

# Early Prediction of Noninvasive Ventilation Failure in Critically Ill Patients with Acute Respiratory Failure: Role of Respiratory Rate, PaO<sub>2</sub>/FiO<sub>2</sub> Ratio, and HACOR Score

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## Abstract

**Background:** Noninvasive ventilation (NIV) is widely used for acute respiratory failure in critically ill patients. However, NIV failure requiring invasive mechanical ventilation can occur, and delayed recognition may worsen outcomes. This study evaluated readily available physiological predictors of NIV failure in ICU patients receiving NIV. **Material and Methods:** This prospective observational study included 120 adult patients with acute respiratory failure admitted to the ICU and initiated on NIV. Initial respiratory rate (RR) and PaO<sub>2</sub>/FiO<sub>2</sub> ratio were recorded at NIV initiation, while the heart rate, acidosis, consciousness, oxygenation, and respiratory rate (HACOR) score was assessed after one hour. Patients were categorized into NIV success and failure groups. **Results:** NIV was successful in 72 (60.0%) patients, while 48 (40.0%) required invasive mechanical ventilation. Initial RR was significantly higher in the failure group than in the success group (38.30 ± 4.59 vs 31.10 ± 3.46 breaths/min,  $p < 0.001$ ). The initial PaO<sub>2</sub>/FiO<sub>2</sub> ratio was significantly lower among patients with NIV failure (190.27 ± 52.95 vs 266.84 ± 42.35,  $p < 0.001$ ). A one-hour HACOR score >5 was present in 83.3% of failure cases compared with 4.2% of successful cases ( $p < 0.001$ ). Higher RR independently increased the odds of failure (OR 1.60, 95% CI 1.36 to 1.88), whereas higher PaO<sub>2</sub>/FiO<sub>2</sub> reduced the odds (OR 0.69, 95% CI 0.60 to 0.79). HACOR >5 was the strongest predictor (OR 115.00, 95% CI 28.85 to 458.44). AUCs were 0.900, 0.880, and 0.981 for RR, PaO<sub>2</sub>/FiO<sub>2</sub>, and HACOR, respectively. **Conclusion:** Initial RR, PaO<sub>2</sub>/FiO<sub>2</sub> ratio, and one-hour HACOR score can help identify ICU patients at high risk of NIV failure, with HACOR demonstrating the strongest predictive performance.

**Keywords:** Noninvasive ventilation, Acute respiratory failure, HACOR score, Respiratory rate, PaO<sub>2</sub>/FiO<sub>2</sub> ratio.

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## INTRODUCTION

Acute respiratory failure is a common and serious cause of admission to the intensive care unit (ICU) and is associated with substantial morbidity and mortality. It may occur as hypoxemic respiratory failure, hypercapnic respiratory failure, or a combination of both, depending on the underlying pulmonary or systemic disease. Acute respiratory failure is classically characterized by a PaO<sub>2</sub> below 60 mmHg, a PaCO<sub>2</sub> above 45 mmHg, or both.<sup>[1,2]</sup> The clinical management of these patients requires timely assessment of respiratory distress, oxygenation, ventilation, and the need for respiratory support.<sup>[3]</sup> Noninvasive ventilation (NIV) has become an important component of respiratory support in critically ill patients with acute respiratory failure. It can reduce the need for endotracheal intubation and invasive mechanical ventilation in appropriately selected patients, particularly those with acute exacerbation of chronic obstructive pulmonary disease and cardiogenic pulmonary edema.<sup>[4,5]</sup> NIV may also be used in selected patients with hypoxemic respiratory failure and mild to moderate acute respiratory distress syndrome.<sup>[6]</sup> However, NIV is not successful in all patients.

NIV failure requiring endotracheal intubation may occur because of persistent hypoxemia, severe respiratory distress, worsening hypercapnia, impaired consciousness, hemodynamic instability, or progression of the underlying disease.<sup>[7]</sup>

Failure of NIV is particularly important in the ICU because delayed recognition of treatment failure may result in prolonged respiratory distress and delayed initiation of invasive mechanical ventilation. Therefore, early identification of patients who are unlikely to respond to NIV is essential. Several clinical and physiological variables have been investigated for their ability to predict NIV failure. Respiratory rate (RR) is a

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simple bedside parameter that reflects the severity of respiratory distress and work of breathing. A persistently elevated RR despite NIV has been associated with a higher probability of NIV failure.<sup>[8,9]</sup> Similarly, the PaO<sub>2</sub>/FiO<sub>2</sub> ratio provides an objective assessment of oxygenation and has been associated with NIV outcomes. A lower PaO<sub>2</sub>/FiO<sub>2</sub> ratio indicates more severe impairment of oxygenation and may identify patients at increased risk of NIV failure.<sup>[10]</sup>

The HACOR score, incorporating heart rate, acidosis, consciousness, oxygenation, and respiratory rate, provides a multidimensional assessment of a patient's response to NIV. Unlike individual physiological variables, the score integrates several important determinants of NIV outcome and can be calculated at the bedside using routinely available clinical and arterial blood gas parameters. Previous research has demonstrated that the HACOR score assessed after the initial period of NIV can provide useful prediction of NIV failure.<sup>[11]</sup> A HACOR score greater than 5 after 1 hour of NIV has been associated with a substantially increased risk of treatment failure and may assist clinicians in deciding whether escalation to invasive mechanical ventilation is required.<sup>[12]</sup>

Although predictors of NIV failure have been investigated in different clinical settings, early prediction remains particularly relevant among critically ill patients managed in the ICU, where disease severity and the need for respiratory support may be greater. The present study therefore focuses on ICU patients with acute respiratory failure receiving NIV and evaluates readily available clinical and physiological parameters for predicting NIV failure. Specifically, the study assesses the relationship of initial RR, initial PaO<sub>2</sub>/FiO<sub>2</sub> ratio, and HACOR score after 1 hour of NIV with treatment outcome. Identification of reliable early predictors may facilitate timely recognition of NIV failure and help avoid inappropriate prolongation of unsuccessful NIV therapy in critically ill patients.

## **MATERIALS AND METHODS**

**Study Design and Setting:** This prospective observational study was conducted in the ICU of a tertiary care teaching hospital over duration of one year from 01 Aug 2021 to 31 July 2022. The study was designed to evaluate the ability of readily available clinical and physiological parameters to predict NIV failure among adult patients with acute respiratory failure. The study was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from the patients or their legally authorized representatives, as applicable. Patient information was kept confidential and the collected data were used exclusively for research purposes.

**Study Population:** Adult patients aged  $\geq 18$  years who were admitted to the ICU with acute respiratory failure and initiated on NIV were consecutively evaluated for inclusion. Patients with type I, type II, or mixed respiratory failure were eligible. Patients were assessed at the initiation of NIV and again after 1 hour of NIV to evaluate early respiratory and physiological parameters and their association with subsequent NIV outcome.

**Inclusion Criteria:** Patients aged  $\geq 18$  years with acute respiratory failure requiring noninvasive ventilation (NIV), including type 1, type 2, or mixed respiratory failure, were included in the study. Eligible patients were required to have adequate spontaneous respiratory effort with an intact cough reflex, a preserved level of consciousness, the ability to protect their airway, and the capacity to cooperate with NIV therapy.

**Exclusion Criteria:** Patients aged  $< 18$  years, pregnant women, and those with facial trauma, facial deformity, or any other anatomical condition precluding an adequate NIV interface seal were excluded. Patients with significantly impaired consciousness, absent spontaneous respiratory effort, or an inability to maintain adequate airway protection were also excluded. Additional exclusion criteria included impending cardiorespiratory arrest requiring immediate invasive airway management, do not resuscitate status, and any clinical condition in which NIV was considered inappropriate or contraindicated by the treating intensivist.

**Study Procedure:** Patients fulfilling the eligibility criteria were initiated on NIV according to the clinical indication and decision of the treating intensivist. Baseline demographic and clinical characteristics were recorded at the initiation of NIV. Initial respiratory rate (RR) and arterial blood gas (ABG) parameters were documented at the beginning of NIV therapy. The PaO<sub>2</sub>/FiO<sub>2</sub> ratio was calculated using the PaO<sub>2</sub> obtained from ABG analysis and the corresponding FiO<sub>2</sub>. RR was assessed by counting respiratory movements for 1 minute.

**Assessment of HACOR Score:** The HACOR score was assessed after 1 hour of NIV. The score incorporates five parameters: heart rate, acidosis, consciousness, oxygenation, and respiratory rate. Heart rate was recorded clinically, acidosis was assessed using pH from ABG analysis, consciousness was assessed using the Glasgow Coma Scale, oxygenation was assessed using the PaO<sub>2</sub>/FiO<sub>2</sub> ratio, and RR was recorded at the time of assessment.

**Assessment of NIV Outcome:** Patients were followed throughout the NIV trial and categorized into either the NIV success group or NIV failure group. NIV success was defined as successful management with NIV without the need for endotracheal intubation and invasive mechanical ventilation. NIV failure was defined as clinical deterioration or inadequate response to NIV requiring endotracheal intubation and initiation of invasive mechanical ventilation.

**Study Variables:** The primary variables evaluated for prediction of NIV failure were initial RR, initial PaO<sub>2</sub>/FiO<sub>2</sub> ratio, and HACOR score at 1 hour after initiation of NIV. Demographic and relevant clinical variables, including age, sex, indication for NIV, type of respiratory failure, and comorbidities, were also recorded to describe the study population and assess their potential association with NIV outcome.

**Statistical Analysis:** Statistical analysis was performed using IBM SPSS Statistics version 27.0. Categorical variables were expressed as frequency and percentage, while continuous variables were presented as mean  $\pm$  SD or median (IQR), as appropriate. Differences between the NIV success and failure groups were assessed using the independent samples t test or Mann Whitney U test for continuous variables and the chi square test or Fisher's exact test for categorical variables.

Logistic regression analysis was performed to identify predictors of NIV failure, with ORs and 95% CIs reported. ROC curve analysis was performed for initial RR, PaO<sub>2</sub>/FiO<sub>2</sub> ratio, and 1-hour HACOR score, with AUC, sensitivity, specificity, PPV, and NPV calculated. A two-sided p value <0.05 was considered statistically significant.

## RESULTS

Among the 120 patients, 72 (60.0%) had successful NIV, while 48 (40.0%) experienced NIV failure. The mean age was 61.01 ± 15.74 years in the NIV success group and 62.79 ± 14.05 years in the failure group (p = 0.519). Males constituted 62.5% in both groups (p = 1.000). Type I respiratory failure was present in 38.9% vs. 45.8%, type II in 45.8% vs. 27.1%, and mixed respiratory failure in 15.3%

vs. 27.1% of the success and failure groups, respectively (p = 0.083). NIV indications differed significantly (p = 0.047), with pneumonia more frequent in the failure group (54.2% vs. 29.2%), while COPD was more common in the success group (34.7% vs. 25.0%). Acute pulmonary edema occurred in 18.1% vs. 8.3% and other indications in 18.1% vs. 12.5%, respectively [Table 1].

The initial RR was significantly higher in the NIV failure group than in the success group (38.30 ± 4.59 vs. 31.10 ± 3.46 breaths/min, p < 0.001). Initial PaO<sub>2</sub> was lower in the failure group (109.82 ± 27.60 vs. 125.39 ± 25.80 mmHg, p = 0.007), while FiO<sub>2</sub> was higher (0.56 ± 0.09 vs. 0.48 ± 0.08, p < 0.001). Consequently, the initial PaO<sub>2</sub>/FiO<sub>2</sub> ratio was significantly lower in the failure group (190.27 ± 52.95 vs. 266.84 ± 42.35, p < 0.001) [Table 2].

**Table 1: Baseline characteristics of patients according to NIV outcome.**

| Variable                           | NIV success (n = 72) | NIV failure (n = 48) | p value |
|------------------------------------|----------------------|----------------------|---------|
| Age, years, mean ± SD              | 61.01 ± 15.74        | 62.79 ± 14.05        | 0.519   |
| Male, n (%)                        | 45 (62.5)            | 30 (62.5)            | 1.000   |
| Female, n (%)                      | 27 (37.5)            | 18 (37.5)            |         |
| Type I respiratory failure, n (%)  | 28 (38.9)            | 22 (45.8)            | 0.083   |
| Type II respiratory failure, n (%) | 33 (45.8)            | 13 (27.1)            |         |
| Mixed respiratory failure, n (%)   | 11 (15.3)            | 13 (27.1)            |         |
| COPD, n (%)                        | 25 (34.7)            | 12 (25.0)            | 0.047   |
| Pneumonia, n (%)                   | 21 (29.2)            | 26 (54.2)            |         |
| Acute pulmonary edema, n (%)       | 13 (18.1)            | 4 (8.3)              |         |
| Other indications, n (%)           | 13 (18.1)            | 6 (12.5)             |         |

**Table 2: Comparison of initial respiratory parameters between NIV success and failure groups.**

| Parameter                                                   | NIV success (n = 72) | NIV failure (n = 48) | p value |
|-------------------------------------------------------------|----------------------|----------------------|---------|
| Initial RR, breaths/min, mean ± SD                          | 31.10 ± 3.46         | 38.30 ± 4.59         | <0.001  |
| Initial PaO <sub>2</sub> , mmHg, mean ± SD                  | 125.39 ± 25.80       | 109.82 ± 27.60       | 0.007   |
| Initial FiO <sub>2</sub> , mean ± SD                        | 0.48 ± 0.08          | 0.56 ± 0.09          | <0.001  |
| Initial PaO <sub>2</sub> /FiO <sub>2</sub> ratio, mean ± SD | 266.84 ± 42.35       | 190.27 ± 52.95       | <0.001  |

Among the 120 patients, a 1-hour HACOR score >5 was significantly associated with NIV failure (p < 0.001). A score ≤5 was observed in 95.8% of the NIV success group

compared with 16.7% of the failure group, whereas a score >5 was present in 4.2% and 83.3%, respectively. Overall, 43 (35.8%) patients had a HACOR score >5 [Table 3].

**Table 3: Association between 1-hour HACOR score and NIV outcome.**

| 1-hour HACOR score | NIV success, n (%) | NIV failure, n (%) | Total, n (%) | p value |
|--------------------|--------------------|--------------------|--------------|---------|
| ≤5                 | 69 (95.8)          | 8 (16.7)           | 77 (64.2)    | <0.001  |
| >5                 | 3 (4.2)            | 40 (83.3)          | 43 (35.8)    |         |
| Total              | 72 (100)           | 48 (100)           | 120 (100)    |         |

Logistic regression showed that higher initial RR was independently associated with increased odds of NIV failure (OR 1.60, 95% CI 1.36–1.88, p < 0.001), while a higher initial PaO<sub>2</sub>/FiO<sub>2</sub> ratio was associated with lower odds of

failure (OR 0.69, 95% CI 0.60–0.79, p < 0.001). A 1-hour HACOR score >5 was the strongest predictor of NIV failure (OR 115.00, 95% CI 28.85–458.44, p < 0.001) [Table 4].

**Table 4: Logistic regression analysis of predictors of NIV failure.**

| Predictor                                                              | OR     | 95% CI       | p value |
|------------------------------------------------------------------------|--------|--------------|---------|
| Initial RR, per 1 breath/min increase                                  | 1.60   | 1.36–1.88    | <0.001  |
| Initial PaO <sub>2</sub> /FiO <sub>2</sub> ratio, per 10-unit increase | 0.69   | 0.60–0.79    | <0.001  |
| HACOR >5 at 1 hour                                                     | 115.00 | 28.85–458.44 | <0.001  |

ROC analysis showed good discriminatory performance for all three predictors. An initial RR >35 breaths/min had an AUC of 0.900, with 81.3% sensitivity, 91.7% specificity, 86.7% PPV, and 88.0% NPV (p < 0.001). An initial

PaO<sub>2</sub>/FiO<sub>2</sub> ratio ≤219 had an AUC of 0.880, with 79.2% sensitivity, 86.1% specificity, 79.2% PPV, and 86.1% NPV (p < 0.001). The 1-hour HACOR score >5 showed the highest discriminatory ability, with an AUC of 0.981,

83.3% sensitivity, 95.8% specificity, 93.0% PPV, and

100.0% NPV ( $p < 0.001$ ) [Table 5].

**Table 5: Diagnostic performance of predictors for NIV failure.**

| Predictor                                        | Cutoff          | AUC   | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) | p value |
|--------------------------------------------------|-----------------|-------|-----------------|-----------------|---------|---------|---------|
| Initial RR                                       | >35 breaths/min | 0.900 | 81.3            | 91.7            | 86.7    | 88.0    | <0.001  |
| Initial PaO <sub>2</sub> /FiO <sub>2</sub> ratio | ≤219            | 0.880 | 79.2            | 86.1            | 79.2    | 86.1    | <0.001  |
| 1-hour HACOR score                               | >5              | 0.981 | 83.3            | 95.8            | 93.0    | 100.0   | <0.001  |

## DISCUSSION

In the present ICU based study of 120 patients with acute respiratory failure receiving NIV, 72 (60.0%) achieved NIV success, whereas 48 (40.0%) required invasive mechanical ventilation. Higher initial RR, lower initial PaO<sub>2</sub>/FiO<sub>2</sub> ratio, and a 1-hour HACOR score >5 was significantly associated with NIV failure.

The demographic characteristics were comparable between the two groups. Mean age did not differ significantly between NIV success and failure groups ( $61.01 \pm 15.74$  vs  $62.79 \pm 14.05$  years,  $p = 0.519$ ), and sex was similarly distributed. Mathen et al. also found no significant association between sex and NIV failure. Their study reported a higher proportion of type II respiratory failure, whereas the present study showed a greater proportion of type I and mixed respiratory failure in the failure group, although this difference was not statistically significant.<sup>[13]</sup> Pneumonia was significantly more frequent among patients who failed NIV, whereas COPD was more frequent among successful cases. Mathen et al. similarly identified COPD as the most common comorbidity among patients receiving NIV.<sup>[13]</sup>

Initial RR was significantly higher among patients with NIV failure ( $38.30 \pm 4.59$  vs  $31.10 \pm 3.46$  breaths/min,  $p < 0.001$ ). Logistic regression demonstrated a 60% increase in the odds of NIV failure for each 1 breath/min increase in RR (OR 1.60, 95% CI 1.36–1.88). ROC analysis showed good discrimination at a cutoff of >35 breaths/min (AUC 0.900). Mathen et al. similarly reported significantly higher RR among NIV failures ( $40.65 \pm 3.88$  vs  $31.98 \pm 3.15$  breaths/min). Antonelli et al. reported increased NIV failure with RR ≥38, while Bastiansen also demonstrated increasing odds of failure with higher RR.<sup>[14,15]</sup> Ozyilmaz et al. described an average RR >25 breaths/min during NIV as a predictor of failure, reflecting increased work of breathing.<sup>[16]</sup>

The initial PaO<sub>2</sub>/FiO<sub>2</sub> ratio was significantly lower in the failure group ( $190.27 \pm 52.95$  vs  $266.84 \pm 42.35$ ,  $p < 0.001$ ). A higher PaO<sub>2</sub>/FiO<sub>2</sub> ratio was associated with reduced odds of NIV failure (OR 0.69, 95% CI 0.60–0.79), while a cutoff ≤219 demonstrated an AUC of 0.880. Mathen et al. similarly reported significantly lower initial PaO<sub>2</sub>/FiO<sub>2</sub> among NIV failures ( $184.57 \pm 50.33$  vs  $277.29 \pm 34.70$ ) (13). Carrillo et al. also demonstrated that lower oxygenation after NIV initiation predicted failure, while Ozyilmaz et al. recommended particular caution when the PaO<sub>2</sub>/FiO<sub>2</sub> ratio is <150.<sup>[16,17]</sup>

The 1-hour HACOR score demonstrated the strongest predictive performance. A score >5 occurred in 83.3% of failures compared with only 4.2% of successful cases ( $p < 0.001$ ), with an OR of 115.00 (95% CI 28.85–458.44). ROC

analysis showed an AUC of 0.981, with 83.3% sensitivity, 95.8% specificity, 93.0% PPV, and 100% NPV. Mathen et al. reported a similarly strong association, with almost all patients having HACOR >5 experiencing NIV failure (13). Duan et al. demonstrated good predictive performance using a cutoff of 5, with sensitivity 72.6% and specificity 90.2%.<sup>[18]</sup>

Overall, the present findings support the use of initial RR, PaO<sub>2</sub>/FiO<sub>2</sub> ratio, and particularly the 1-hour HACOR score for early identification of patients at high risk of NIV failure. Early recognition of these predictors may facilitate timely escalation to invasive ventilation and help avoid potentially harmful delays in intubation. As with Mathen et al., interpretation should consider the observational, single center design and potential interobserver variability in parameters such as RR and GCS.

This study has several limitations. Its prospective observational design and single center setting may limit the generalizability of the findings to other ICU populations and healthcare settings. The sample size was relatively small, which may have reduced the precision of the estimated associations and diagnostic performance measures. RR and GCS assessments may have been subject to interobserver variability. NIV management, including interface selection and ventilatory settings, was determined by the treating intensivist and was not standardized, potentially introducing management related variability. Additionally, only initial RR and PaO<sub>2</sub>/FiO<sub>2</sub> and the 1-hour HACOR score were evaluated, while changes in these parameters over time were not assessed. External validation in larger, multicenter cohorts is warranted before routine clinical implementation.

## CONCLUSION

In ICU patients with acute respiratory failure receiving NIV, higher initial RR, lower initial PaO<sub>2</sub>/FiO<sub>2</sub> ratio, and a 1-hour HACOR score >5 was significantly associated with NIV failure. Among these predictors, the 1-hour HACOR score demonstrated the highest discriminatory ability, followed by initial RR and PaO<sub>2</sub>/FiO<sub>2</sub> ratio. These readily available bedside parameters may help clinicians identify patients at high risk of NIV failure at an early stage. Their timely assessment may facilitate appropriate escalation to invasive mechanical ventilation and help prevent delays in intubation among critically ill patients requiring respiratory support.

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## Conflicts of interest

There are no conflicts of interest.

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