte count, NLR, CRP, PCT, BUN, Cr, albumin, BNP). The categorical variables were analyzed using the Chi-squared test. Multivariate logistic regression analyses (including gender, APACHE II, heartbeat, respiratory rate, $PaO_2/FiO_2$, $PaCO_2$, Vte, leukocyte count NLR, CRP, albumin, kidney failure) with a conditional forward stepwise regression model were conducted to determine whether any of the factors were independently associated with NIV failure. An equation was developed based on the results of the multivariate logistic regression analyses, and the combination value of each patient was calculated according to the equation. Receiver-operating characteristic (ROC) curves were constructed to evaluate the ability of markers to predict NIV failure. For each ROC curve, the optimal cutoff values, sensitivity, specificity, positive predictive value, negative predictive value, diagnostic accuracy, Youden's index, area under the curve (AUC), and 95% confidence interval (CI) were calculated. Kaplan-Meier 28-day survival curves were constructed, and log-rank tests were used to compare the curves. Differences were considered statistically significant at $P<0.05$ (two-sided). The SPSS software package (version 21.0) was used for all the statistical analysis.

## Results

### *Baseline characteristics and laboratory data at admission between NIV failure and NIV success*

As *Figure 1* shows, NIV failure occurred in 33.3% of the mild and 69.9% of the moderate ARDS patients. As a whole, the rate of NIV failure was 48.9% in this study. The proportion of males was higher (76.6%) in the NIV

failure group than the NIV success group (52.2%) (see *Table 1*). Additionally, the NIV failure subjects had a higher APACHE II score (P<0.001), respiratory rate (P=0.007), and expired tidal volume (Vte) (P<0.001) than the NIV success subjects. Subjects in the NIV failure group presented with worse laboratory data than those in the NIV success group (see *Table 1*). More specifically, they had lower $PaO_2/FiO_2$, arterial carbon dioxide tension ($PaCO_2$), and albumin levels, and a higher leukocyte, neutrophil/lymphocyte ratio (NLR) and C-reactive protein (CRP) values than the NIV success group. Additionally, kidney failure (P=0.005) was more commonly observed among patients in the NIV failure group than the NIV success group.

### *Risk factors of NIV failure*

According to the multivariate logistic regression analyses (see *Table 2*), the APACHE II score [odds ratio (OR) =0.77; 95% CI: 0.654–0.907; P=0.002], Vte (OR =0.343; 95% CI: 0.153–0.768; P=0.009), and NLR (OR =0.838; 95% CI: 0.704–0.997; P=0.046) were independent factors for predicting NIV failure. The multivariate logistic regression analyses were conducted with a number of covariates, including gender, heart beats, respiratory rates, $PaO_2/FiO_2$, $PaCO_2$, leukocyte counts, CRP levels, albumin levels, and kidney failure.

The following logistic regression equation was developed based on the β-coefficient of the APACHE II core, Vte, and NLR:

$$\begin{aligned} L &= APACHE + \frac{1.069}{0.261} * Vte + \frac{0.177}{0.261} * NLR \\ &= APACHE + 4.096 * Vte + 0.678 * NLR \end{aligned} \quad [1]$$

where L is the combination value of the APACHE II score, Vte, and NLR.

### *Ability of the APACHE II score, Vte, NLR, and the combination value to predict NIV failure*

The ROC curves are displayed in *Figure 2*. As *Table 3* shows, the AUC of the combination value (0.9; 95% CI: 0.845–0.955) was higher than that of the APACHE II (0.818), NLR (0.839), or Vte (0.805) alone. The combination value had the highest sensitivity (0.922), specificity (0.806), positive predictive value (0.819), negative predictive value (0.915), and diagnostic accuracy (0.863) among all the markers. The cutoff value for predicting NIV failure was a combination value >59.17, an APACHE II score >16.5, a NLR >7.22, and a Vte >8.96 mL/kg.

### *Patients' 28-day survival*

As *Figure 3* shows, the cumulative survival probability within 28 days was lower in patients with an APACHEII score >16.5 (P<0.001 by the log-rank test), a NLR >7.22 (P<0.001 by the log-rank test), a Vte >8.96 mL/kg (P<0.001 by log-rank test), and a combination value >59.17 (P<0.001 by the log-rank test).

## Discussion

In the current study, we developed a novel equation for predicting NIV failure in pneumonia-induced mild to moderate ARDS patients. This equation takes into account the APACHE II score, NLR and Vte, which can be easily obtained at patients' bedsides by conducting assessments and laboratory tests. Thus, this equation may be a concise and convenient tool for evaluating patients and predicting NIV failure.

Initially, the use of NIV in patients with ARDS focused on immunocompromised patients, such as those with hematologic malignancies (22,23). However, mounting evidence suggested that a subgroup of ARDS patients could benefit from NIV and avoid intubation (21). Patients with NIV treatment for acute respiratory failure had a substantially lower intubation rate, shorter ICU stay, and lower hospital mortality compared with those using standard or conventional oxygen therapy (24).

Our study showed that the NLR (>7.22) was an independent contributor of NIV failure among pneumonia-induced ARDS patients. Previous studies have demonstrated that an elevated NLR is an independent predictor of mortality in ARDS patients (25,26). The current study included pneumonia patients, for whom the original cause of ARDS was infection, and the infection-derived signals activated the release of neutrophils from the bone morrow into circulation and targeted organs (27). During ARDS, neutrophils are the first leukocytes recruited to sites of inflammation in response to chemotactic factors released by activated macrophages and pulmonary epithelial and endothelial cells (28). The neutrophils recruited to the lung execute its function by releasing reactive oxygen species, antimicrobial peptides, and multiple proteinases, and by forming the neutrophil extracellular traps (29). However, the inappropriate or excessive activation of neutrophils can cause by-stander damage to tissues (30), including increased alveolar-capillary barrier permeability, lung edema, and ultimately irreversible hypoxemia. Hoenderdos *et al.* demonstrated that

**Table 1** Comparisons of the baseline characteristics and laboratory data at admission

| Characteristics | NIV failure (n=64) | NIV success (n=67) | P value |
|---|---|---|---|
| Age, years | 65 [57–77] | 66 [59–76] | 0.68 |
| Gender (male), n (%) | 49 (76.6) | 35 (52.2) | 0.006 |
| LOS | 17 [9–26] | 15 [10–20] | 0.437 |
| APACHE II | 20±4.6 | 14±3.6 | <0.001 |
| Heart rate (beats/min) | 97 [80–111] | 88 [78–100] | 0.032 |
| Systolic pressure | 120 [110–131] | 128 [117–148] | 0.004 |
| Temperature | 36.8 [36.5–37.3] | 36.5 [36.3–37] | 0.083 |
| Respiratory rate | 23 [20–30] | 21 [20–24] | 0.007 |
| Expired tidal volume (mL/kg) | 10.03±1.07 | 8.87±0.88 | <0.001 |
| pH | 7.44±0.062 | 7.44±0.052 | 0.789 |
| $PaO_2/FiO_2$ (mmHg) | 194±78 | 236±53 | 0.001 |
| $PaCO_2$ (mmHg) | 33.9 [30.4–36] | 35.6 [32.7–42.2] | 0.004 |
| $HCO_3^-$ (mmol/L) | 25.4 [22.5–26.4] | 24.8 [23.6–27.3] | 0.624 |
| Leukocyte count ($\times10^9$/L) | 9.5 [7.6–12.2] | 7.4 [5.3–9.6] | 0.001 |
| Neutrophil count ($\times10^9$/L) | 8.6 [6.5–10.9] | 5 [3.2–7.8] | <0.001 |
| Lymphocyte count ($\times10^9$/L) | 0.65 [0.44–0.92] | 1.29 [0.90–1.87] | <0.001 |
| NLR | 9.93 [8.31–11.95] | 3.84 [2.83–7.16] | <0.001 |
| CRP (mg/L) | 99 [35–120] | 38 [8–62] | <0.001 |
| PCT (ng/mL) | 0.29 [0.05–5.47] | 0.1 [0.05–5.27] | 0.204 |
| BUN (mmol/L) | 6.23 [4.62–9.75] | 6.40 [4.02–9.80] | 0.411 |
| Cr (μmol/L) | 77.3 [58.5–98] | 68.5 [56.7–96.4] | 0.331 |
| Albumin (g/L) | 28.4 [23.9–33] | 33 [29.2–37] | 0.001 |
| BNP (ng/mL) | 737 [196–3,517] | 461 [40–2,278] | 0.05 |
| Glucocorticoid use | 19 (29.7) | 10 (14.9) | 0.058 |
| Kidney failure | 34 (53.1) | 19 (28.4) | 0.005 |
| Respiratory diseases | 22 (34.4) | 24 (35.8) | 1 |
| Malignancy | 12 (18.8) | 5 (7.5) | 0.07 |
| Heart failure | 13 (20.3) | 23 (34.3) | 0.081 |
| Liver function impairment | 14 (21.9) | 14 (20.9) | 1 |
| Gastrointestinal bleeding | 5 (7.8) | 2 (3.0) | 0.267 |
| Diabetes | 17 (26.6) | 23 (34.3) | 0.35 |
| Hypertension | 25 (39.1) | 31 (46.3) | 0.156 |

Data are shown as number (percentage), median [interquartile range], or mean ± standard deviation. LOS, length of stay in hospital; APACHE II, Acute Physiology And Chronic Health Evaluation II; $PaO_2$, arterial oxygen tension; $FiO_2$, fraction of inspired oxygen; $PaCO_2$, arterial carbon dioxide tension; $HCO_3^-$, bicarbonate; NLR, neutrophil/lymphocyte ratio; CRP, C-reactive protein; PCT, procalcitonin; BUN, blood urea nitrogen; Cr, Creatinine; BNP, brain natriuretic peptide.

**Table 2** Multivariate logistic regression analyses of risk factors for NIV failure

| Variables | B | OR | 95% CI | P value |
|---|---|---|---|---|
| Gender | 1.201 | 3.323 | 0.949–11.64 | 0.06 |
| APACHE II | −0.261 | 0.77 | 0.654–0.907 | 0.002 |
| Heart beats | 0.023 | 1.024 | 0.988–1.061 | 0.199 |
| Respiratory rate | −0.074 | 0.929 | 0.811–1.064 | 0.285 |
| $PaO_2/FiO_2$ | −0.002 | 0.998 | 0.987–1.008 | 0.646 |
| $PaCO_2$ | −0.013 | 0.987 | 0.877–1.111 | 0.832 |
| Vte | −1.069 | 0.343 | 0.153–0.768 | 0.009 |
| Leukocyte | 0.067 | 1.069 | 0.883–1.294 | 0.494 |
| NLR | −0.177 | 0.838 | 0.704–0.997 | 0.046 |
| CRP | −0.013 | 0.987 | 0.973–1.002 | 0.094 |
| Albumin | −0.021 | 0.979 | 0.886–1.082 | 0.68 |
| Kidney failure | 0.366 | 1.442 | 0.384–5.419 | 0.588 |

APACHE II, Acute Physiology And Chronic Health Evaluation II; $PaO_2$, arterial oxygen tension; $FiO_2$, fraction of inspired oxygen; $PaCO_2$, arterial carbon dioxide tension; Vte, expired tidal volume; NLR, neutrophil/lymphocyte ratio; CRP, C-reactive protein; B, beta coefficient; OR, odds ratio; CI, confidence interval.

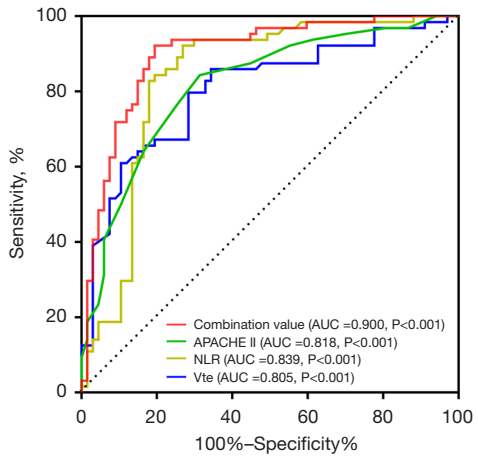


**Figure 2** ROC curves for the combination value, APACHE II score, NLR, and Vte for predicting NIV failure. AUC, area under the curve; ROC, receiver operating characteristic curve; APACHE II, Acute Physiology And Chronic Health Evaluation II; NLR, neutrophil/lymphocyte ratio; Vte, expired tidal volume.

hypoxia inhibits the apoptosis of neutrophils and augments neutrophil-mediated injury by upregulating neutrophil degranulation (31), and this conclusion indicated that hypoxemia and excessive neutrophil activation perpetuated a vicious cycle. It has been demonstrated that the concentration of neutrophils in the bronchoalveolar lavage fluid of patients with ARDS correlates with the severity of disease and poor outcomes (32). Additionally, the neutrophils isolated from sepsis patients with a diagnosis of ARDS were also shown to mediate a profound loss of endothelial barrier integrity *in vitro* (33). Further, a reduced lymphocyte count was found to be an independent predictor of mortality in severe infectious patients (34). In the current study, NIV failure patients presented a significantly higher count of circulating neutrophils, a lower lymphocyte count and a lower level of $PaO_2/FiO_2$ than NIV success patients did, which could mean that more neutrophils had been released from the bone marrow, and more neutrophil apoptosis could have been inhibited by worse hypoxemia in the NIV failure group. More prominent alveolar-capillary barrier damage and lung edema mediated by neutrophils make it difficult to maintain oxygenation with NIV, and it is logic that patients with a higher NLR would require intubation.

The other main finding of our study is that Vte (>8.96 mL/kg) was independently associated with NIV failure in pneumonia-induced ARDS patients. Our conclusion was consistent with that of a previous study which showed that a Vte >9.5 mL/kg predicted body weight could accurately predicted NIV failure in ARDS patients (35). During NIV, the tidal volume is the result of both the airway pressure delivered by the ventilator and the respiratory muscle pressure generated by the patient's

**Table 3** ROC curve data

| Variables | APACHE II | NLR | Vte (mL/kg) | Combination value |
|---|---|---|---|---|
| Cutoff | 16.5 | 7.22 | 8.96 | 59.17 |
| Sensitivity, % | 0.844 | 0.922 | 0.859 | 0.922 |
| Specificity, % | 0.687 | 0.731 | 0.657 | 0.806 |
| Positive predictive value, % | 0.72 | 0.766 | 0.705 | 0.819 |
| Negative predictive value, % | 0.821 | 0.907 | 0.83 | 0.915 |
| Diagnostic accuracy | 0.763 | 0.824 | 0.756 | 0.863 |
| Youden's index | 0.531 | 0.653 | 0.516 | 0.728 |
| AUC | 0.818 | 0.839 | 0.805 | 0.9 |
| 95% CI | 0.745–0.891 | 0.765–0.913 | 0.729–0.881 | 0.845–0.955 |

ROC, receiver-operating characteristic; AUC, area under the curve; CI, confidence interval; APACHE II, Acute Physiology And Chronic Health Evaluation II; Vte, expired tidal volume; NLR, neutrophil/lymphocyte ratio.

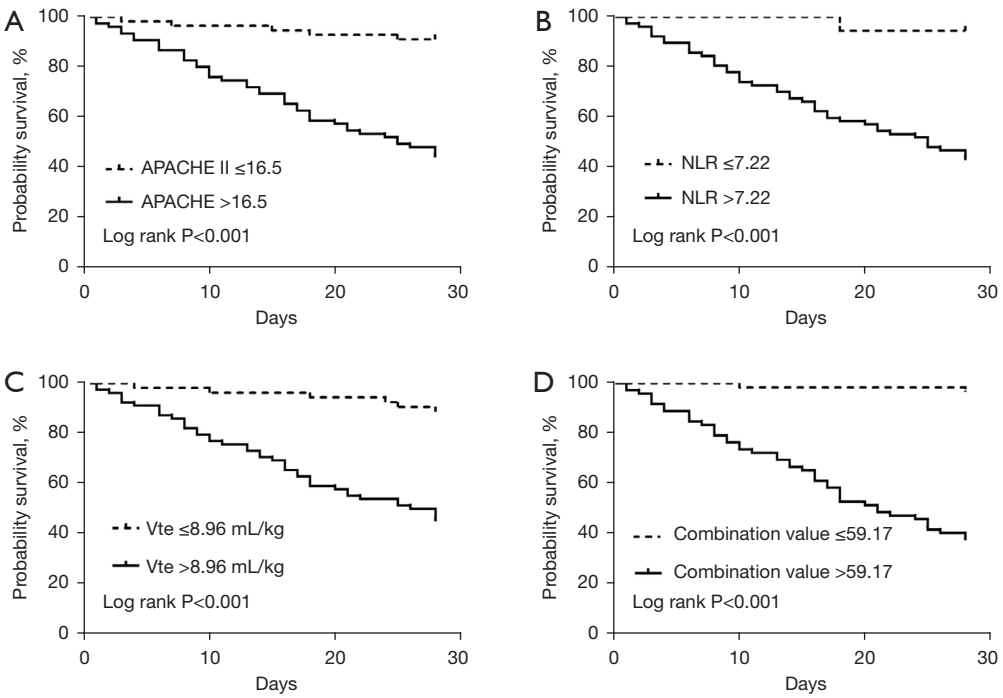


**Figure 3** Kaplan-Meier curves for 28-day survival categorized by the APACHEII score (A), NLR (B), Vte (C), and combination value levels (D). APACHE II, acute physiology and chronic health evaluation II; NLR, neutrophil/lymphocyte ratio; Vte, expired tidal volume.

respiratory drive. The reasons for increased respiratory drive include hypoxia due to lung collapse and shunt, raised concentrations of $CO_2$ due to high dead space, and elevated metabolic demand. Tonelli *et al.* reported that an elevated inspiratory effort (defined as a lack of reduction in the swing of esophageal pressure 2 hours after the start of NIV) is an accurate predictor of NIV failure among moderate-to-severe acute hypoxemic respiratory failure patients (36). We found that NIV failure patients tended to have a faster respiratory rate and a lower level of $PaCO_2$, which implied that these patients had a higher respiratory drive than NIV success patients.

A higher tidal volume is a potential surrogate of the severity of the ongoing disease process. In the current study,

 

patients with a higher Vte had lower $PaO_2/FiO_2$, and a higher inflammatory response (e.g., a higher CRP level and leukocyte count). Additionally, a high Vte may also serve as a worsening factor during NIV by inducing superimposed ventilator-induced lung injury (VILI). In invasively ventilated ARDS patients, the fundamental ventilation strategy is the small tidal volume (37). Many previous studies have shown that a low tidal volume improves survival in patients with ARDS by reducing the VILI (38-40), and a high tidal volume increases the cytokines released into systemic circulation by activating the inflammatory cells within the pulmonary vasculature (41). Patients with a higher Vte are prone to have more severe pneumonia and a more prominent inflammation response, which would lead to NIV failure.

APACHE II scores (>16.5) were also found to be an independent factor of NIV failure and mortality, and this conclusion is in line with previous studies (42,43). In summary, the equation based on the logistic regression analyses included 3 independent contributors to NIV failure. The APACHE II score, including multiple organ function and laboratory tests, could serve as an overall evaluation tool, the NLR could serve as a surrogate for systematic inflammation (as reflected by the severity of infection and neutrophil activation), and the Vte could act as a marker of pulmonary local inflammation reflected by respiratory drive and lung overdistention. As the equation consists of variables that are easily acquired at the bedside, it can be used to evaluate the efficacy of NIV. Pneumonia-induced ARDS patients with a combination value of >59.17 are at risk of NIV failure, and high-risk patients should be handled with caution and intubation should not be delayed.

## Conclusions

This study indicated that a combination value comprising the APACHE II score, NLR, and Vte is a preferable marker for predicting NIV failure among pneumonia-induced ARDS patients. We suggest that for patients with a higher combination value, NIV support should be assessed with caution to avoid delays to intubation. However, further studies with larger sample sizes need to be conducted to determine whether the combination of these 3 markers improves NIV outcomes in pneumonia-induced ARDS patients.

### *Limitations*

This study had a number of limitations. First, it was a single-center study and had a relatively small sample size; thus, the results can only be generalized carefully to other clinical settings. Second, the equation was not validated due to the small sample size of the study. Third, because of the retrospective nature of the study, respiratory mechanics related parameters were not available.

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## Footnote

*Reporting Checklist:* The authors have completed the STARD reporting checklist. Available at https://atm.amegroups.com/article/view/10.21037/atm-22-536/rc

*Data Sharing Statement:* Available at https://atm.amegroups.com/article/view/10.21037/atm-22-536/dss

*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at https://atm.amegroups.com/article/view/10.21037/atm-22-536/coif). The authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was approved by the Institutional Review Board of the Beijing Chao-Yang Hospital (No. 2016-KE-95). Since the current study did not impose any diagnostic and therapeutic influence on patients, the Institutional Review Board of Beijing Chao-Yang Hospital approved the study with a waiver of informed consent. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

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